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Type	Oral communication
Session	Biological Networks
Title	From microbial community model to interaction networks
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Motivation

The microbiota is a complex micro-world characterised by several relationships established among microbes [1-2] and mediated by availability of resources. Since the metabolic products contribute to the available resources, microbial interactions, e.g. mutualism and commensalism (positive interactions), amensalism and competition (negative interactions), are strongly determined by the metabolism of the microorganisms in the community.
Although improvement of metagenome sequencing has identified associations between the microbiota and various diseases [3], little is known about the complex web of these microbial interactions in different conditions, characterizing healthy and pathological states. Several computational models have been developed to reverse engineering microbial networks based on sequence read abundance [4,5]; however, verifying the reliability of inferred networks is challenging since the true underlying interaction structure is unknown.
A ground truth network is necessary to perform a quantitative assessment of algorithm performance and, although cultures of microorganisms can be used to quantify the microbes’ abundance in a sample, defining a ground truth network of interaction based on biological knowledge shows several difficulties including the limited number of microorganisms that can be handled in culture and the lack of information related to their metabolism.
In this work, we introduce a new in-silico approach to simulate ground truth microbial networks of interaction leveraging on Community Simulator [6], a recently developed python simulator of microbial population evolution that, given a set of microorganism, resources, and metabolic parameters, provide as output the abundance values dynamics. Furthermore, we exploit the sequencing count model of metaSPARSim [7] to simulate the sequencing process and obtain a typical metagenomics data matrix.

Methods

The Microbial Consumer Resource Model (MicroCRM) [8-9] underlying the simulator is based on the concept of energy flows to describe the growth and metabolism of each microbe with an energy conservation law given by Jin = Jgrowth + Jout, where: Jin is the energy flux into a bacterial cell, Jgrowth the flux portion used for growth and Jout the outgoing flux due to metabolites production. Basically, two sets of ordinary differential equations describe the dynamics of the population in relation to Jgrowth and the dynamics of resource concentrations as a function of global consumption and production by different bacterial species.
Perturbing an initial steady state with different stimuli (i.e. different availability of resources), different dynamic evolution of the system are obtained. Once absolute abundances are obtained, we exploit our previous sequencing data simulator metaSPARSim to obtain compositional abundance data using the multivariate hypergeometric distribution, as previously done in Patuzzi et al [7]. The simulated sequencing data do not reflect absolute abundance, but rather portions of a whole, i.e. microbiome data are compositional [10].
These data can be given as input to different reverse engineering methods to benchmark their outpu against the ground truth network that we model exploiting the dependence between Jout and the metabolic matrix (resources produced by resources consumed) and between Jin and the consumption matrix (resources consumed by each bacterium). Namely, the weight of the negative interactions between two species Si and Sj is determined by considering both the consumption rates of the different microbes, and their ability to obtain energy from other resources. On the other hand, when Si produces a resource consumed by Sj, the weight of the positive interaction is calculated by considering how much the consumption of that resource is important for the species Sj and the amount of resource Si produces, in relation to Sj consumption.

Results

The overall framework proposed in this work allows to take into account the dependence relationships between species in the simulation process and to plug this information in the metaSPARSim simulator, so to i) generate relative abundance data that reflect the temporal evolution of a community and ii) provide the underlying interaction network. It is worth noting that different ground truth topologies can be obtained acting on the metabolism parameters, e.g. by exploiting known values from BacDive metadatabase [11].
The Community Simulator implements an EM algorithm to identify the steady state faster than the direct numerical integration of the dynamical equations. For example, the simulation of a network of 100 microbes takes a few seconds of computation on a standard personal computer exploiting parallel execution.

Info

References:

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Availability	-

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