

Graph Theory and Global Stability Problem in Heterogeneous Epidemic Models

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Simple Epidemic Models

n -Group Models

An n -Group SIR Model

Previous Results

Global-Stability and
Lyapunov Functions

Derivative of V

Choosing Constants v_k

The Matrix-Tree
Theorem

The Double Sum H_n

Main Results

Summary

Lyapunov functions

Kirchhoff Matrix-Tree
Theorem

Outline of Talk

Part I: Modeling Infectious Diseases in Heterogeneous Populations

- ▶ Simple epidemic models and their dynamics
- ▶ Basic reproduction number and the threshold theorem
- ▶ Multi-group models for heterogeneous populations

Part II: Global-Stability Problem in Multi-Group Models

- ▶ Global-stability problem and Lyapunov functions
- ▶ A Lyapunov function for multi-group models
- ▶ Why is global-stability difficult to prove?

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Part II: Global-Stability Problem in Multi-Group Models

- ▶ Global-stability problem and Lyapunov functions
- ▶ A Lyapunov function for multi-group models
- ▶ Why is global-stability difficult to prove?

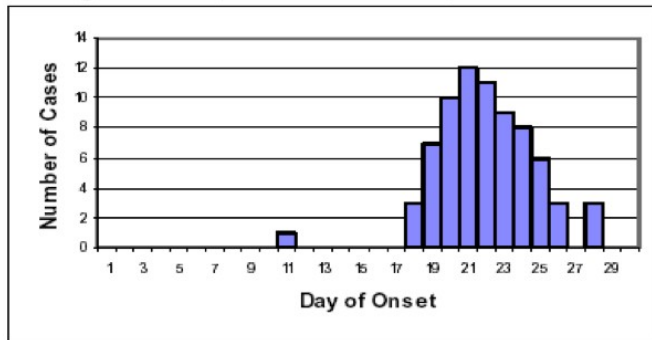
Part III: Matrix-Tree Theorem in Graph Theory

- ▶ Rooted directed trees and unicyclic graphs
- ▶ Kirchhoff's Matrix-Tree Theorem

Part IV: How do all of these come together?

- ▶ Global-stability result for multi-group models.
- ▶ A general theorem

How to Model an Epidemic?

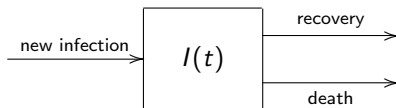


An Epidemic Curve

Graph Theory and Global Stability Problem in Heterogeneous Epidemic Models

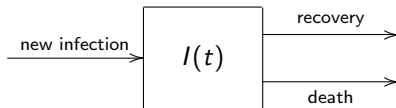
Simple Epidemic Models

How to Model an Epidemic?



$$\begin{aligned} I'(t) &= \boxed{\text{Incidence Rate}} - \boxed{\text{Recovery Rate}} - \boxed{\text{Death Rate}} \\ &= f(I(t), S(t), N(t)) - \gamma I(t) - d I(t) \end{aligned}$$

How to Model an Epidemic?



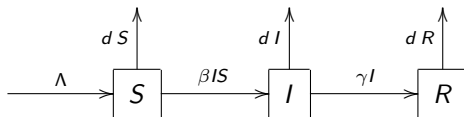
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$$f(I, S, N) = \beta I S : \quad \text{bilinear incidence}$$

$$f(I, S, N) = \lambda \frac{I S}{N} : \quad \text{proportionate incidence}$$

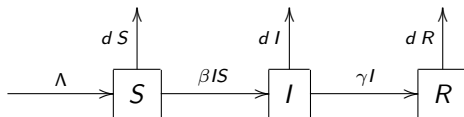
A Single-Group SIR Model

S : Susceptibles I : Infectious R : *Removed*



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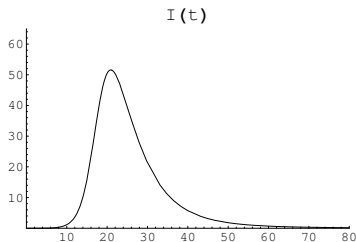


