Bifurcation analysis of microbiome steady states

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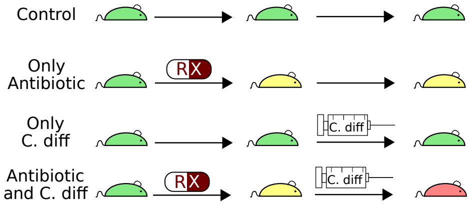
General Goal

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



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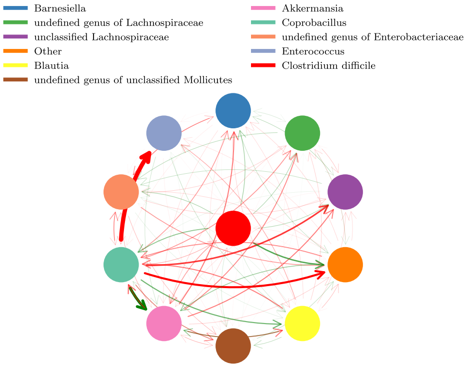
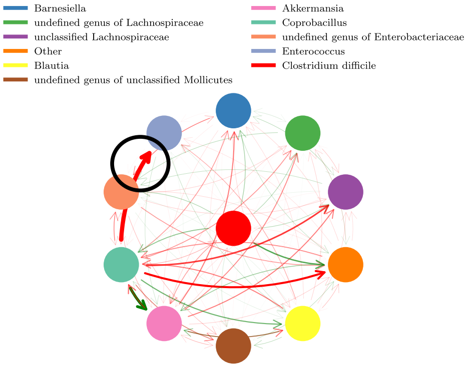


Source: Jones and Carlson, PLoS Comp. Biol. 2018

General Goal

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



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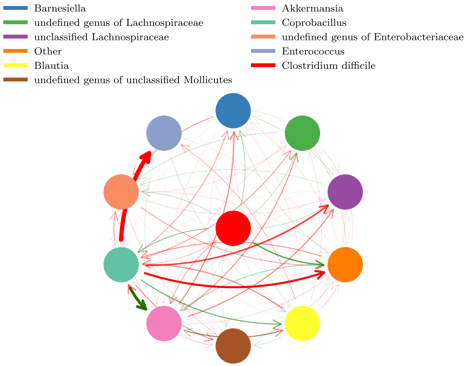
Stein Model

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



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Generalized Lotka-Volterra equations

Taylor Expansion:

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

N-species gLV Equations:

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

2D:

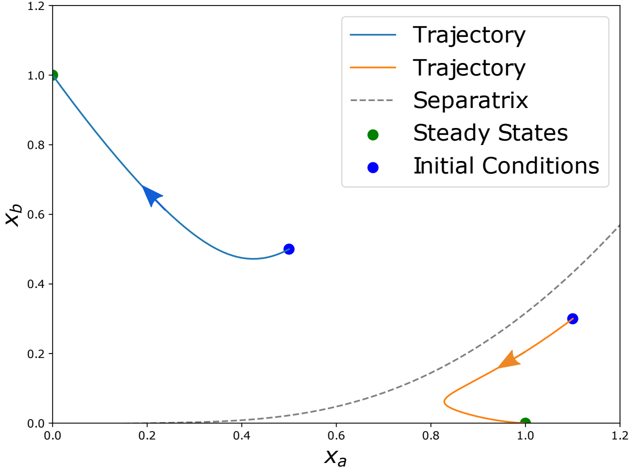
$$\begin{cases} \frac{dx_a}{dt} = \overbrace{\mu_a}^{\text{growth rate}} x_a - \overbrace{M_{aa} x_a^2 - M_{ab} x_a x_b}^{\text{interaction}} \\ \frac{dx_b}{dt} = \mu_b x_b - M_{ba} x_a x_b - M_{bb} x_b^2 \end{cases}$$

Dynamical Landscape

Equivalent form:

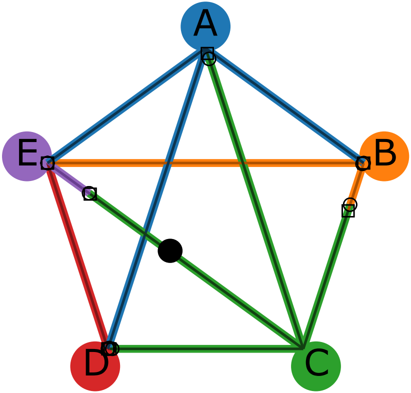
$$\begin{cases} \frac{dx_a}{dt} = x_a(1 - x_a - M_{ab}x_b) \\ \frac{dx_b}{dt} = x_b(\mu_b - M_{ba}x_a - x_b) \end{cases}$$

