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How does the history of microbiology call for a more integrative view of explanation in human gut microbiome research?

&HPS9
16 – 18th March 2023

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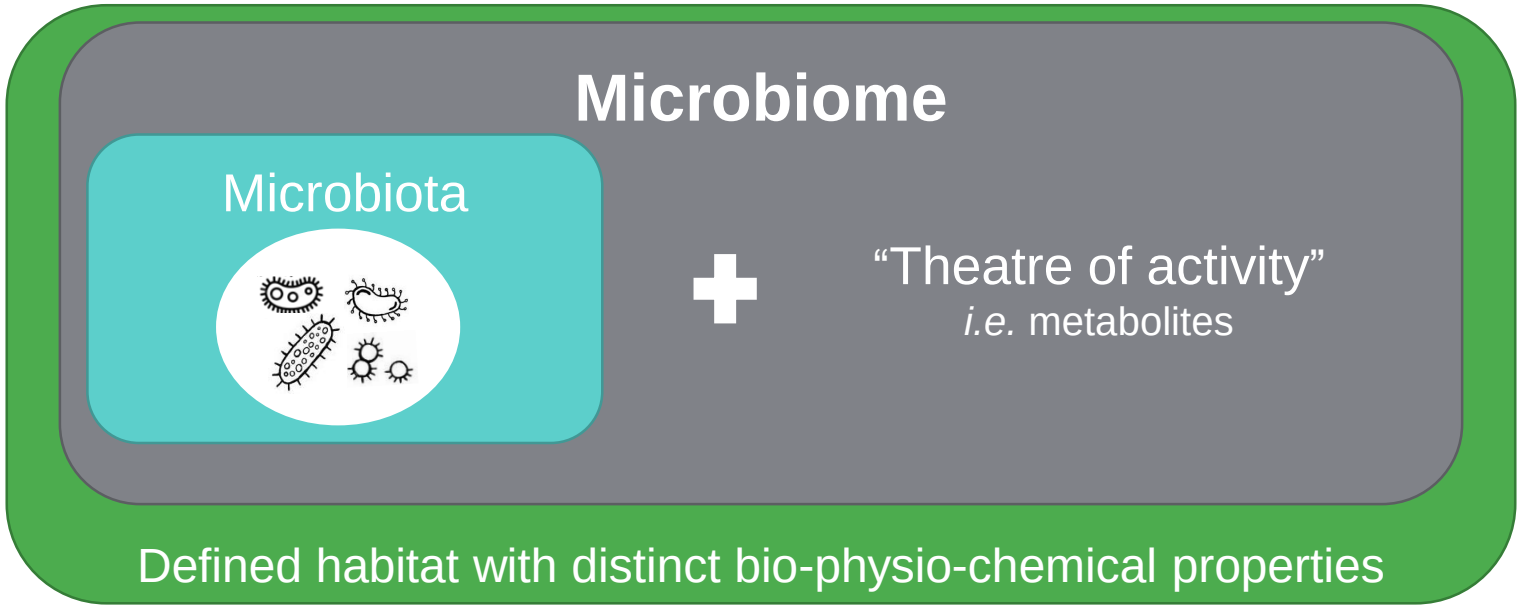
Introduction

- Defining the “microbiome” is difficult, but a recent attempt at consensus has been published. Here, the microbiome is **the microbiota** – the microorganisms and their “**theatre of activity**” – all their activities in a given environment (Berg et al. 2020).

⇒ Complex and multilevel system



Berg, G., Rybakova, D., Fischer, D. *et al*. (2020). Microbiome definition re-visited: old concepts and new challenges. *Microbiome* 8, 103. Doi: 10.1186/s40168-020-00875-0

Introduction

- Human gut microbiomes have been associated with various healthy and diseased human phenotypes.

$\Rightarrow$ There is a scientific worry about how one can explain health and disease states involving the microbiome + how to evaluate these explanations.

- The main philosophical study so far is the one published by Lynch and colleagues (2019) + the various commentaries received on the paper.
  - Focus on **causal explanations** drawing on standards methods to establish causation: **1880s Koch postulates** and **the interventionist view of causation**

  $\Rightarrow$ Causal claims involving the whole microbiome are weak or misleading.

This approach overlooks part of microbiology's history leading to a distorted view of explanation in microbiome research.

