Bifurcation analysis of microbiome steady states

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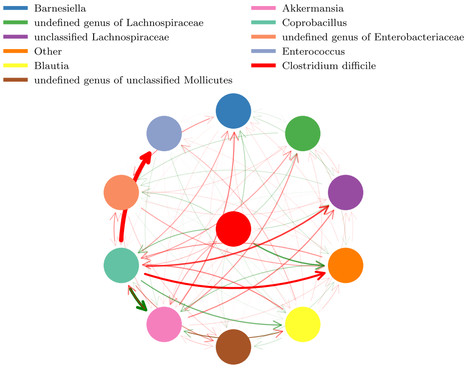
General Goal

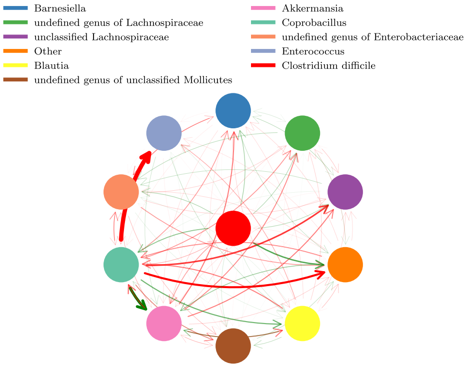
- Ecology $\leftrightarrow$ Microbiome
- Modify diseased states into healthy states
- Change microbial interactions



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

Stein Model

- 11 categories; 11-D vector
- Based on experiments
- Gives several steady states



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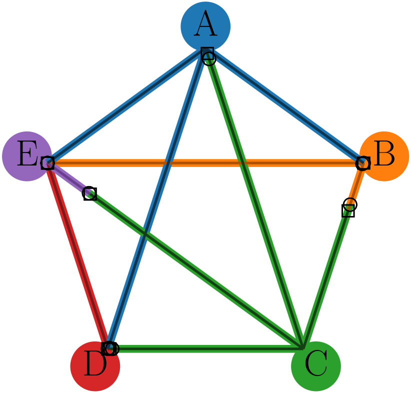


Generalized Lotka-Volterra equations

$$
\begin{aligned}
\frac{d\vec{y}}{dt} = f(\vec{y}) &\approx f(\vec{0}) + Df(\vec{0}) \cdot \vec{y} + \vec{y}^T \cdot Hf(\vec{0}) \cdot \vec{y} \\
\frac{d}{dt} y_i(t) &= y_i(t) \Big(\rho_i + \sum_{j=1}^{N} K_{ij} y_i(t) \Big)
\end{aligned}
$$

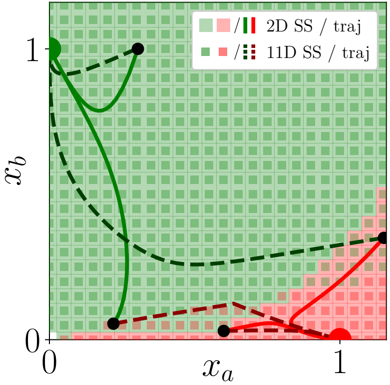
2D:

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

Nondimensionalization and Steady States

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

- Stable steady states at $(0, 1)$ and $(1, 0)$
- Separatrix: the line where color changes
- Unstable steady states on separatrix

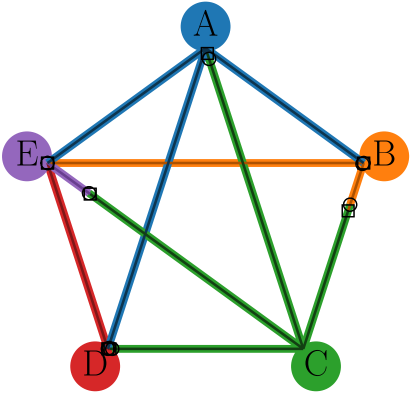


Source: Jones and Carlson, arXiv:1808.01715

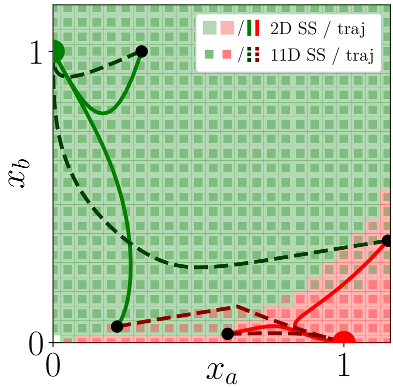
Steady State Reduction(SSR)

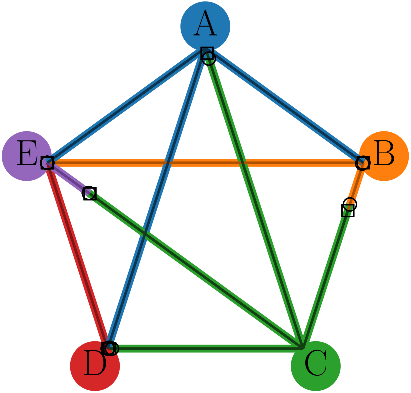
$$\mu_\gamma = \vec{\rho} \cdot \vec{y_\gamma}$$
$$M_{\gamma\delta} = \vec{y_\gamma}^T K \vec{y_\delta}$$
$$\gamma, \delta \in a, b$$

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



Steady State Reduction(SSR)