Taking $\mu_b = 1$:

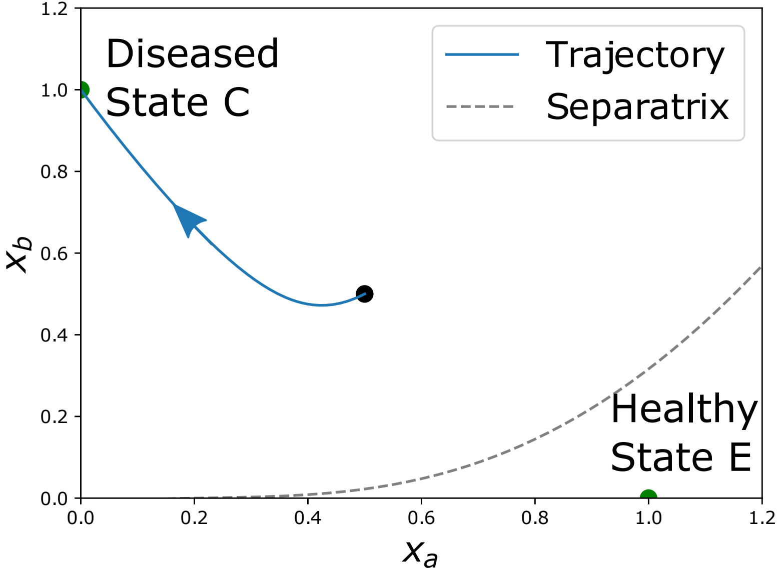


Project Goal

- 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

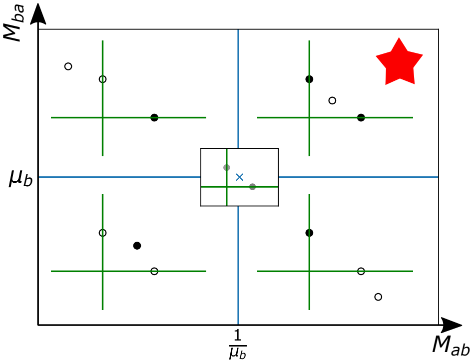


Original Trajectory



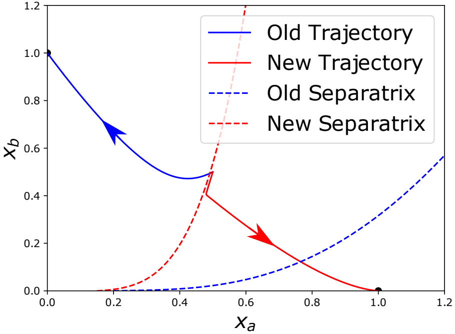
Bifurcation Analysis

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

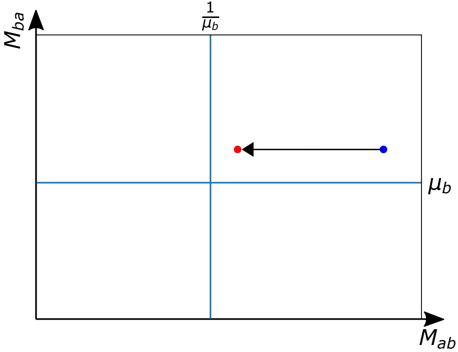


Black dots shows stable steady states, and hollow dots shows unstable steady states

Change in M

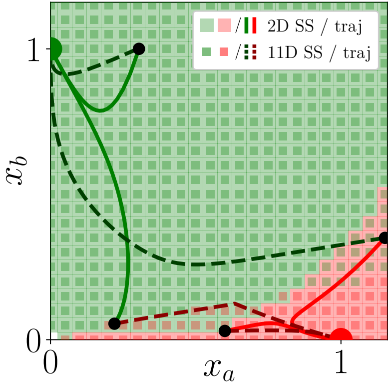


Microbial Phase Space

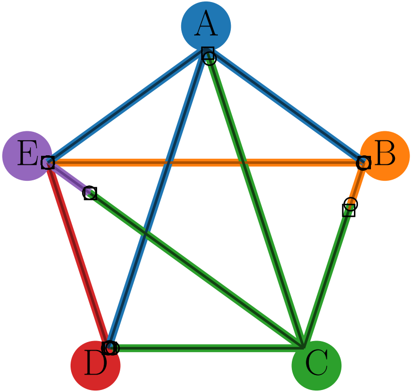


Parameter Space

Steady State Reduction(SSR)



