Microbiome and Philosophy: Origins, Causality, and Human Categorizations

Aline Potiron

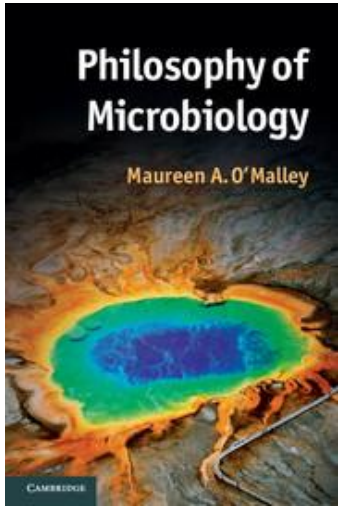
Utrecht University

Microbiology and Philosophy

- Philosophy of biology: species definition and delineation, evolutionary theory, the origin of life, etc.

- General philosophy of science: construction and use of models, issues related to causality

- **Microbiome Research: Individuality issues, causality issues, ethical issues, …**



Microbiomes and Philosophy: Origins, Causality, and Human Categorizations

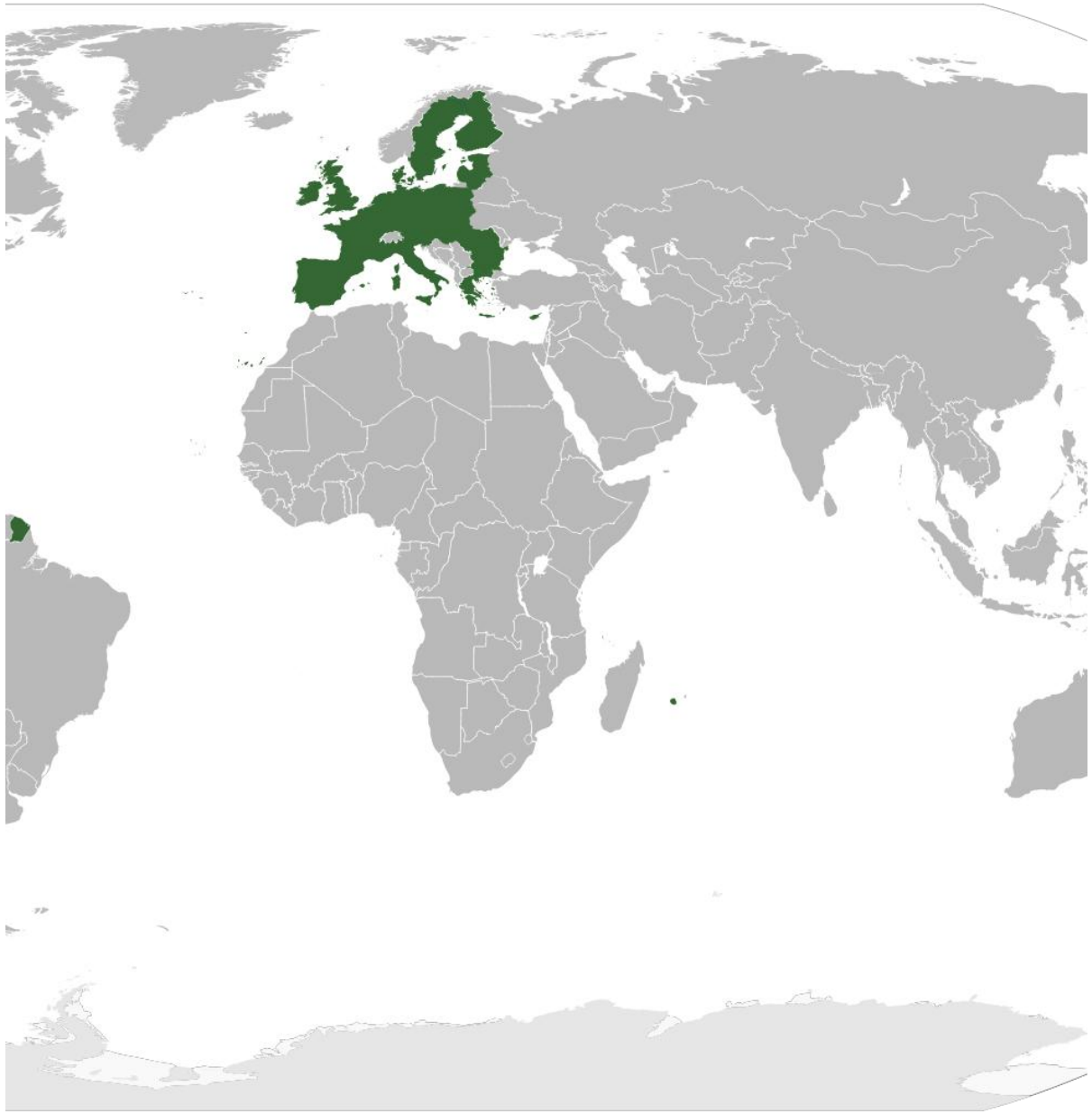
- Build upon these efforts
- Practice-oriented approach to philosophy
- Rely on my background in microbiology
- *Work in progress*

Table of content

- Introduction
- **Origins:** Unearthing the ecological roots of microbiome studies
- **Causality:** A new perspective for microbiome research
- **Human Categorizations:** The myth of ethno-racial categories
- Conclusion

Positionality Statement

- Positionality: an individual's worldview and the stance they take in relation to research and its context (Holmes, 2020).
- **White European woman who spent most of her professional life in Europe.**
- **Biases:**
  - The “history” of microbiology I will present is European/Western-centered.
  - My vision and definition of race
  - My racial experiences are also biased, as I am part of one of the most privileged populations.



Unearthing the ecological roots of microbiome studies

My contributions

1. Explain the current status of microbiome studies and the tensions within it using **the history of microbiology**
2. Better characterization of the “ecological perspective”
3. Propose a **way forward.**

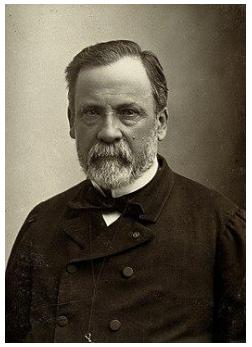
A Brief History of Microbiology

Ecological branch

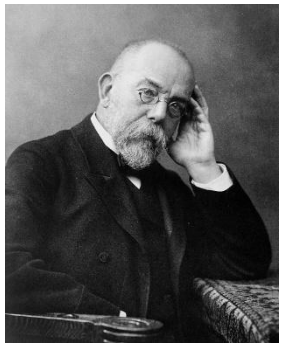
1st Observations 1670s

Ecology
Ernst Haëckel
1866

1870s
Pasteur/Tyndall
Germ theory



1880s
Koch postulates



Beijerinck/Winogradsky
1880s-1950

1930s
Fleming
Antibiotics

1990s
The earliest report of diversity in human gut microbiota using culture-independent methods (Suau et al., 1999)

Human Microbiome Project

2000s

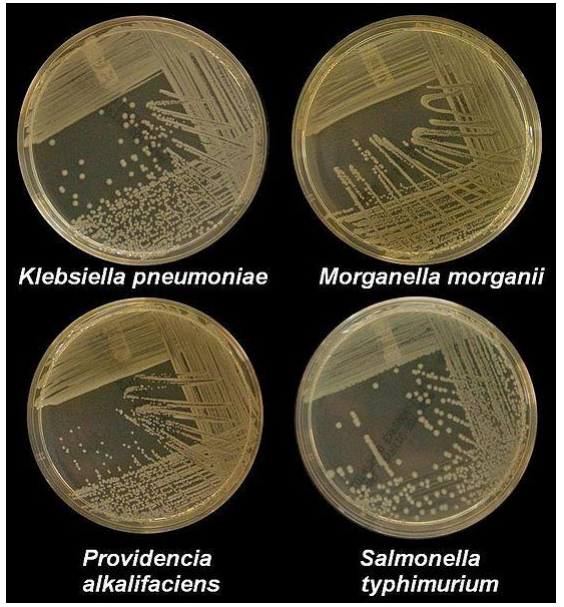
Medical branch

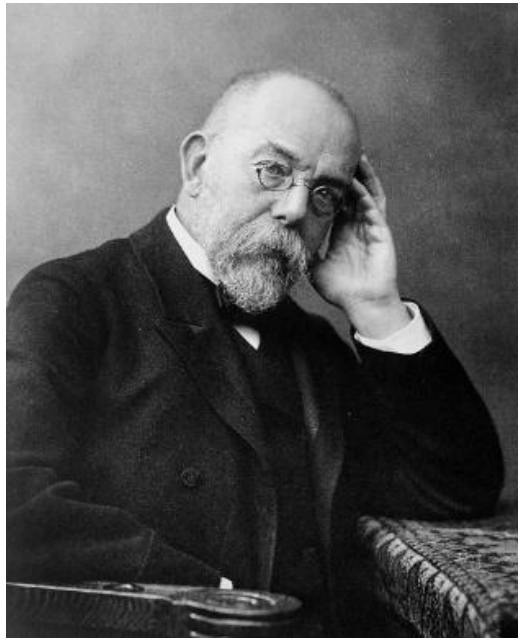
Caumette et al. 2015; Kolter 2021; O'Malley 2014