$$S' = \Lambda - \beta I S - d S$$

$$I' = \beta I S - (\gamma + d) I$$

$$R' = \gamma I - d R$$

A Single-Group SIR Model



Numerical output I: epidemic case

Simple Epidemic Models

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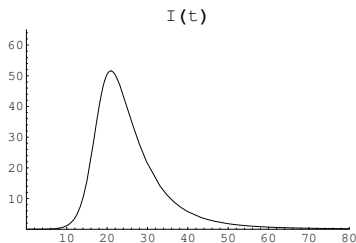
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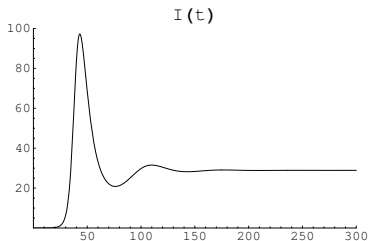
[Lyapunov functions](#)

[Kirchhoff Matrix-Tree
Theorem](#)

A Single-Group SIR Model



Numerical output I: epidemic case



Numerical output II: endemic case

Threshold Theorem

The **basic reproduction number** is

$$R_0 = \frac{\beta \Lambda}{(\gamma + d)d} = \beta \cdot \frac{1}{\gamma + d} \cdot \frac{\Lambda}{d}$$

The average secondary infections produced by a single infective during its entire infectious period.

Threshold Theorem

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The average secondary infections produced by a single infective during its entire infectious period.

Theorem (Threshold Theorem)

- (1) If $R_0 \leq 1$, then the disease-free equilibrium $P_0 = (\Lambda/d, 0)$ is stable and attracts all solutions in R_+^2 .
- (2) If $R_0 > 1$, then P_0 is unstable, and a unique endemic (positive) equilibrium P^* is stable and attracts all positive solutions in R_+^2 .

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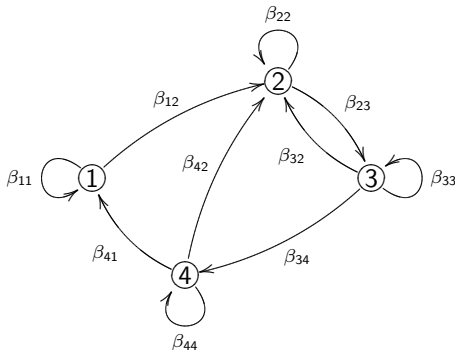
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Proof uses the Poincaré-Bendixson theory for 2d systems.

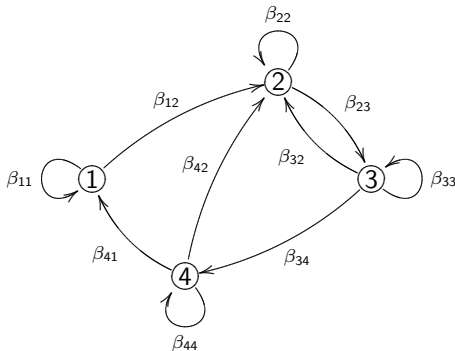
n -Group Models for Heterogeneous Populations



Each circled number represents a homogeneous group.

β_{jk} : transmission coefficient between I_j and S_k .

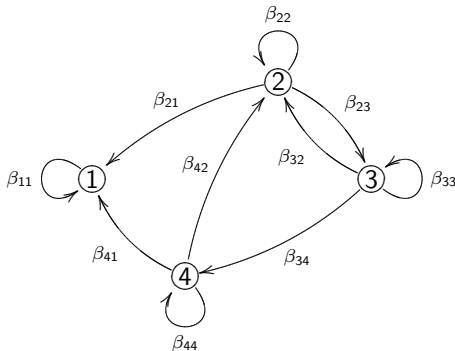
n -Group Models for Heterogeneous Populations



$$B = \begin{bmatrix} \beta_{11} & \beta_{12} & 0 & 0 \\ 0 & \beta_{22} & \beta_{23} & 0 \\ 0 & \beta_{32} & \beta_{33} & \beta_{34} \\ \beta_{41} & \beta_{42} & 0 & \beta_{44} \end{bmatrix}$$

Transmission Matrix B is **irreducible**.