Lynch, K. E., Parke, E. C., and O'Malley, M.A. (2019). How causal are microbiome? A comparison with the *Helicobacter pylori* explanation of ulcers. *Biology and Philosophy* 34 (62), 1-24. Doi: 10.1007/s10539-019-9702-2

Aims

1. Show that microbiology is a medical AND ecological discipline by using the history of microbiology.

2. Argue that in the ecological branch of microbiology, explanations describes mechanism by using an analysis of Sergei Winogradsky's work.

3. Suggest a more integrative view of explanation in human gut microbiome research based on a mechanistic account of explanation.

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Aim 1: Microbiology is also ecological.

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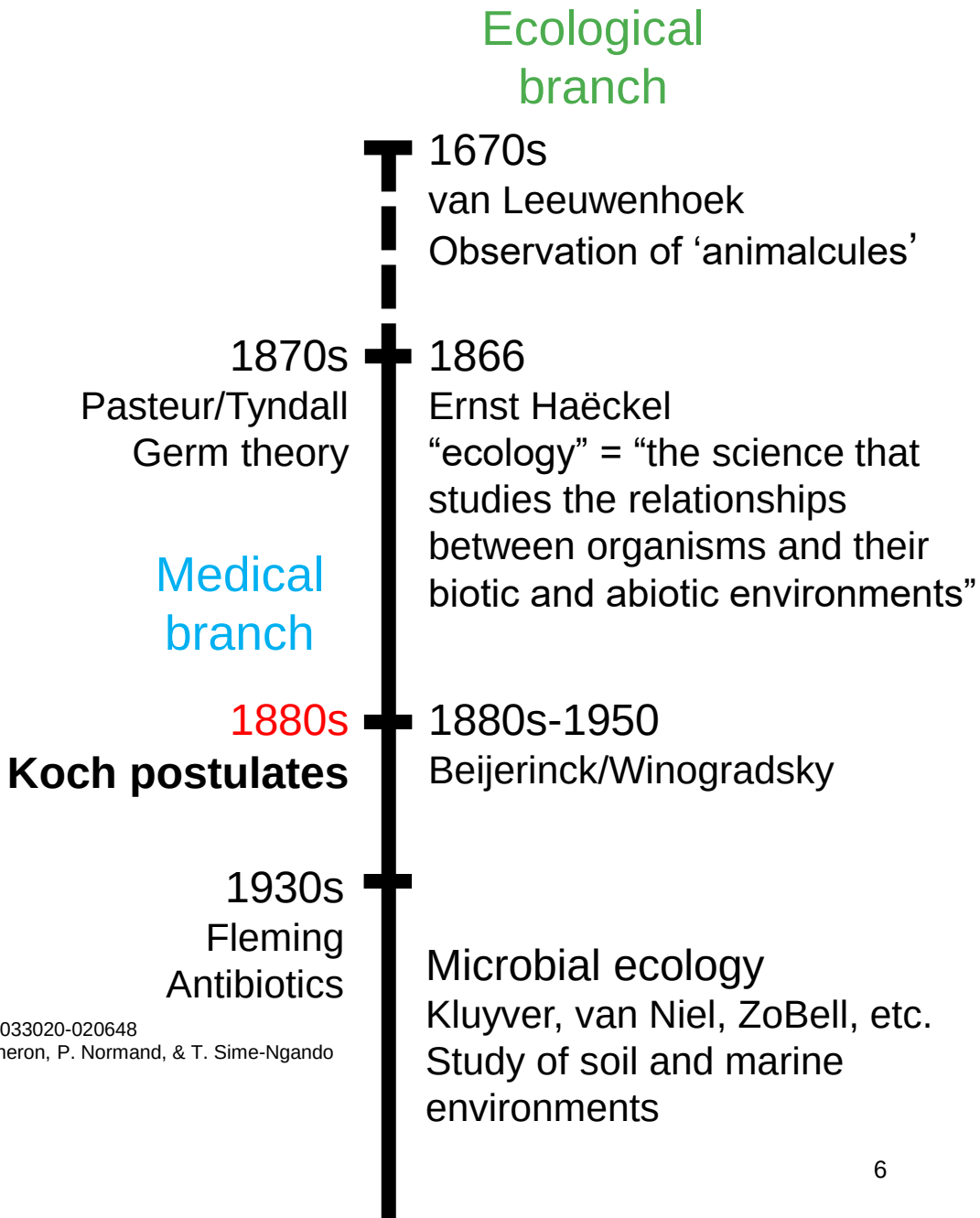
A brief history of Microbiology

- Pasteur, Winogradsky and Beijerinck: “all three recognized the complex interplay of microbes with their environments in the settings they investigated” (Kolter, 2021, 3).
- 1870s-1880s: controversy between Pasteur and Koch leading to the formulation of the **postulates** (Carter, 2005, 115-122):

After being fully isolated in pure culture, the microorganism can infect healthy hosts in producing the classic symptoms of the disease.

