School of Artificial Intelligence Applied to Microbiomes

01-10-2025 – 03-10-2025
AgroParisTech

université PARIS-SACLAY
GRADUATE SCHOOL Biosphera

Ecole Doctorale ABIES

ÉCOLE DOCTORALE
Sciences du végétal : du gène à l'écosystème (SEVE)

METAPROGRAMME HOLOFLUX

MicroEngine project

RÉPUBLIQUE FRANÇAISE
Liberté Égalité Fraternité

FRANCE 2030

Programme EXPLOR'AE

Special thanks to

Daniel Garza for organizing the school, as well as

Aristeidis Litos and all the speakers

Frédérique Delville from Biosphera

THEMATIC PROGRAM
MICROORGANISMS: FROM GENES TO ECO-SYSTEMS

Miguel Iniesto (IDEEV, ESE, miguel.iniesto@universite-paris-saclay.fr)
Ariane Bize (INRAE, PROSE, ariane.bize@inrae.fr)

aims to reinforce the network of Paris-Saclay's students and scientists working in microbiology, at a broad sense, on Biosphera topics

meeting once a year

financial support of collective events related to the thematic program → don't hesitate to contact us!

Journée Scientifique Biosphera

Jeudi 15 janvier 2026 de 9h à 19h – Campus Agro Paris-Saclay

Elle aura pour thématique **Biodiversité & évolution à l'épreuve du changement climatique »**

Le programme est en cours de construction. Il vous sera transmis sous peu avec le lien d'inscription.

School overview & practical information

Daniel Garza

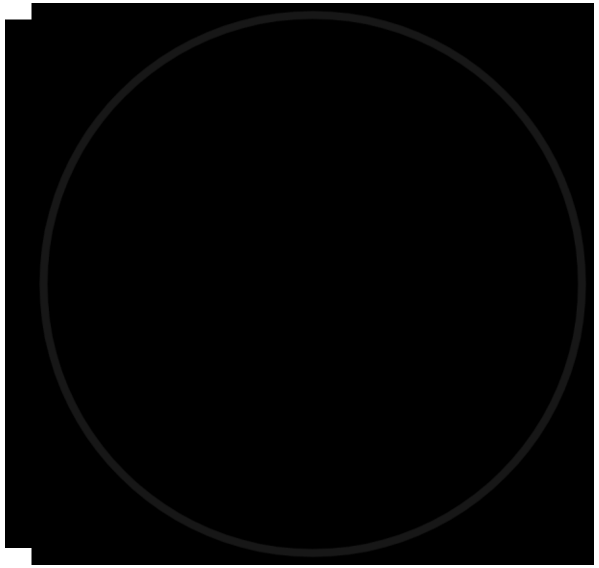
PROSE
PRocédés biOtechnologiques au Service de l'Environnement

RÉPUBLIQUE FRANÇAISE

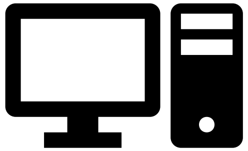
INRAE

SCHOOL OF ARTIFICIAL INTELLIGENCE APPLIED TO MICROBIOMES

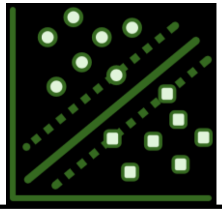
Goal of the School: provide a broad overview of how advanced computational methods, including artificial intelligence, are used in microbiome science



Omics tools



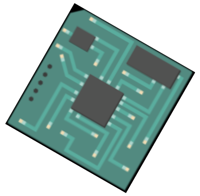
Machine learning



Artificial intelligence

New ways to make sense of large microbiome datasets

New models to predict and explain microbiome dynamics



New approaches to engineering microbial systems for targeted functions or desired community states

SCHOOL OF ARTIFICIAL INTELLIGENCE APPLIED TO MICROBIOMES

Program: research talks & tutorials

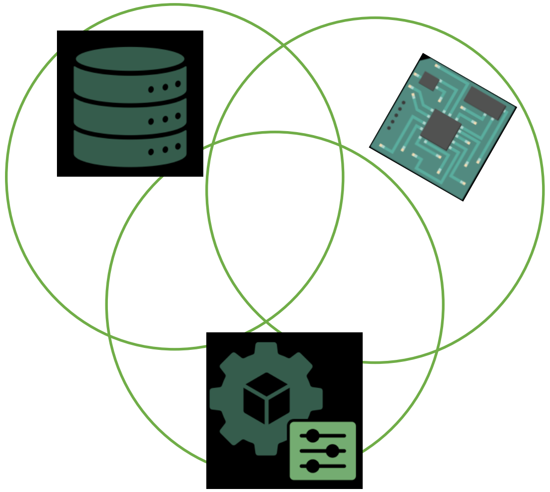
New ways to make sense of large microbiome datasets

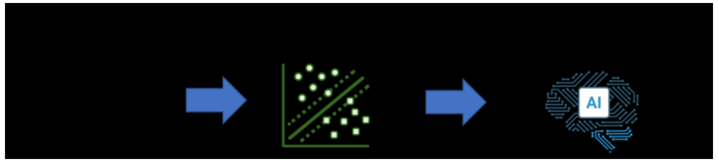
Dr. Julian Tap
INRAE
France

Lecture: *Integrating Human Gut Microbiome Data at Scale: From Individuals to Multi-Layered Features in Clinical and Nutritional Studies*

Prof. Bas Dutilh
Friedrich Schiller University Jena
Germany

Lecture: *Mapping the Microverse and Modelling its Drivers*





Program: research talks & tutorials

New computational models to predict and explain microbiome dynamics

Dr. Clémence Frioux
Inria, University of Bordeaux
France

Lecture: *to be defined*

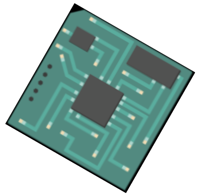
Prof. Jean-Loup Faulon
University of Paris Saclay, INRAE
France

Lecture: *Bacterial Reservoir Computing*

Dr. Haris Zafeiropoulos
KU Leuven
Belgium

Lecture: *to be defined*

Program: research talks & tutorials



New approaches to engineering microbial systems for targeted functions or desired community states

Dr. Djordje Bajić
TU Delft
The Netherlands

Lecture: *Statistical mapping of Structure-Function Landscapes in Microbiomes*

Dr. Lucas Böttcher
Frankfurt School of Finance & Management
Germany

Lecture: *Simulation and Control of High-Dimensional Dynamical Systems Using Artificial Neural Networks*

Dr. Alex Fedorec
University College London
United Kingdom

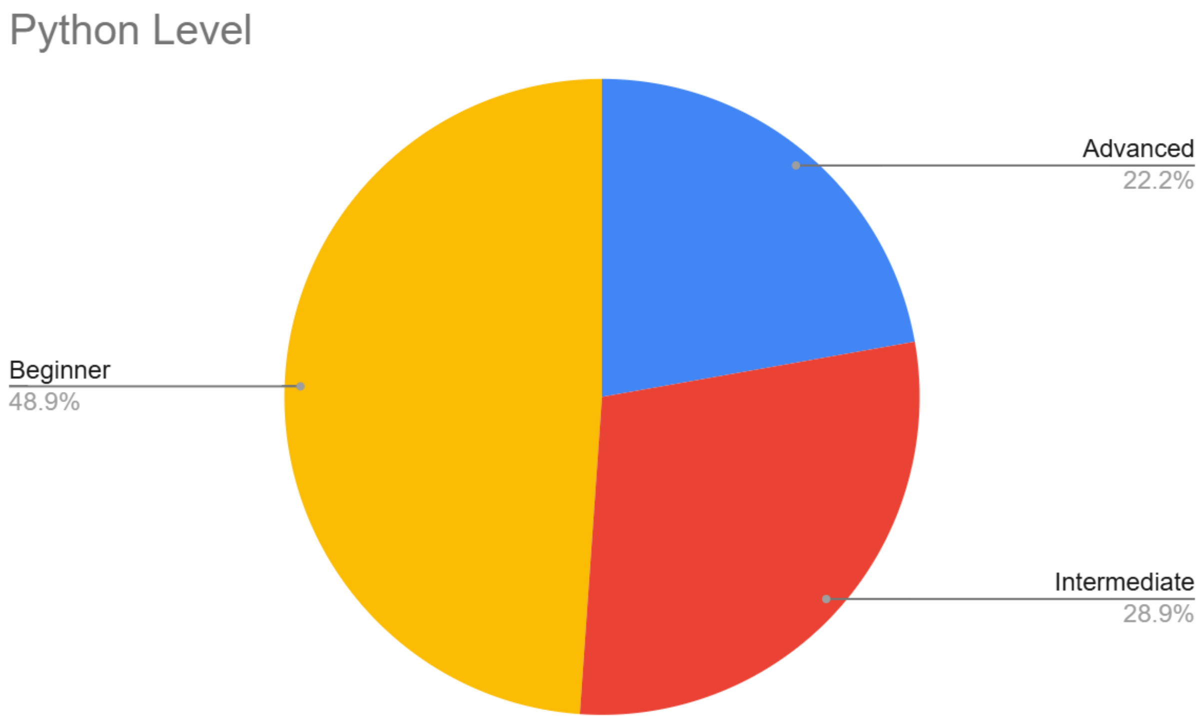
Lecture: *Computational Design of Synthetic Microbial Communities*

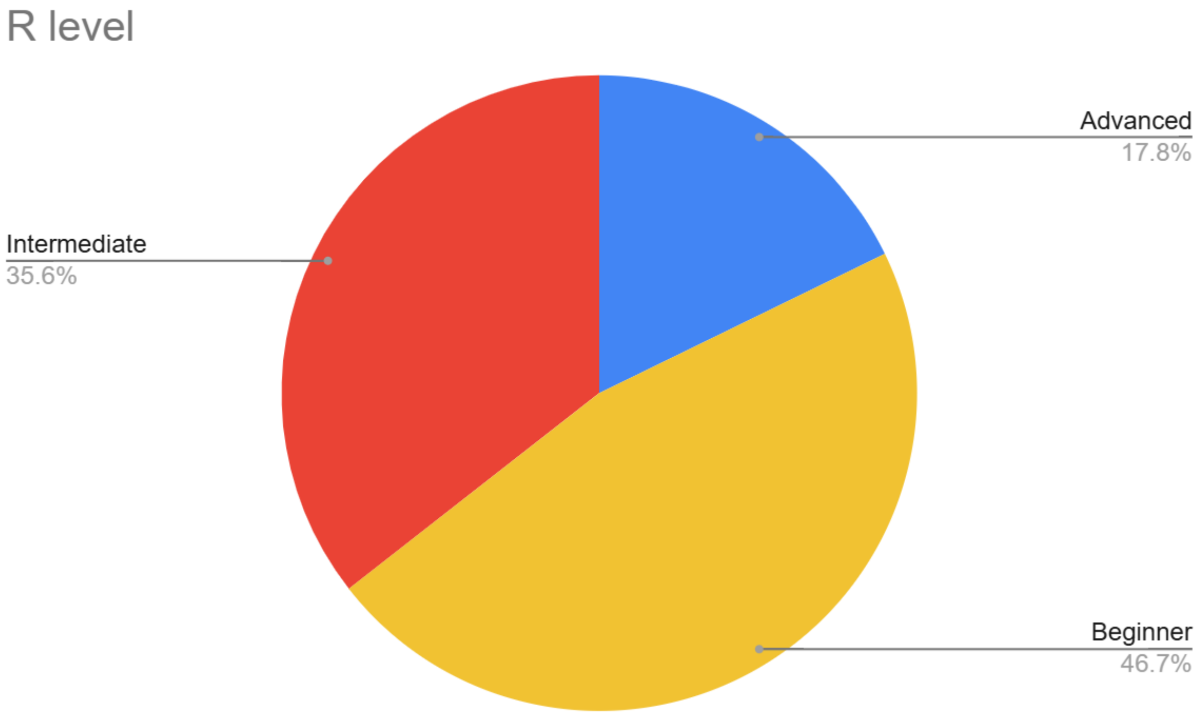
Dr. Daniel Garza
University of Paris Saclay, INRAE
France

Lecture: *Controlling complex microbiomes with computational intelligence: physical and virtual prototypes*

Participants

48 registrations





General Information

Program/Speakers/Participants:
https://ai-microbiome-school.onrender.com/

Slides and materials will be later organized in the "Tutorial & Slides" section of the website.

Most of the code will be available in the GitHub repository:
https://github.com/danielriosgarza/AiSchool.git