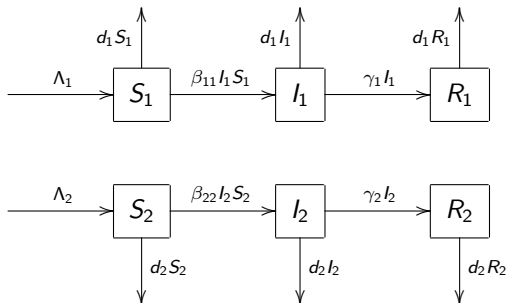
n -Group Models for Heterogeneous Populations



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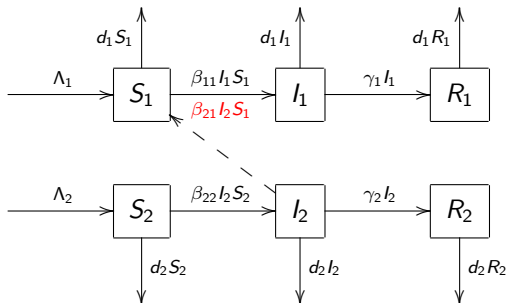
A Two-Group SIR Model



Incidence terms (bilinear):

- ▶ Group 1: $\beta_{11} I_1 S_1$
- ▶ Group 2: $\beta_{22} I_2 S_2$

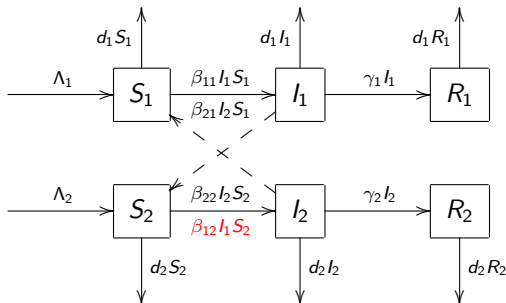
A Two-Group SIR Model



Incidence terms (bilinear):

- ▶ Group 1: $\beta_{11} I_1 S_1 + \beta_{21} I_2 S_1$
- ▶ Group 2: $\beta_{22} I_2 S_2$

A Two-Group SIR Model



Incidence terms (bilinear):

- ▶ Group 1: $\beta_{11} I_1 S_1 + \beta_{21} I_2 S_1$
- ▶ Group 2: $\beta_{22} I_2 S_2 + \beta_{12} I_1 S_2$

An n -Group SIR Model

$$\begin{cases} S'_k = \Lambda_k - d_k S_k - \sum_{j=1}^n \beta_{jk} I_j S_k, \\ I'_k = \sum_{j=1}^n \beta_{jk} I_j S_k - (d_k + \gamma_k) I_k, \end{cases} \quad k = 1, \dots, n.$$

Mathematical Questions:

- If $R_0 > 1$, is P^* unique?

An n -Group SIR Model

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Mathematical Questions:

- ▶ If $R_0 > 1$, is P^* unique?
- ▶ When P^* is unique, is it globally stable?

Previous Results on GAS of P^*

For Models using **bilinear incidence**:

- Lajmanovich and Yorke (1976)
 - ▶ n -group SIS model, by Lyapunov function
 - ▶ later extended by Nold, Hirsch
- Hethcote (1975)
 - ▶ n -group SIR model with no vital dynamics
- Thieme (1983)
 - ▶ n -group SEIRS model, small latent and immune periods
- Beretta and Capasso (1986)
 - ▶ n -group SIR model, constant group sizes
- Lin and So (1993)
 - ▶ n -group SIRS model, constant group sizes
 - ▶ β_{ij} ($i \neq j$) small

Non-uniqueness of P^* when $R_0 > 1$

- ▶ Lin (1992)
 n -group model for HIV
- ▶ Huang, Cooke, Castillo-Chavez (1992)
 n -group model for HIV with delay

These models use **proportionate incidence**.

Global-Stability and Lyapunov Functions

Consider a general system of ODE

$$x' = F(x), \quad x \in D \subset \mathbb{R}^d.$$

\bar{x} is an **equilibrium** if $F(\bar{x}) = 0$.

An equilibrium \bar{x} is globally stable in D if it is locally stable and all solutions in D converge to \bar{x} as $t \rightarrow \infty$.

