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Simplification and control of microbial ecosystems

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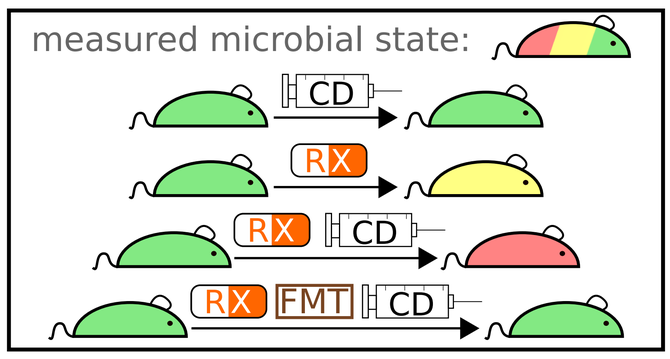
Overview



Motivation: Reverse onset of antibiotic-induced *C. difficile* infection in an ecological model of the microbiome

Objective: Develop ecological theory that describes how external interventions [e.g. fecal microbiota transplantation (FMT)] alter a microbiome's state

Approach: Identify meaningful ecological steady states ( ), examine how to efficiently transition between pairs of states

Outcomes:

- ★ Theoretical machinery studies how direct (e.g. FMT) and indirect (e.g. diet changes) interventions drive a microbiome towards a target state
- ★ Dimensionality-reduction tool links complex ecosystem models to analytically tractable ones
- ★ Noise enriches observed ecological dynamics and affects efficacy of direct interventions

Background

Ecological generalized Lotka-Volterra (gLV) model of microbial dynamics fit to *C. difficile* infection experiment[1]

$$\underbrace{\frac{\mathrm{d}}{\mathrm{d}t}y_i(t)}_{\text{change in abundance of population } i} = \underbrace{\rho_i y_i(t)}_{\text{stand-alone growth}} + \underbrace{y_i(t)\sum_{j=1}^{N} K_{ij}y_j(t)}_{\text{pairwise interactions}}$$

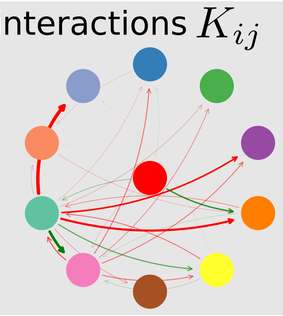
microbial populations y_i

- Barnesiella
- undefined genus of Lachnospiraceae
- unclassified Lachnospiraceae
- Other
- Blautia
- undefined genus of unclassified Mollicutes
- Akkermansia
- Coprobacillus
- undefined genus of Enterobacteriaceae
- Enterococcus
- Clostridium difficile

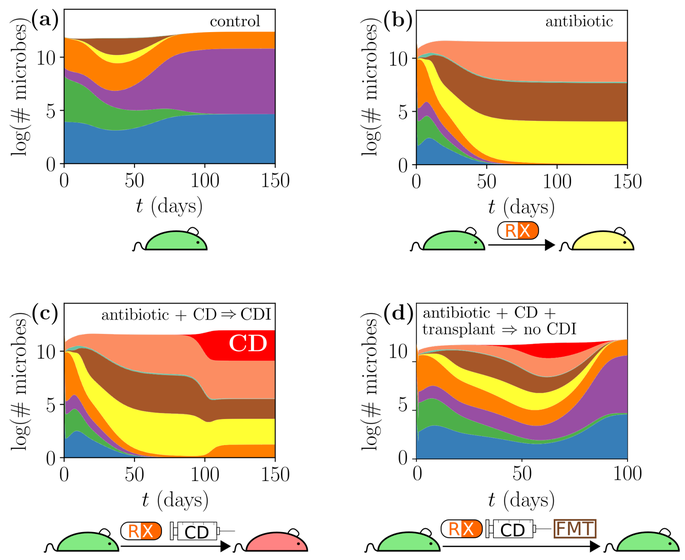
pairwise interactions K_{ij}

facilitation $j \rightarrow i$

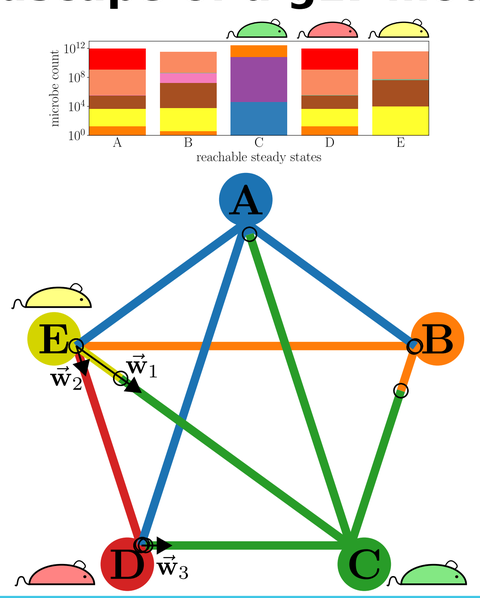
inhibition $j \dashrightarrow i$



Interventions alter steady-state outcomes[2]

