Modelling the dynamics and long-term stability of perturbed gut microbiota

Brian Gardner[1, *], Marwa M. Hassan[1], Mark Chambers[1, 2], Roberto M. La Ragione[1, 2], Giovanni Lo Iacono[1]

1. School of Veterinary Medicine, University of Surrey, Guildford, UK 2. School of Biosciences and Medicine, University of Surrey, Guildford, UK

Introduction

- The gut microbiota play a key role in the health of animals and humans. However, the *dynamic properties and stability* of the microbiota are poorly understood.
- We propose a *regression technique for parameter inference of a mechanistic model* to describe the temporal dynamics of these microbial communities. The model could be used for measuring community resilience against *external perturbing factors*, such as antibiotic therapy.

Methodology

- For model validation, we generated our own in silico time-series data of microbial abundances, based on an agent-based method that recreates the essential characteristics of experimental data [1].
- To model these data, we applied a set of stochastic differential equations to realistically mimic microbial growth, mortality, and species synergy.
- An external signal was included to represent the impact of perturbations such as periodic circadian rhythms or administration of antibiotics. The model parameters were inferred using Bayesian linear regression.

The generative model (Lotka-Volterra):

$$\frac{\mathrm{d}}{\mathrm{d}t}x_i(t) = x_i(t)\left(\alpha_i + \sum_j \beta_{ij}x_j(t) + \gamma_i u(t) + \sigma\dot{W}(t)\right)$$

This dynamical equation specifies the change in the abundance, x_i, of the *i*-th simulated taxon at each time point, *t*.

- Specifically, we modelled five microbial taxa: each of which grows with rate α_i and interacts with other taxa according to interaction matrix $\boldsymbol{\beta}$.
- The interaction components β_{ij} refer to the impact of taxa *j* on *i*, which can be negative (parasitism), zero, or positive (symbiosis). The self-interaction ($\beta_{ii} < 0$) represents the mortality of taxon *i*.
- The susceptibility term γ_i refers to the impact of a perturbation signal, *u*, on the taxon, and *W* is a stochastic process with noise amplitude σ.

Numerical integration procedure

Generates artificial taxon counts for each simulated time step

In-silico time-series data

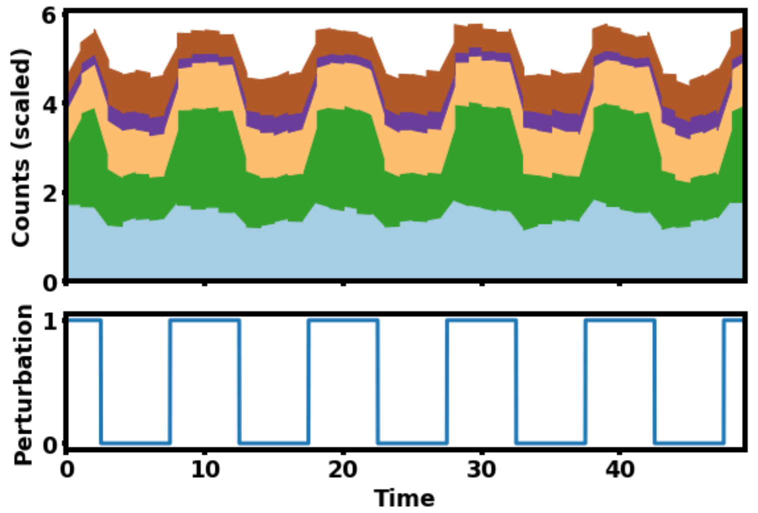

Figure 1. Arbitrary composition data of five taxa perturbed by an external, periodic signal. These taxonomic units respond differently to the perturbing signal.

Results

- We successfully produced time-series data from preliminary simulations that are qualitatively similar to those measured from experiments.
- We implemented an external perturbation signal, modelled as a periodic step function (Figure 1).
- For demonstrative purposes, the abundances of five taxa were simulated: two received positive perturbation (increased growth), two negative (increased mortality), and the remaining one was unaffected.
- Figure 2 demonstrates the strong potential of our regression technique for parameter estimation on real data. This regression is also robust against noise.
- The entire set of 'self-interaction' parameters are inferred as negative, and the 'growth rates' as positive: indicating a reliable fit to these data.