NB: *Work in progress*
Medical "path", "perspective", or "worldviews"...

Medical Microbiology

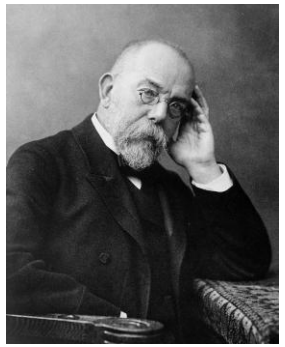
- A methodological **reductionism** (e.g., pure culture)
- The assumption of **a simple causal architecture** (e.g., the germ theory of diseases)
- A clear separation between different causal elements (e.g., the host and the microorganisms)
- Incarnated by **the germ theory of diseases** and the **Koch's postulates**



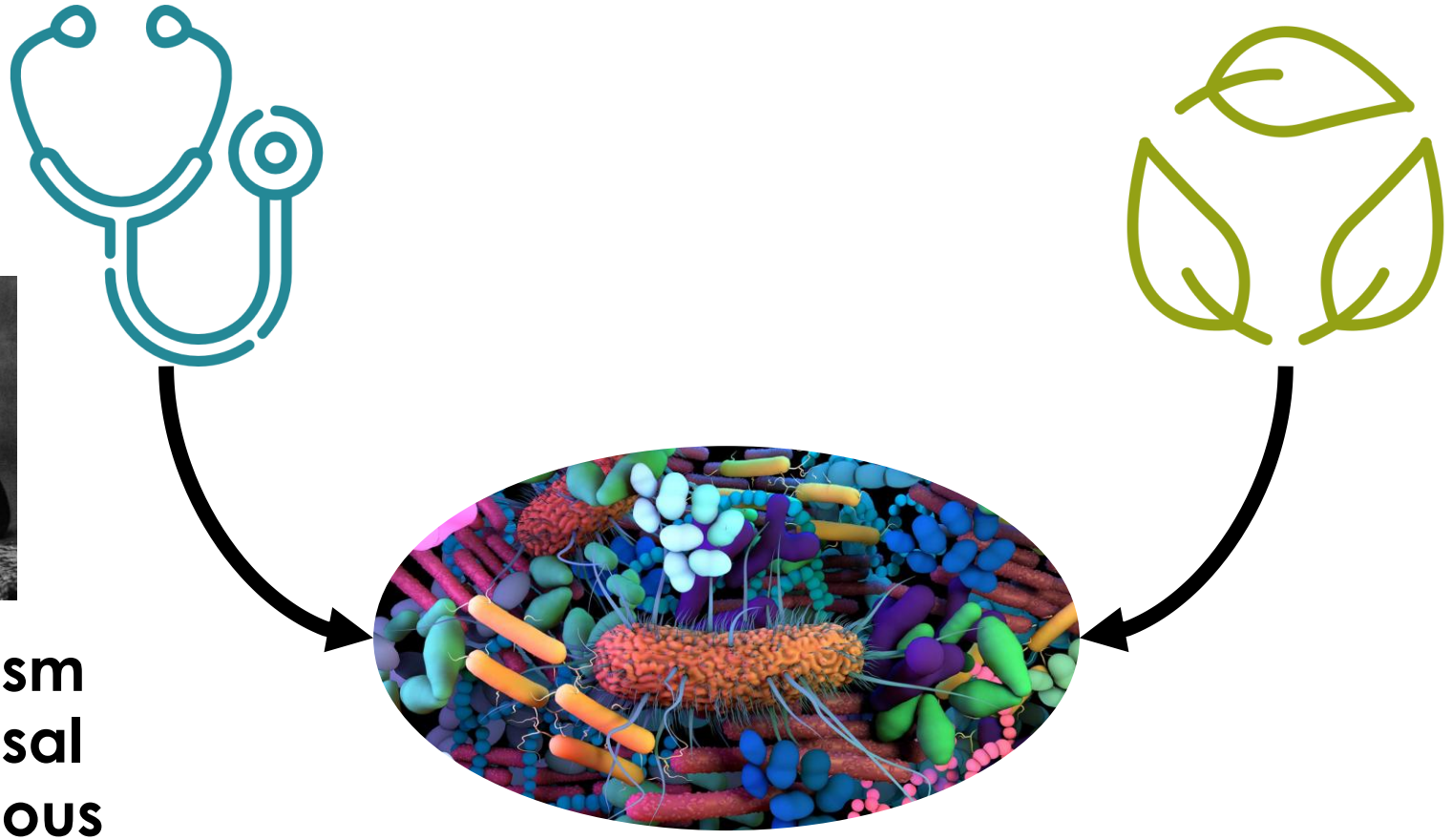


Carter 2003; Ross and Woodward 2016

A Brief History of Microbiology



Reductionism
Mono-causal
Homogeneous



?