⇒ **Look for causal explanations – Interventionism**



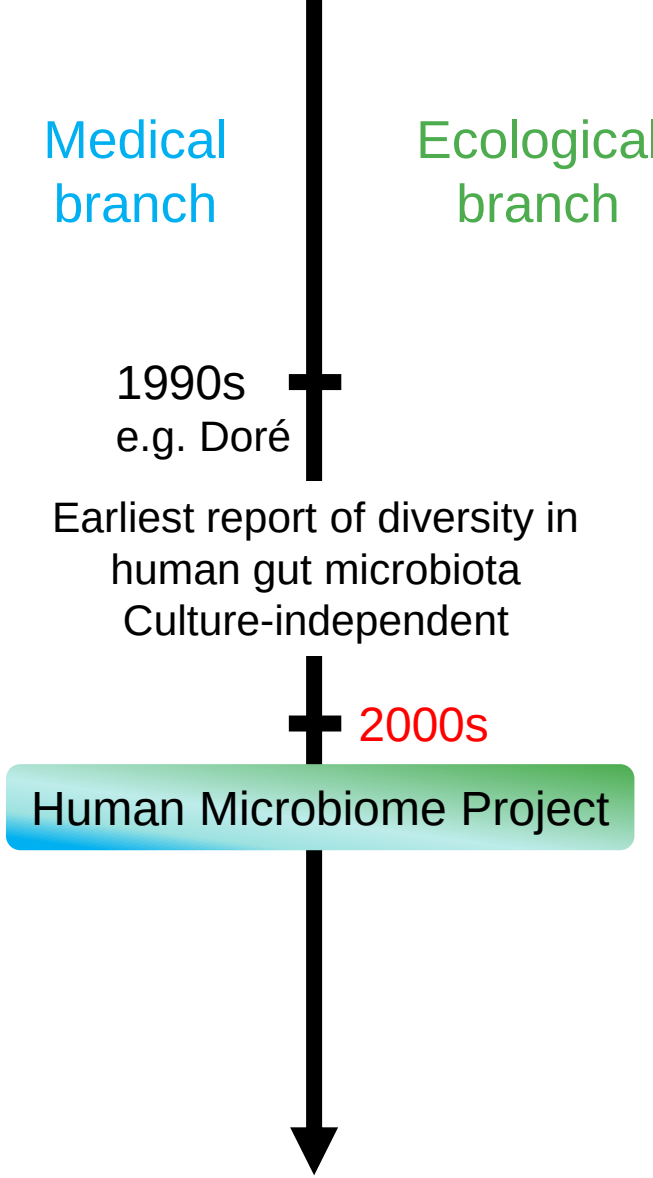
Kolter, R. (2021). The History of Microbiology-A Personal Interpretation. *Annual Review of Microbiology*, 75, 1–17. https://doi.org/10.1146/annurev-micro-033020-020648
Caumette, P., Bertrand, J.-C., & Normand, P. (2015). Some Historical Elements of Microbial Ecology. In J.-C. Bertrand, P. Caumette, P. Lebaron, R. Matheron, P. Normand, & T. Sime-Ngando (Eds.), Environmental Microbiology: Fundamentals and Applications (pp. 9–24). Springer.
Carter, K. C. (2003). *The rise of causal concept of disease: case histories*. New York: Routledge,

A brief history of Microbiology

- The studies of the intestinal gut microbiota **bring together** these sub-disciplines:
  - Diversity – ecological approach
  - Human (gut microbiota) – medical approach
  - Culture-independent – molecular tools

Research on the human gut microbiome has a dual heritage: a medical approach and an environmental approach

⇒Focusing on explanation in the medical branch is legitimate but overlooks insights from the second branch



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Aim 2: Microbial ecology historically looks for mechanisms.