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Global-Stability and Lyapunov Functions

Theorem (Lyapunov)

Suppose \exists a Lipschitz function $V(x)$ such that

$$(1) \quad V(x) \geq V(\bar{x}) \text{ and } V(x) = V(\bar{x}) \iff x = \bar{x}.$$

$$(2) \quad \begin{aligned} &V^*(x) = \nabla V(x) \cdot F(x) \leq 0, \quad x \in D, \text{ and} \\ &V^*(x) = 0 \iff x = \bar{x}. \end{aligned}$$

Then \bar{x} is globally stable in D .

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$$\overset{*}{V}(x) = 0 \iff x = \bar{x}.$$

Then \bar{x} is globally stable in D .

$V(x(t))$ strictly decreasing along a solution $x(t)$

Constructing a Lyapunov Function for the n -Group Model

Consider a candidate

$$V = \sum_{k=1}^n v_k \left[\underbrace{(S_k - S_k^* \ln S_k) + (I_k - I_k^* \ln I_k)}_{\text{A Lyapunov function for a single-group model}} \right]$$

Constructing a Lyapunov Function for the n -Group Model

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Choose appropriate v_k so that $V(x)$ is negative definite.

Derivative of V

$$V' = \sum_{k=1}^n v_k \left[(S'_k - \frac{S_k^*}{S_k} S'_k) + (I'_k - \frac{I_k^*}{I_k} I'_k) \right]$$

Derivative of V

$$\begin{aligned} V' &= \\ & \sum_{k=1}^n v_k \left[(S'_k - \frac{S_k^*}{S_k} S'_k) + (I'_k - \frac{I_k^*}{I_k} I'_k) \right] \\ &= \sum_{k=1}^n v_k \left[d_k S_k^* \left(2 - \frac{S_k^*}{S_k} - \frac{S_k}{S_k^*} \right) \right] \\ &+ \sum_{k=1}^n v_k \left[\sum_{j=1}^n \beta_{jk} S_k^* I_j - (d_k + \gamma_k) I_k \right] \\ &+ \sum_{j,k=1}^n v_k \beta_{kj} I_k^* S_j^* \left(2 - \frac{S_j^*}{S_j} - \frac{S_j}{S_j^*} \frac{I_j}{I_j^*} \frac{I_k^*}{I_k} \right) \end{aligned}$$

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Choosing Constants v_k

Choose v_k so that

$$\sum_{k=1}^n v_k \left[\sum_{j=1}^n \beta_{jk} S_k^* I_j - (d_k + \gamma_k) I_k \right] \equiv 0$$

for all $I_1, \dots, I_n > 0$.

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$$\begin{bmatrix} \beta_{11} I_1^* S_1^* & \cdots & \beta_{n1} I_n^* S_1^* \\ \vdots & \ddots & \vdots \\ \beta_{1n} I_1^* S_n^* & \cdots & \beta_{nn} I_n^* S_n^* \end{bmatrix} \begin{bmatrix} v_1 \\ \vdots \\ v_n \end{bmatrix} = \begin{bmatrix} \sum_{j=1}^n \beta_{j1} I_j^* S_1^* v_1 \\ \vdots \\ \sum_{j=1}^n \beta_{jn} I_j^* S_n^* v_n \end{bmatrix}$$

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since, at P^* ,

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Set $\bar{\beta}_{jk} = \beta_{jk} I_j^* S_k^*$. Then (v_1, \dots, v_k) are determined by the linear system

$$\begin{bmatrix} \sum_{l \neq 1} \bar{\beta}_{1l} & -\bar{\beta}_{21} & \cdots & -\bar{\beta}_{n1} \\ -\bar{\beta}_{12} & \sum_{l \neq 2} \bar{\beta}_{2l} & \cdots & -\bar{\beta}_{n2} \\ \vdots & \vdots & \ddots & \vdots \\ -\bar{\beta}_{1n} & -\bar{\beta}_{2n} & \cdots & \sum_{l \neq n} \bar{\beta}_{nl} \end{bmatrix} \begin{bmatrix} v_1 \\ \vdots \\ v_n \end{bmatrix} = \begin{bmatrix} 0 \\ \vdots \\ 0 \end{bmatrix}$$

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The solution space is 1d and a basis is given by

$v_k = C_{kk}$, the k -th principal minor, $k = 1, \dots, n$.