IFB Cluster

INSTITUT FRANÇAIS DE BIOINFORMATIQUE

https://ondemand.cluster.france-bioinformatique.fr

INSTITUT FRANÇAIS DE BIOINFORMATIQUE

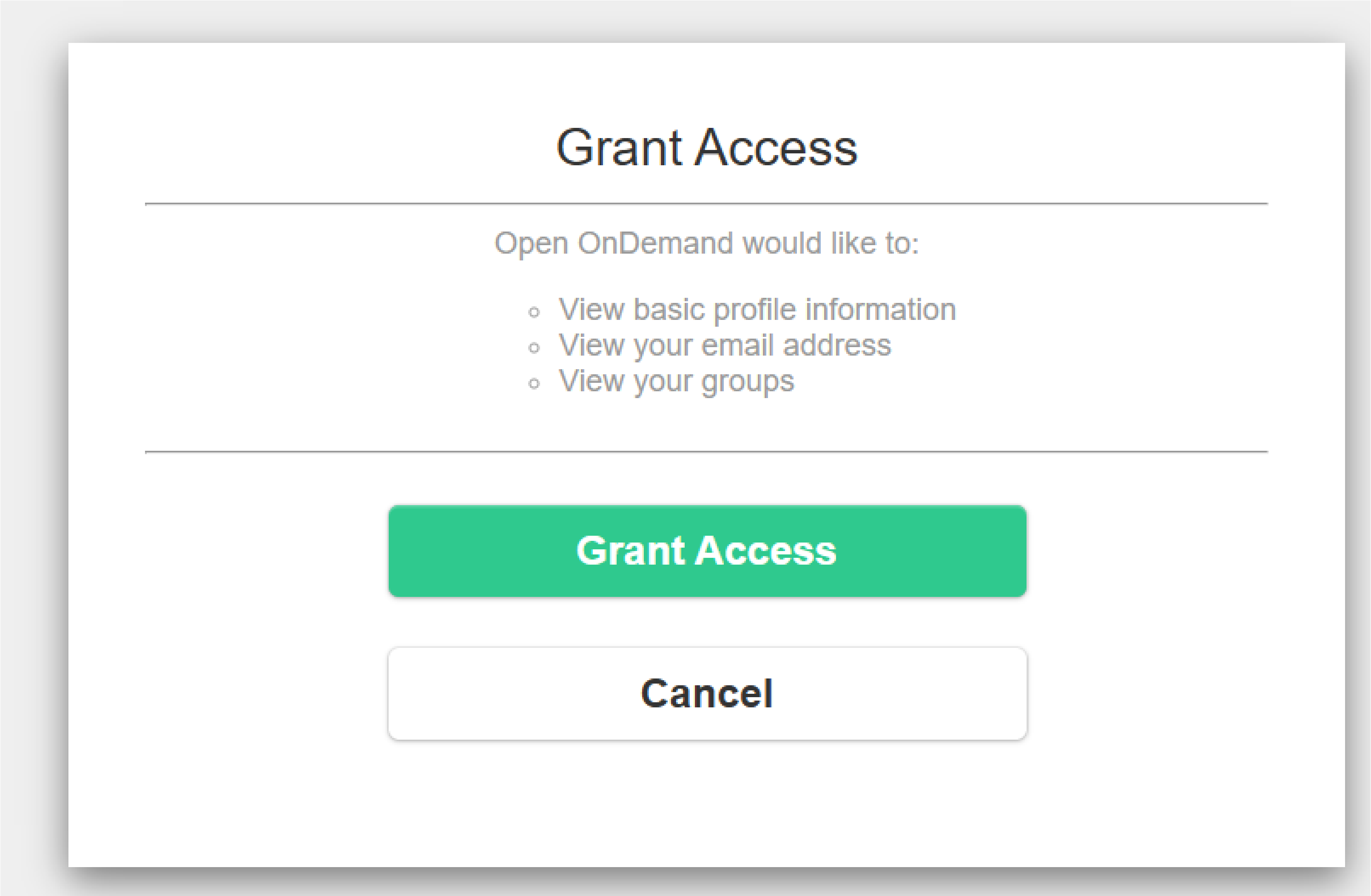
Sign in to access your account

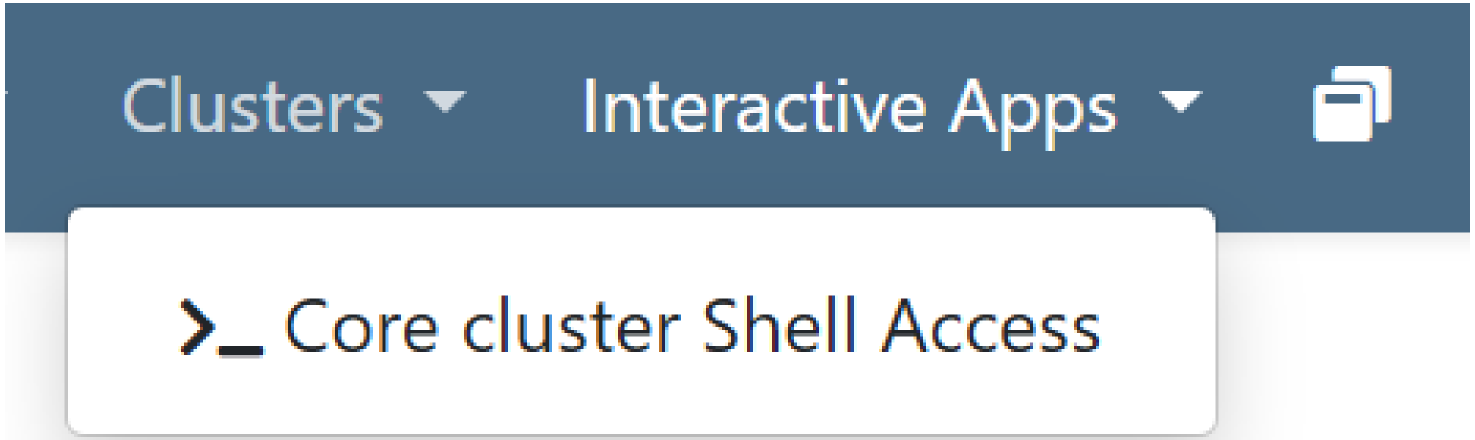
User id

Password

Sign in

Lost your password? RESET


Grant Access
Open OnDemand would like to:
View basic profile information
View your email address
View your groups
Grant Access
Cancel


Clusters
Interactive Apps
Core cluster Shell Access

```
Warning: Permanently added 'core-login1.cluster.france-bioinformatique.fr,192.168.16.205' (ECDSA) to the list of known hosts.
tp182674@core-login1.cluster.france-bioinformatique.fr's password:

  Welcome to the

  📗 Documentation: https://doc.cluster.france-bioinformatique.fr
  🛟 Cluster Support: https://support.cluster.france-bioinformatique.fr
  🧪 Community Forum: https://community.france-bioinformatique.fr

   ⚠️ ATTENTION MAINTENANCE 6-10 Octobre 2025 🚧
   Arrêt du Cluster le Lundi 6 octobre à 14h
   Reprise du service le Vendredi 10 Octobre à 18h

Last login: Sat Sep 27 14:39:52 2025 from 192.168.16.235

                         HOME [#-------------------]       7 /     100 GB
Update: 2025-09-29 17:00 - Your current default account is tp_2534_ai_microbiomes_181502 - More info: status_bars --help
tp182674@clust-slurm-client:~$
```

```
tp182674@clust-slurm-client:~$ git clone https://github.com/danielriosgarza/AiSchool.git
```

git clone https://github.com/danielriosgarza/AiSchool.git

```
tp182674@clust-slurm-client:~$ git clone https://github.com/danielriosgarza/AiSchool.git
Cloning into 'AiSchool'...
remote: Enumerating objects: 506, done.
remote: Counting objects: 100% (98/98), done.
remote: Compressing objects: 100% (69/69), done.
remote: Total 506 (delta 61), reused 57 (delta 27), pack-reused 408 (from 1)
Receiving objects: 100% (506/506), 54.14 MiB | 39.26 MiB/s, done.
```

OPEN OnDemand

OnDemand provides an integrated, single access point for all of your HPC resources.

Pinned Apps A featured subset of all available apps

JupyterLab: Core
System Installed App

RStudio Server: Core
System Installed App

RTrainer: Core
System Installed App

Desktop: Core
System Installed App

Reservation

2534_AI_microbiomes

Account

tp_2534_ai_microbiomes_181502

Partition

fast

Number of CPUs

3

A least one CPU is required for the JupyterLab webserver

Amount of memory

10G

Unit can be specified using the suffix M, G or T (default is megabytes).