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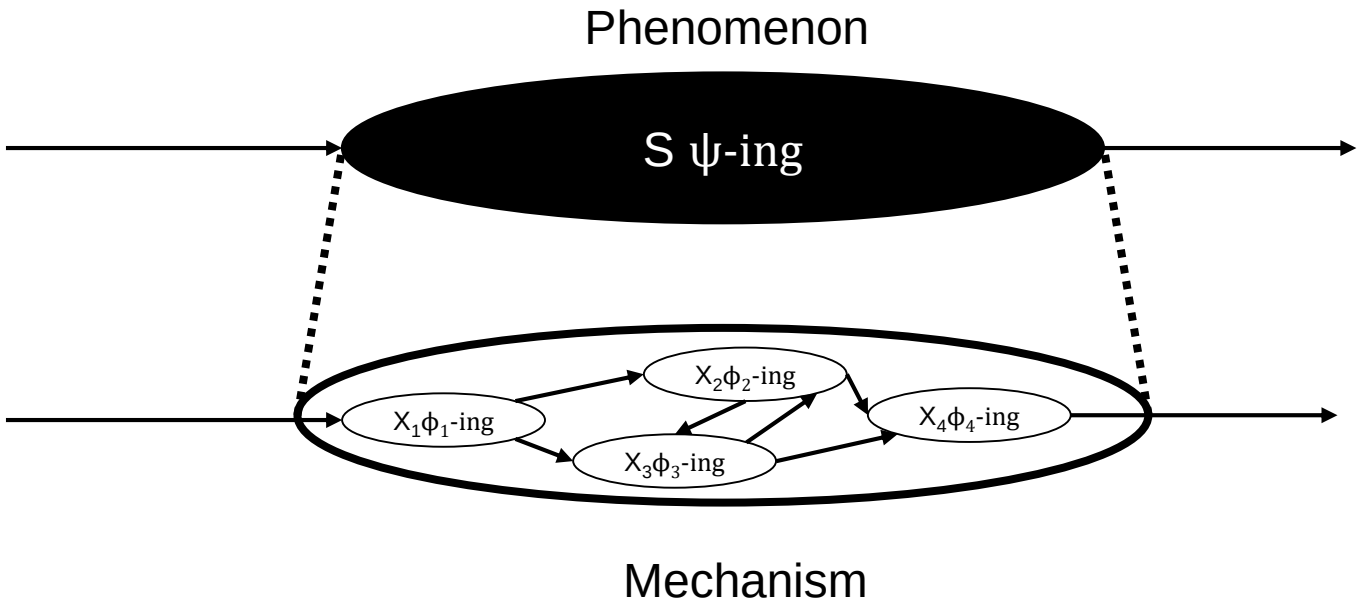
Explanations in microbial ecology

- Several definitions of ‘mechanisms’ in philosophy.
- **Central idea**: mechanism is a complex causal system with multiple components that exhibit activities and a certain organization – that interact – to produce one or more overall phenomenon (Fagan, 2012, 450).



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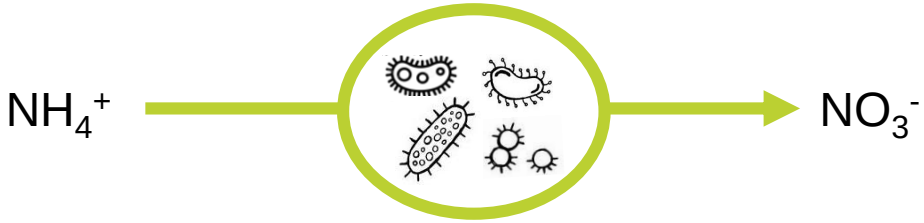
Fagan, M. B. (2012). The Joint Account of Mechanistic Explanation. *Philosophy of Science, 79(4), pp. 448-472.* http://www.jstor.org/stable/10.1086/668006

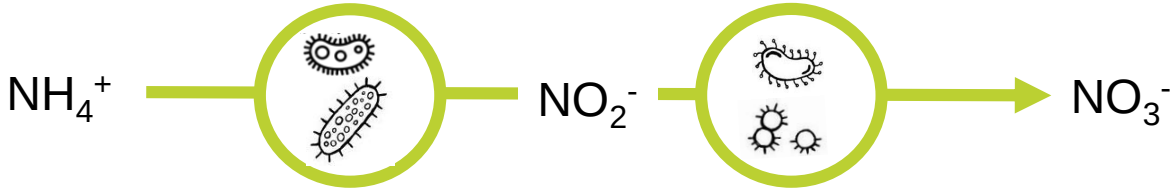
Explanations in microbial ecology

1856-1953

- Sergeï Winogradsky puts into question the transferability of results observed in pure cultures to natural phenomena.
- **Nitrification phenomenon**: transformation of ammonium to nitrates.



