

Bifurcation analysis of microbiome steady states

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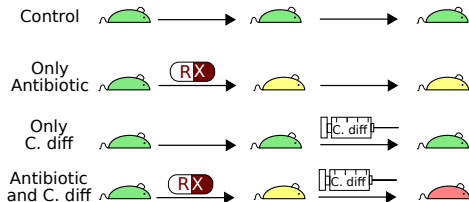
Josh Mueller

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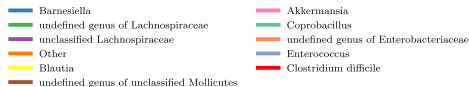
General Goal

- ▶ Modify diseased states into healthy states
- ▶ Ecology \leftrightarrow Microbiome
- ▶ Change microbial interactions



General Goal

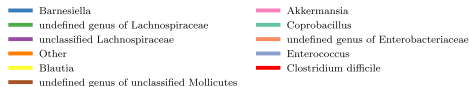
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Source: Jones and Carlson, PLoS Comp. Biol. 2018

General Goal

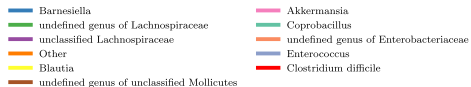
- ▶ Modify diseased states into healthy states
- ▶ Ecology \leftrightarrow Microbiome
- ▶ Change microbial interactions
- ▶ Example: change acidity of environment



Source: Jones and Carlson, PLoS Comp. Biol. 2018

Stein Model

- ▶ Based on experiments
- ▶ 11 categories; 11-D vector



Source: Jones and Carlson, PLoS Comp. Biol. 2018

Generalized Lotka-Volterra equations

Taylor Expansion:

$$\frac{d\vec{y}}{dt} = f(\vec{y}) \approx f(\vec{0}) + Df(\vec{0}) \cdot \vec{y} + \vec{y}^T \cdot Hf(\vec{0}) \cdot \vec{y}$$

N-species gLV Equations:

$$\frac{d}{dt}y_i(t) = y_i(t) \left(\rho_i + \sum_{j=1}^N K_{ij} y_j(t) \right)$$

2D:

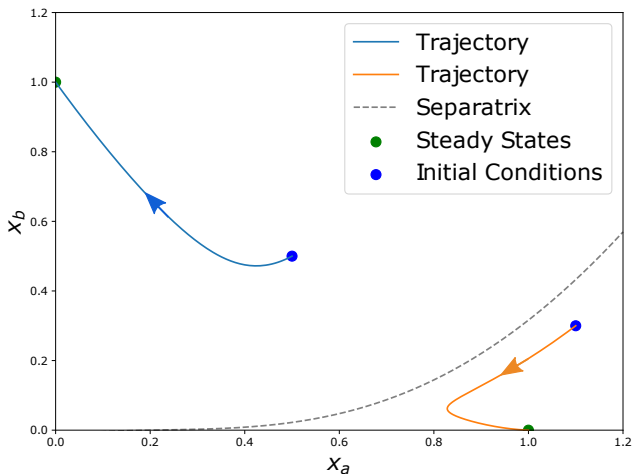
$$\begin{cases} \frac{dx_a}{dt} = \underbrace{\mu_a}_{\text{growth rate}} x_a - \overbrace{M_{aa}x_a^2 + M_{ab}x_ax_b}_{\text{interaction}} \\ \frac{dx_b}{dt} = \mu_b x_b - \overbrace{M_{ba}x_ax_b + M_{bb}x_b^2}_{\text{interaction}} \end{cases}$$

Dynamical Landscape

Equivalent form:

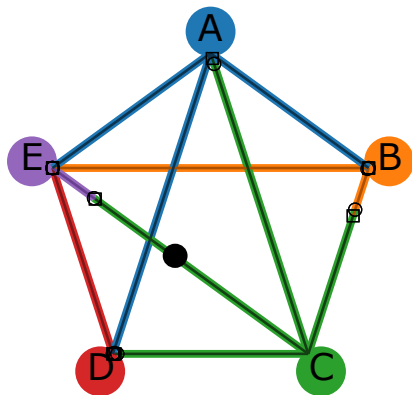
$$\begin{cases} \frac{dx_a}{dt} = x_a(1 - x_a - M_{ab}x_b) \\ \frac{dx_b}{dt} = x_b(\mu_b - M_{ba}x_a - x_b) \end{cases}$$

Taking $\mu_b = 1$:

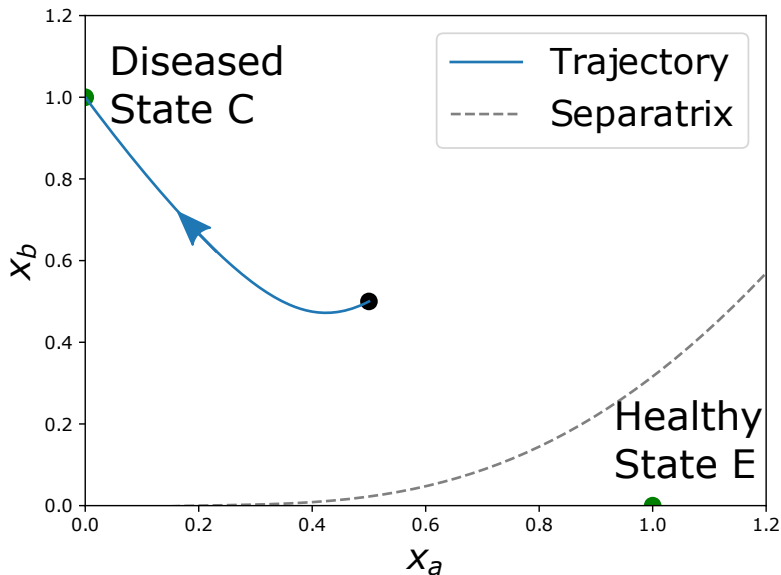


Project Goal

- ▶ Consider steady states C and E
- ▶ Start at the middle point
- ▶ Use SSR to reduce K to M
- ▶ Modify interaction matrix M
- ▶ Change system from C to E

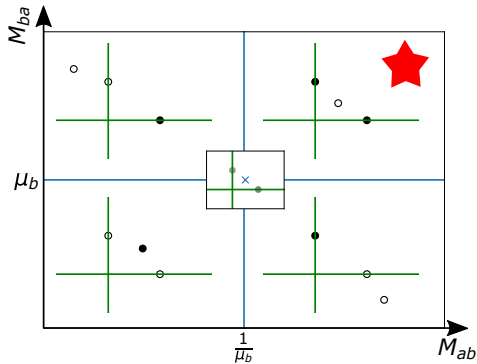


Original Trajectory



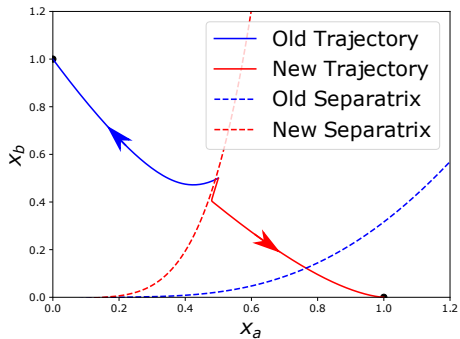
Bifurcation Analysis

- ▶ Separatrix moves with the third steady state
- ▶ Originally in upper right region
- ▶ going towards upper left

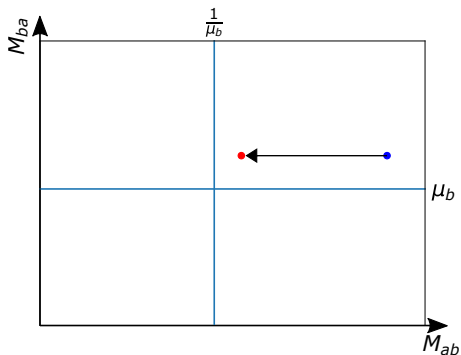


Black dots shows stable steady states, and hollow dots shows unstable steady states

Change in M

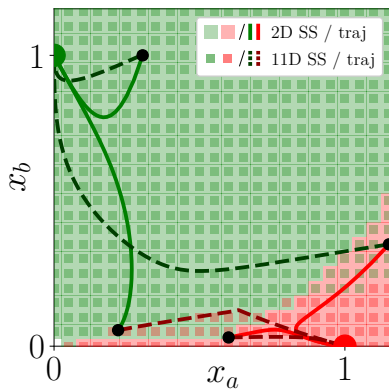


Microbial Phase Space

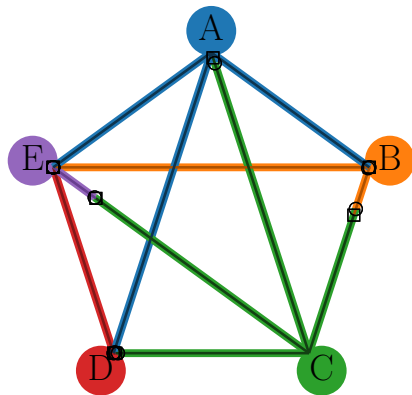


Parameter Space

Steady State Reduction(SSR)