GPUs

No GPU

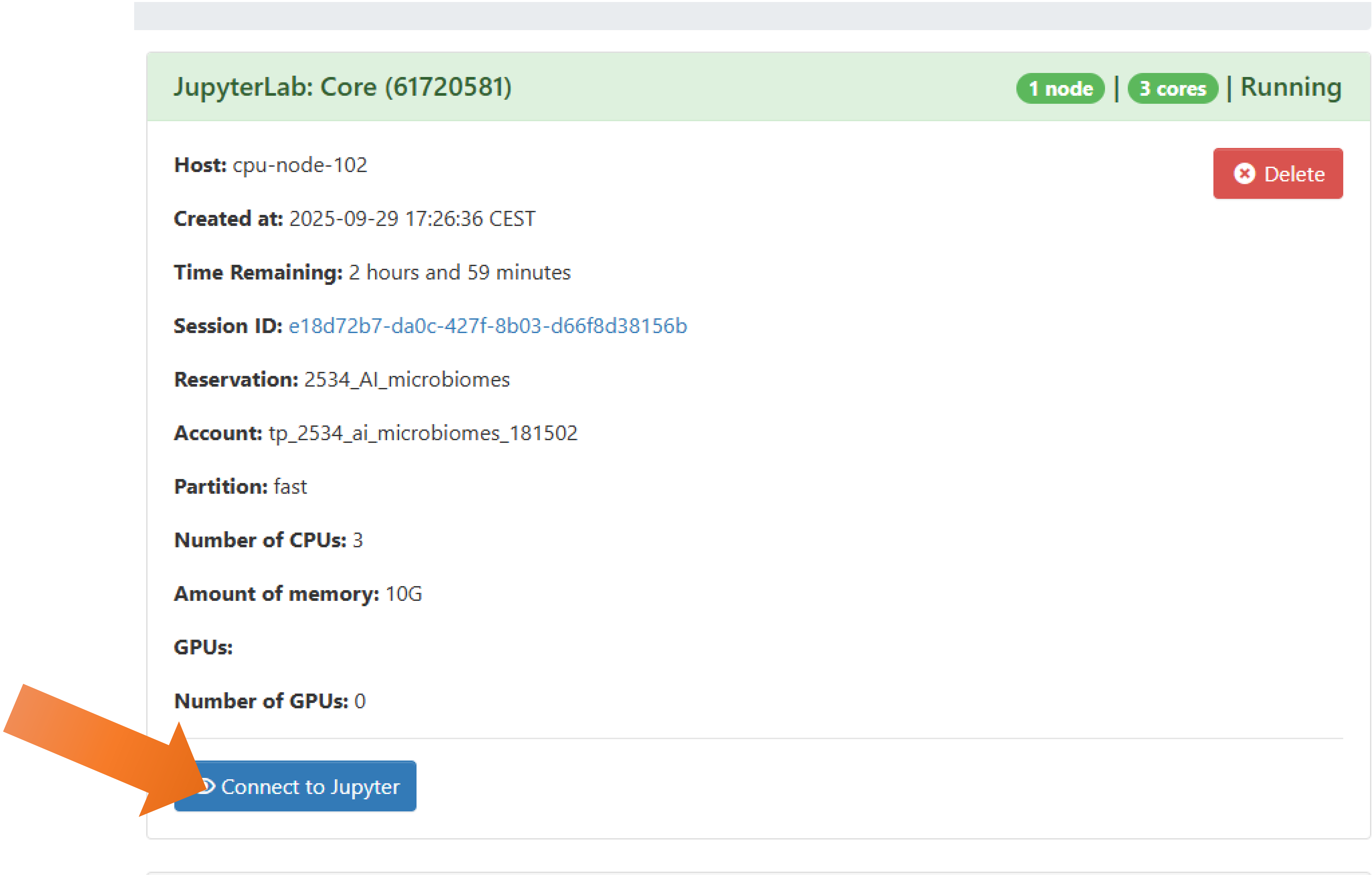
Number of GPUs

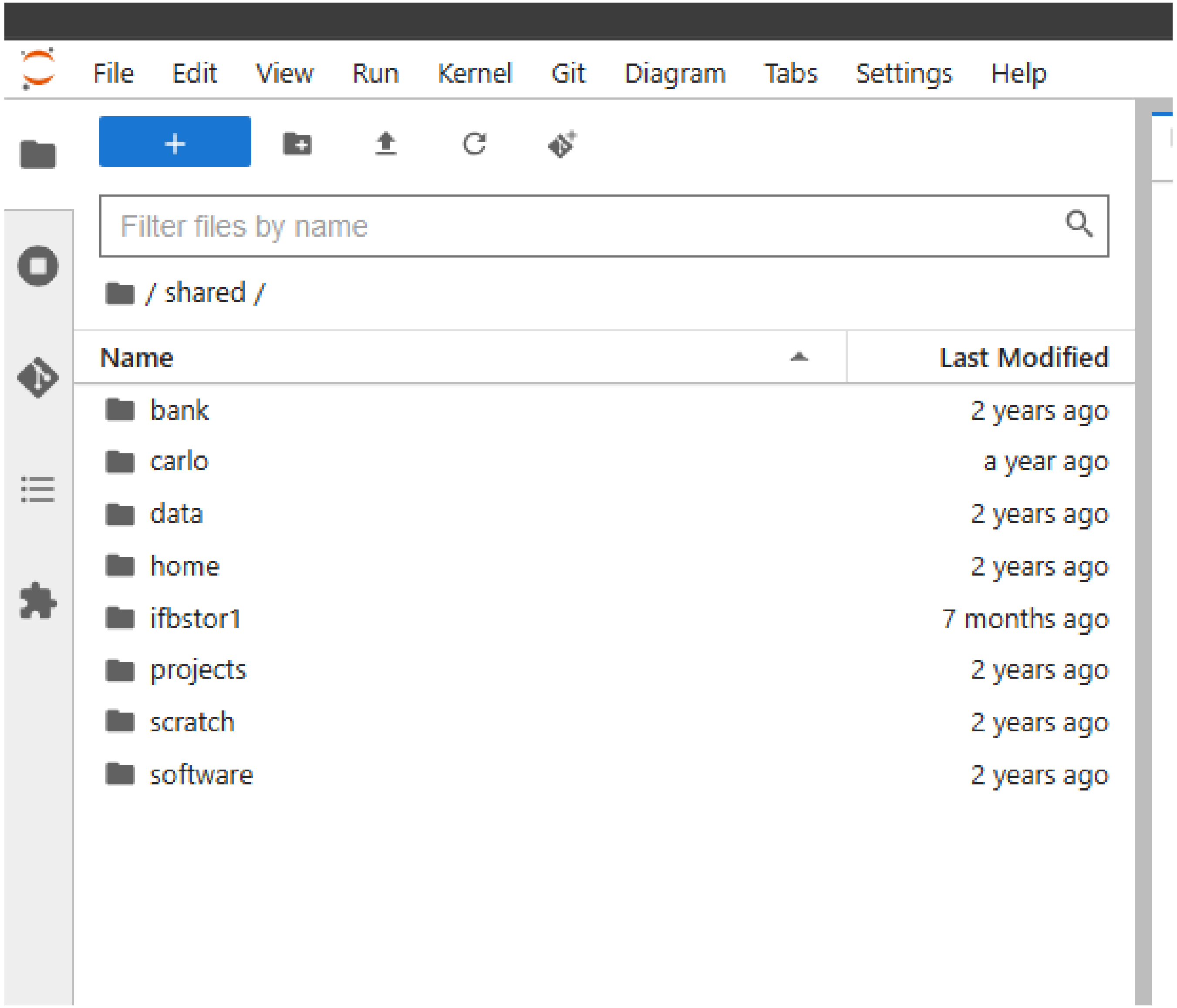
0

Number of hours

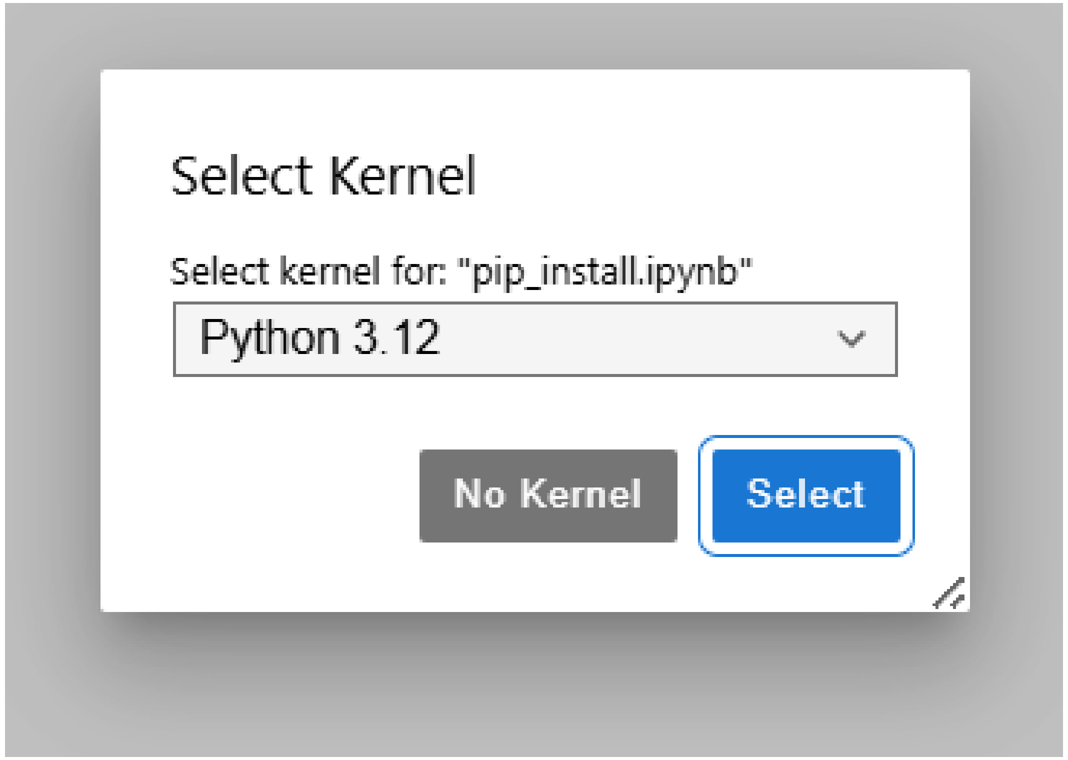
3

Launch

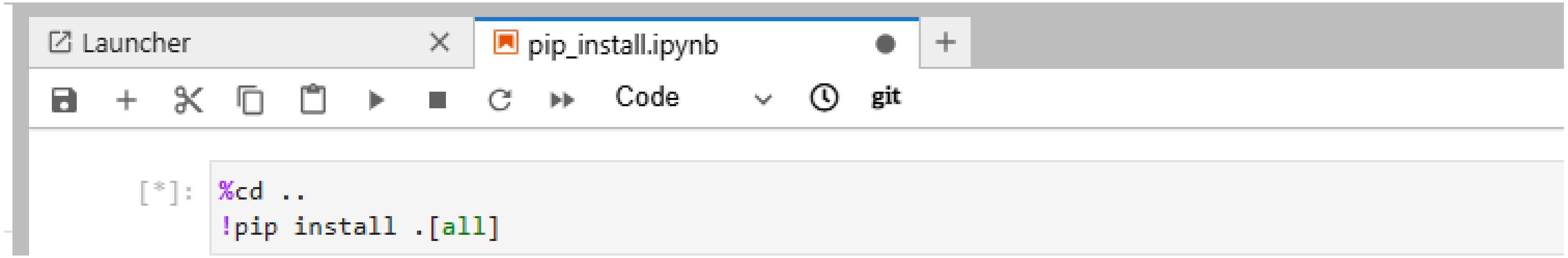

JupyterLab: Core (61720581)
1 node | 3 cores | Running
Delete
Host: cpu-node-102
Created at: 2025-09-29 17:26:36 CEST
Time Remaining: 2 hours and 59 minutes
Session ID: e18d72b7-da0c-427f-8b03-d66f8d38156b
Reservation: 2534_AI_microbiomes
Account: tp_2534_ai_microbiomes_181502
Partition: fast
Number of CPUs: 3
Amount of memory: 10G
GPUs:
Number of GPUs: 0
Connect to Jupyter

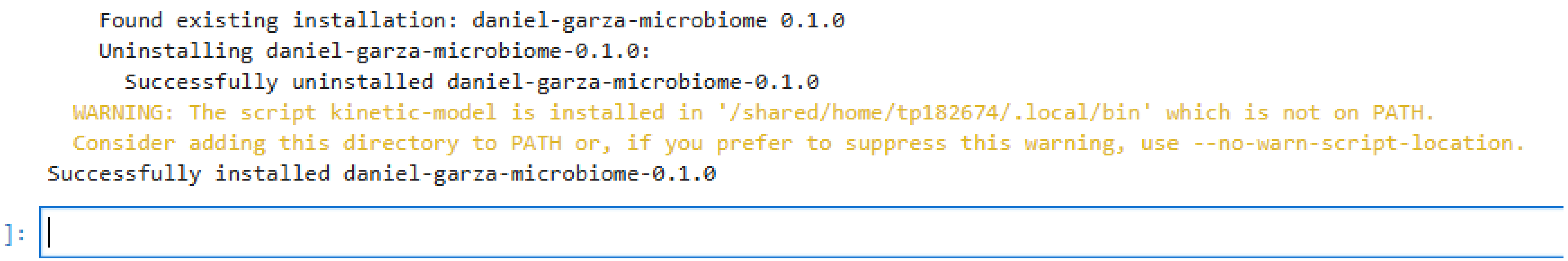


Go to: shared/home/<tp user name>/
AiSchool/content/DanielGarza/notebooks/pip_install.ipynb


Select Kernel
Select kernel for: "pip_install.ipynb"
Python 3.12
No Kernel
Select

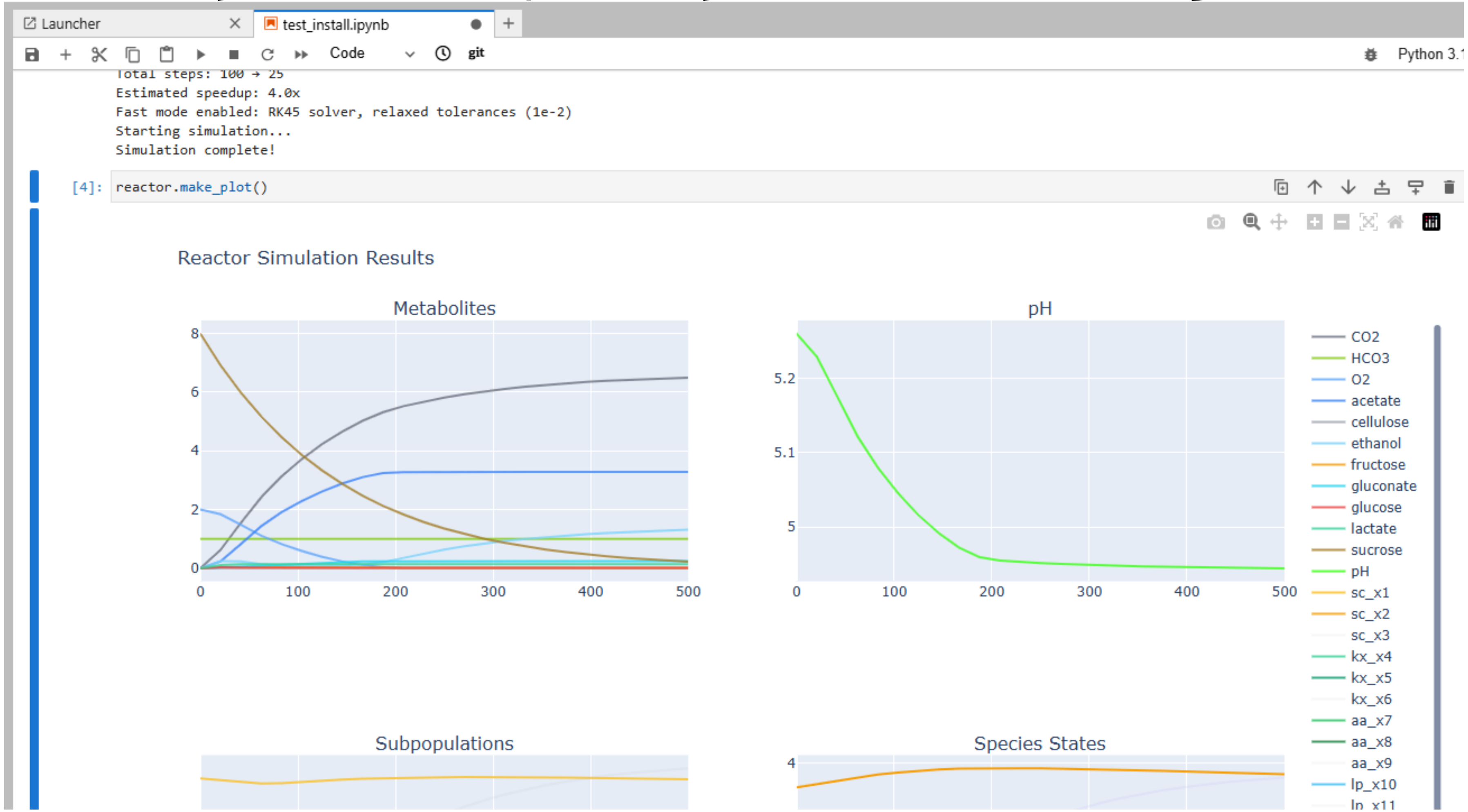
Run “play button” or “shift + enter”





Open and run the notebook “test_install.ipynb

Wait a min… if you see the plots, you are all set to go.



Controlling complex microbiomes with computational intelligence: physical and virtual prototypes

Daniel Garza

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PRocédés biOtechnologiques au Service de l'Environnement

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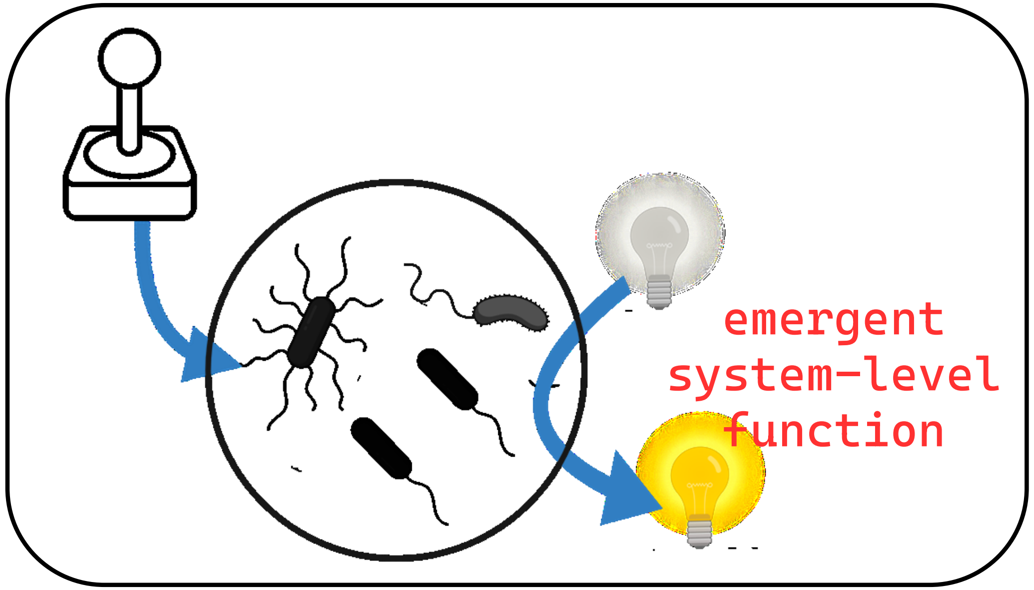
SCHOOL OF ARTIFICIAL INTELLIGENCE APPLIED TO MICROBIOMES

Microbiome engineering is the rational control of microbial ecosystems to make a desired collective function emerge and persist.

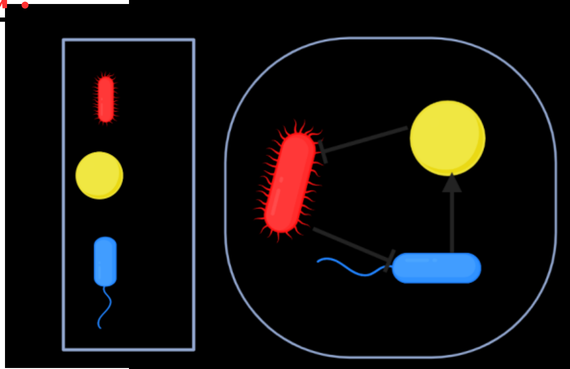


However, there are some important problems...

Problem #1: microbiomes are difficult to predict

One way uncover a system's dynamics is to model it. But classical modeling assumes that parameters are fixed and identifiable.

For example, the generalized Lotka–Volterra model, widely used in ecology, is built on the premise that growth rates and interaction strengths are fixed and can be uniquely identified.



1. Micro[redacted] space a[redacted]

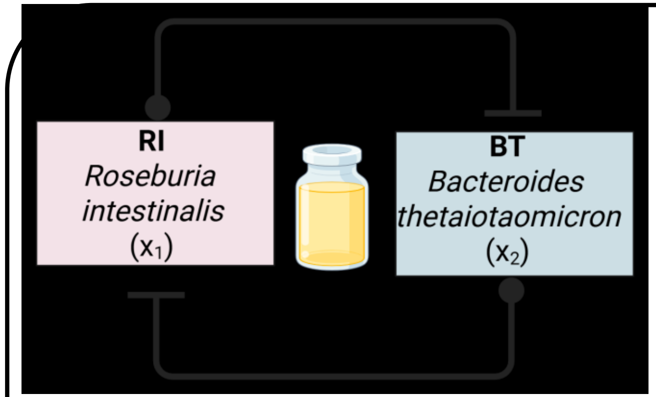
	A	B	C
A	-1.00	0.00	-0.05
B	-0.10	-1.00	0.00
C	0.00	0.20	-1.00

2. By identifying their interactions (and growth rates), we can derive an interactions matrix

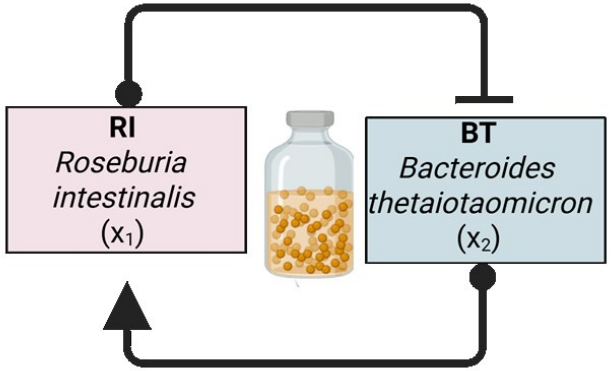
3. Allowing us to predict their temporal dynamics

[redacted]

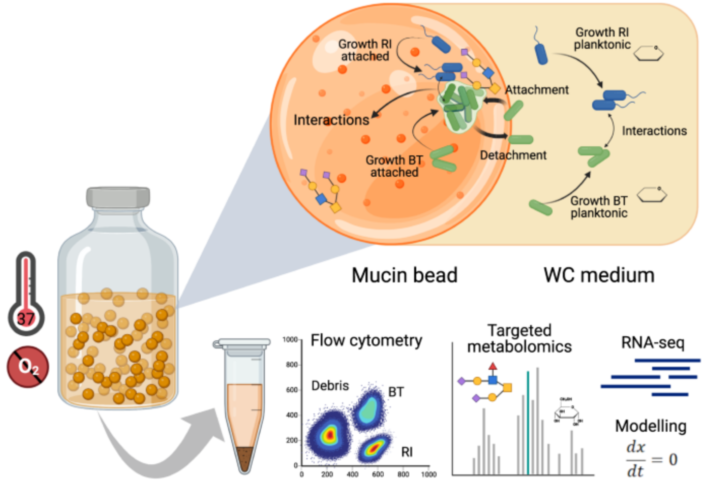
Interactions emerge from local, context-specific dynamics



