Bifurcation analysis of microbiome steady states

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General Goal

- Modify diseased states into healthy states
- Ecology ↔ Microbiome
- Change microbial interactions
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Source: Jones and Carlson, PLoS Comp. Biol. 2018
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- 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:

\[
\begin{cases}
\frac{dx_a}{dt} = \mu_a x_a - M_{aa} x_a^2 - M_{ab} x_a x_b \\
\frac{dx_b}{dt} = \mu_b x_b - M_{ba} x_a x_b - M_{bb} x_b^2
\end{cases}
\]

growth rate  interaction
Dynamical Landscape

Equivalent form:

\[
\begin{align*}
\frac{dx_a}{dt} &= x_a(1 - x_a - M_{ab}x_b) \\
\frac{dx_b}{dt} &= x_b(\mu_b - M_{ba}x_a - x_b)
\end{align*}
\]

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

Diseased State C

Healthy State E
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)

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

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

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

$$M_{ab} = y_a^T K y_b$$

$$= \sum_{i=1, j=1}^{11, 11} \alpha_{ij} K_{ij}$$

- 121 coefficients
- Most are 0
- $M_{ab}$ most sensitive to change in $k_{ij}$ with the largest $\alpha_{ij}$ coefficient
11-D Trajectory

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

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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?