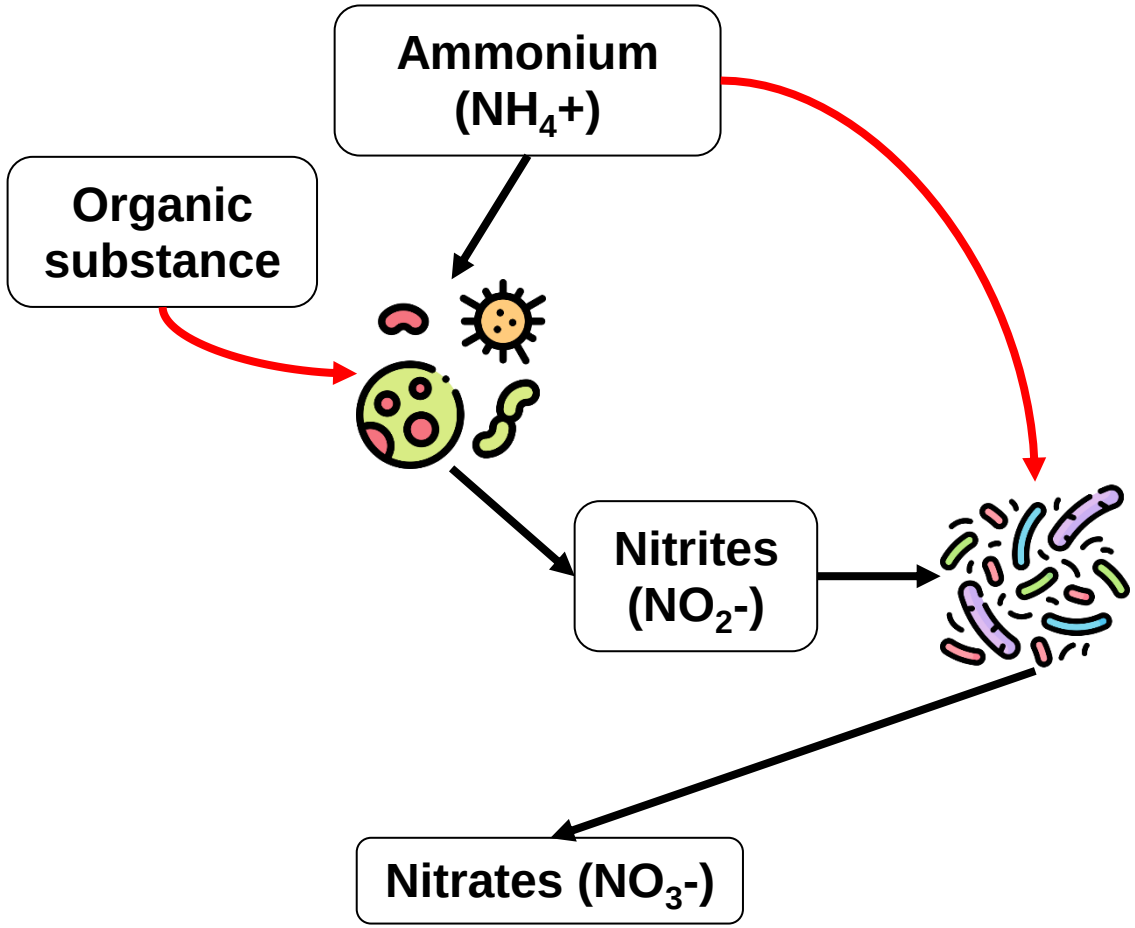
Microbial Ecology

- Incarnated by Sergei Winogradsky (1856-1953)
- **Methodology:** elective method, whole communities

UPVD-BioEcoL3-2010, CC BY-SA 3.0 <https://creativecommons.org/licenses/by-sa/3.0>

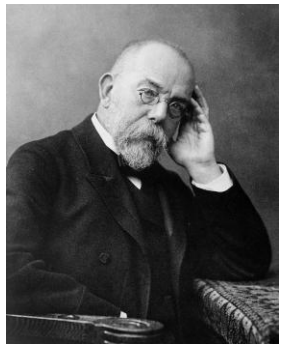
Microbial Ecology

- What kind of phenomena? Looking for **the flow of material or energy**.
- How are those phenomena explained?
  - **Functions**
  - **Dynamic Processes**



Winogradsky, 1949

A Brief History of Microbiology



Reductionism
Mono-causal
Homogeneous

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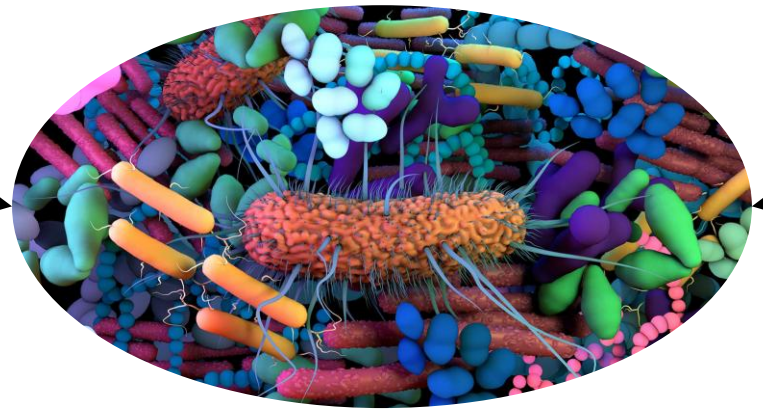


Elective method
Cycles/Flows
Dynamic

Contemporary Microbiome Studies

Medical Perspective

- **Mono-causal** and **homogeneous**
- Conceptually tries to **modify the Koch postulates**
- **Affiliations of the authors**: medical centers or research institutes tightly linked to a hospital

Vonaesh et al., 2018; Neville et al., 2018; Byrd and Segre, 2016

Contemporary Microbiome Studies

Ecological Perspective

- **Network constructions and analysis**, but often few experimental data – simulations

- Conceptually, look at **the patterns of interactions,** the network, to explain the outcome of **a community**

- **Affiliations of the authors:** Systems biology laboratory or team, computer sciences

MICROBIOME

The ecology of the microbiome: Networks, competition, and stability

Katharine Z. Coyte,[1,2*] Jonas Schluter,[1,2,3*†] Kevin R. Foster[1,2†]

ARTICLE

https://doi.org/10.1038/s41467-020-17180-x OPEN

An ecological framework to understand the efficacy of fecal microbiota transplantation

Yandong Xiao[1,2], Marco Tulio Angulo[3,4], Songyang Lao[1], Scott T. Weiss[2] & Yang-Yu Liu[2,5✉]

nature ecology & evolution

REVIEW ARTICLE

https://doi.org/10.1038/s41559-022-01746-7

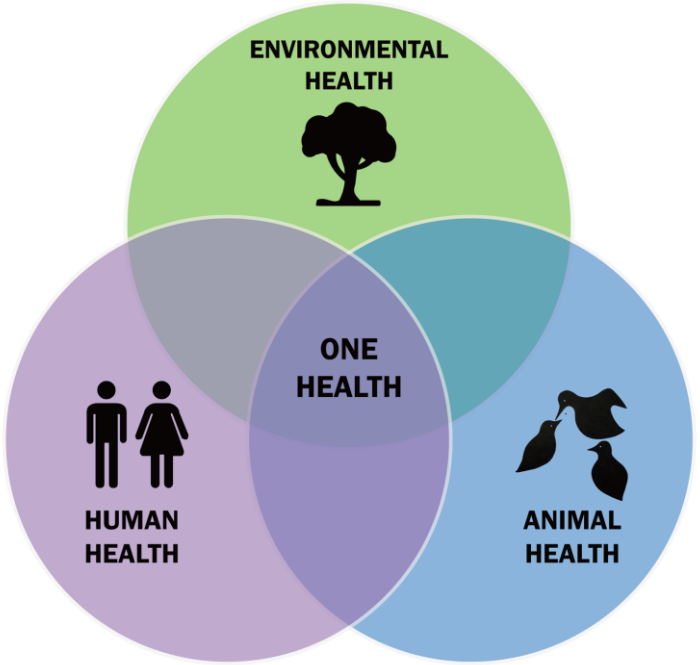
Ecological modelling approaches for predicting emergent properties in microbial communities

Naomi Iris van den Berg[1], Daniel Machado[2], Sophia Santos[3], Isabel Rocha[4], Jeremy Chacón[5], William Harcombe[5], Sara Mitri[6] and Kiran R. Patil[1✉]

Coyte et al. 2015; Xiao et al., 2020; van den Berg et al. 2022

Integrating both perspectives

- More integration
  - **Conceptually**: move from targeting specific pathogens or “silver bullet” microorganisms to managing the entire microorganismal community and studying dynamic interactions
  - **Methodologically**: Complement multiomics approaches with microbial cultures, computational approaches, and simulations.
- **Problems**:
  - How to integrate meaningfully different knowledge?
  - Lack of actionability



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Conclusion

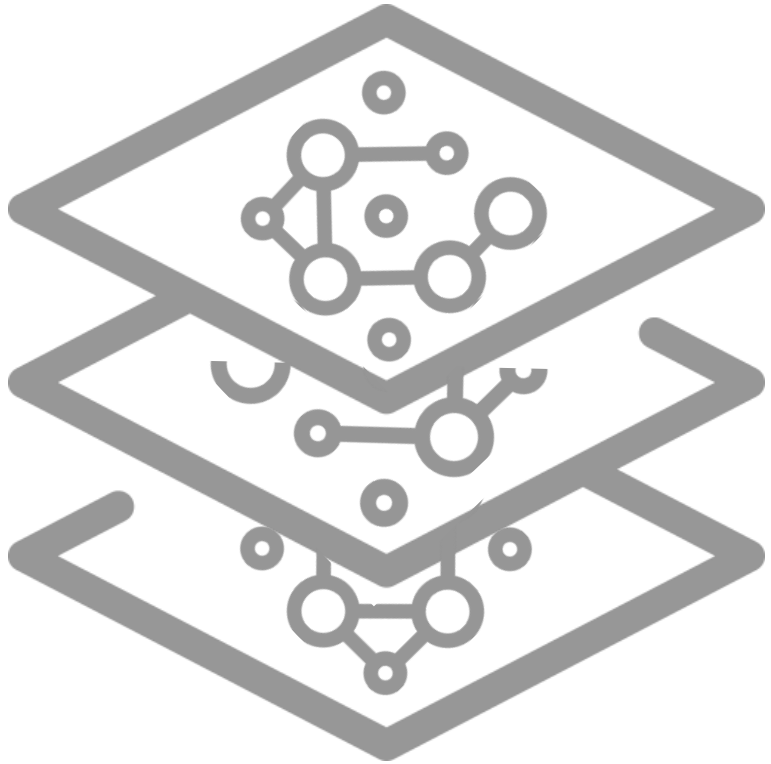
1. The **history of microbiology** can explain the current status of microbiome studies and the tensions within it.
2. Characterization of the “ecological perspective”: **actual functions** (and not only predicted functions), **flow** of material or energy, microorganismal **interactions**, **dynamic and context-dependent** processes – **complex causal architecture**.
3. **A way forward**: Integration of the methods and the concepts used, more collaborative and interdisciplinary work.