Initially predicted to compete for pyruvate and glucose



Adding mucin beads is predicted to create positive interactions

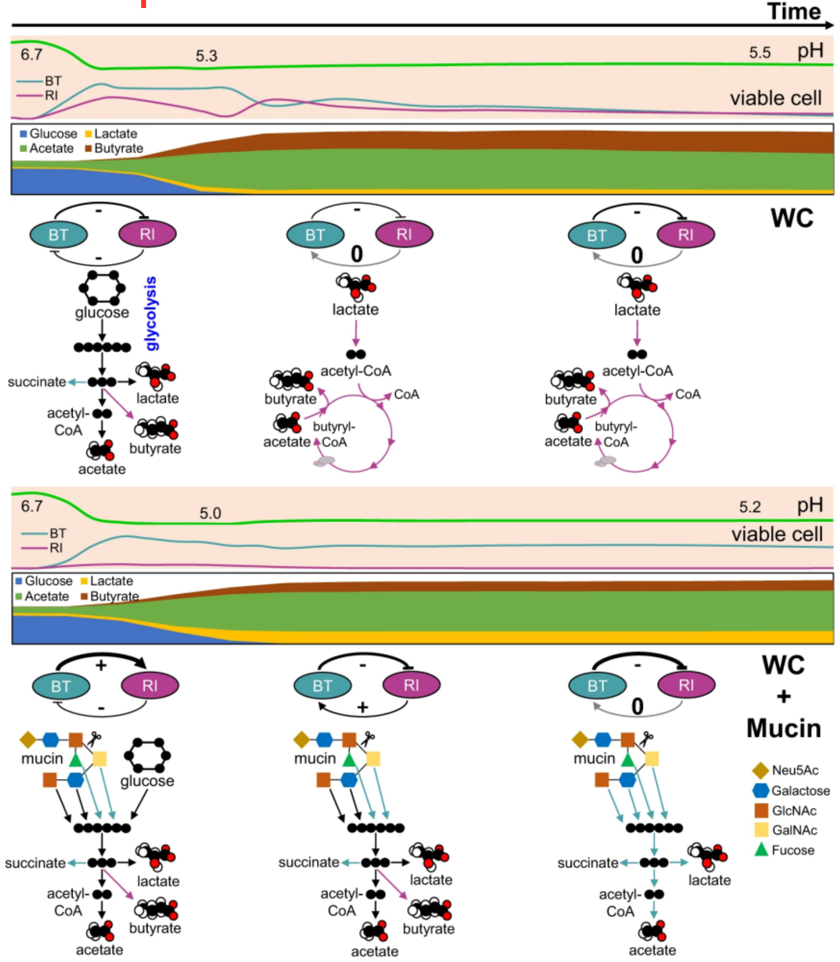


BT Degrades mucin

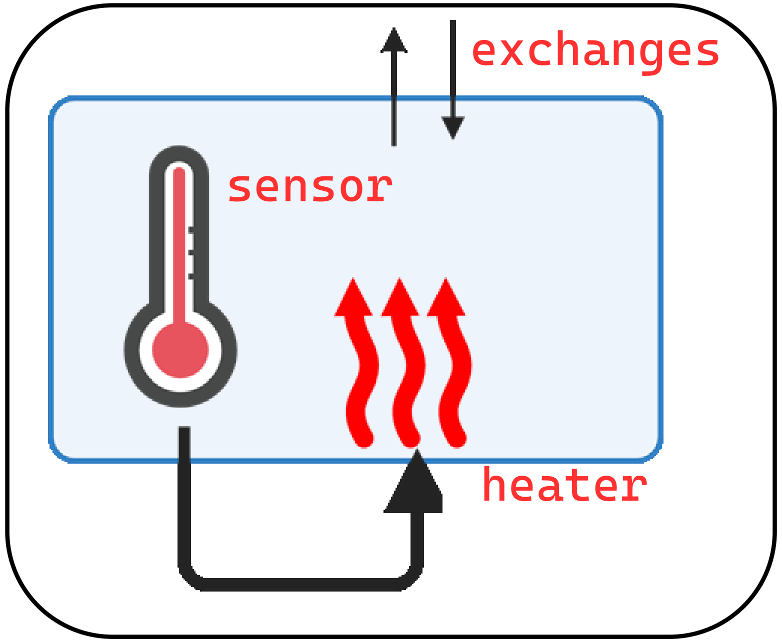
Both feed on mucin degradation products

ISME J. 2023

Environmental factors lead to multiple modes of interactions



Problem #2: Controlling complex systems requires different control principles

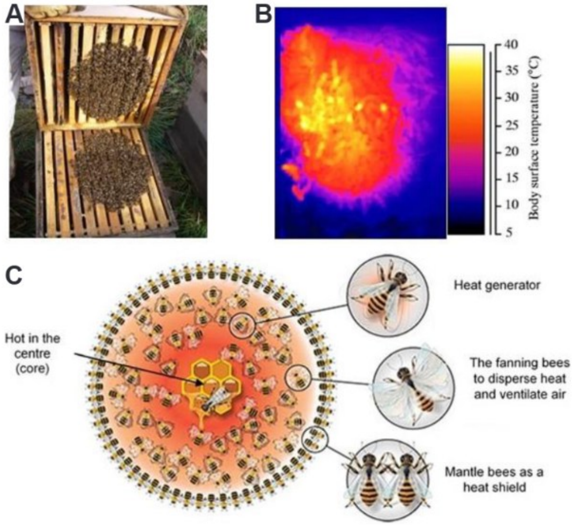


Simple thermostat (outside temperature assumed lower)

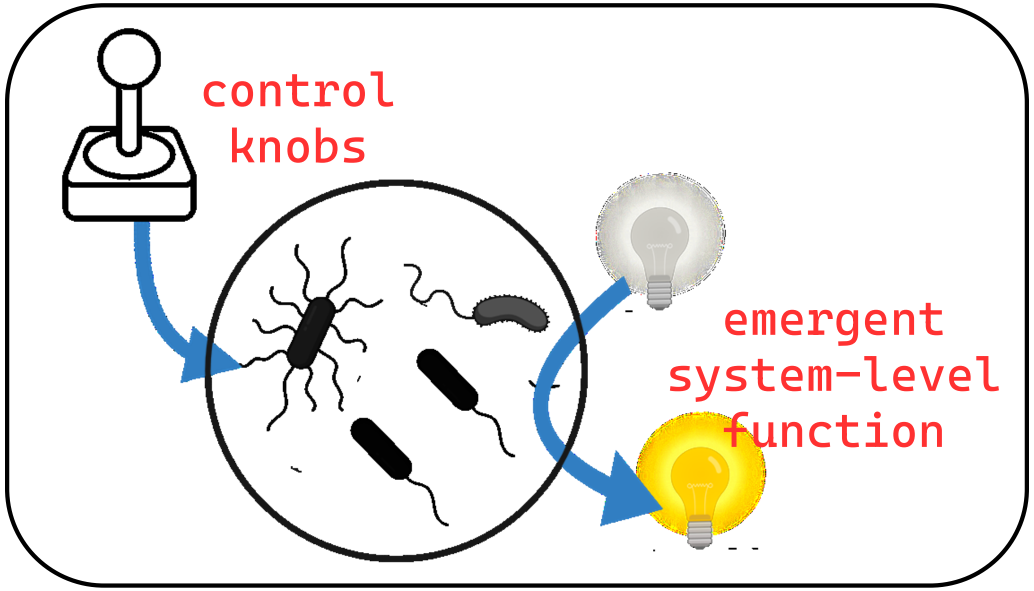
Collective fanning, clustering, and heat sharing maintain brood temperature

Broods need a temperature of 36⁰C to become healthy adults

Rodriguez-Vasquez et al. 2024



Microbiome engineering is the rational control of microbial ecosystems to make a desired collective function emerge and persist.



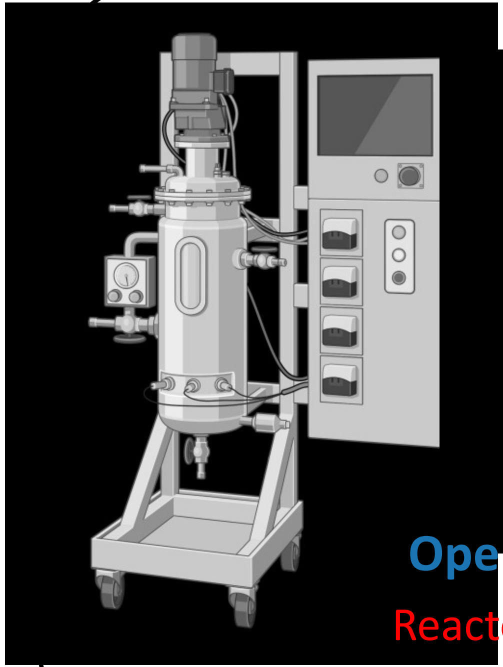
Engineering microbiomes means engineering a complex system.

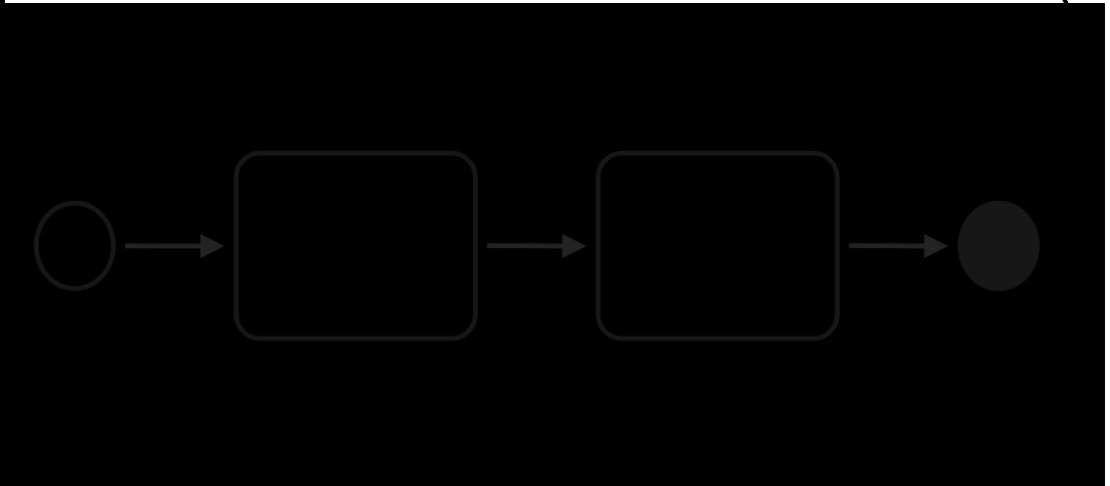
Complex systems are difficult to predict because their dynamics emerge from local, context-specific interactions.

They require fundamentally different control principles.

Most microbiome biotechnologies are insufficient to control complex systems – fundamental ingredients are missing

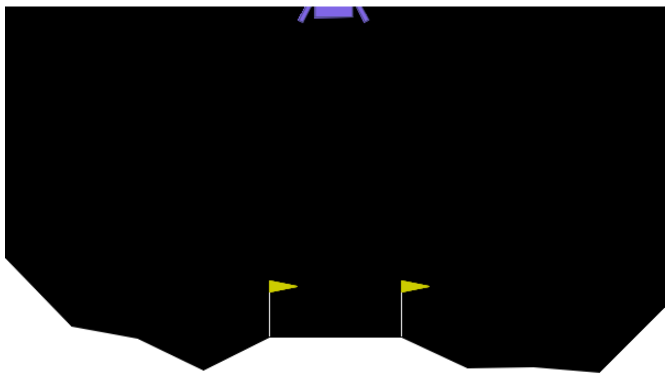
Missing ingredient #1: feedback control seen from the microbiome's perspective, not just the environment's.





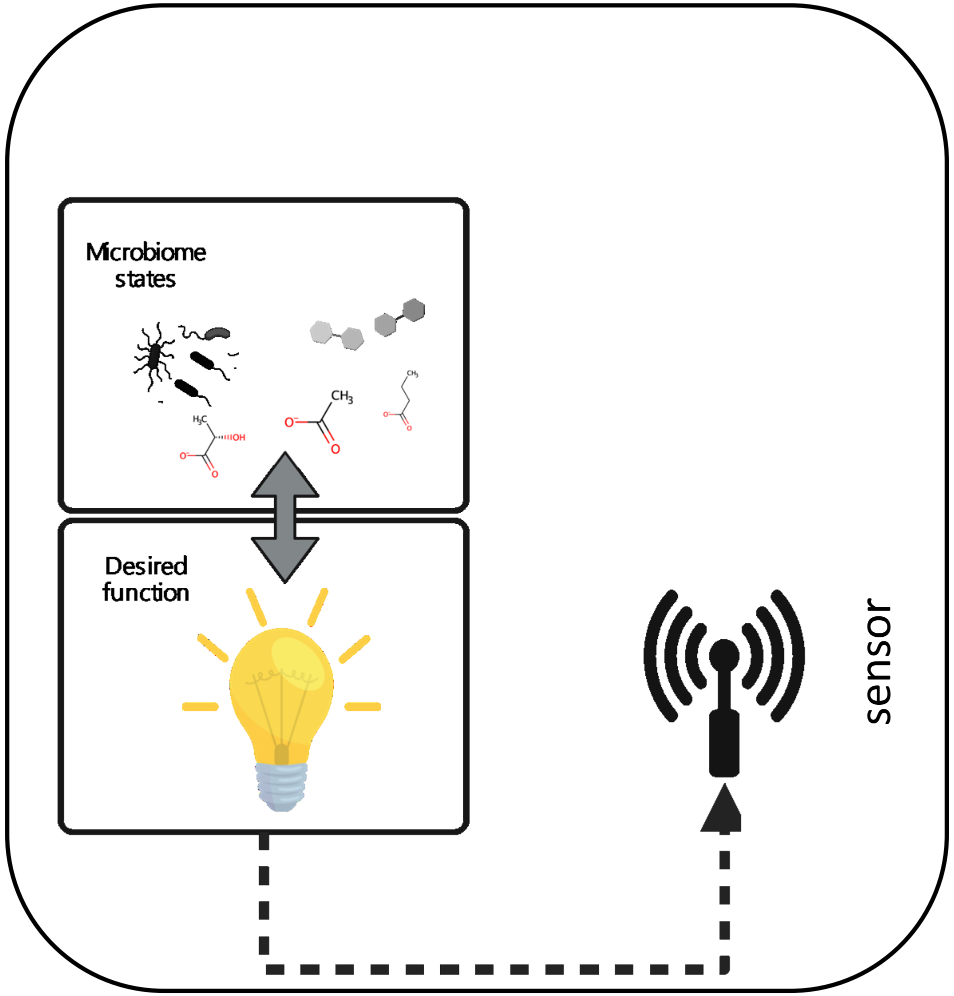
Open-loop control strategy

Reactor that is set to stably operate "optimal" conditions



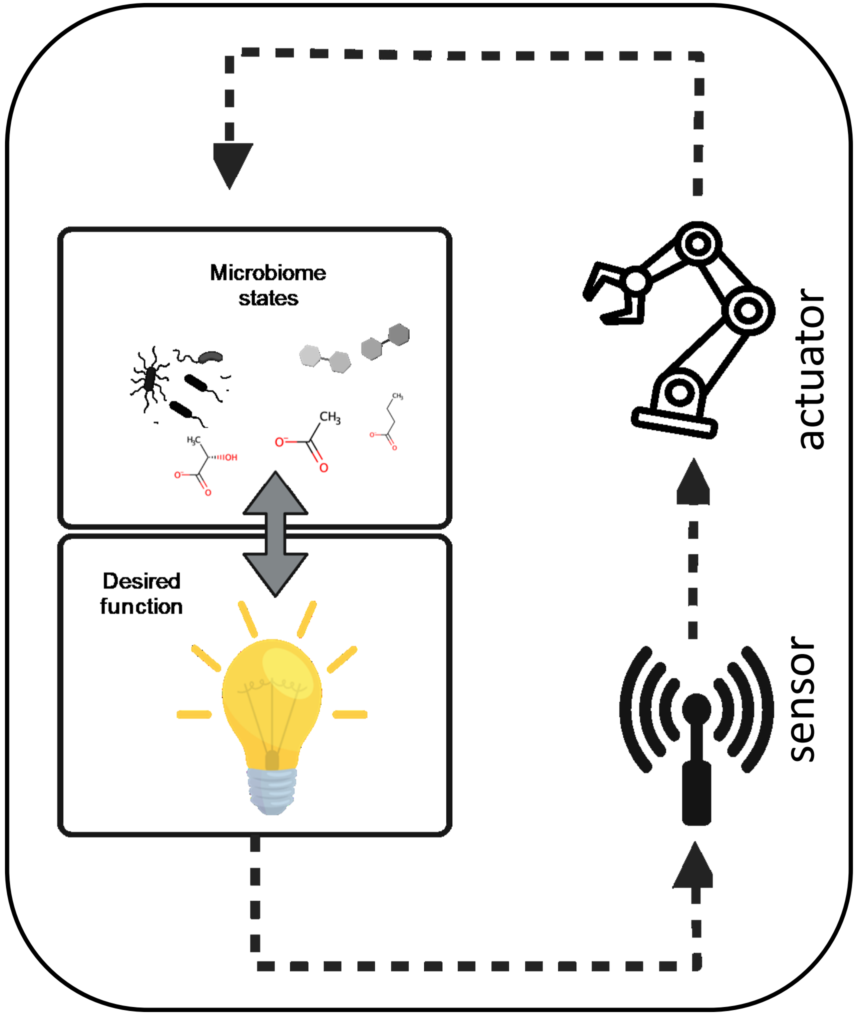
Local dynamics shift; the system drifts away despite a correct start

