

# Interacting Hosts with Microbiome Exchange:

An Extension of Metacommunity Theory for  
Discrete Interactions

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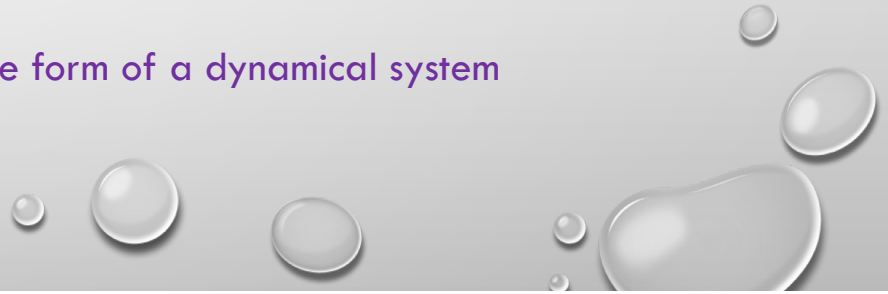
# Introduction

Microbiomes + Metacommunity Theory





# Microbiomes

- Microbiome: A community of microorganisms that are living together in some habitat
  - Microbiomes substantially impact the environmental patches or living hosts that they occupy, and they play a critical role in their functioning and health
  - A host's social interactions significantly impact its microbiome composition
  - Model a microbiome with local ecological dynamics in the form of a dynamical system
- 



# Examples of Local Ecological Dynamics

- Generalized Lotka–Volterra model:

$$\frac{dN_k}{dt} = r_k N_k + \sum_{l=1}^m \alpha_{kl} N_k N_l$$

- $m$  coexisting microbe species  $N_k$
- Each species  $k$  has an intrinsic birth rate and death rate, which are combined into  $r_k$
- Interaction parameter  $\alpha_{kl}$ 
  - $\alpha_{kl} > 0 \rightarrow$  species  $l$  is beneficial to species  $k$
  - $\alpha_{kl} < 0 \rightarrow$  species  $l$  is harmful to species  $k$

- Niche model (a consumer–resource model):

$$\begin{aligned} \frac{dN_k}{dt} &= N_k A_k(\mathbf{R}), \\ \frac{dR_l}{dt} &= B_l(\mathbf{R}) - \sum_{k=1}^m N_k C_{kl}(\mathbf{R}) \end{aligned}$$

# Metacommunity Theory

- Ecological metacommunity: A set of interacting communities that are linked by the dispersal of multiple, potentially interacting species
- Metacommunity ecology combines local factors (e.g., predation, competition, and environmental conditions) and regional factors (e.g., dispersal of individuals, immigration, and emigration) to explain patterns of species distributions across multiple spatial scales.
- Often studied using the so-called “mass-effects paradigm”, which has continuous dispersal of microbes (and yields a coupled set of differential equations).
  - We change this by using discrete interactions.



# Our Modeling Framework

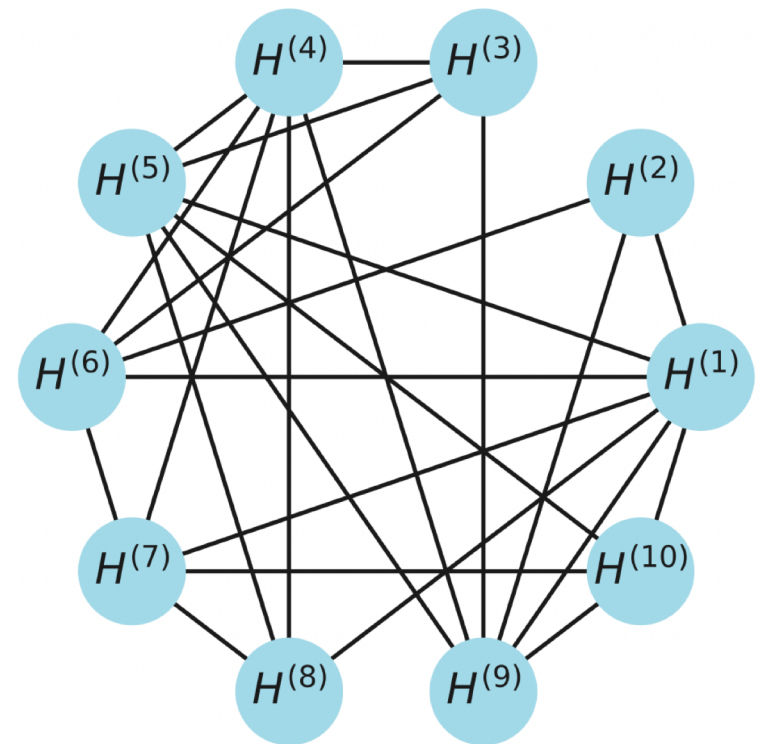
Interaction Network + Exchange Dynamics + Local Dynamics



