## Inferring Generalized Lotka-Volterra parameters from longitudinal microbial data

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Microorganisms like bacteria, archaea and other eukaryotic cells coexist in large and complex ecosystems. Actually, microbial communities form the largest and more diverse ecosystems on the planet. The interactions among their individuals are diverse, encompassing predation, mutualism, comensalism, amensalism or competition. Measuring these interactions in direction and strength at a large scale is a challenging process that requires a combination of data analysis and modeling. Furthermore, the dynamic nature of the abundances of different species of microorganisms cannot be ignored to present a sound theory on microbial interactions.

*Data.* We use experimental data that reported the OTU relative abundance – operational taxonomic units, which are quasi-equivalent to a species definition – every day for a period of 20 days in 5 different experiments, with 2 replicates for each. So, for each OTU *i* we have the relative abundance  $x_i^t$  for each  $t = 1d, \ldots, 20d$ .

*Model.* We will assume a Generalized Lotka-Volterra model to fit the data. The choice of this model is motivated by the power-law variation in OTU abundances, which suggests a multiplicative process. Other features of longitudinal microbial relative abundance point also to this kind of model [1]. The model is defined by the following system of non-linear ordinary differential equations

$$\frac{1}{x_i}\frac{d}{dt}x_i = a_i + \sum_{j=1}^N \beta_{ij}x_j,\tag{1}$$

where N is the total number of OTUs considered. They consist of a local growth term and an interaction term that encodes the effect of other OTU abundances on the self abundance of one OTU. The particular values of  $\beta_{ij}$  as compared to  $\beta_{ji}$  let us define different types of interaction (see Tab. 1).

$\beta_{ij}\beta_{ji}$	$\beta_{ij} + \beta_{ji}$	Interaction type
< 0	_	Predation
> 0	> 0	Mutualism
	< 0	Competition
	> 0	Comensalism
0	< 0	Amensalism
	0	Neutral

Table 1. Different interaction types depending on the values of the interaction matrix  $\beta$ .

Parameter estimation. In order to estimate the best parameters that fit the data we minimize  $\chi^2$  assuming the model in Eq. (1). We assume that the fitting is to  $\frac{1}{x_i} \frac{dx_i}{dt}$ , which is approximated by  $W_i^t = \frac{x_i^t - x_i^{t-1}}{x_i^{t-1}}$  from the data. The result of this minimization has the solution

$$a_i = \langle W_i \rangle - \beta_{ij} \langle x_j \rangle$$
 and  $\beta_{ij} = \Omega_{ik} C_{kj}^{-1}$ , (2)

where  $\Omega_{ij} = \langle W_i x_j \rangle - \langle W_i \rangle \langle x_j \rangle$ ,  $C_{kj}^{-1}$  are the elements of the inverse of the covariance matrix  $(C_{ij} = \langle x_i x_j \rangle - \langle x_i \rangle \langle x_j \rangle)$  and the operator  $\langle \cdot \rangle$  denotes the average over all time points. This fitting procedure is made in steps by adding first the interactions that reduce most  $\chi^2$  and later the best model is selected based on the AIC (Akaike information criterion). This methodology avoids overfitting of the data and produces sparse interaction matrices  $\beta$ .

*Results*. The results of the fitting procedure let us explore the parameters that best fit the data. We find that the fixed points defined by these parameters do not correspond to feasible configurations of the model. We also explore the different types of interactions that are present in the system. As can be seen in Fig. 1 neutral and non-reciproval (commensalist and amensalist) dominate, while reciprocal interactions account for a small percentage of the interactions. These results are statistically significant when compared to randomizations of the interaction matrices.

*Discussion.* The fitted model reveals thus the intrinsic growth rates and the interaction network among OTUs. The estimated parameters imply fixed points that are not feasible, pointing to the fact that the dynamics might be operating around more complex attractors. The interaction types that dominate the results are non-reciprocated. These type of interactions have been mostly ignored in the modeling literature and deserve more attention for a proper description of microbial ecosystems.

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Fig. 1. Percentage of each type of interaction for the different experiments in the dataset.

[1] J. Grilli, Macroecological laws describe variation and diversity in microbial communities, Nat. Comm. **11**, 4743 (2020).