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MODELING INTRA-HOST DYNAMICS WITHIN THE MICROBIOTA.

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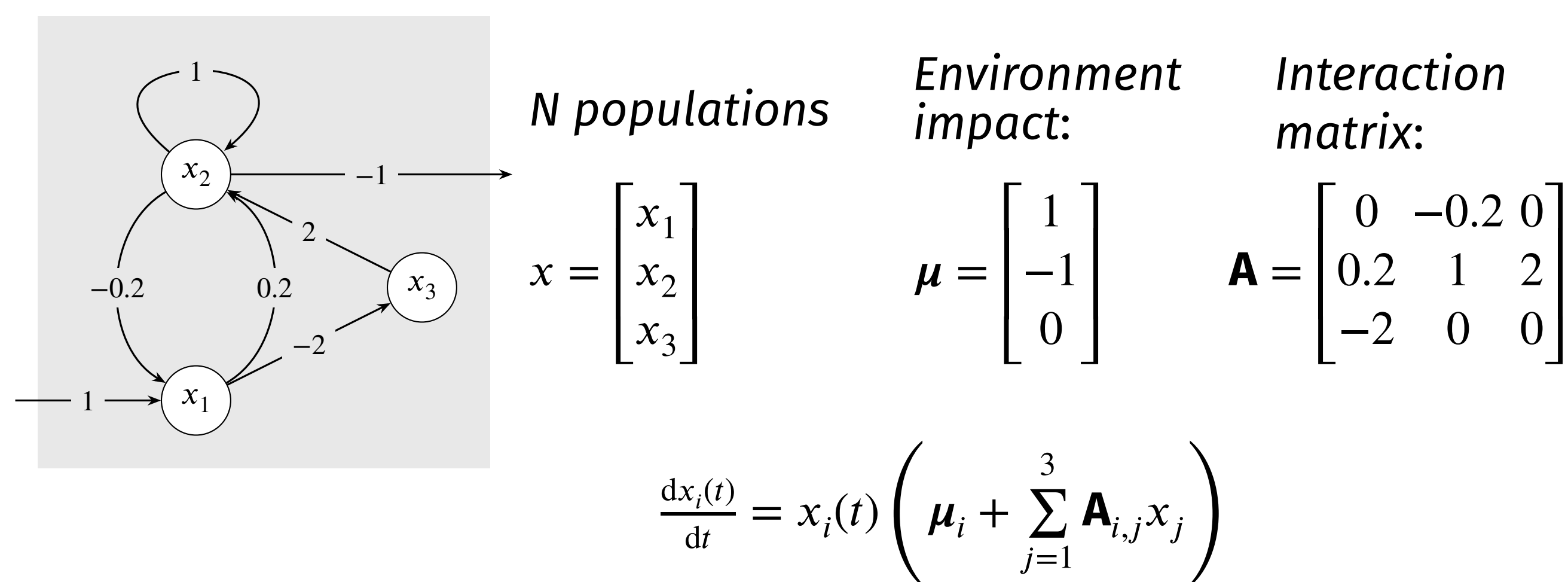
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Abstract

Microbiota is a major reservoir of bacteria in the humans and animals organism. It is home to numerous commensal species, some of which can be sources of infection, such as staphylococcus aureus[1]. While the composition and properties of microbiota are increasingly understood, their dynamics remain difficult to model, due to the large number of species and their interactions. **Generalized Lotka Volterra (LV)** model is particularly interesting, since it allows simulations of a large number of interacting microbial populations. However, calibrating this model requires abundance data, while classical metagenomic analyses, which quantify the composition of microbiota, only provide "**frequency**" data, i.e. the proportion of each population among those present. Currently, to address this issue, either imprecise proxies of total microbiota abundance are used [2], or strong assumptions are made about the system, for example by assuming that total abundance is fixed [3]. Applying this model to microbiota data without using such assumptions is therefore a key challenge:

- We **characterize analytically** the **identifiability** conditions of the LV model on frequency data.
- We demonstrate analytically that such **identifiability is possible in the general case**, without requiring strong assumptions.
- We validate this result by **numerical analysis of simulations** of microbiotic dynamics.

The Lotka-Volterra model



The identifiability problem

Is it possible to calibrate the Lotka-Volterra model using frequency data?