Causal Inference: A new perspective for microbiome research

Causal Inference in Microbiome Research

Tension between the need **for causal explanations** (health and disease phenotype) and the **complexity** of the microbiome.

How to understand causal claims? How to establish them? How to evaluate them?



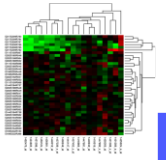
Understanding Causal Claims

Experimental Evidence

- Example: epidemiological studies using dietary interventions, RCTs, animal models called human microbiota-associated

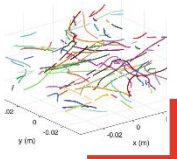
Evidence from Simulations

- Example: Mendelian randomization analysis, mediation analysis, potential-outcomes framework, etc.



Evidence of Mechanisms

- Example: longitudinal and prospective studies, measures of the expressions of host and bacterial genes, measures of the molecules produced by the intestinal tract, etc.



Evidence of Pathways

- Example: the tracking of molecules by using stable isotope probes

Fischbach 2018; Lv et al. 2021; Hanage 2014; Walter et al. 2020; Chaudhari et al. 2021; Maruvada et al. 2017; Hall et al. 2018

Image par Pete Linforth de Pixabay; By Federico Toschi, Marcello Sega - https://link.springer.com/chapter/10.1007/978-3-030-23370-9_6, CC BY 4.0, https://commons.wikimedia.org/w/index.php?curid=138193897

My contributions

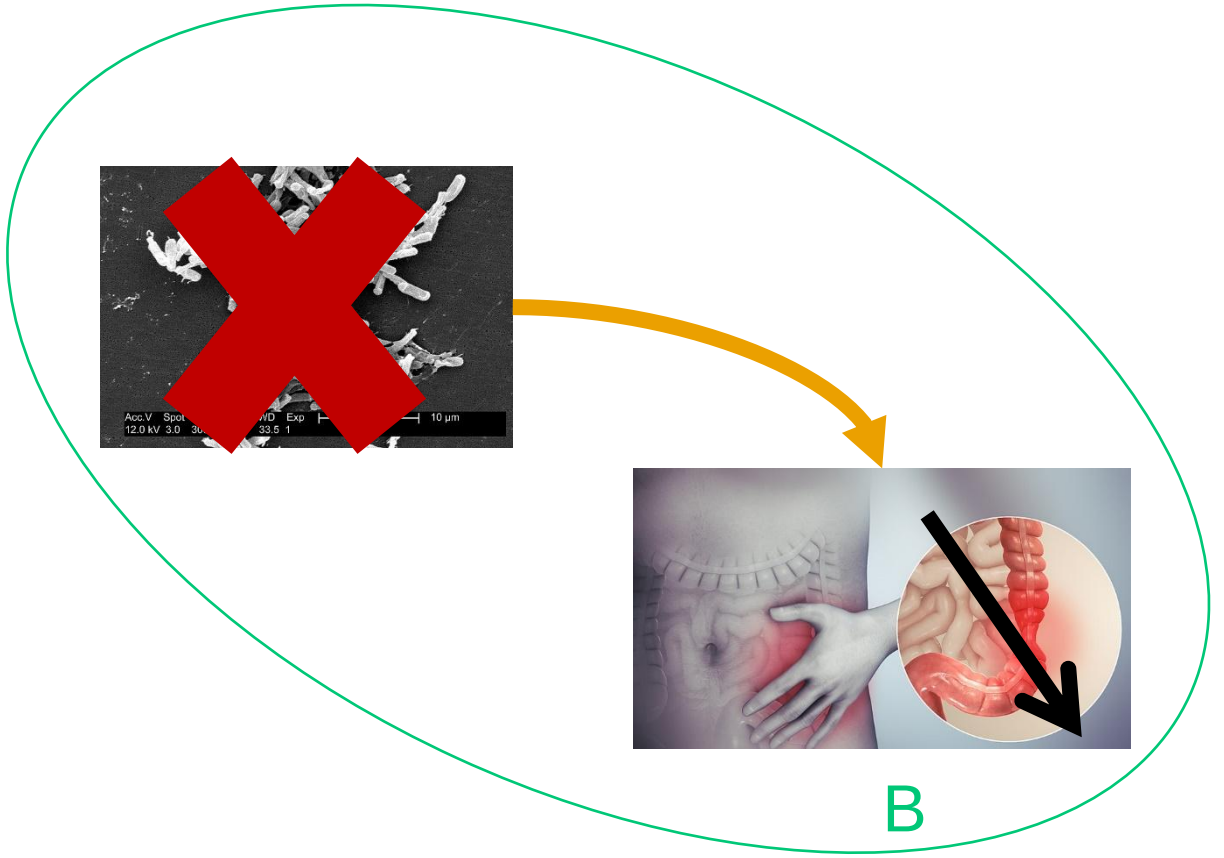
1. Criticize the two philosophical accounts (interventionism and functionalism)
2. Propose an alternative: Inferentialism.

Yes, I know, a lot of “ism”…

Interventionism

Definition: *"The microbiome causes disease Y"* = *"There is an intervention (e.g., inhibition) on the microbiome (or an element of the microbiome), such that disease Y is mitigated."*

- **Normative aspect**: specificity, stability, and proportionality
- **Advantages:** In accordance with scientific practice, & Can accommodate the need for mechanistic evidence
- **Conclusion**: Causal claims linking the whole microbiome to disease are **weak, often misleading, and sometimes not causal**



Woodward 2003; Woodward 2010; Lynch et al. 2019

Functionalism(s)

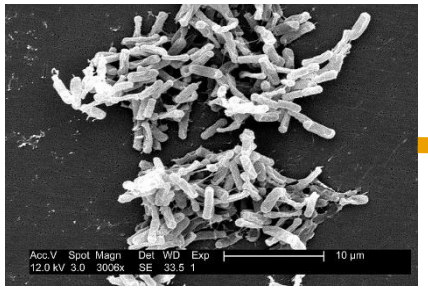
Selected-Effect Function

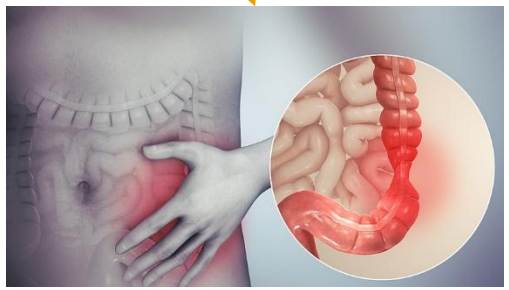
- The **function** of an item is to produce the effects for which the item was selected by **natural selection.**

Definition: *"The microbe X causes Y" = "The microbe X expressed the selected effect function Y."*

- A microbe is a cause of an effect if its niche "co-occurs with the expressed traits that this microbe uses to establish that niche" (Klassen 2020, p. 2).
- **Conclusion:** Microbiomes are **too complex to fully understand their interactions with the hosts.**

C. difficile expresses traits to **realize i**ts niche. Those traits are **selected.**





IBD **co-occurs** with the realization of the *C. difficile* niche.