Feedback control means sensing the system and acting to keep it on course



$$X_o \Rightarrow (X_o - X_d)$$

Feedback control means sensing the system and acting to keep it on course



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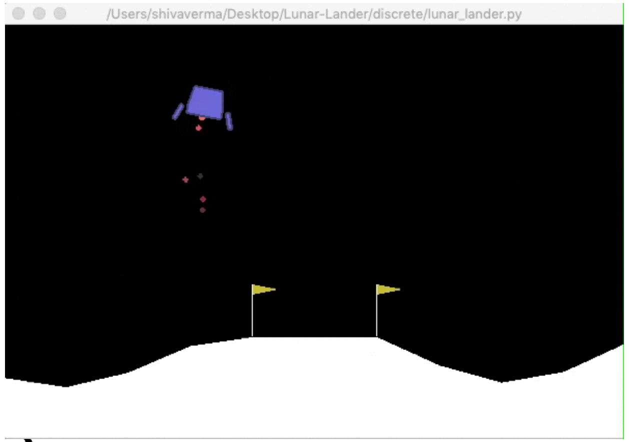
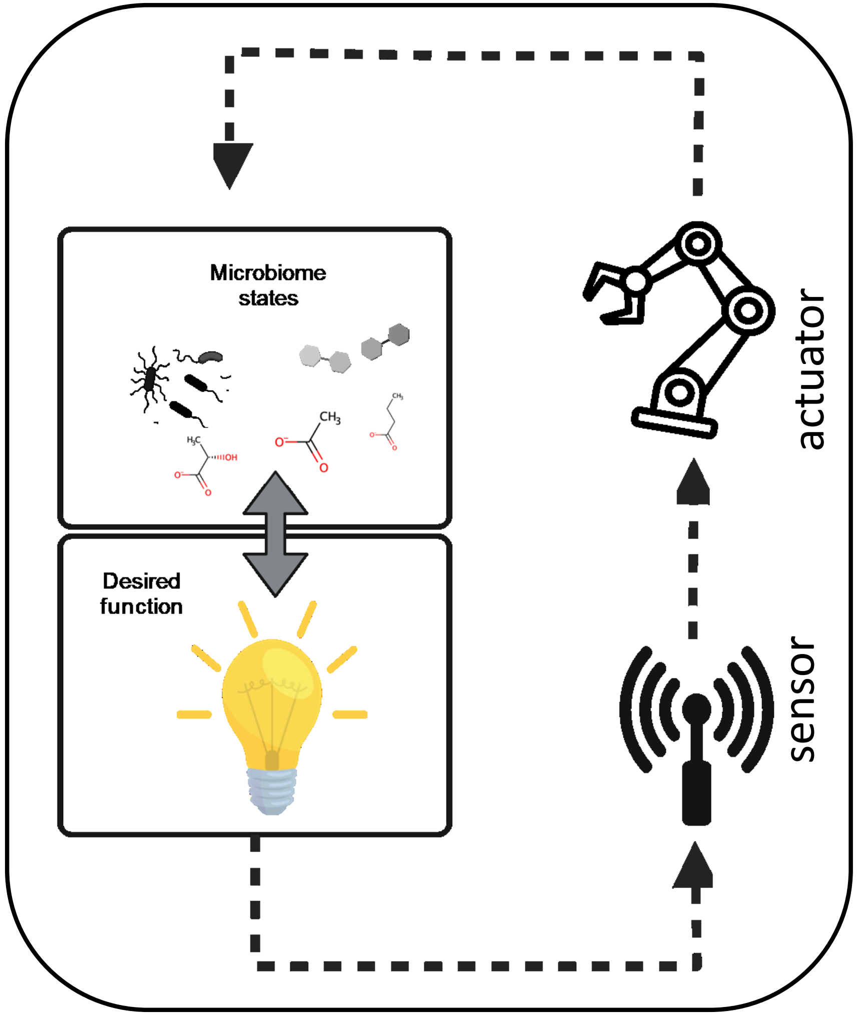
$$X_o \rightarrow (X_o - X_d)$$

Adapts to changes and reaches otherwise unreachable states



Missing ingredient #2: computational intelligence



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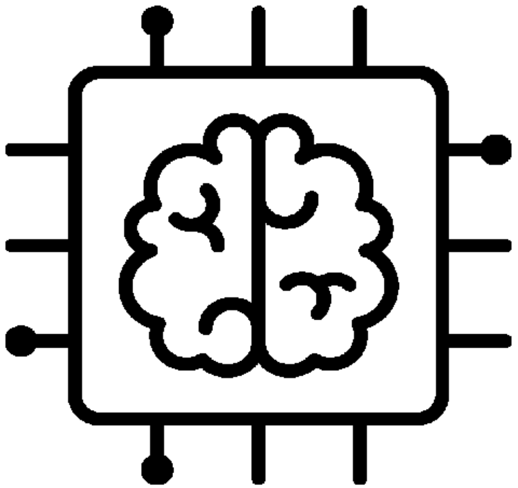
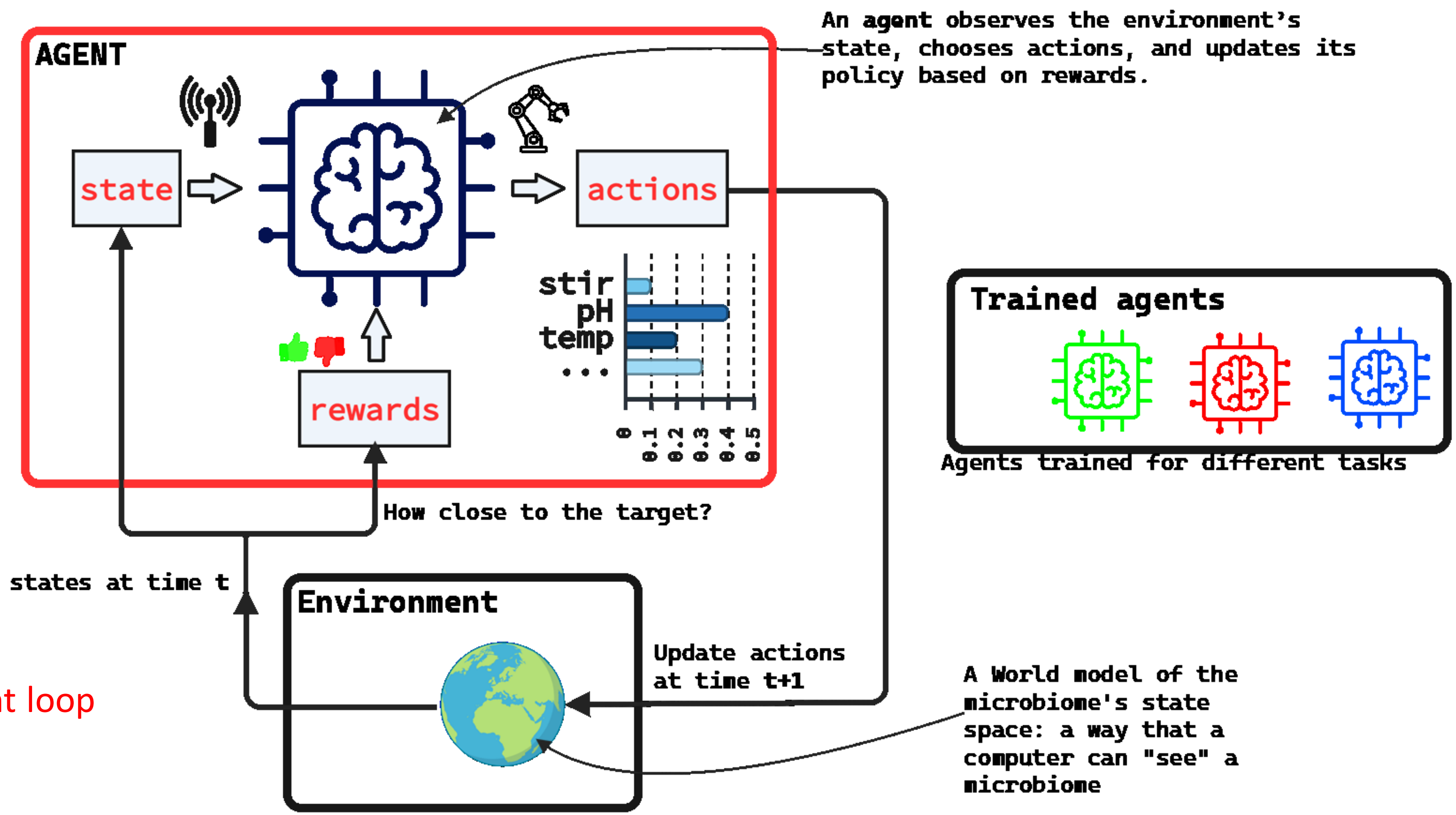


$$X_o \rightarrow (X_o - X_d)$$

"The global capacity to act purposefully, to think rationally, and to deal effectively with one's environment" – David Weschler

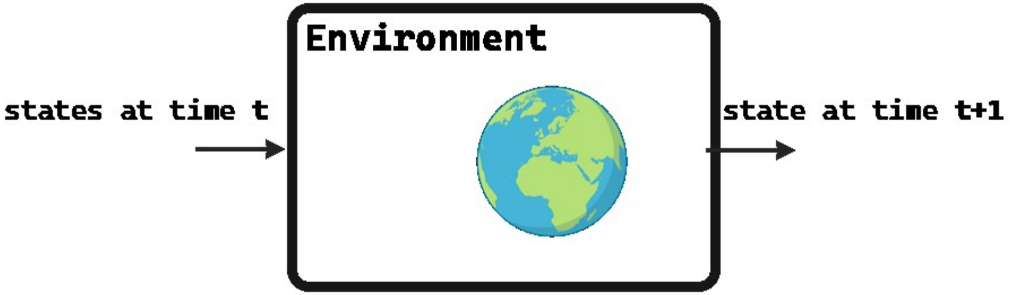
Controlling complex systems by synchronizing local interactions into the correct group-level behavior is a classical problem of intelligence

Computational intelligence is an agent's ability to achieve goals in many environments



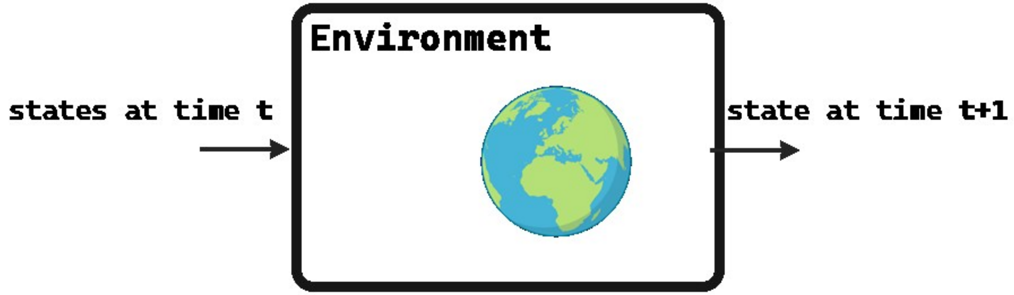
Agent-Environment loop

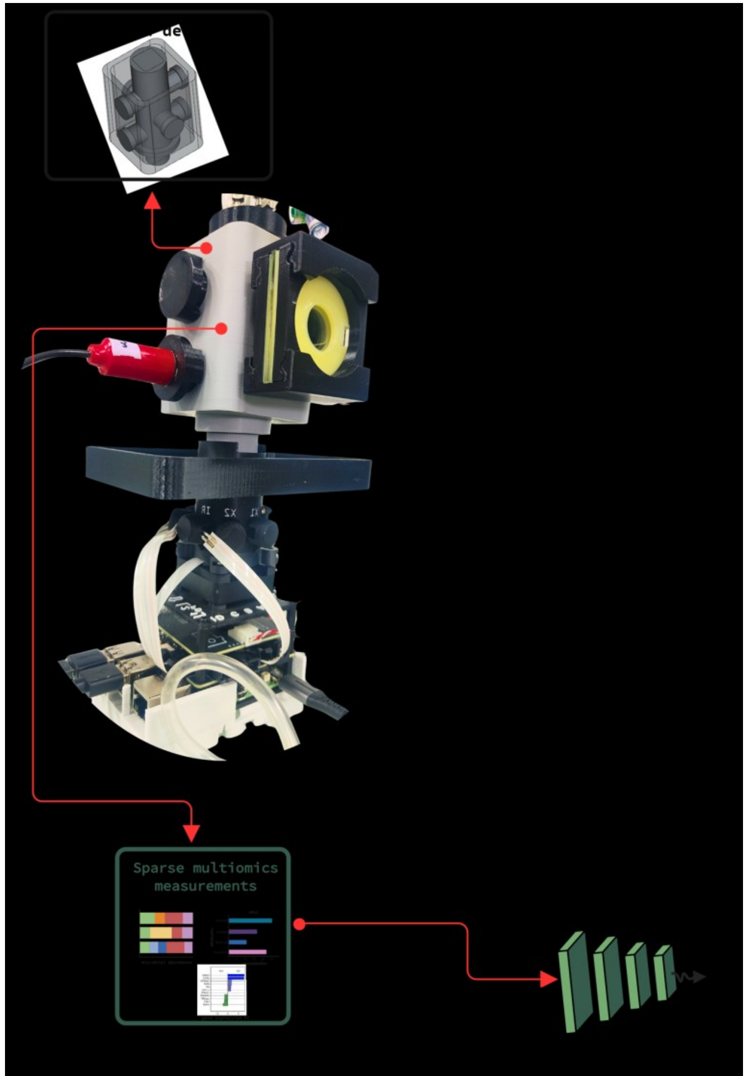
The environment: presentint the microbiome (physical entity) to the agent (digital entity)



Prototype that directly couples trained agents with living microbiomes to control them in real time.