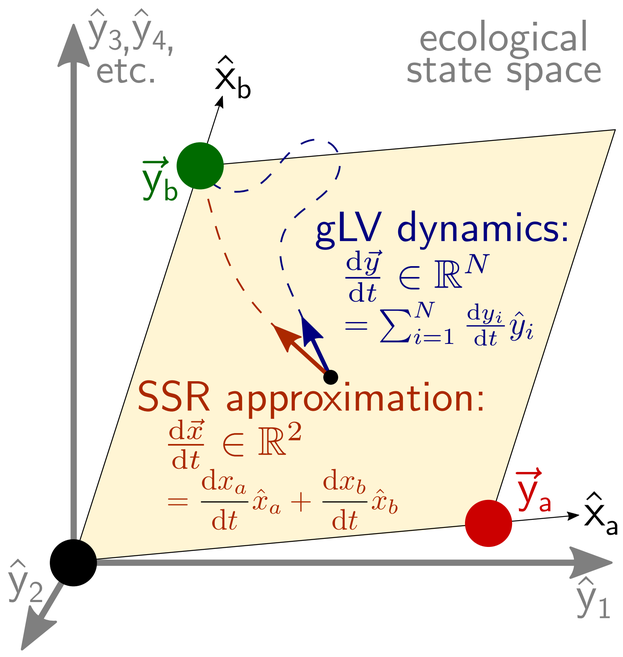


Mapping the dynamical landscape of a gLV model[3]



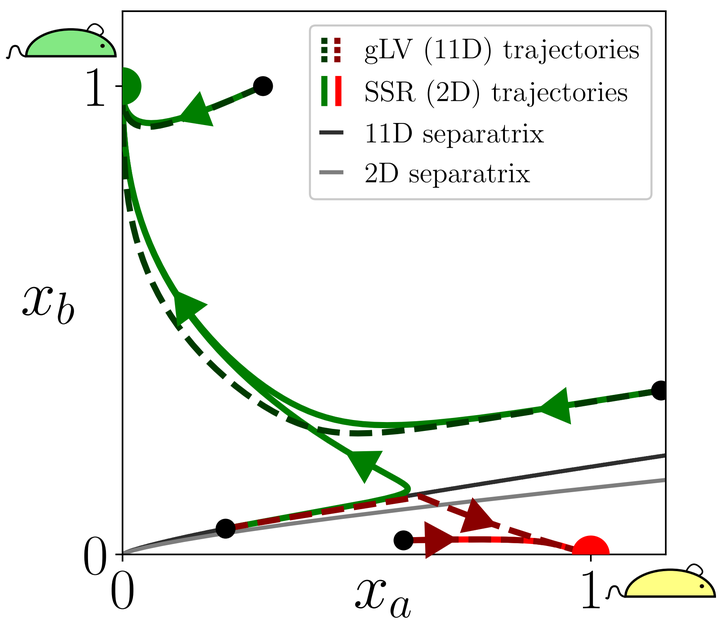
Steady-state reduction[4] (SSR)

approximates bistable region of high-dimensional gLV model by analytically tractable 2D gLV model