Wouters 2005; Klassen 2020

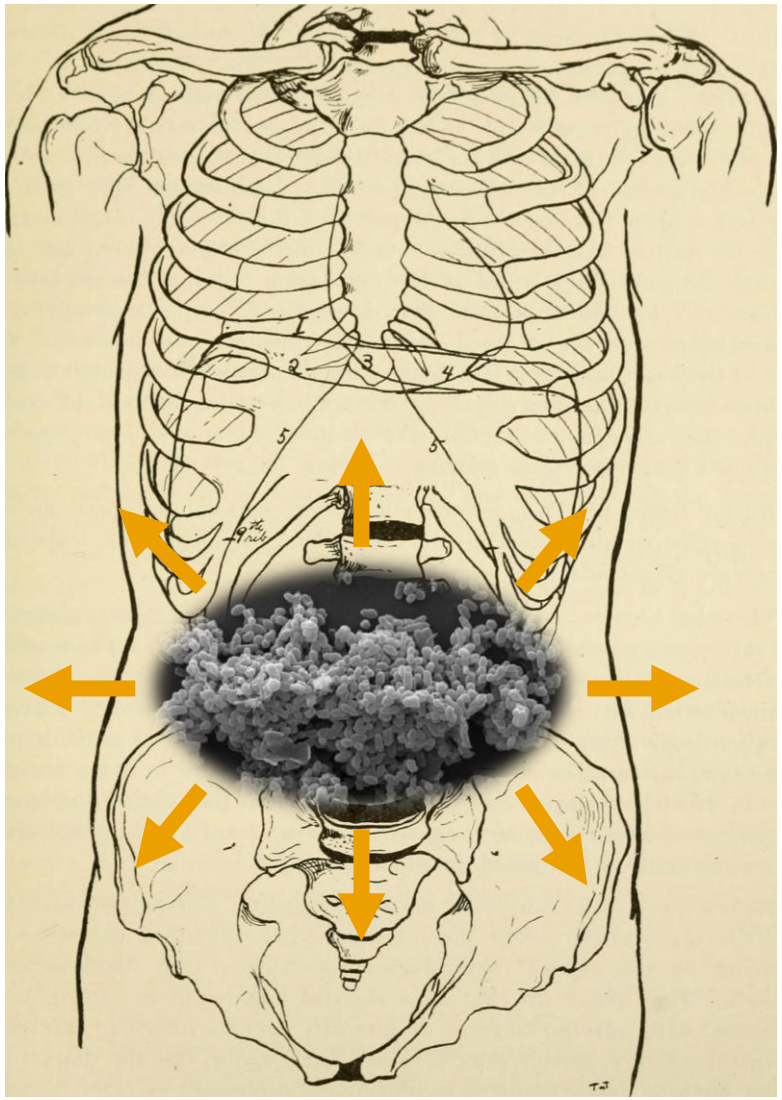
Functionalism(s)

Causal-Role Function

- The term **function** is helpful when we want to **explain the capacity of a containing system**.

Definition: *The microbiome "contributes to the containing system (O), the host, in its capacity for maintaining the stability and persistence of its physiological functioning systems (e.g., digestion, metabolism, development, and immunity)" (Schneider 2023).*

- **Conclusion:** Closer to the natural causal architecture of microbiomes.



Cummins 1975; Schneider 2023

Issues with Interventionism

- It is silent on the role of **other types of evidence** other than interventions.
- It is too **stringent** for the causal architecture of microbiomes.

- **Consequences: Lack of available fine-grained interventions** in microbiome studies and a **lack of empirical justification** for the focus on reductionist approaches.

Reiss 2015; Steel 2005; Schneider 2023

Issues with Functionalism(s)

Selected-Effect Function

- It implies **second-order causation** of the type *"X exists/persists because it causes Y"*

⇒**Needs an evolutionary history**

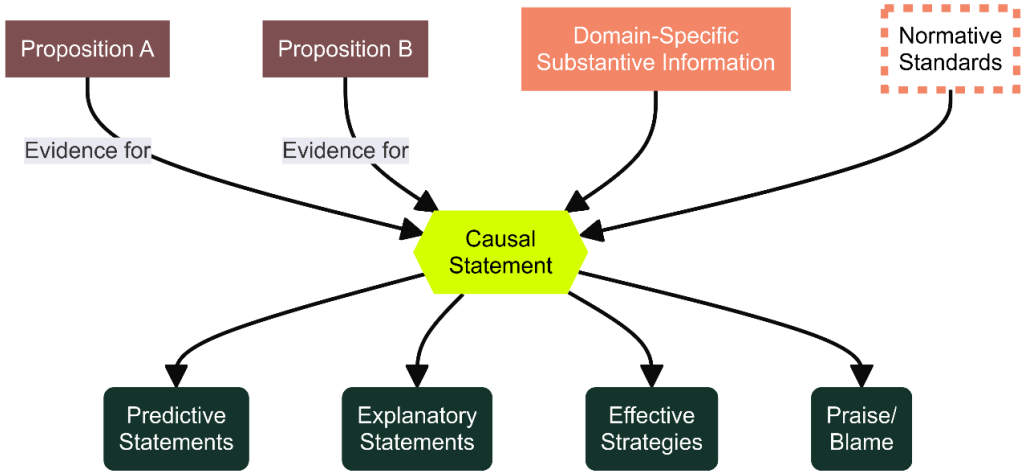
- No means to assign biological functions **to not yet selected traits in the microbiome**

- **Partial explanation**: It focuses on the microbes and not on background conditions or more complex contexts

Causal-Role Function

- Liberality of what can be a function.
- **Teleological**
- Might be sufficient in the context of health and disease conceptualized as those of the hosts, but…
- It restricts the significance of the biological functions of the microbiome **to those related to the host.**
- Not clear what types of evidence are necessary to establish causal claims.

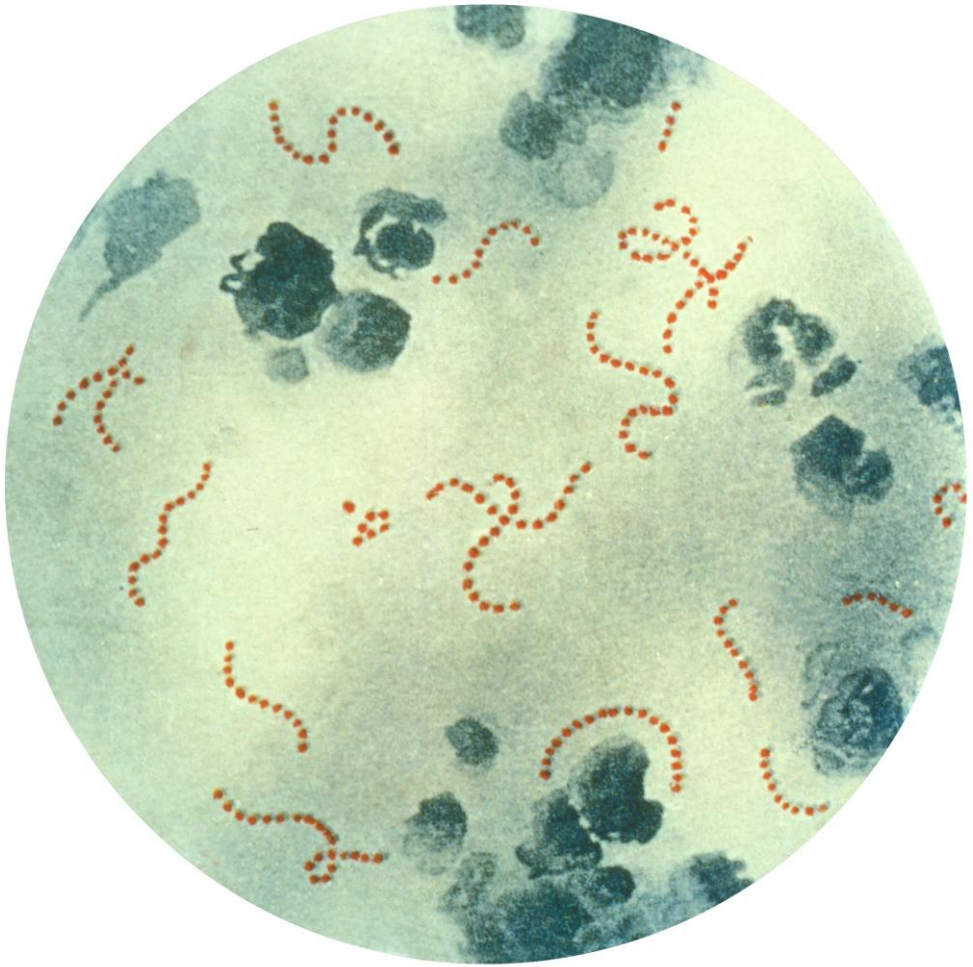
Reiss 2015; Steel 2005; Schneider 2023



An alternative: Inferentialism

- *"The microbiome causes obesity"* are to be understood by studying their places within an inferential network available to a scientific community.
- **Evidential pluralism**: Different kinds of evidence can play a role in establishing causal claims
- Causal inferences are licensed only locally in a given inquiry with **specific goals, substantive information, and normative standards.**
- The normative standards for causal claims are those of the **scientific community**.