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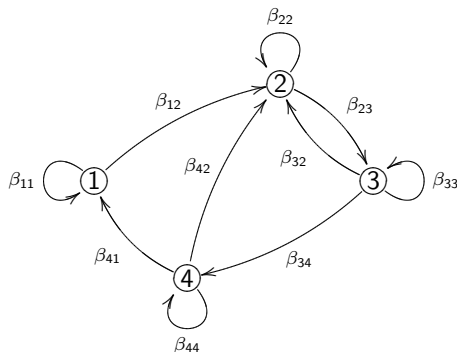
Need to show

$$V' \leq H_n = \sum_{j,k=1}^n v_k \bar{\beta}_{kj} \left(2 - \frac{S_j^*}{S_j} - \frac{S_j}{S_j^*} \frac{I_j}{I_j^*} \frac{I_k^*}{I_k} \right) \leq 0,$$

for all $S_1, I_1, \dots, S_n, I_n \geq 0$.

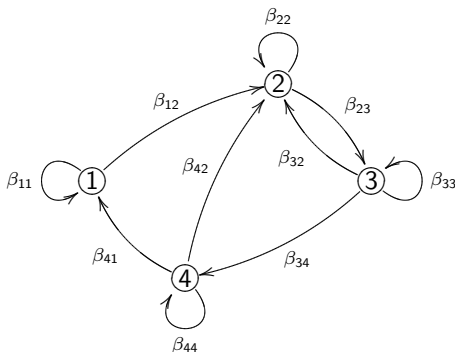
Directed Graphs and Rooted Spanning Trees

Let G be a directed graph with vertex set $V(G) = \{1, \dots, n\}$ and weight matrix $B = (\beta_{ij})_{n \times n}$.



Directed Graphs and Rooted Spanning Trees

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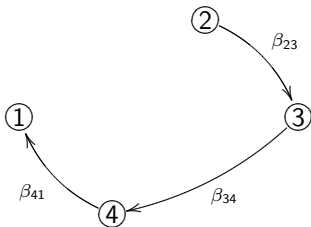


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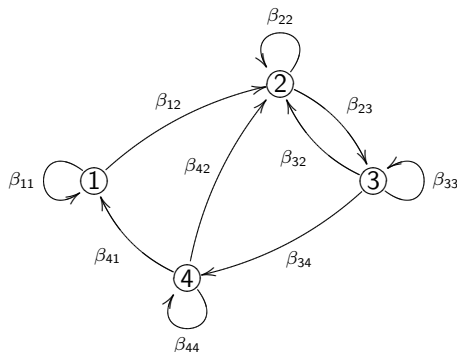
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The Matrix-Tree Theorem

Let $B = (\bar{\beta}_{ij})_{n \times n}$ be the weight matrix of graph G .

The **Kirchhoff Matrix** (combinatorial Laplacian) of B is

$$\bar{B} = \begin{bmatrix} \sum_{l \neq 1} \bar{\beta}_{1l} & -\bar{\beta}_{21} & \cdots & -\bar{\beta}_{n1} \\ -\bar{\beta}_{12} & \sum_{l \neq 2} \bar{\beta}_{2l} & \cdots & -\bar{\beta}_{n2} \\ \vdots & \vdots & \ddots & \vdots \\ -\bar{\beta}_{1n} & -\bar{\beta}_{2n} & \cdots & \sum_{l \neq n} \bar{\beta}_{nl} \end{bmatrix}.$$

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Theorem (Matrix Tree Theorem, Kirchhoff 1847)

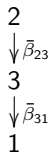
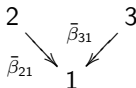
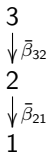
$$C_{kk} = \sum_{T \in \mathbb{T}_k} w(T).$$

\mathbb{T}_k : The set of spanning trees rooted at vertex k .

