Implementation of a Python simulator for microbial communities evolution via agent-based modeling

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Motivation. Human gut microbiota composition has been proved fundamental for our health; thus, modeling of microbial ecology is a hot topic in computational, systems and synthetic biology [1-3]. Classical bioinformatic approaches leverage on co-occurrence networks obtained from metagenomic data, investigated via topological analysis; those methods still lack in generalizability, not providing information on molecular mechanisms generating the observed scenarios nor being able to model environmental, spatial and temporal features [4-6].

Agent based modeling (ABM) is a solution to efficiently describe systems counting for billions of bacteria from hundreds of different species. ABM allows to develop mechanistic descriptions of simple agents, dynamically interacting with the surrounding - arbitrarily modeled - environment; then, from agents decoupled behaviors, the complex microbial ecologies should emerge without the need of describing hard-to-identify interaction networks [7-10].

In this work, we blueprint a Python-coded simulator exploiting ABM to study microbial ecologies. Specifically, the model aims to simulate the migration of bacteria along an intestinal tract, running into different metabolites across the whole space length. Each bacterial species counts for a certain number of random initial instances; bacterial growth and survival is governed by their metabolism, in turn function of the metabolites present in each specific intestinal tract. Every iteration of the model implies the bacterial processing of the metabolites (i.e., metabolite consumption and production by bacterial metabolism), computed for each intestinal section and depending on the specific bacterial composition. Eventually, bacterial growth, death and migration is computed for each species in each tract, depending on the locally processed metabolites pool.

The technology to cheaply and reliably characterize bacterial metabolisms in an high-throughput fashion is still to be developed. However, we believe that the modular structure of our simulator is generalizable enough to be already used for roughly defined communities, but also to be directly adoptable in a near future, when all the require data for a full identification of the model will be achievable.

Methods. The gut is abstracted as a series of boxes called Cells - each one containing a specific set of metabolites - connected in sequences of neighbors cells. Bacterial agents (i.e., bacteria of different species) can process the metabolites in the cell, grow and move into the next cell of the line.

This is implemented in Python through two classes:

The class Cell, whose instances implement the spatial unity, is defined by:

-an array of metabolites available at the current iteration

-a matrix of metabolites produced by the bacteria at each past iteration

-a dictionary of the bacteria in the cell, with the number of agents for each Bact instance

At each iteration, bacteria can migrate from the i-th to the (i+1)-th Cell (to mimic the direction of chime), grow, die, metabolize available metabolites and produce a new set of metabolites for the

next iteration.
The class Bact, whose instances implement bacterial species with specific metabolism, is defined by:
-a string with the species name
-a vector with the metabolisms, indicating for each metabolite if it is consumed or produced
-a vector indicating which metabolites lead to toxic effects
-two integers describing the maximum growth rate and the toxicity level, to be adopted in Hill equations computing population growth and death.
In addition to the accessor ones, the Cell class includes methods to update the number of metabolites and of bacteria in each cell at each iteration.
Analogously, the class Bact include methods to compute the variation in each species abundance, depending on the nutrients available in a certain cell and the presence of toxic metabolites.

Results. Starting from randomly generated data (metabolites concentration and bacterial abundance), the model was able to simulate a number of different conditions such as bad fitness (no nutrient in a Cell is metabolized by any of the species), perfect fitness (most of the nutrients in a Cell are highly metabolized by a specific species) and commensalism (most metabolites produced by a certain species are metabolized by another specific one and vice versa).
Despite the current implementation still needs to be significantly enriched and refined, this is already a meaningful result since the generated community behavior emerges from random metabolic patterns and nutrient distribution, mimicking a natural evolution.
Our model describes bacterial communities growing in a linear space (e.g., a gut section) with not motile metabolites; thus, the primary upgrade will be to model more in details spatial constraints and dynamics for both bacterial spreading and bolus flux.
Further enrichments will be addressed to include the possibility of importing metabolite and metabolisms data from curated databases [11].

References

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Availability
The Python code will be adapted for enabling parallel computing, to allow simulations of gut-like dimension communities with reasonable time.
We aim to release a documented and ready to use Python package on GitHub by the end of the year; a Dash-implemented GUI will be also enclosed, to facilitate the usage to non-python - and non-IT in general - users.
Finally, we are planning to validate this model on a synthetic bacterial mock community (for small number of bacterial species and highly defined metabolite composition) and on public metagenomic datasets involving longitudinal compositional and metabolomic analyses (for large number of bacterial species and decently quantified metabolite composition).