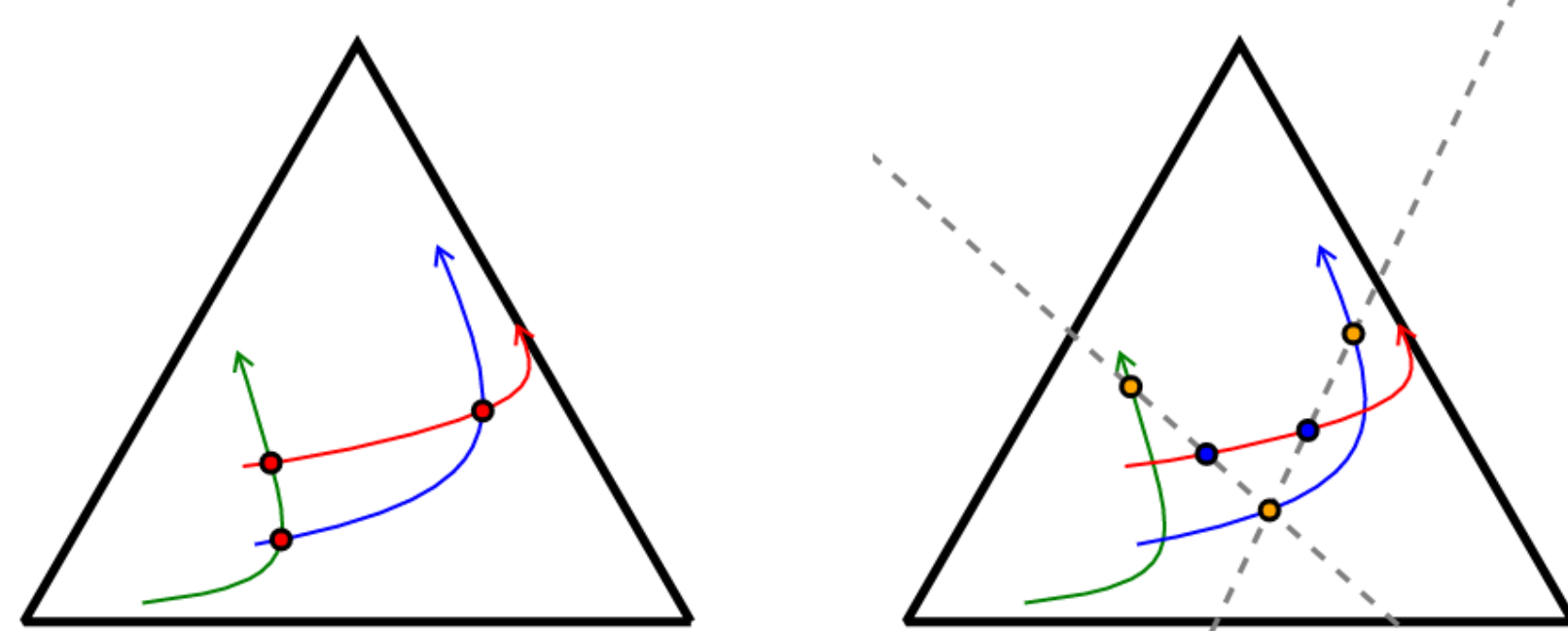
$$\frac{dx_i(t)}{dt} = x_i(t) \left(\mu_i + \sum_{j=1}^N A_{i,j} x_j \right) \quad \frac{dx'_i(t)}{dt} = x'_i(t) \left(\mu'_i + \sum_{j=1}^N A'_{i,j} x'_j \right)$$

$$\frac{1}{\sum_{j=1}^N x_j(t)} x(t) = \frac{1}{\sum_{j=1}^N x'_j(t)} x'(t) \stackrel{?}{\Rightarrow} \mu' = \mu \ \& \ A' = A$$

Identifiability of the generalised Lotka-Volterra model

Theorem:

If the frequency data is rich enough:



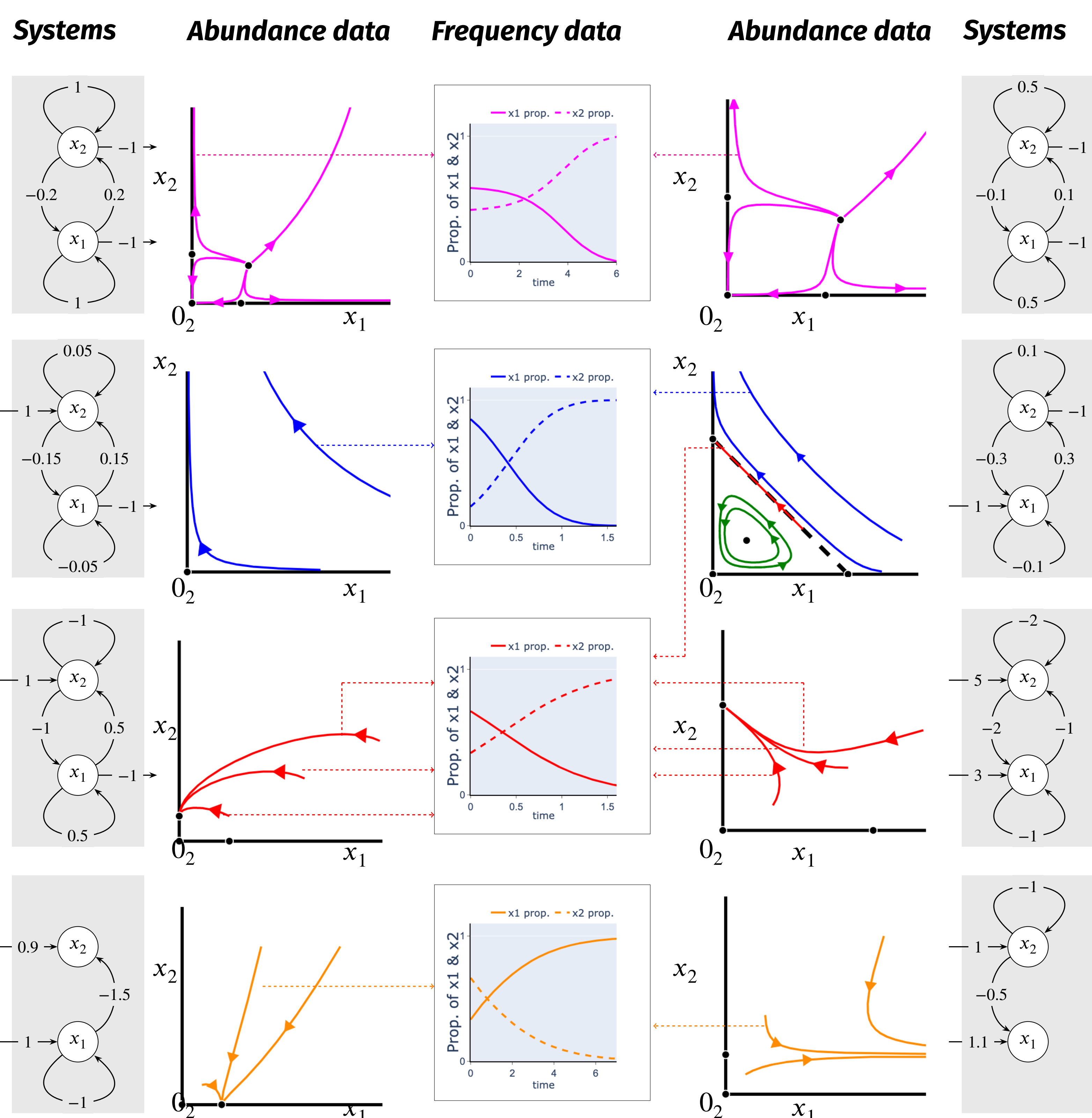
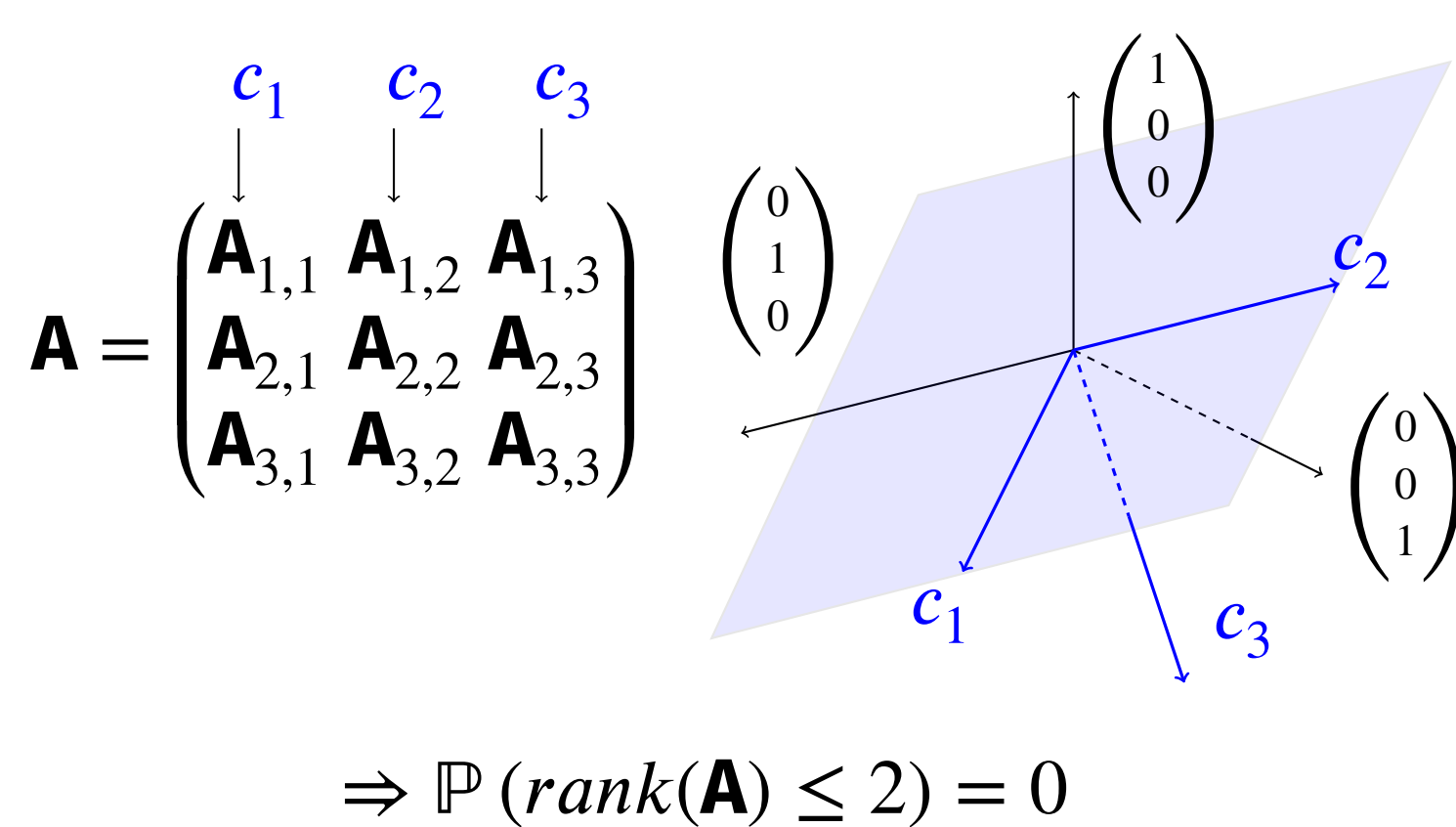
And $\frac{1}{\sum_{j=1}^N x_j(t)} x(t) = \frac{1}{\sum_{j=1}^N x'_j(t)} x'(t)$

Then 1) either $\text{rank}(A) > 2 \Rightarrow \mu' = \mu \ \& \ A' = \rho A$ with $\rho > 0$

Identifiability!

2) or $\text{rank}(A) \leq 2$

If $n \geq 3$: $\text{rank}(A) \leq 2 \iff c_1, c_2 \text{ and } c_3 \text{ are in the same plane}$



Conclusion and perspectives

- It is possible to **reconstruct the total abundance** of a microbiota **using only its frequency data**.
- It is possible to use the **Lotka-Volterra model** on frequency data of the microbiota.

Acknowledgements

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