Solving System $\bar{B} v = 0 : n = 3$

$$v_1 = C_{11} = \sum_{T \in \mathbb{T}_1} w(T) = \bar{\beta}_{32}\bar{\beta}_{21} + \bar{\beta}_{21}\bar{\beta}_{31} + \bar{\beta}_{23}\bar{\beta}_{31}$$

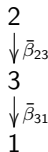
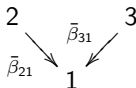
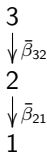
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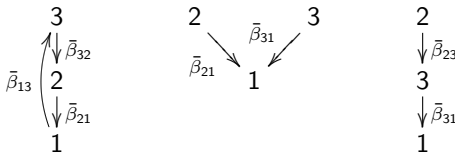
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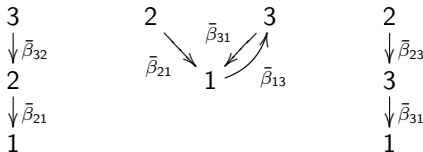
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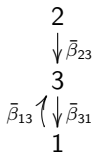
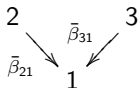
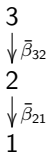
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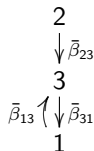
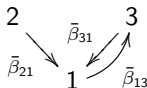
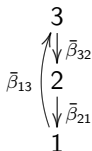
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Each product is the weight of a **unicyclic graph** with a cycle of length $1 \leq r \leq 3$.

Unicyclic Graphs and Rooted Trees

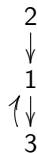
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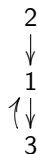
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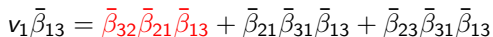


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Graph Theory and Global Stability Problem in Heterogeneous Epidemic Models

The Matrix-Tree Theorem



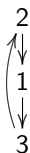
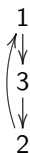
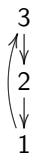
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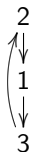
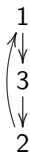
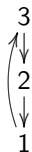


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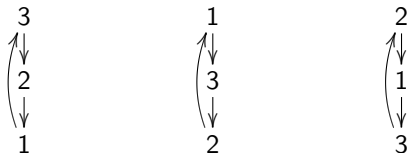


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$$V' \leq H_n = \sum_{j,k=1}^n v_k \bar{\beta}_{kj} \left(2 - \frac{S_j^*}{S_j} - \frac{S_j}{S_j^*} \frac{I_j}{I_j^*} \frac{I_k^*}{I_k} \right)$$

H_n is Summed over all Unicyclic Graphs

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Finally, because C_Q is a cycle,

$$\prod_{(p,q) \in E(C_Q)} \frac{S_p^*}{S_p} \cdot \frac{S_p}{S_p^*} \cdot \frac{I_p}{I_p^*} \cdot \frac{I_q^*}{I_q} = \prod_{(p,q) \in E(C_Q)} \frac{I_p}{I_p^*} \cdot \frac{I_q^*}{I_q} = 1.$$

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Main Result

For the n -group SIR model with bilinear incidence,

Theorem (Guo, Li, Shuai, 2007)

Assume that transmission matrix B is irreducible.

If $R_0 > 1$, then P^ is unique and is globally stable in R_+^{2n} .*

The same graph-theoretical approach can be used to:

Build Lyapunov function V for a large-scale system

$$V = \sum_{k=1}^n c_k V_k$$

using the known Lyapunov function V_k for each component.

Construction of Lyapunov Functions for Complex Networks

Given a coupled system over a digraph \mathcal{G} :

$$u_i' = f_i(t, u_i) + \sum_{j=1}^n g_{ij}(t, u_i, u_j), \quad i = 1, 2, \dots, n. \quad (1)$$

Assume: Each vertex system $u_i' = f_i(t, u_i)$ has a global Lyapunov function V_i .

Question: How to construct a global Lyapunov function for the coupled system?

A simple idea: For $u = (u_1, \dots, u_n)$, try

$$V(u) = \sum_{i=1}^n c_i V_i(u_i)$$

and find suitable constants c_i .

A New Result

Theorem [Z. Shuai and ML, 2009] Assume

- (1) There exist $F_{ij}(t, u)$ such that, for $t > 0, u \in D$,

$$\dot{V}_i(u) \leq \sum_{j=1}^n a_{ij} F_{ij}(t, u). \quad (2)$$

Let \mathcal{G}_A be the weighted graph with weight matrix $A = (a_{ij})$.