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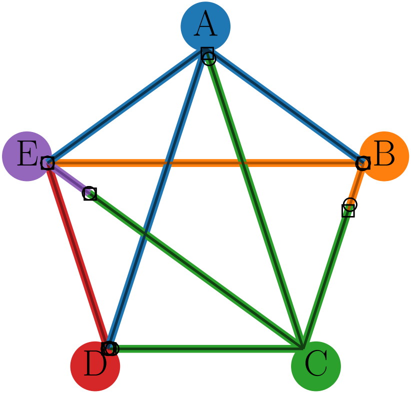
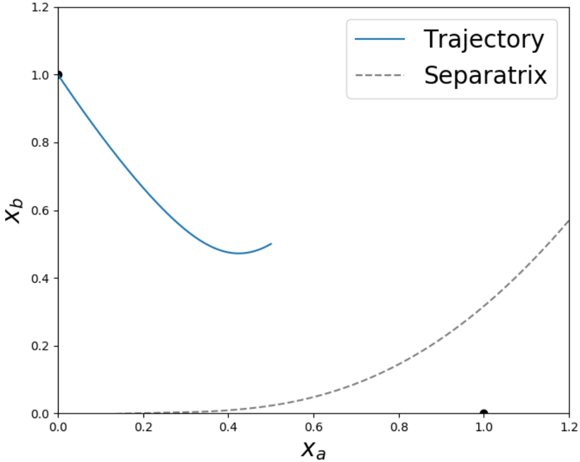
Project Goal

- Interested in steady states C and E
- Start at the middle point
- Using SSR to reduce K to M
- Modify interaction matrix M
- Changing system from C to E



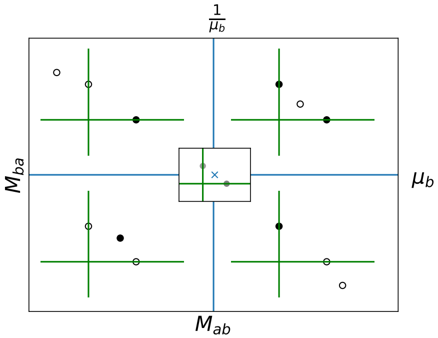
Original Trajectory



(1,0) shows steady state E, and (0,1) shows steady state C.

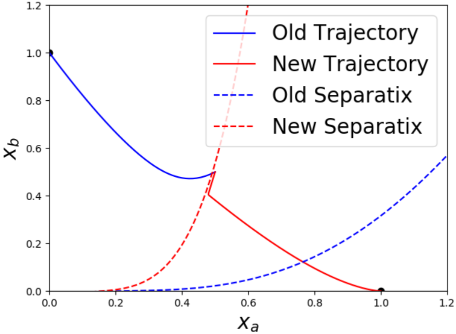
Bifurcation Analysis

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

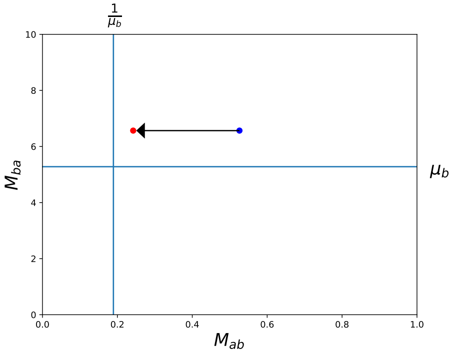


Black dots shows stable steady state, and hollowed dots shows unstable steady states.

Change in M



Old Trajectory
New Trajectory
Old Separatix
New Separatix
x_b
x_a
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0.0
0.2
0.4
0.6
0.8
1.0
1.2

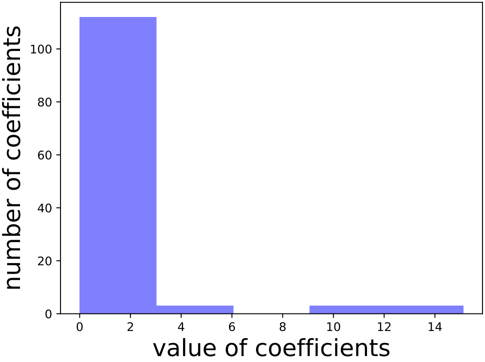


$\frac{1}{\mu_b}$
μ_b
M_{ba}
M_{ab}
10
8
6
4
2
0
0.0
0.2
0.4
0.6
0.8
1.0

Change in K

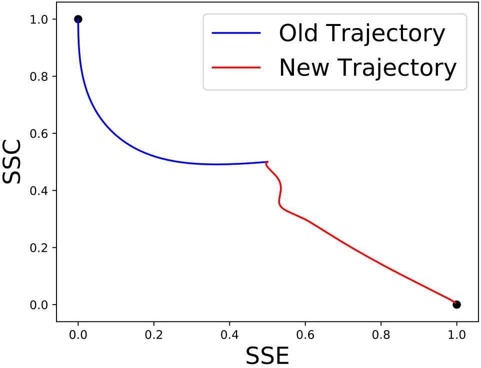
$$M_{ab} = \vec{y_a}^T K \vec{y_b}$$
$$= \sum_{1,1}^{11,11} \alpha_{ij} K_{ij}$$

- 121 coefficients
- Most are 0
- Change K using the large coefficient



11-D Trajectory

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



Summary

- Reduce to 2-D; Use bifurcation analysis to guide; project to 11-D
- Can be applied to any complex system where trying to switch steady states
- Gene regulatory network
- neural networks

Acknowledgement

Eric Jones
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