Reiss 2015; Reiss 2024



Conclusion

1. Current philosophical frameworks (interventionism and functionalism) to explain causal claims in microbiome **have flaws**
2. Better alternative: **Inferentialism**
3. Further work: **test if this framework is useful in science**.

The myth of ethno-racial categories

Human Categorizations in Microbiomes

- Microbiome research uses **human categorizations**, including ethno-racial categories.

- **Civilizational ghosts**(Nieves-Delgado and Baedke, 202; for a review, see Rawson 2024).

- **Microbiomization** (Helmreich 2014).

My contribution

- Microbiome studies **from 2018**, where ethno-racial categories are used to study human health disparities to inform **personalized medicine**.

- I question **the inferential power** of ethno-racial categories in this context.

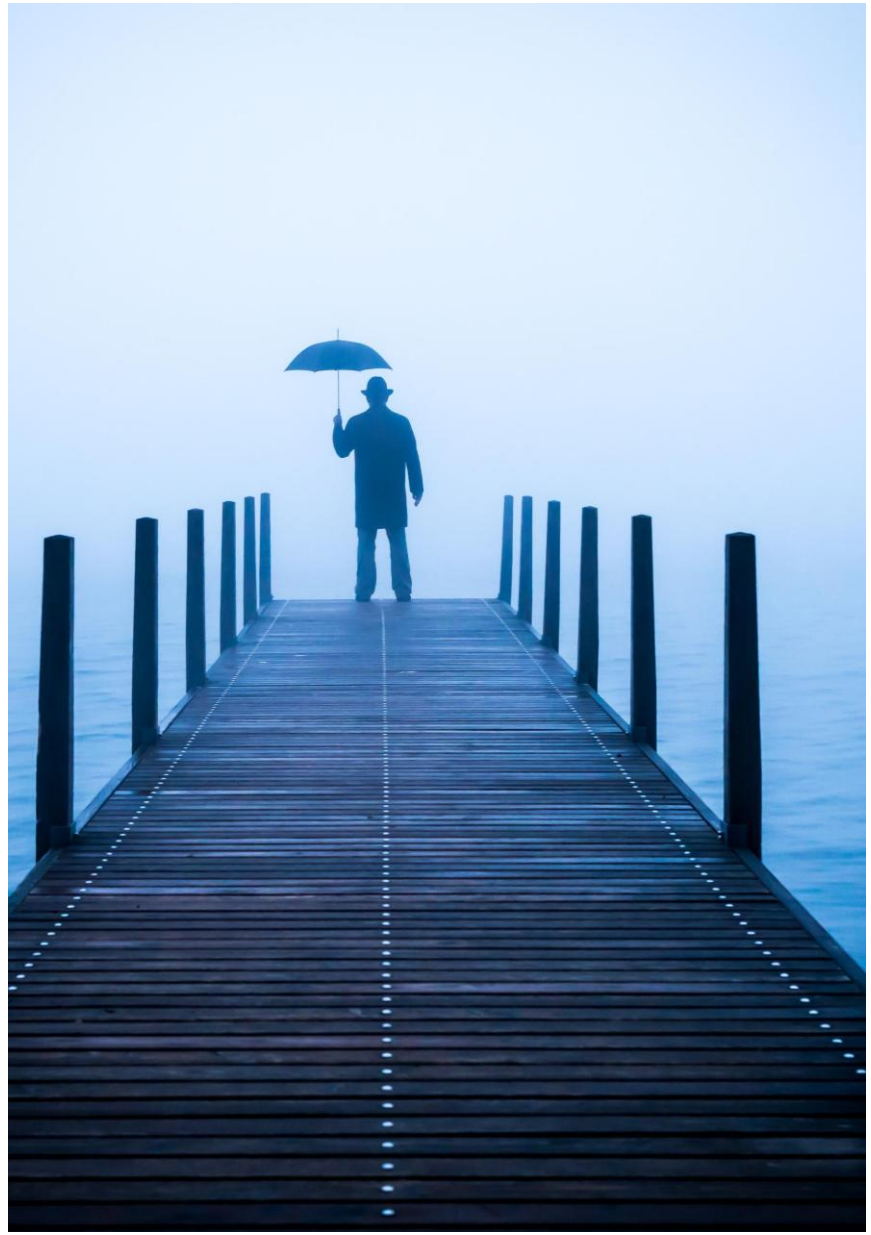
My contribution

1. The definitions of ethno-racial categories are imprecise, creating **epistemic uncertainty**.
2. These categories **reduce multiple dimensions** into one category, which can result **in stereotyping and essentializing ethno-racial categories through the microbiome.**
3. The **instability of these categories** makes them useless for treating a particular individual.

Conclusion: Using ethno-racial categories in microbiome studies in the context of personalized medicine is **problematic and should be abandoned**.

Conceptual Imprecision

- Ethno-racial categories are ambiguous and inconsistent, creating **epistemic uncertainty** (Malinowska and Serpico, 2023).
- This **conceptual imprecision also plagues microbiome studies**.
- **Method** (ongoing): non-systematic review in PubMed, EuroPMC, and Web of Science – terms “ethnicity”, “race” in Title and Abstracts associated with “human gut microbiome”



Thomas Leuthard

Conceptual Imprecision

Articles	Terms employed	Define (not explicitly) as
Amato et al. (2021)	Race and ethnicity	“Structurally imposed differences in lifestyle and environmental factors”, often associated with ancestry
Borello et al. (2022)	Race and ethnicity	Proxy for diet
Brooks et al. (2018)	Ethnicity	Self-declared, aspects of human genetic variation, social, economic and cultural variations
Deschasaux et al. (2018)	Ethnicity	HELIUS definition, people with same “diet, lifestyle, or genetics”, Western and non-Western
Gaulke and Sharpton (2018)	Ethnicity	Genetic diversity, geography
Syromyatnikov et al. (2022)	Race and ethnicity	Genetic diversity, living conditions, nationalities and religions

Conceptual Imprecision

01

These studies often **use interchangeably different concepts** such as “race,” “ethnicity,” “geography,” and “nationality.”

02

Few studies **define** these terms before using them, or **do not use them consistently** throughout one paper.

03

When institutional or more general definitions backed up such papers, those **definitions are not consistent globally and depend mainly on the location of the researchers**.