- One example of explanation: “[…], the conclusion that these are in fact two autonomous functions, each exercised by its own ferment, appears necessary.” (MS, 252)

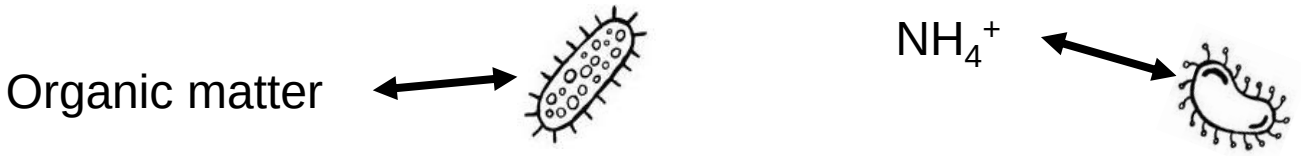


Explanations in microbial ecology

- The “microflora” can thus be decomposed **into parts** – microorganisms – that **interact** with each other – by transforming chemical compounds into others. But it is not a mere aggregate:

  the functioning of the “Microflora” “should not be seen as the sum of individual activities, but as the work of a self-regulating collective.” (MS, 845)

- Integration of **biotic and abiotic components** of the environment:

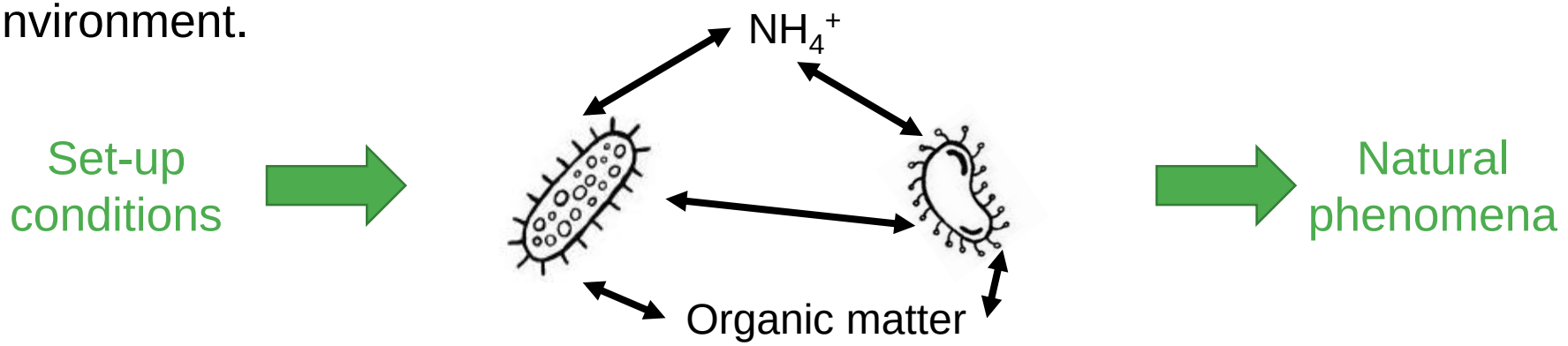


- **Localization and spatial organization** of the microorganisms and the other components within the environment:

  e.g. “These [autochthonous microbes] are always lodged on flakes of colloidal material, [...] from which they cannot be detached. […]”(MS, 453).

Explanations in microbial ecology – Summary

- Natural phenomena are thus explained in terms of interactions between the microorganisms in a given environment.



- Microorganisms are more often found in **community** in which **interactions** and communication are critical to population dynamics and function.

⇒Call for a holistic view in methods (interdisciplinarity) and explanation (Berg et al., 2020).

⇒**We need a comprehensive account of explanation in human gut microbiome research that can accommodate this search for mechanisms.**

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Aim 3: Towards an integrative view of explanation in human gut microbiome research.