# Interaction Network

- A graph  $G = (H, E)$  of hosts (i.e., nodes)  $H$  and edges  $E$
- An undirected edge  $e = (H^{(i)}, H^{(j)})$  has an associated *interaction-frequency parameters*  $\lambda_{ij}$
- *Total interaction-frequency parameter*  $\lambda_{\text{tot}}$ 
  - A key model parameter

$$\lambda_{\text{tot}} = \sum_{i=1}^{|H|} \sum_{j=i+1}^{|H|} \lambda_{ij}$$



# Exchange Dynamics

- $\mathbf{N}^{(i)}(t)$  = microbiome abundance vector = vector of species abundances in host  $i$
- If two hosts interact at time  $t_I$ , they instantaneously exchange a proportion  $\gamma$  of their microbiomes with each other
  - $\gamma$  governs the strength of an interaction and is a key model parameter
  - Simplifying assumption: the same constant  $\gamma$  for each pair of hosts

$$\begin{aligned}\mathbf{N}^{(i)}(t_I^+) &= (1 - \gamma)\mathbf{N}^{(i)}(t_I^-) + \gamma\mathbf{N}^{(j)}(t_I^-) \\ \mathbf{N}^{(j)}(t_I^+) &= (1 - \gamma)\mathbf{N}^{(j)}(t_I^-) + \gamma\mathbf{N}^{(i)}(t_I^-)\end{aligned}$$

- We model the time between consecutive interactions between a host pair as an exponentially distributed random variable:

$$f_{ij}(t) = \lambda_{ij}e^{-\lambda_{ij}t}$$

$$l_{ij} = \Pr(X_{ij} = X) = \frac{\lambda_{ij}}{\lambda_{\text{tot}}}$$

# Local Dynamics of the Hosts

- Between interactions, the microbiome abundance vector of each host satisfies an autonomous dynamical system:

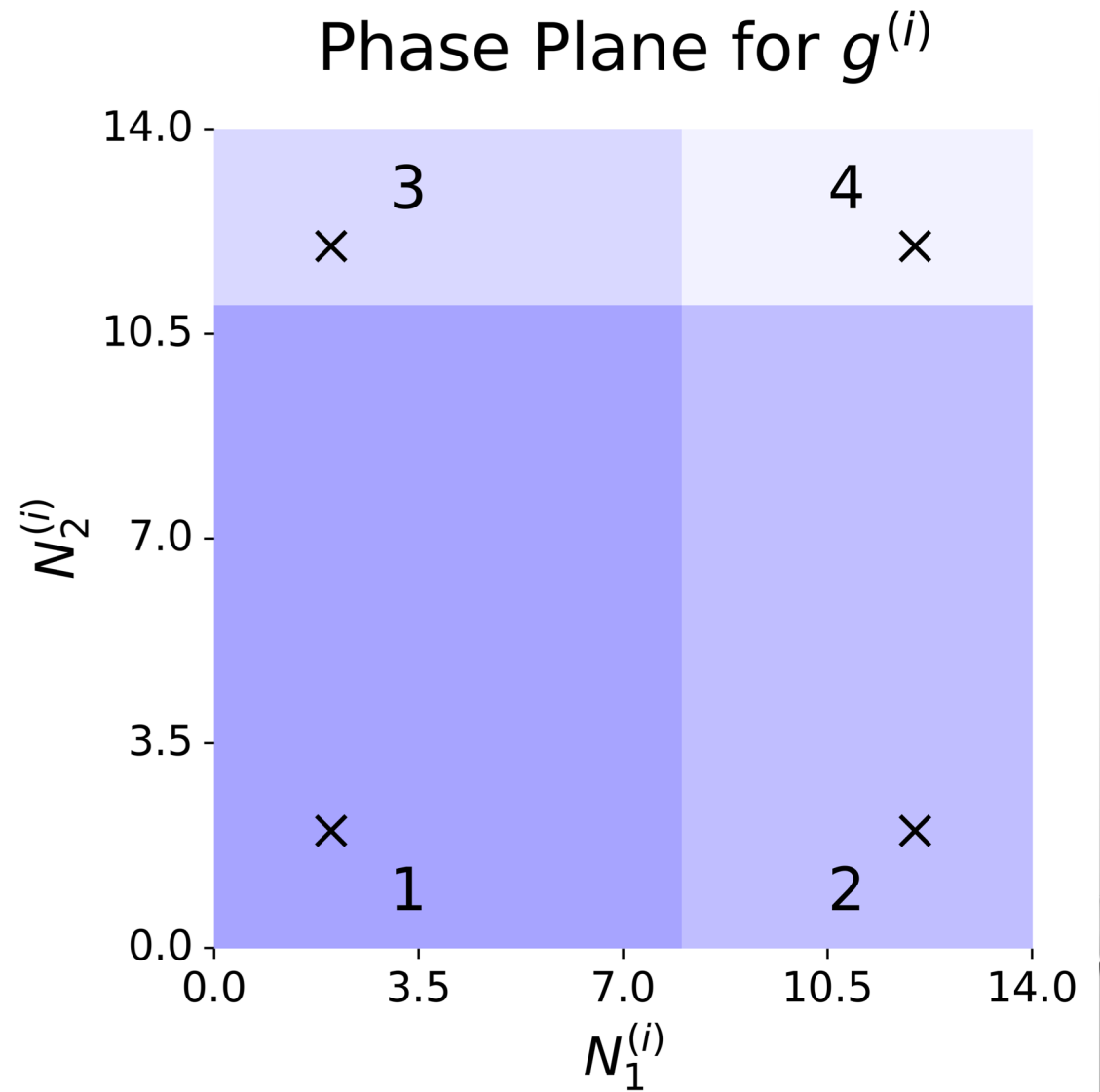
$$\frac{d\mathbf{N}^{(i)}}{dt} = g^{(i)} \left( \mathbf{N}^{(i)} \right)$$

- Toy model of local dynamics (for our numerical illustrations):

$$\begin{aligned} \frac{dN_1^{(i)}}{dt} &= -\frac{N_1^{(i)}}{10} \left( N_1^{(i)} - 2 \right) \left( N_1^{(i)} - 8 \right) \left( N_1^{(i)} - 12 \right) , \\ \frac{dN_2^{(i)}}{dt} &= -\frac{N_2^{(i)}}{10} \left( N_2^{(i)} - 2 \right) \left( N_2^{(i)} - 11 \right) \left( N_2^{(i)} - 12 \right) \end{aligned}$$



- The four stable equilibrium points of the local dynamics, with their basins of attraction