The environment: presentint the microbiome (physical entity) to the agent (digital entity)





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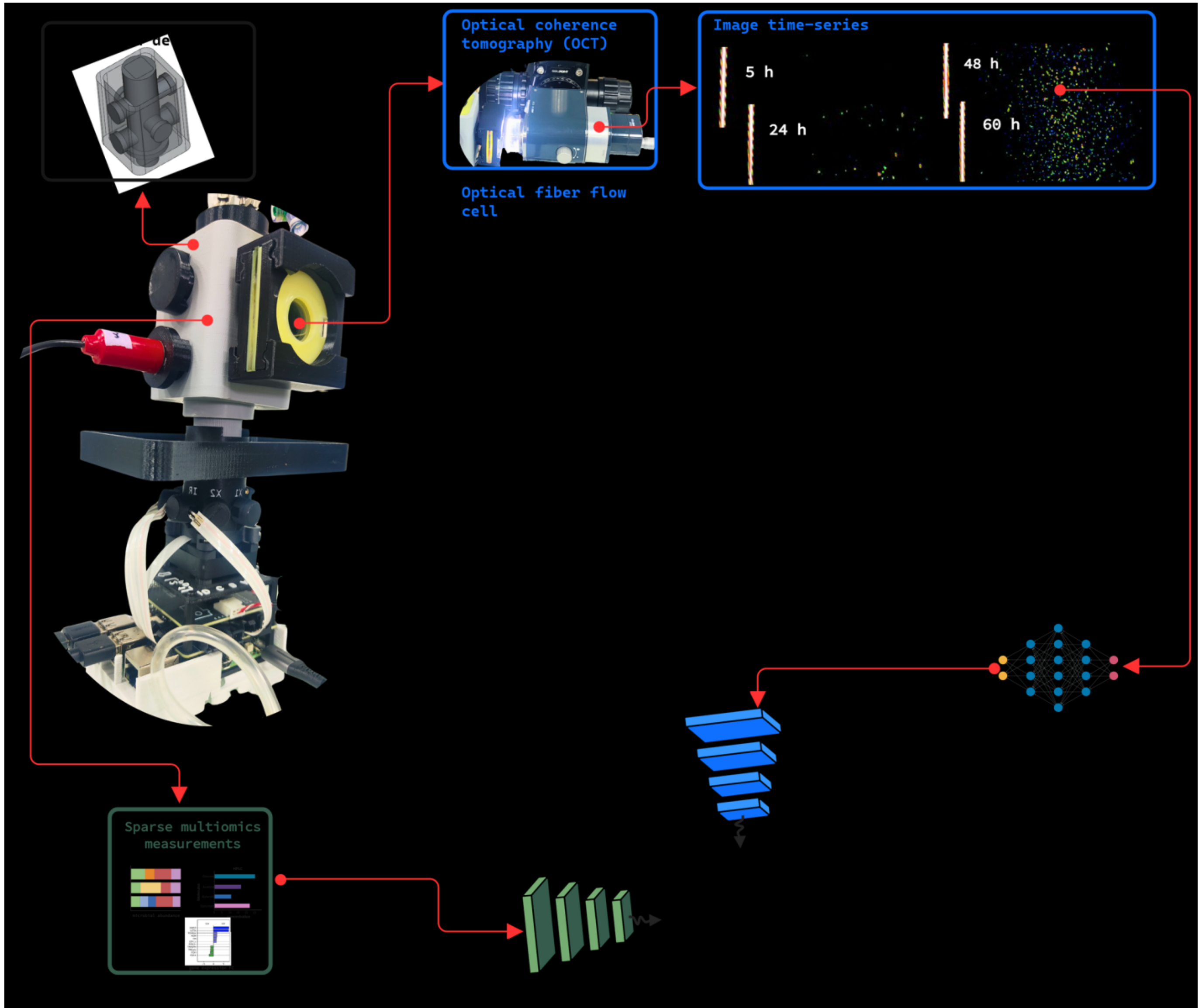

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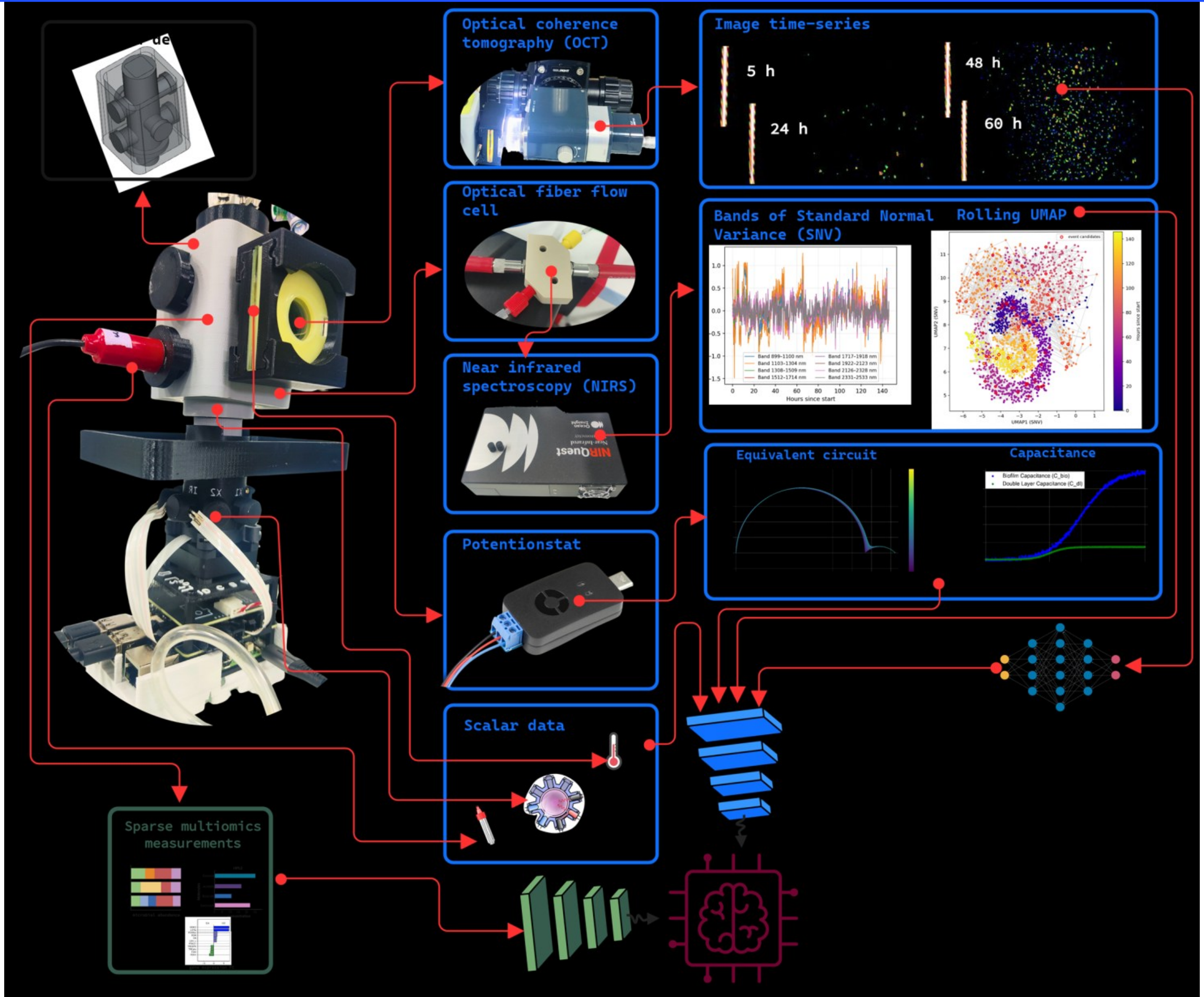

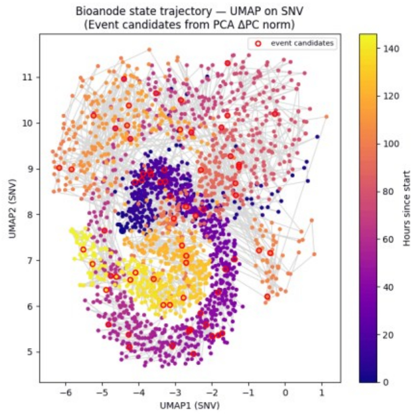

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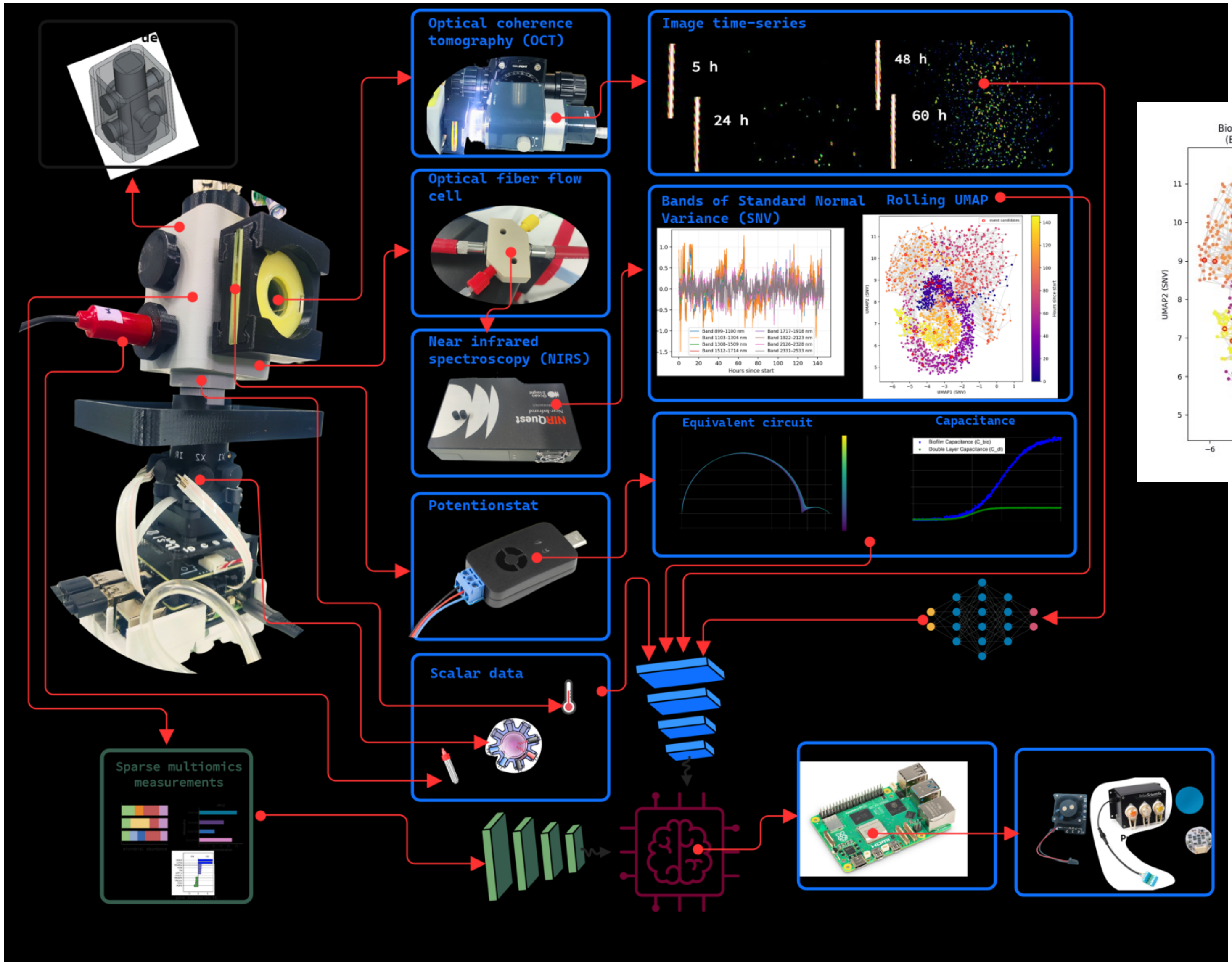
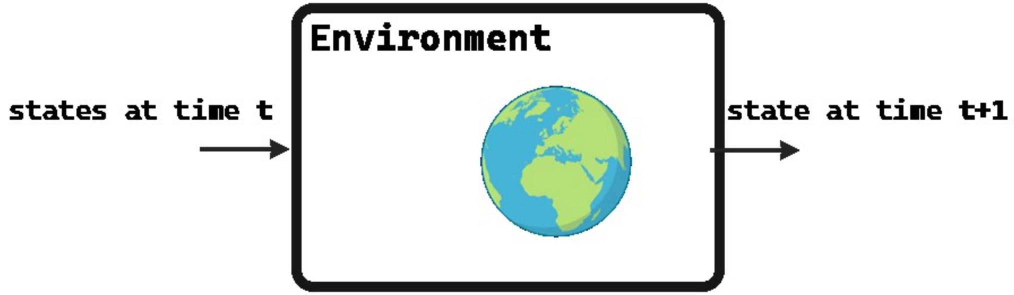
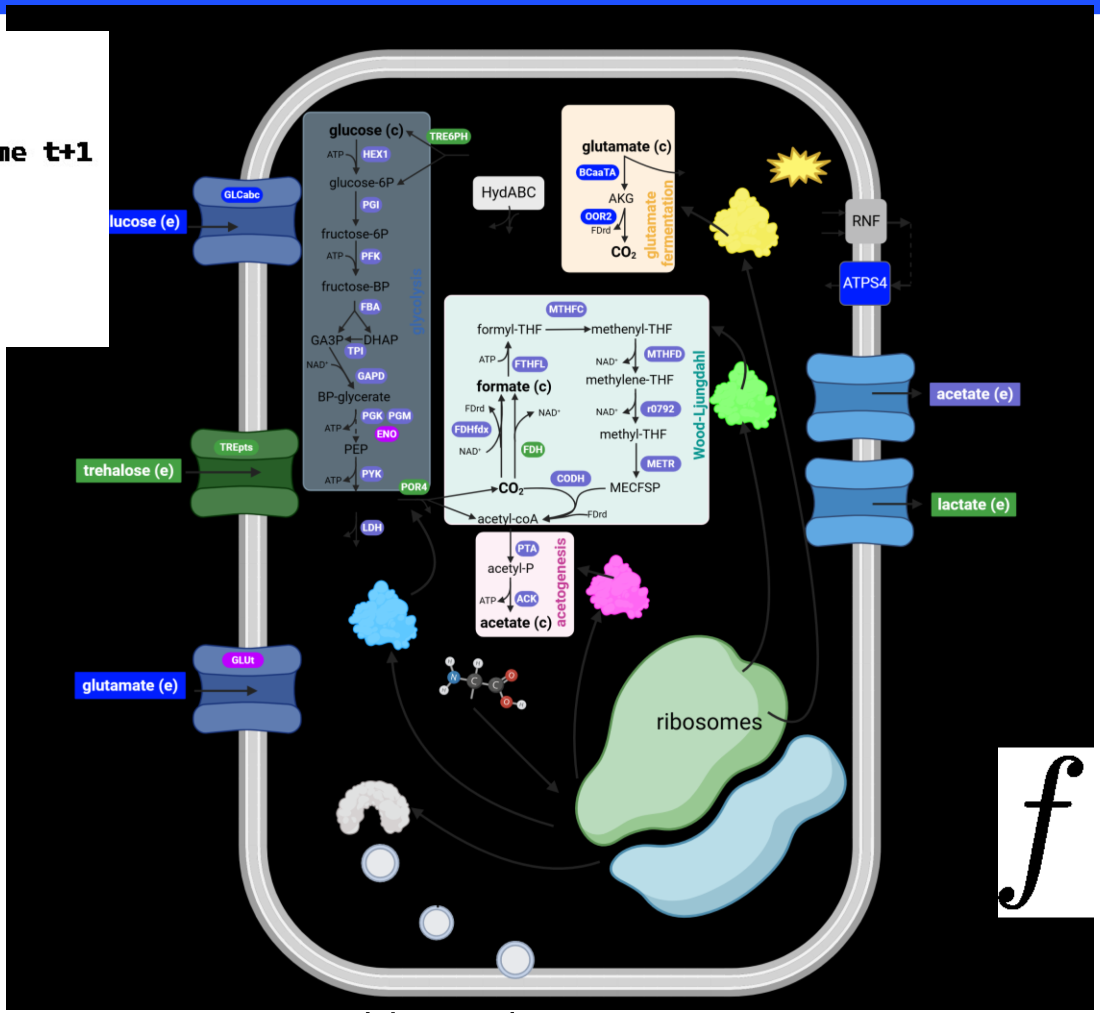
Prototype that directly couples trained agents with living microbiomes to control them in real time.