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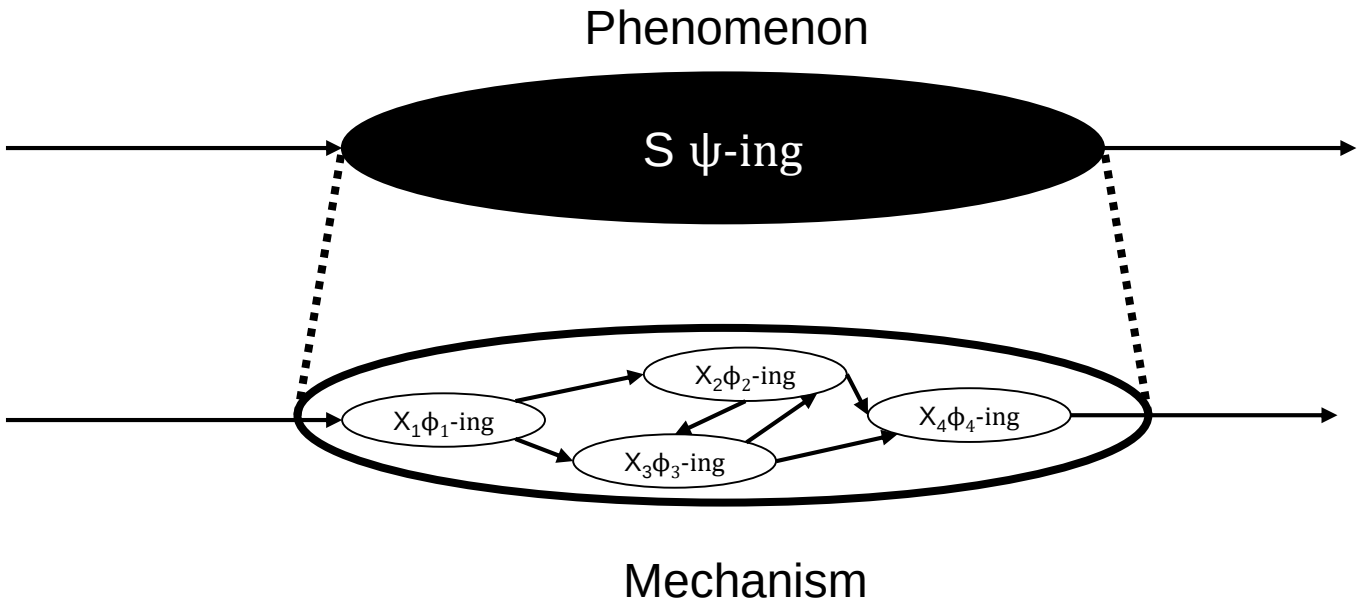
Towards an integrative view of explanation

- I propose to apply and adapt the mechanistic view of explanation developed by Craver (2007).
- Craver's account: A mechanism (the explanans) explains an explanandum phenomenon when it describes relevant components, their activities and their spatial and temporal organization such that they will produce the phenomenon (Craver, 2007).



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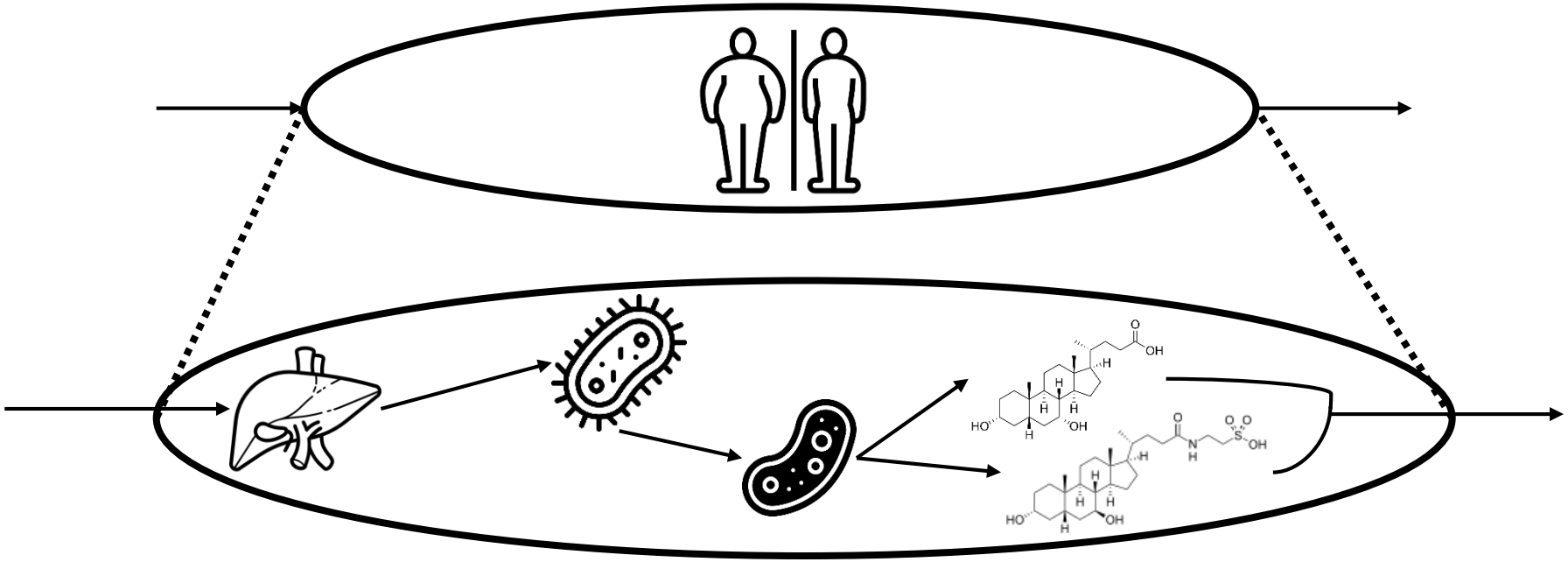
Towards an integrative view of explanation