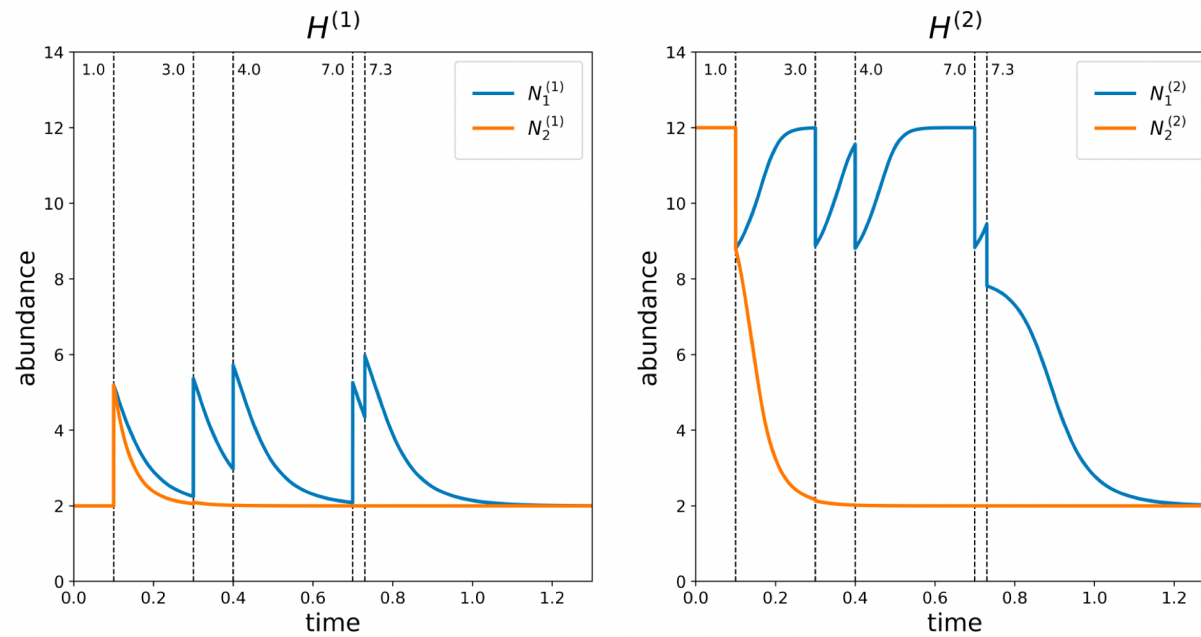
The slide features a light gray gradient background. In the top-left corner, there are several water droplets of varying sizes, some partially cut off by the edge. In the top-right corner, there is one large droplet and a smaller one below it. In the bottom-right corner, there is a cluster of droplets, including a large one and several smaller ones. In the bottom-center area, there are a few more small droplets.

# Approximations in Three Different Regimes



# Low-Frequency Approximation (LFA)

- All interaction-frequency parameters  $\lambda_{ij}$  are small



**Figure 4.** Two hosts with local dynamics (2.9). These hosts have initial states  $\mathbf{N}^{(1)}(0) = (2, 2)$  and  $\mathbf{N}^{(2)}(0) = (12, 12)$ . We show the abundances of microbe species 1 and 2 in each host through the course of five interactions at times 0.1, 0.3, 0.4, 0.7, and 0.73.

# Low-Frequency-Approximation Theorem

- When the local dynamics is much faster than the exchange dynamics, each microbiome abundance vector becomes close to an attractor before the next exchange interaction occurs, so a total-interaction operator accurately describes the probabilities in a basin probability tensor.
  - The basin probability tensor gives the probabilities of being in each basin of attraction.

**Theorem 3.1 (Low-Frequency-Approximation Theorem).** *Suppose that the attractors of each host's local dynamics consist of a finite set of stable equilibrium points at which the local-dynamics function  $g^{(i)}$  is inward pointing, and let each  $g^{(i)}$  be continuous and bounded (see subsection 2.3). Fix  $\gamma \notin \mathcal{B}$ , all  $l_{ij}$ , and a frequency-scaled time  $T^*$ . As  $\lambda_{\text{tot}} \rightarrow 0$ , the basin probability tensor  $\Psi(t^*)$  converges uniformly to  $\tilde{\Psi}(t^*)$  on  $[0, T^*]$ , where*

$$(3.9) \quad \begin{aligned} \frac{d}{dt^*} \tilde{\Psi}_{b_1, \dots, b_{|H|}}(t^*) &= \Phi_{b_1, \dots, b_{|H|}, a_1, \dots, a_{|H|}} \tilde{\Psi}_{a_1, \dots, a_{|H|}}(t^*) - \tilde{\Psi}_{b_1, \dots, b_{|H|}}(t^*), \\ \tilde{\Psi}(0) &= \Psi(0). \end{aligned}$$

# High-Frequency, Low-Strength Approximation (HFLSA)

- Interactions between hosts are very frequent but very weak.
- The HFLSA approximation becomes increasingly accurate as the total frequency-interaction parameter  $\lambda_{\text{tot}} \rightarrow \infty$  and the interaction strength  $\gamma \rightarrow 0$  for fixed relative interaction-frequency parameters  $l_{ij}$  and fixed product  $(\lambda_{\text{tot}} \times \gamma)$ .
- The HFLSA approximation yields a model that takes the form of a mass-effects model.