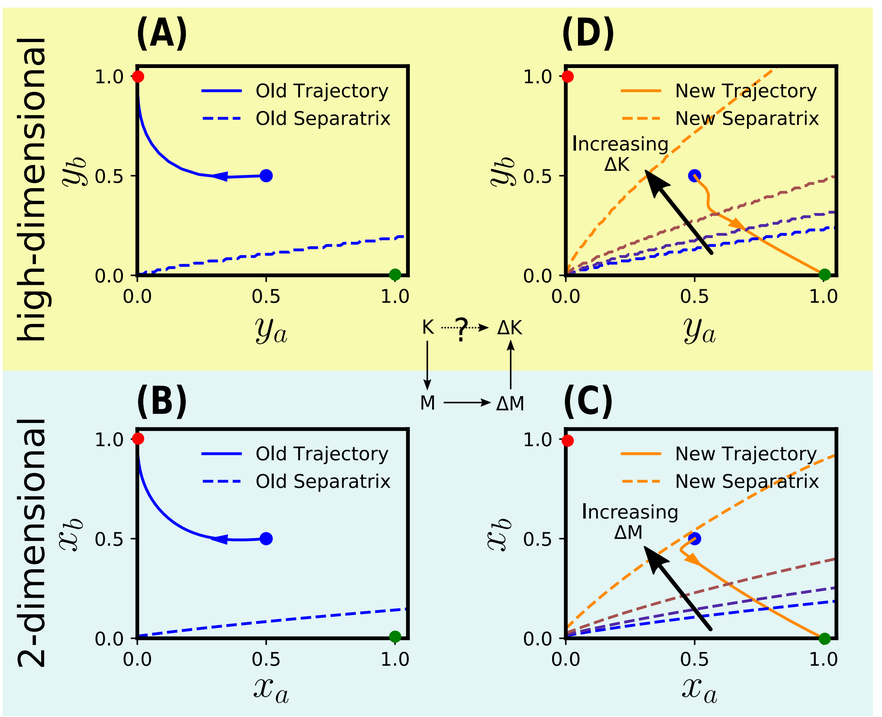
SSR correspondence suggests

2D SSR-reduced systems can be used as gateway to study realistic high-dimensional gLV models



Control of steady-state outcomes

via deliberate parameter perturbations[5]



Results

true microbiome (trillions of microbes) → **gLV model (11-dimensional)** → **SSR-reduced model (2-dimensional)**

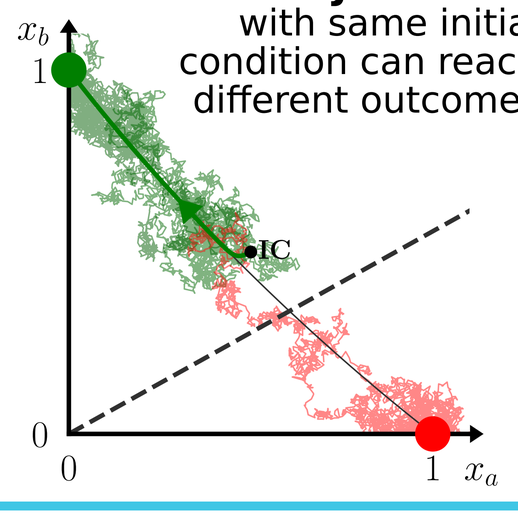
Spatial inhomogeneity in the microbiome looks like **noise** (when using coarse-grained abundance data)

Introduce stochasticity to a 2D gLV model:

$$\begin{bmatrix}\mathrm{d}x_a\\ \mathrm{d}x_b\end{bmatrix} = \underbrace{\mathrm{d}t\begin{bmatrix}x_a(\mu_a - M_{aa}x_a - M_{ab}x_b)\\ x_b(\mu_b - M_{ba}x_a - M_{bb}x_b)\end{bmatrix}}_{\text{drift (deterministic)}} + \underbrace{\mathrm{d}\boldsymbol{W}(t)\begin{bmatrix}\sigma_\phi^{1/2}\\ \sigma_\phi^{1/2}\end{bmatrix}}_{\text{immigration noise}} + \underbrace{\begin{bmatrix}0\\ v\end{bmatrix}}_{\text{transplant}}$$

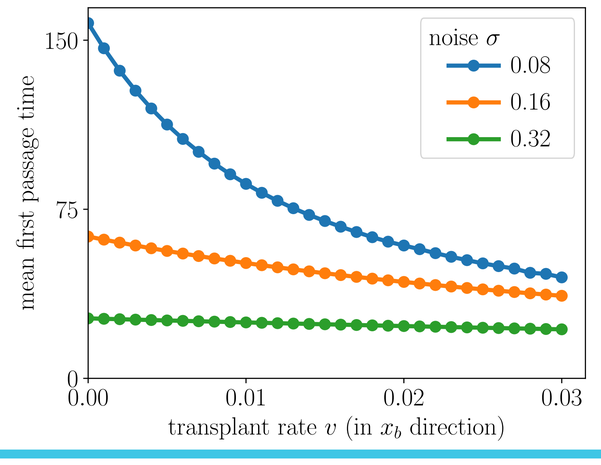
Stochastic trajectories

with same initial condition can reach different outcomes



Transplant efficacy

is influenced by noise



References

[1] Stein et al., PLOS Comp. Biol. 2013; [2] Jones and Carlson, PLOS Comp. Biol. 2018; [3] Jones et al., AIMS Special Issue on Biol. Systems Modeling 2020; [4] Jones and Carlson, Phys. Rev. E 2019; [5] Wang et al., Phys. Rev. E. 2020

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