- Mechanisms are searched by scientists in human gut microbiome research, but there is no (not yet) archetypal example of a clear explanation in this discipline.
- Yet, the gut microbiome has been associated multiple times +/- with obesity, for example:



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Towards an integrative view of explanation

- I consider two important points of Craver's account:
  - **Causal relevance**: components of the underlying mechanism are linked by causal relations. These are relationships of manipulability (Craver, 2007, 139).

  ⇒Uses the interventionist account to decipher causal relevance relations.

⇒ **By integrating the interventionist account in the selection of relevant causes, the mechanistic account integrates the view on explanation inherited from the medical branch, i.e. the search for causes.**

⇒ **But it is not all there is to explanation...**

Craver, C. F. (2007). *Explaining the Brain: Mechanisms and the Mosaic Unity of Neuroscience*. New York: Oxford University Press.
Woodward, J. (2010). Causation in biology: stability, specificity, and the choice of levels of explanation. *Biology and Philosophy*, 25:287–318. doi:10.1007/s10539-010-9200-z

Towards an integrative view of explanation

- **Constitutive explanation**: “how the behavior of a whole is explained in terms of the behavior of its parts” (Craver, 2007, 160).
  - **Mutual manipulability criterion**: “a component is relevant to the behavior of a mechanism as a whole when:
    - one can wiggle the behavior of the whole by wiggling the behavior of the component and

Antibiotic treatments – **bottom-up experiment:** the microorganisms are wiggled, their activities are suppressed. And the detection method is at the level of the phenomenon, i.e. obesity (reduction of body weight).

- one can wiggle the behavior of the component by wiggling the behavior as a whole.

Increasing of energy expenditure – **top-down experiment**: the phenomenon as a whole is wiggled and the detection is at the level of the mechanism, i.e. the components/activities supposed to be involved in the production of obesity.

The two are related as part to whole and they are mutually manipulable.” (Craver, 2007, 153)

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Towards an integrative view of explanation

- Problem: Risk of confounding causal vs. constitutive relationships – noticed elsewhere (Fagan, 2012 and Kästner and Andersen, 2018).
  - Both are based on manipulability criteria.
  - The problem of interventions in the mechanism as a whole is that they are **fat-handed**, i.e. the top-down experiment doesn't wiggle only one component – even understood as the whole microbiome – but also a variety of host-related mechanisms.
  - Experiments to prove constitutive relationships are taken as proving causality (Chaudhari et al., 2021).

  $\Rightarrow$ **Need to develop the mechanistic account to consider this issue.**

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Kästner, L. and Andersen, L. M. (2018). Intervening into mechanisms: Prospects and challenges. *Philosophy Compass, 13:e12546*. https://doi.org/10.1111/phc3.12546

Conclusion

- **Aim 1**: Microbiology is also an ecological discipline & Human gut microbiome research is at the crossroad between a medical and an ecological approach of microbiology.

- **Aim 2**: Microbial ecology – as well as human gut microbiome research – is looking for mechanisms.

- **Aim 3**: Sketch of an integrative account of explanation that
  - Considers the multipath history of human gut microbiome research
  - Broadens our understanding of explanation in this discipline and might find **satisfactory explanatory claims after all**.

Thank you for your attention