$$\frac{d\mathbf{N}^{(i)}}{dt} = g^{(i)}(\mathbf{N}^{(i)}) + \sum_j \sigma_{ij} \left( \mathbf{N}^{(j)} - \mathbf{N}^{(i)} \right)$$

# High-Frequency, Low-Strength Approximation Theorem

**Theorem 4.1 (High-Frequency, Low-Strength Approximation Theorem).** *Fix the relative interaction-frequency parameters  $l_{ij}$ , the product  $\lambda_{\text{tot}}\gamma$ , and a time  $T$ . Let each local-dynamics function  $g^{(i)}$  be continuously differentiable and bounded (see [subsection 2.3](#)), and let  $\varepsilon \in (0, 1]$  and  $\delta > 0$  be arbitrary but fixed. For sufficiently large  $\lambda_{\text{tot}}$ , each host's microbiome abundance vector  $\mathbf{N}^{(i)}(t)$  satisfies*

$$(4.1) \quad \left\| \mathbf{N}^{(i)} - \tilde{\mathbf{N}}^{(i)} \right\|_{L^\infty[0, T]} < \delta$$

*with probability larger than  $1 - \varepsilon$ , where*

$$(4.2) \quad \begin{aligned} \frac{d\tilde{\mathbf{N}}^{(i)}}{dt} &= g^{(i)}(\tilde{\mathbf{N}}^{(i)}) + \sum_j \lambda_{ij}\gamma \left( \tilde{\mathbf{N}}^{(j)} - \tilde{\mathbf{N}}^{(i)} \right), \\ \tilde{\mathbf{N}}^{(i)}(0) &= \mathbf{N}^{(i)}(0). \end{aligned}$$

# High-Frequency, Constant-Strength Approximation (HFCSA)

- Interactions are very frequent and have constant strength.
- The HFCSA approximation becomes increasingly accurate as the total interaction-frequency parameter  $\lambda_{\text{tot}} \rightarrow \infty$  for fixed relative interaction-frequency parameters  $l_{ij}$  and fixed interaction strength  $\gamma$ .
- In this regime, all microbiome abundance vectors converge rapidly to the mean of these vectors, and then the “synchronized” microbiome abundance vectors follow the mean of their local dynamics.



# High-Frequency, Constant-Strength Approximation Theorem

**Theorem 4.2 (High-Frequency, Constant-Strength Approximation Theorem).** *Fix the relative interaction-frequency parameters  $l_{ij}$ , the interaction strength  $\gamma > 0$ , and a time  $T$ . Suppose that each local-dynamics function  $g^{(i)}$  is Lipschitz continuous and bounded (see [subsection 2.3](#)). Let  $\varepsilon \in (0, 1]$ ,  $\delta > 0$ , and  $\eta > 0$  be arbitrary but fixed constants. For sufficiently large  $\lambda_{\text{tot}}$ , each host microbiome abundance vector  $\mathbf{N}^{(i)}(t)$  satisfies*

$$(4.14) \quad \left\| \mathbf{N}^{(i)} - \tilde{\mathbf{N}} \right\|_{L^\infty[\eta, T]} < \delta$$

*with probability larger than  $1 - \varepsilon$ , where*

$$(4.15) \quad \begin{aligned} \frac{d\tilde{\mathbf{N}}}{dt} &= \frac{1}{|H|} \sum_{j=1}^{|H|} g^{(j)}(\tilde{\mathbf{N}}) , \\ \tilde{\mathbf{N}}(0) &= \overline{\mathbf{N}}(0) . \end{aligned}$$



# Conclusions

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# Conclusions

- We developed a framework to model the microbiome dynamics of living hosts that incorporates both local dynamics within an environment and exchanges of microbiomes between environments.
  - Our framework extends metacommunity theory by accounting for the discrete nature of host interactions.
  - Our framework incorporates distinct parameters that control interaction frequencies and interaction strength.
    - We analyzed three different regimes of these parameters.
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