Making microbiomes computable and visible to the computer



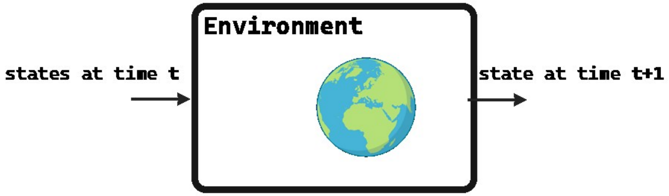


$$f(X, S)$$

1. Build a multi-omics map to reveal system structure

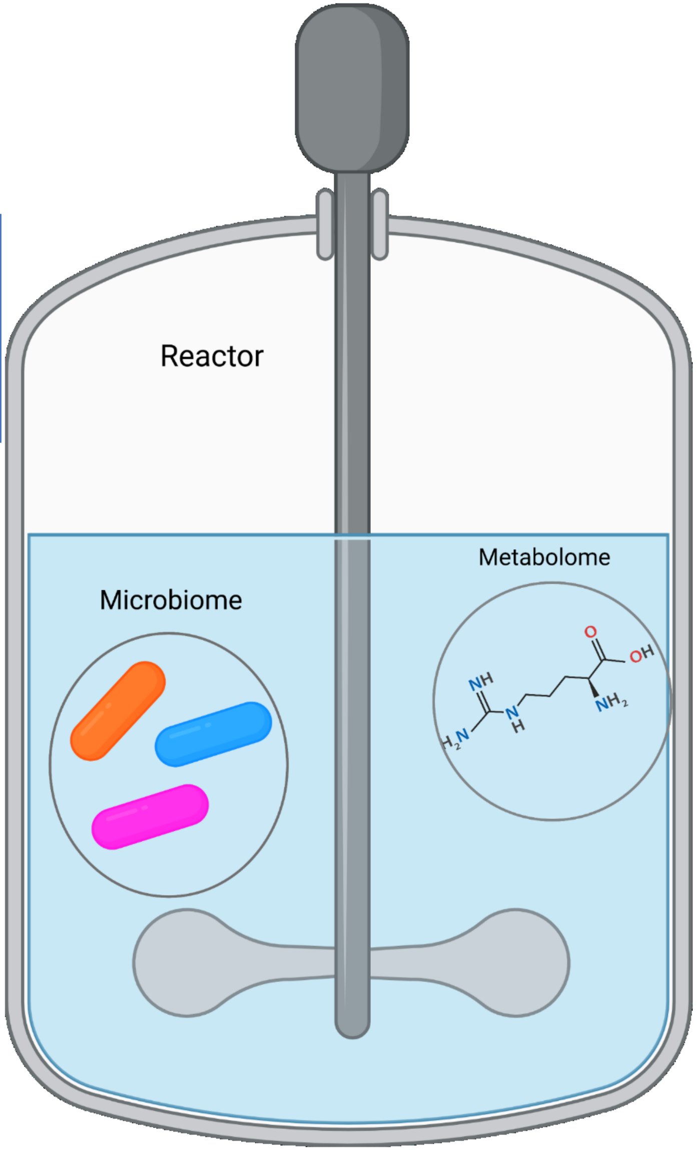
2. Formulate mathematical models that enable forward simulation

Another way to represent the environment is through a kinetic model



Reactor
- Volume
- control "pulses" (temperature, pH, stirring…)

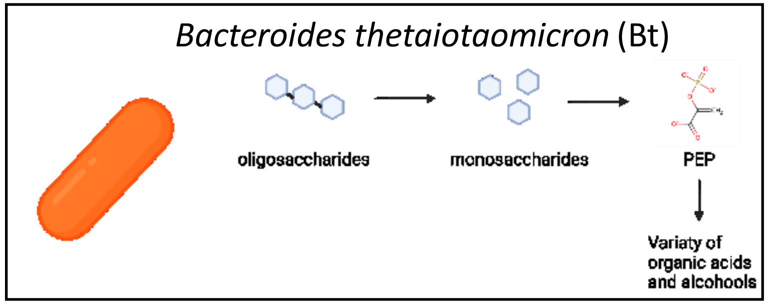
Microbiome
- Microbial subpopulations
- Growth functions



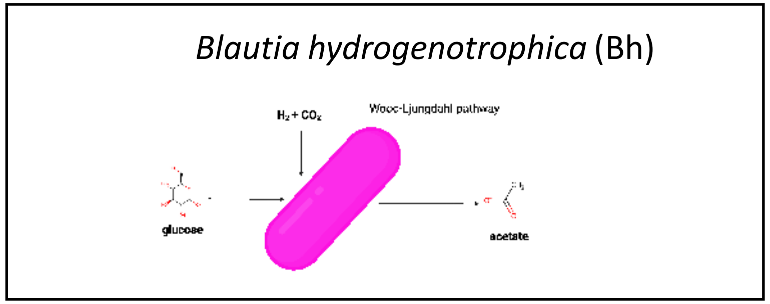
Metabolome
- Added in the media
- Consumed and produced by microbes

Nat. Comm. 2025
Accepted in Sep. 23/2025

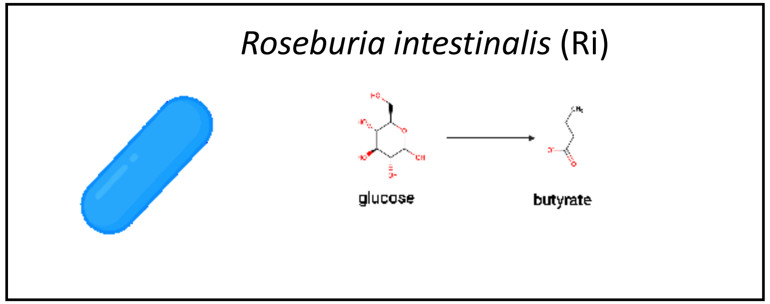
Example of a kinetic model applied to a consortium of three gut bacteria



Primary fermenter

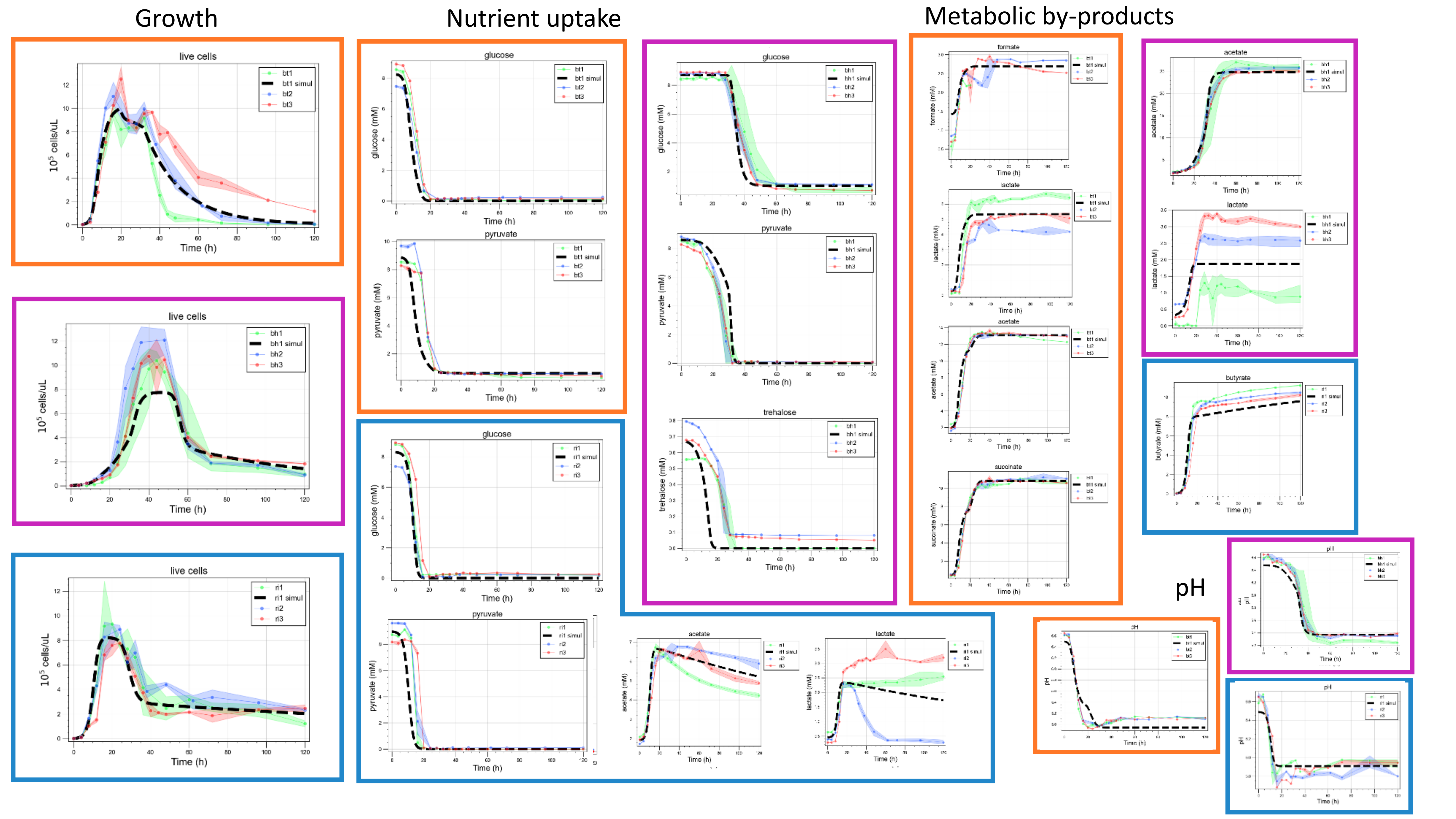


Acetogen

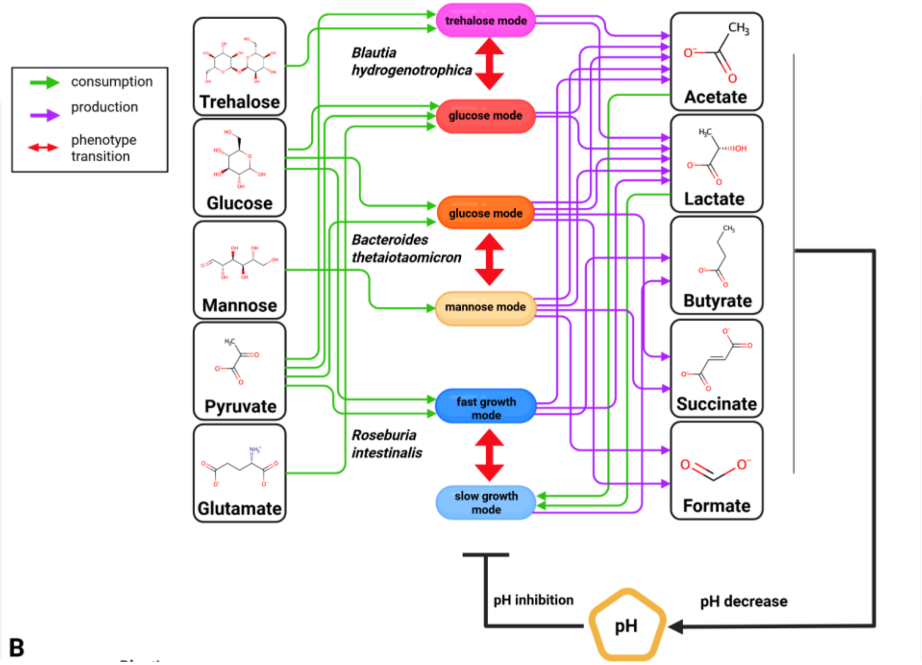


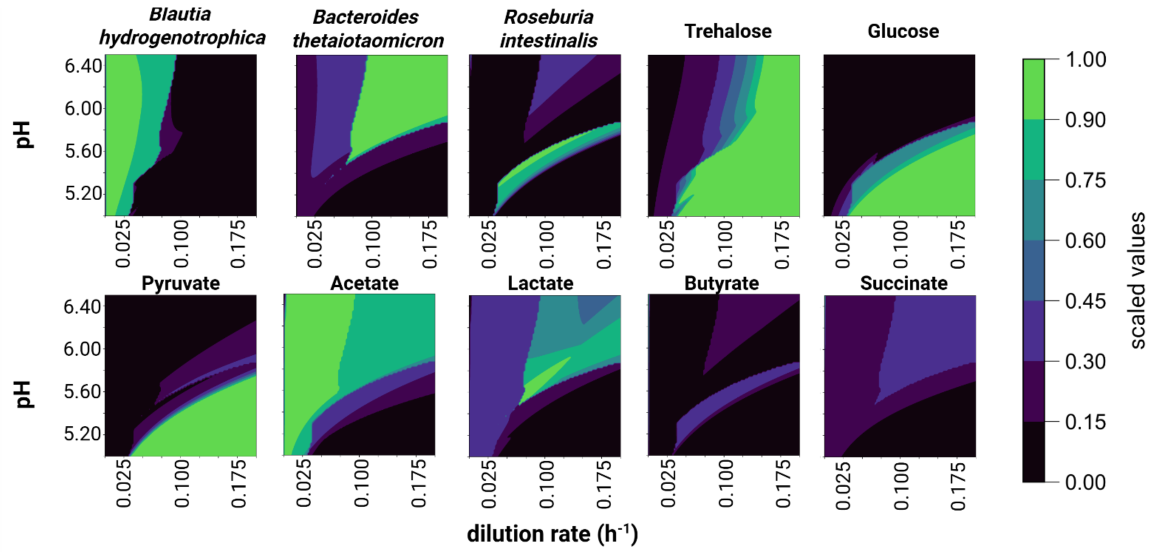
Butyrate producer

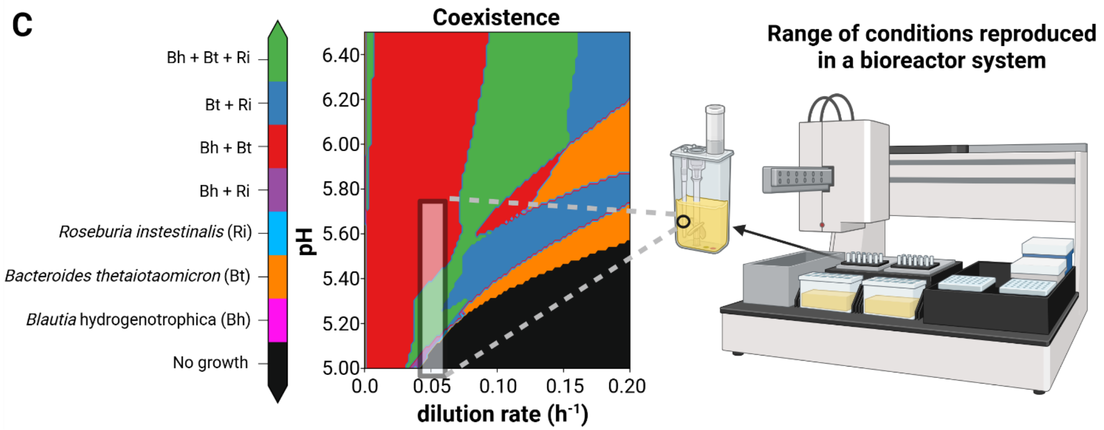
Nat. Comm. 2025
Accepted in Sep. 23/2025