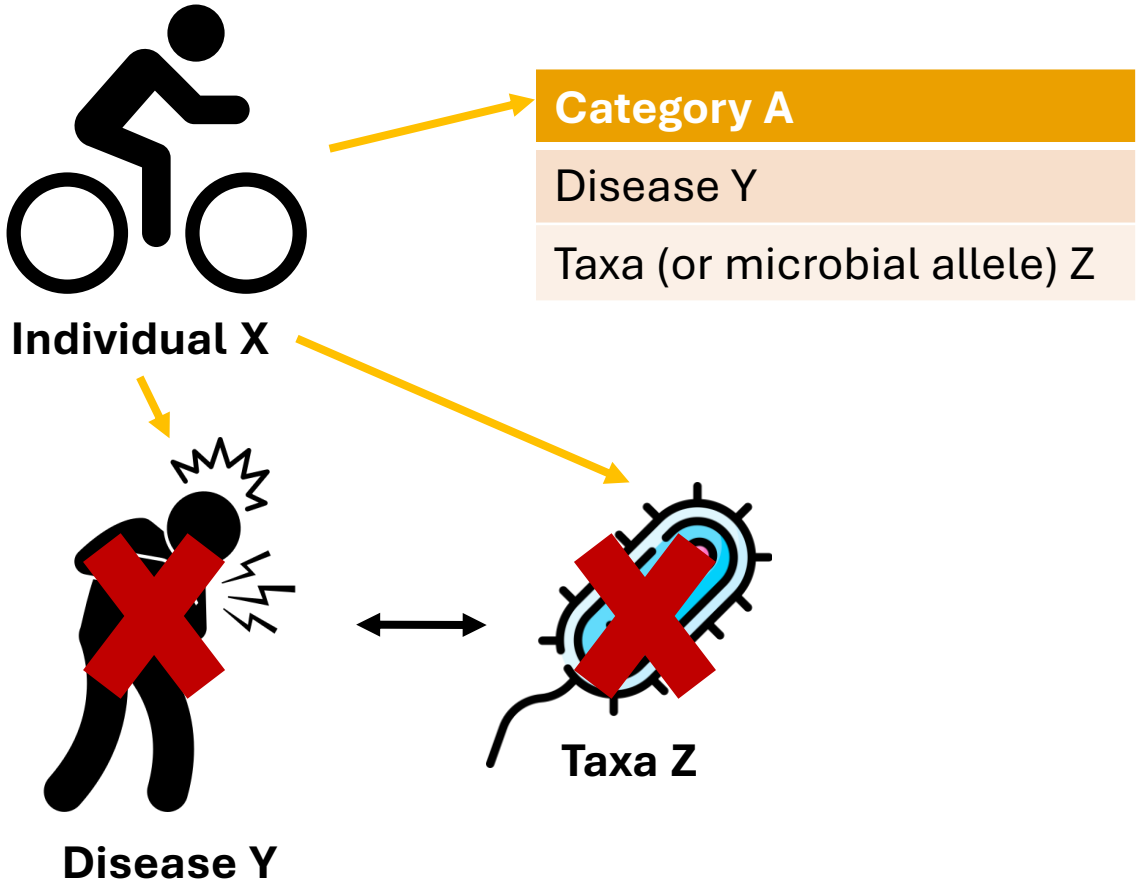
04

This situation prevents **comparative analyses** of different studies and **hinders scientific communication.**

Heuristic Limits of Ethno-racial Categories

- Ethno-racial categories help make inferences:

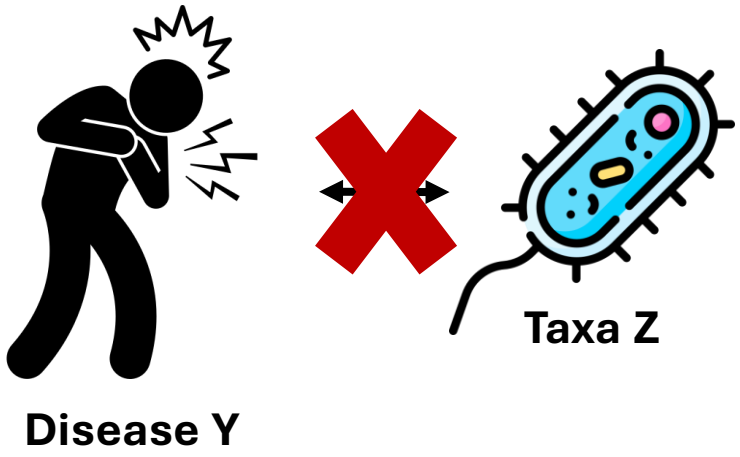
- *Which disease will they be susceptible to?*
- *How to treat them?*
- *Etc.*



images: Flaticon.com

Heuristic Limits of Ethno-racial Categories

- Few studies have found **consistent, reliable associations between microbial taxa and disease or health phenotypes.**

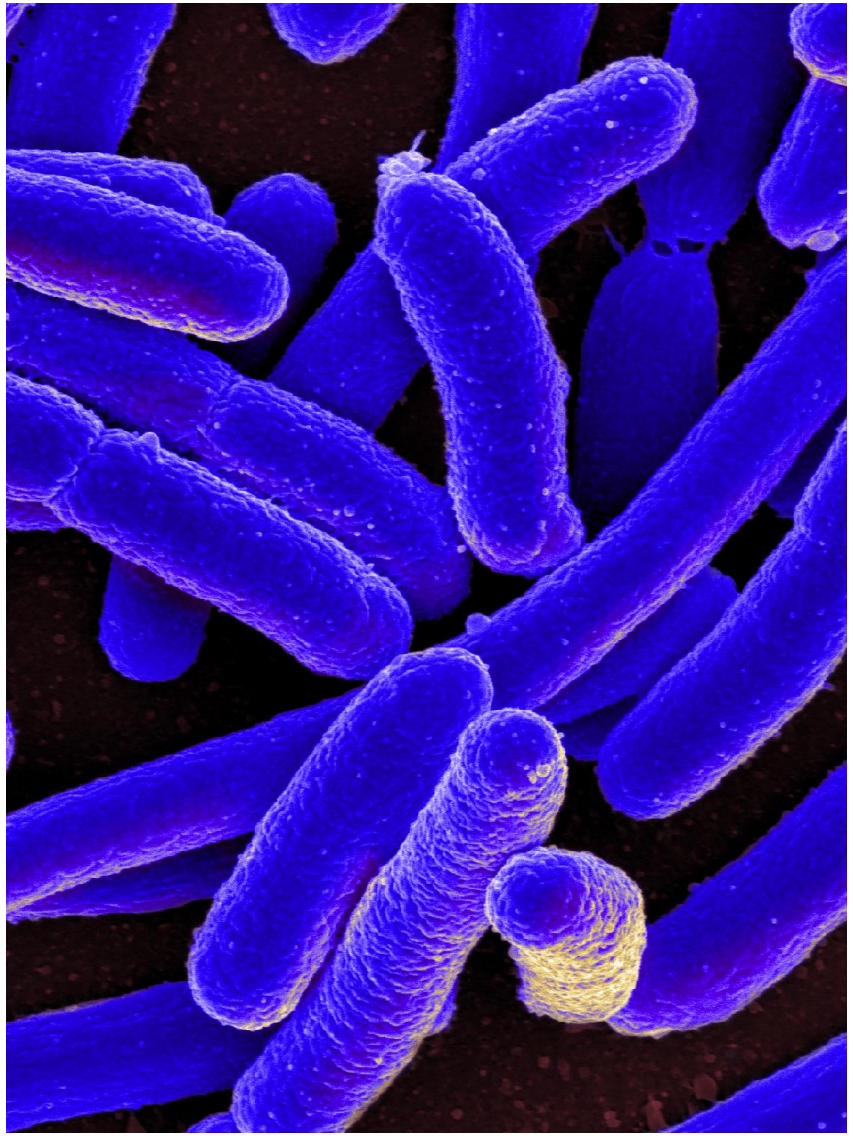


Category A
Disease Y
Taxa (or microbial allele) Z

- What is category A? How is ethnicity/race understood?

Heuristic Limits of Ethno-racial Categories

HUMAN GENETIC DIVERSITY	DIET/LIFESTYLE	OTHER?
“Ethno-racial groups cannot be expected to be homogeneous for every biological and environmental factor that is relevant to a given pathological phenotype” (Malinowska and Serpico, 2023)	Some associations between nutrients (e.g., glucose) and certain diseases (e.g., obesity).	
No microbial taxa (or alleles) are reliably and consistently associated with a particular **human allele**.	Some associations between nutrients (e.g., fibers) and certain microbial functions (e.g., SCFAs production).	