Source: Jones and Carlson, arXiv:1808.01715



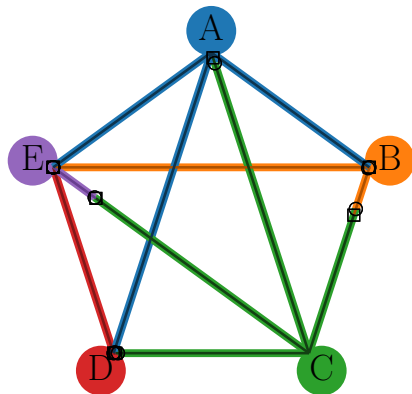
A-E: Steady states

Circle and square: Separatrices

Steady State Reduction(SSR)

$$\begin{aligned}\mu_\gamma &= \vec{\rho} \cdot \vec{y}_\gamma \\ M_{\gamma\delta} &= \vec{y}_\gamma^T K \vec{y}_\delta \\ \gamma, \delta &\in a, b\end{aligned}$$

- ▶ Simplify 11-D to 2-D
- ▶ Works well for Stein model



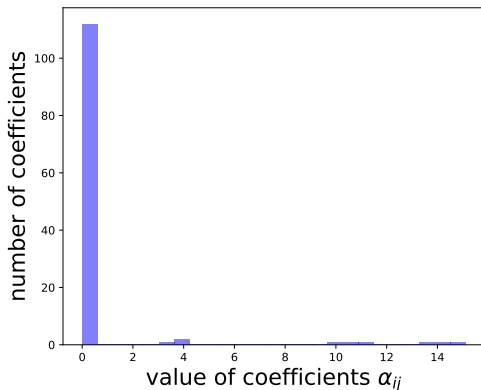
A-E: Steady states

Circle and square: Separatrices

Change in K

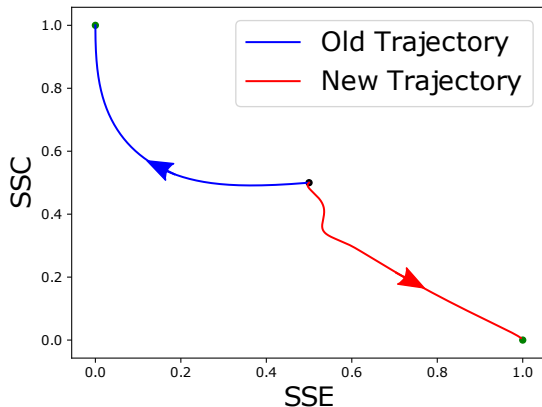
$$M_{ab} = \vec{y}_a^T K \vec{y}_b$$
$$= \sum_{i=1, j=1}^{11, 11} \alpha_{ij} K_{ij}$$

- ▶ 121 coefficients
- ▶ Most are 0
- ▶ M_{ab} most sensitive to change in k_{ij} with the largest α_{ij} coefficient



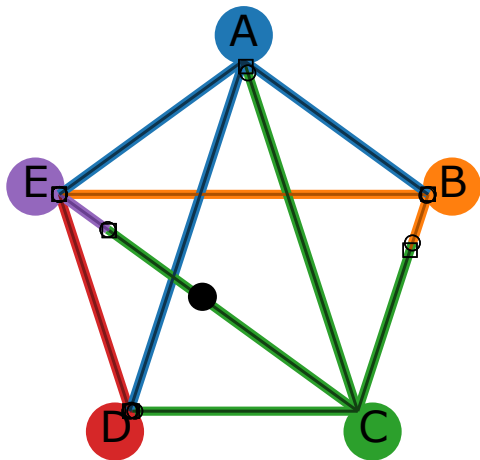
11-D Trajectory

- ▶ 11-D Trajectory projected to plane spanned by SSC and SSE
- ▶ It works!



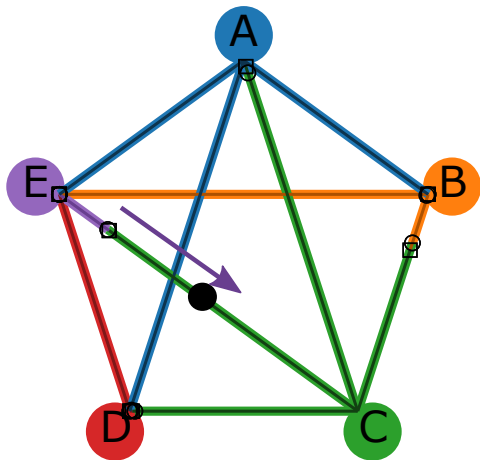
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Summary

- ▶ Reduce to 2-D; use bifurcation analysis to guide; project to 11-D
- ▶ Can be applied to other complex system with favorable and unfavorable steady states such as...
 - ▶ Gene regulatory networks
 - ▶ Neural networks
- ▶ Questions?