- (2) $\{F_{ij}(t, u)\}$ satisfies the following **cycle condition**: along each directed cycle \mathcal{C} of graph \mathcal{G}_A ,

$$\sum_{(r,s) \in E(\mathcal{C})} F_{rs}(t, u) \leq 0, \quad t > 0, u \in D. \quad (3)$$

Then there exist constants $c_i \geq 0$ such that

$$V(u) = \sum_{i=1}^n c_i V_i(u)$$

satisfies

$$\dot{V}(u) \leq 0, \quad u \in D_1 \times \cdots \times D_n.$$

Kirchhoff Matrix-Tree Theorem

Let \mathcal{G}_A be a weighted digraph with weight matrix $A = (a_{ij})$.
The **Laplacian matrix** of graph \mathcal{G}_A is

$$L = \begin{bmatrix} \sum_{k \neq 1} a_{1k} & -a_{12} & \cdots & -a_{1n} \\ -a_{21} & \sum_{k \neq 2} a_{2k} & \cdots & -a_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ -a_{n1} & -a_{n2} & \cdots & \sum_{k \neq n} a_{nk} \end{bmatrix}.$$

Let c_i be the **cofactor** of the i -th diagonal element of L .

Matrix-Tree Theorem [Kirchhoff (1847)] Assume $n \geq 2$. Then

$$c_i = \sum_{\mathcal{T} \in \mathbb{T}_i} w(\mathcal{T}), \quad i = 1, 2, \dots, n, \quad (4)$$

where \mathbb{T}_i is the set of all spanning trees \mathcal{T} of \mathcal{G}_A rooted at vertex i , and $w(\mathcal{T})$ is the **weight** of \mathcal{T} .

The Tree-Cycle Identity

Tree-Cycle Identity (Z. Shuai and ML, 2009) Let c_i be given by the Matrix-Tree Theorem. Then the following identity holds.

$$\sum_{i,j=1}^n c_i a_{ij} F_{ij}(x) = \sum_{Q \in \mathcal{Q}} w(Q) \sum_{(r,s) \in E(\mathcal{C}_Q)} F_{rs}(x), \quad (5)$$

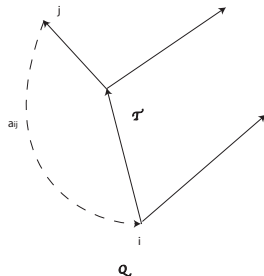
where $F_{ij}(x)$, $1 \leq i, j \leq n$, are arbitrary functions, \mathcal{Q} is the set of all spanning unicyclic graphs Q of \mathcal{G}_A , $w(Q)$ is the weight of Q , and \mathcal{C}_Q denotes the oriented cycle of Q .

The Tree-Cycle Identity

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Proof: Note $w(\mathcal{T}) a_{ij} = w(Q)$,

where Q is the unicyclic graph obtained by adding an arc (j, i) to \mathcal{T} .

Proof of Main Theorem

Let

$$V = \sum_{i=1}^n c_i V_i.$$

Choose c_i as in the Matrix-Tree Theorem

$$c_i = \sum_{\mathcal{T} \in \mathbb{T}_i} w(\mathcal{T}), \quad i = 1, 2, \dots, n.$$

Then

$$\begin{aligned} \dot{V} &= \sum_{i=1}^n c_i \dot{V}_i \leq \sum_{i,j=1}^n c_i a_{ij} F_{ij}(u) \quad (\text{assumption (1)}) \\ &= \sum_{Q \in \mathcal{Q}} w(Q) \sum_{(r,s) \in E(\mathcal{C}_Q)} F_{rs}(u) \quad (\text{Tree-Cycle Identity}) \\ &\leq 0. \end{aligned}$$

Our Theorem offers a systematic way to construct global Lyapunov functions for complex networks, utilizing individual Lyapunov functions for the vertex systems.

Thank you!

Simple Epidemic Models

n-Group Models

An *n*-Group SIR Model

Previous Results

Global-Stability and
Lyapunov Functions

Derivative of V

Choosing Constants v_k

The Matrix-Tree
Theorem

The Double Sum H_n

Main Results

Summary

Lyapunov functions

**Kirchhoff Matrix-Tree
Theorem**