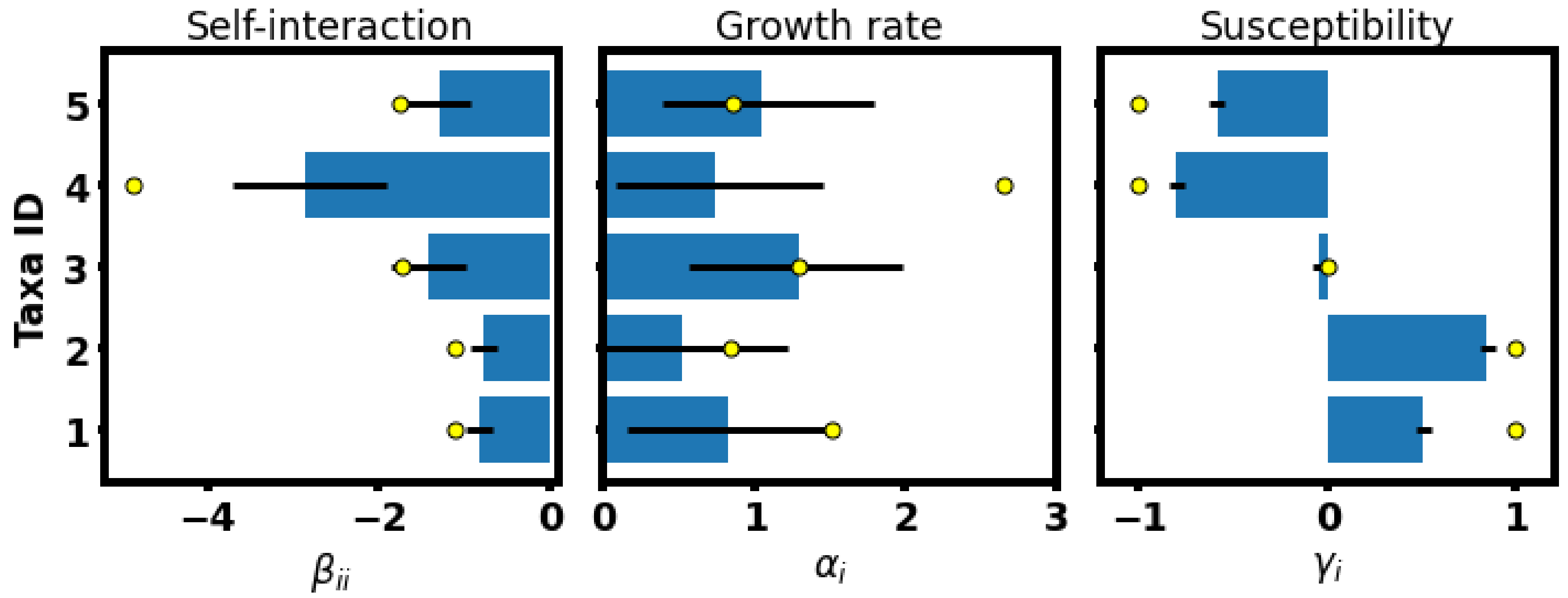

Figure 2. Inference of the ground-truth parameters using Bayesian linear regression. Yellow markers indicate the target/actual values, and the errors bars a confidence interval of 95 %.

Conclusions

- Mathematically modelling microbial dynamics is valuable for predicting the long-term stability of the gut microbiota in response to a wide variety of perturbing factors.
- Future work will explore the application of this probabilistic regression technique to data that will be obtained from an in vitro pig gut model that is subject to perturbation.

Literature cited and aknowledgments

[1] Descheemaeker, L., & De Buyl, S. (2020). Stochastic logistic models reproduce experimental time series of microbial communities. Elife, 9, e55650. doi: https://doi.org/10.7554/eLife.55650

This poster is part of the European Joint Programme One Health EJP. This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 773830. We acknowledge and thank all FED-AMR OHEJP consortium partners.

Further information

* E-mail: b.gardner@surrey.ac.uk