Growth
Nutrient uptake
Metabolic by-products
pH
live cells
bt1
bt1 simul
bt2
bt3
10^5 cells/uL
Time (h)
live cells
bh1
bh1 simul
bh2
bh3
live cells
ri1
ri1 simul
ri2
ri3
glucose
pyruvate
trehalose
formate
lactate
acetate
succinate
butyrate
glucose (mM)
pyruvate (mM)
trehalose (mM)
acetate (mM)
lactate (mM)
butyrate (mM)
pH

Next we predict the model's phase plane—an open-loop controller



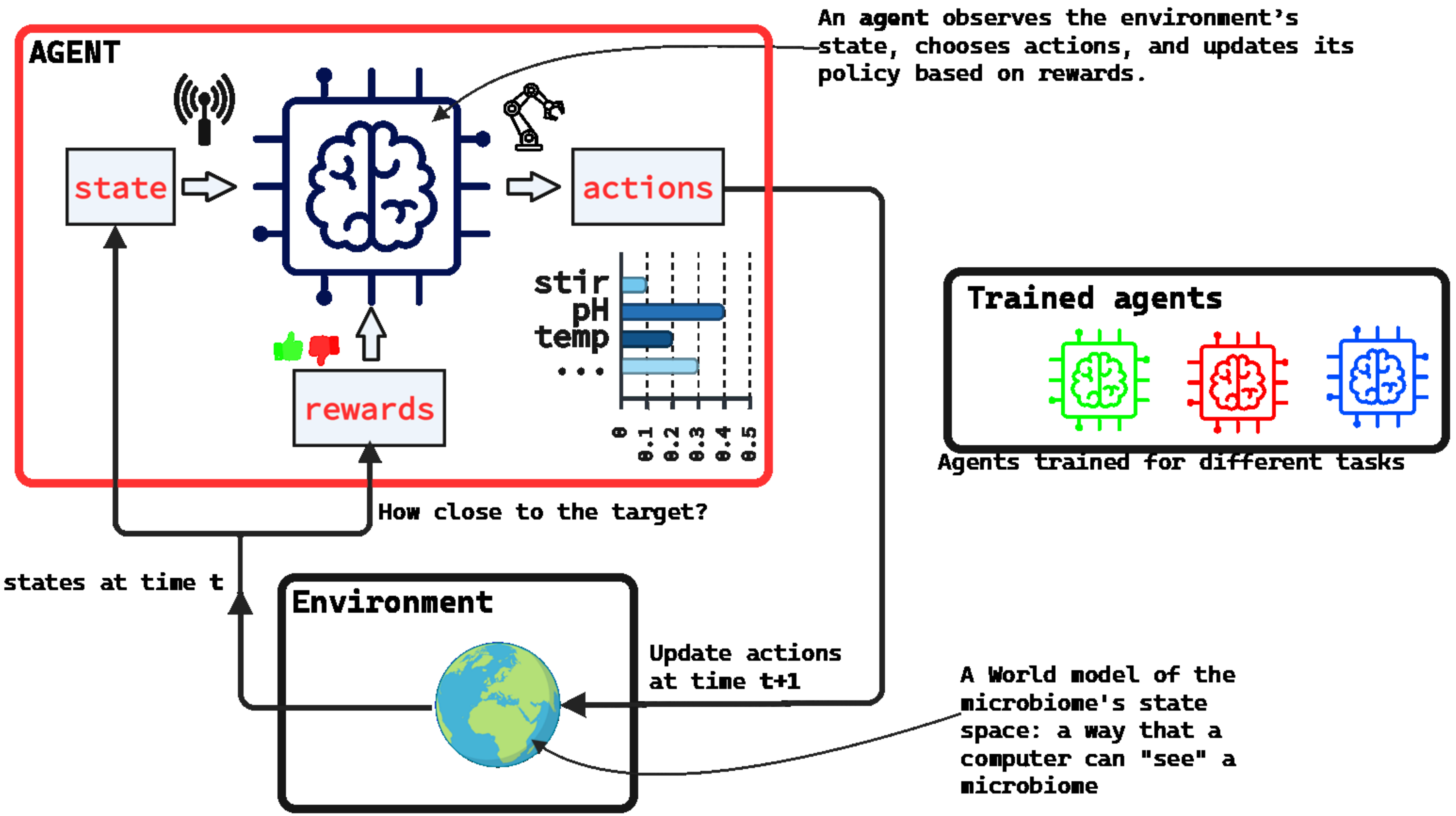




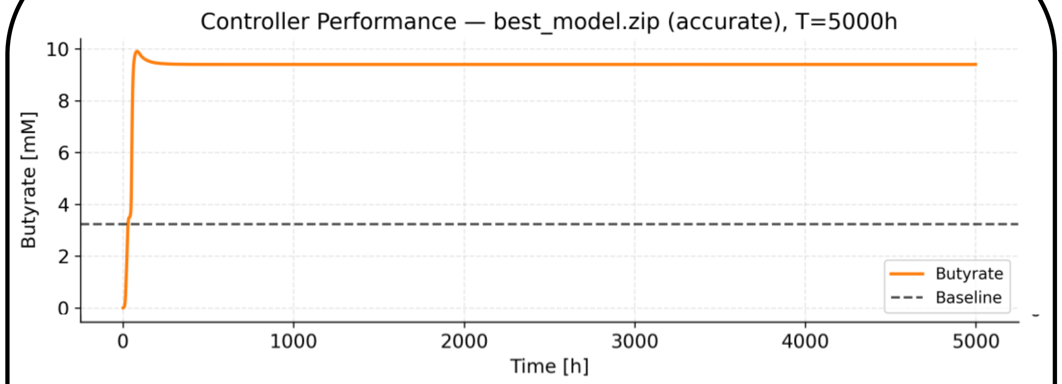
Nat. Comm. 2025
Accepted in Sep. 23/2025

Doing better with an artificially intelligent closed-loop controller?

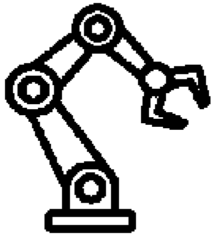
Agent-Environment loop



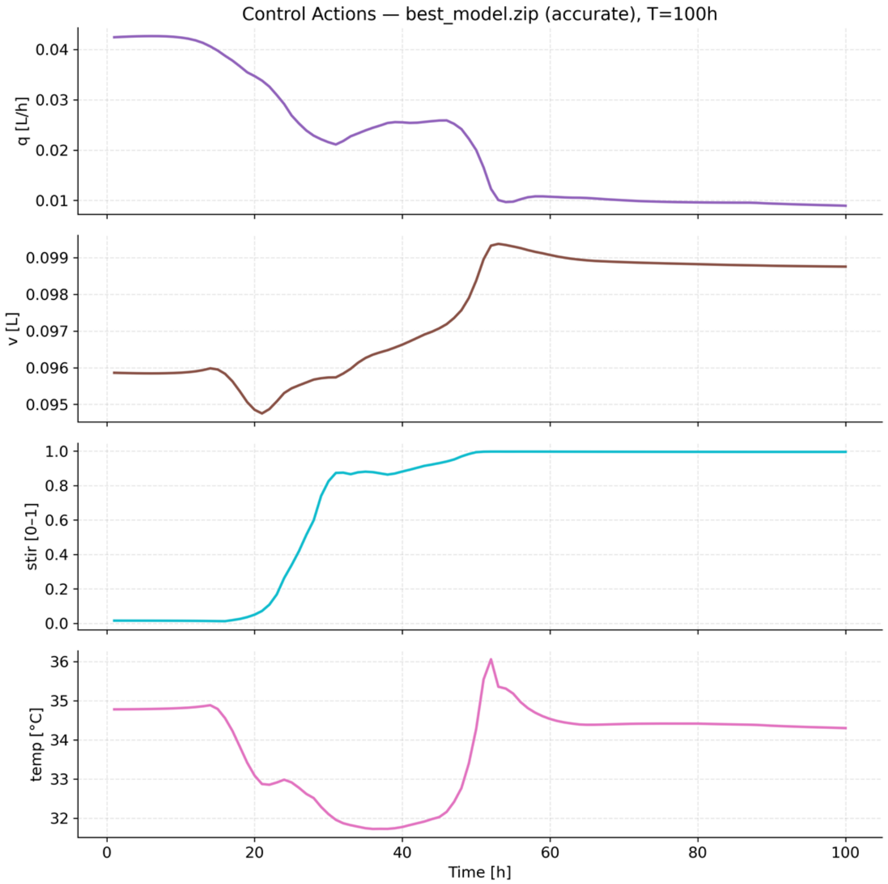
Example: controlling butyrate production



The model significantly improves over the open-loop controller (dashed line)



Four actuators:
1) Continuous feed.
2) Perioding feed (serial dilution).
3) Stirring.
4) Temperature.

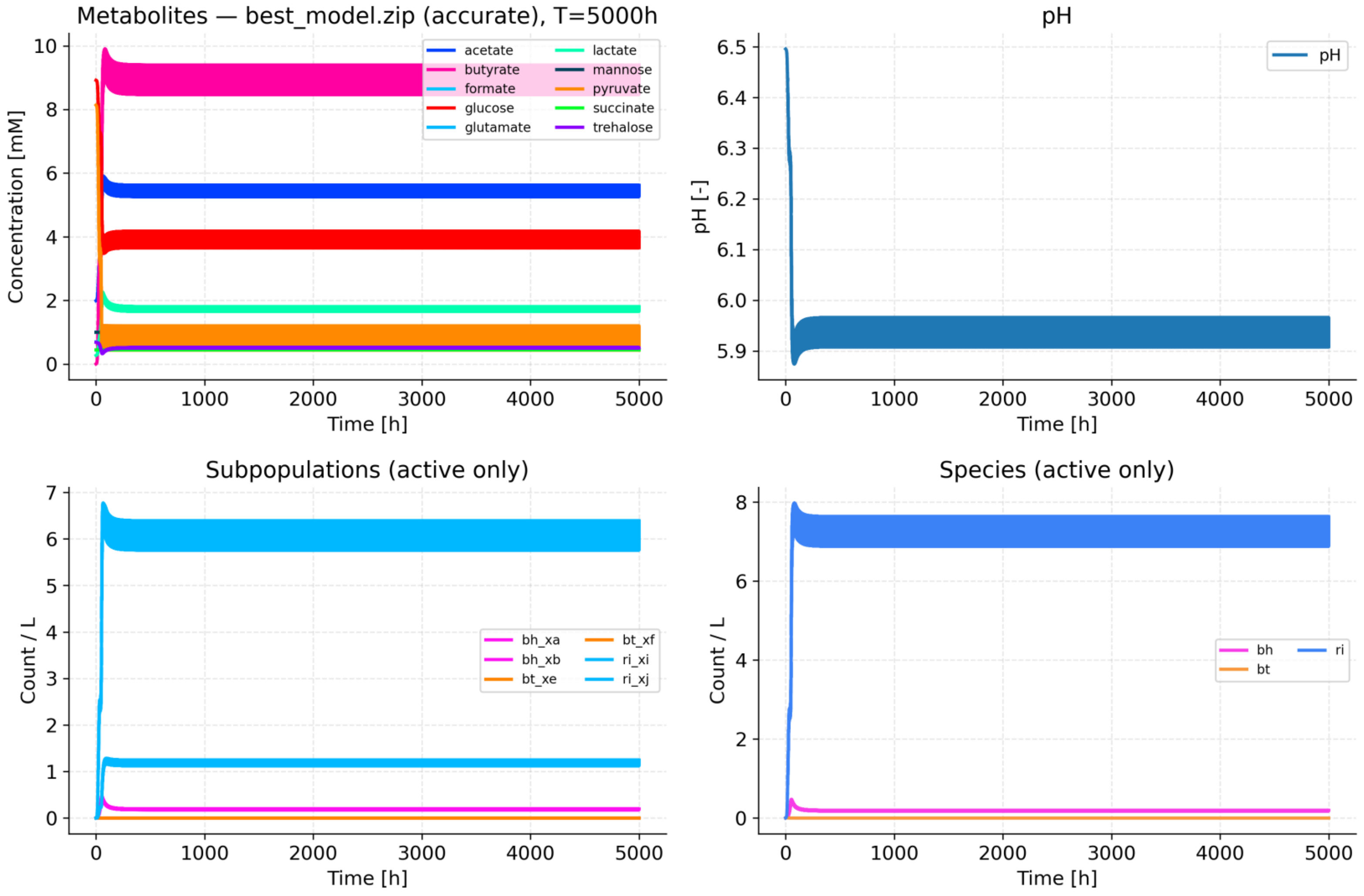


It learns a creative strategy: decreasing continuous feed while increasing periodic feed.

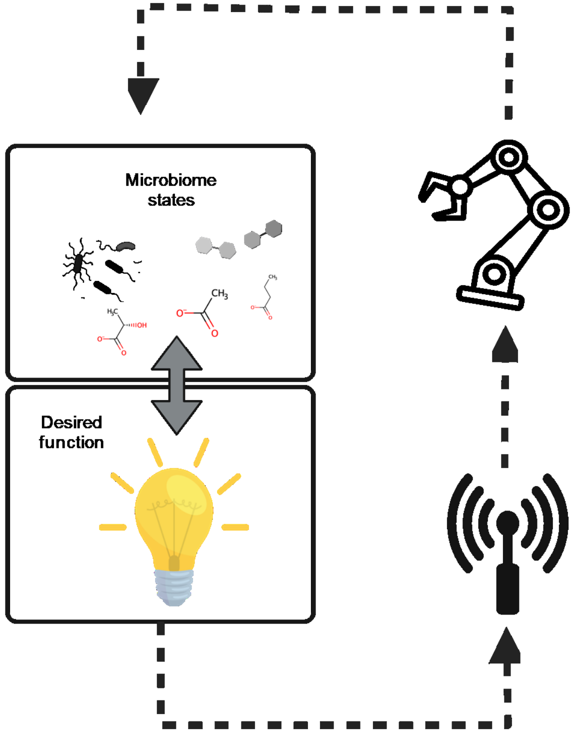
Example: how butyrate is maximized

The solution keeps a small population of the acetogen (*Blautia hydrogenotrophica*) feeding on trehalose, while producing acetate that the butyrate producer (*Roseburia intestinalis*) can use to make more butyrate.

When feeding on trehalose, the acetogen does not compete with for the other carbon sources (glucose and pyruvate)



Summary



1) Microbiomes are complex system that are difficult to predict and control

2) We need intelligent feedback controllers to move them towards desired states, which are often far from their natural equilibrium.

3) Essentially, the challenge of closed-loop microbiome control is the challenge of developing intelligent agents capable of interpreting the current state and finding actions to move the system towards desired states.

Practical task: Use the kinetic model to compare a random controller with a trained controller