Source: Jones and Carlson, arXiv:1808.01715

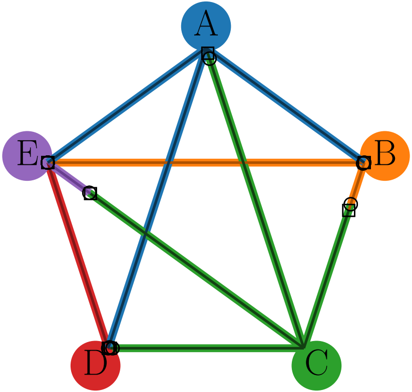


A-E: Steady states
Circle and square: Separatrices predicted by 11-D model and 2-D model

Steady State Reduction(SSR)

$$\mu_\gamma = \vec{\rho} \cdot \vec{y_\gamma}$$
$$M_{\gamma\delta} = \vec{y_\gamma}^T K \vec{y_\delta}$$
$$\gamma, \delta \in a, b$$

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

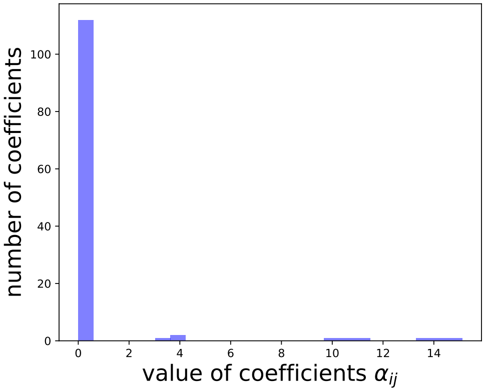


A-E: Steady states
Circle and square: Separatrices predicted by 11-D model and 2-D model

Change in K

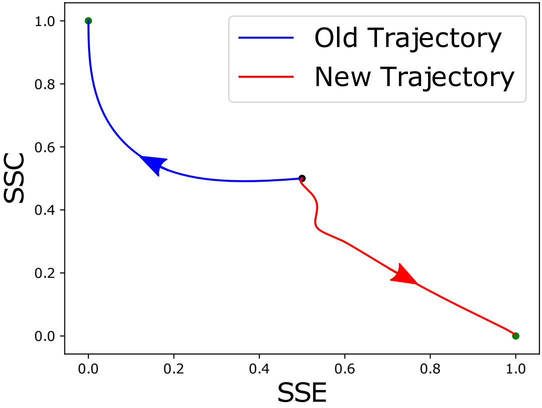
$$M_{ab} = \vec{y_a}^T K \vec{y_b}$$
$$= \sum_{i=1,j=1}^{11,11} \alpha_{ij} K_{ij}$$

- 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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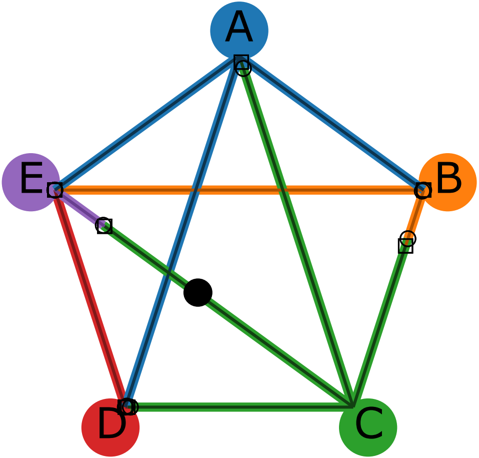

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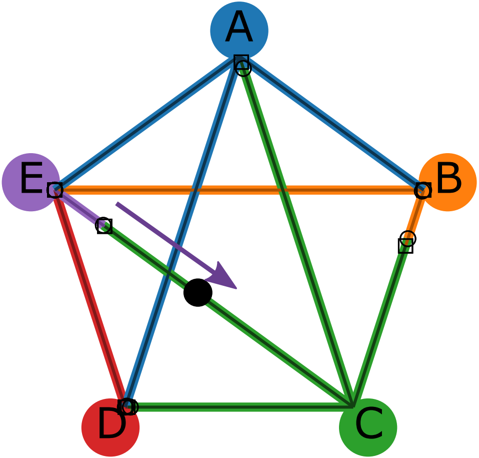

Summary

- 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?

Acknowledgement: Jean Carlson; Eric Jones; Josh Mueller