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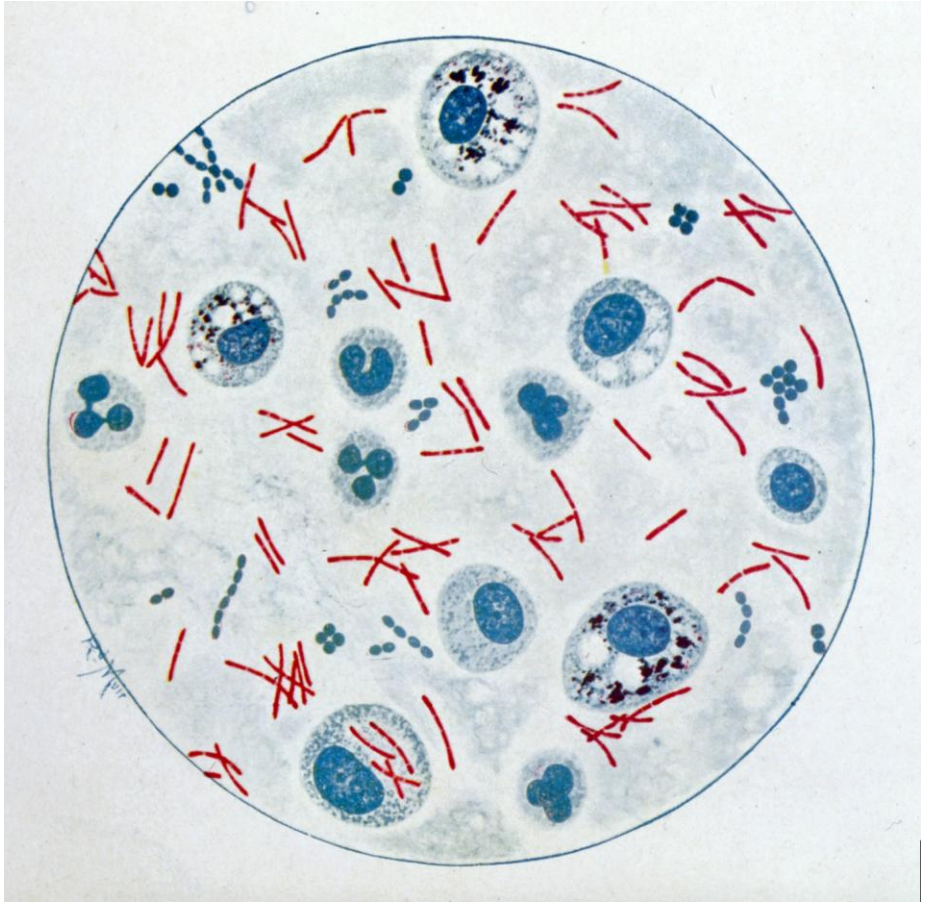
Heuristic Limits of Ethno-racial Categories

- Even if stable associations were found, these factors could lead **to different classifications of the same human population**, not necessarily consistent with more classical (US-centered) definitions of race, nor consistent between diseases.

- Thus, ethno-racial categories **are useless for treating a particular individual**.

Conclusion

- Ethno-racial categories in microbiome **studies have limited inferential power.**
- The risks of using ethno-racial categories in microbiome studies, including **poor scientific communication**, attributing **a spurious causal role** to these categories, **stereotyping**, and **misplacing individuals** into categories that may not be relevant for treatment or risk-factor assessment, **outweigh any potential benefits**.
- Instead, researchers should focus on the **actual variables** they are interested in, such as diet, to avoid racist descriptions and the microbiomization of ethno-racial categories.



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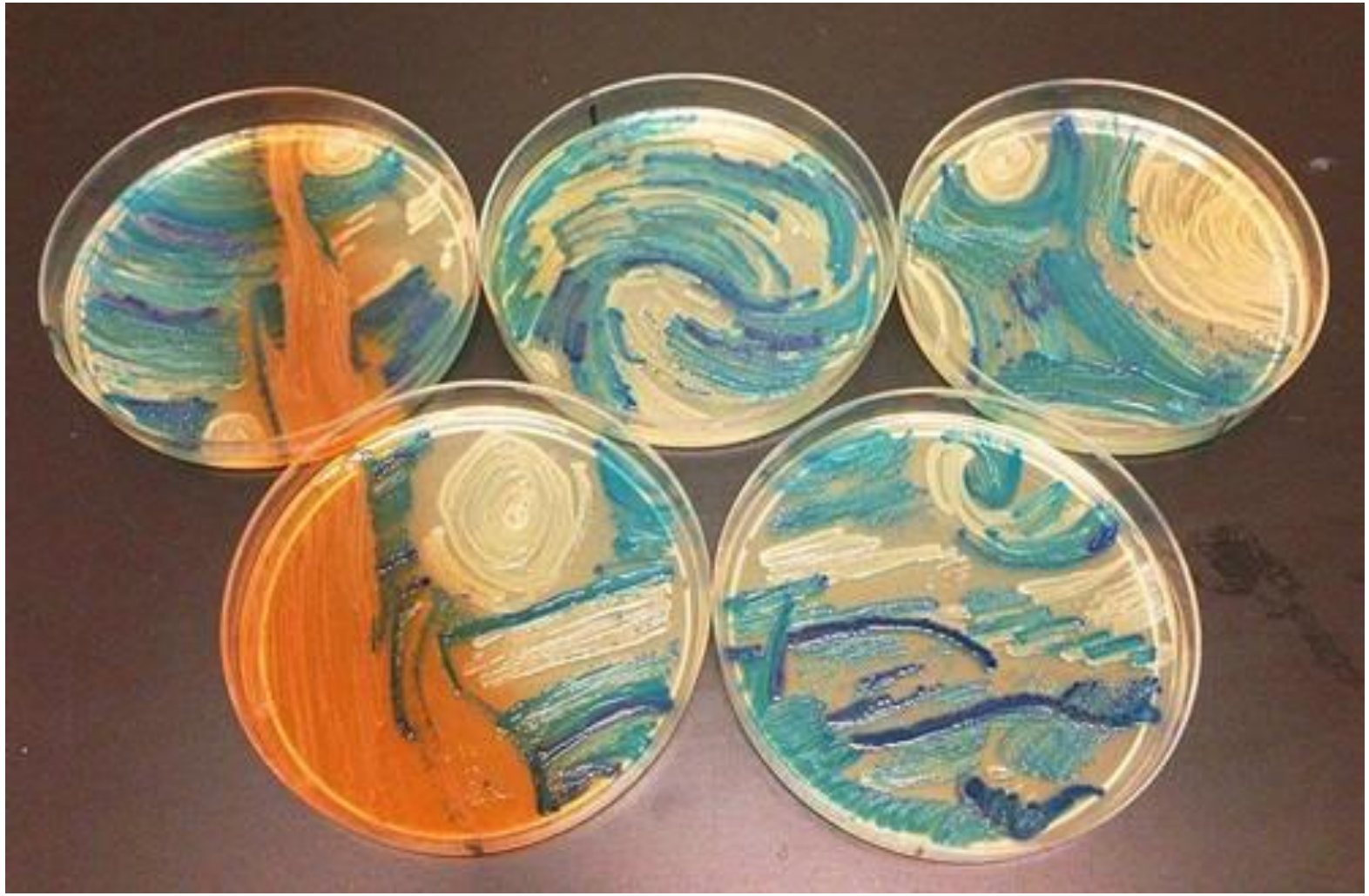
General Conclusion

- **Origins: Unearthing the ecological roots of microbiome studies**
  - Explain the **current status** of the discipline and the tensions within it using the history of microbiology
  - Perspective in microbial ecology: **dynamic processes, complex causal systems, interactions, etc.**
  - For practitioners: **more integration**
- **Causality:** Alternative causal framework: **Inferentialism**
- **Human Categorizations: The myth of ethno-racial categories**
  - **Limited inferential power** of ethno-racial categories
  - **Abandon** of the use of these categories
  - Focus on the **real variables of interest**



Thank you!

Vincent van Gogh's "The Starry Night" by Melanie Sullivan of Missouri. *American Society of Microbiology.*

Acknowledgments – Future Event

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- https://perspectivesrace.wixsite.com/the-human-diversity/home-2