2022

Population Persistence and Disease Invasion in Heterogenous Networks

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POPULATION PERSISTENCE AND DISEASE INVASION IN HETEROGENOUS NETWORKS

by

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A dissertation submitted in partial fulfilment of the requirements
for the degree of Doctor of Philosophy
in the Department of Mathematics
in the College of Sciences
at the University of Central Florida
Orlando, Florida

Fall Term
2022

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ABSTRACT

The problem of understanding how biological species and infectious diseases can persist and spread in heterogeneous networks has brought a wide attention, recently highlighted due to the COVID-19 pandemic. This dissertation investigates the connection between the structures of heterogeneous networks and population persistence/disease invasion. To do so, we propose a new index for network heterogeneity by employing the Laplacian matrix of population dispersal and its corresponding group inverse. The network growth rate and reproduction number can be evaluated using the network average and the network heterogeneity index as the first and second order approximation, respectively. We also illustrate the impact of arrangement of ecological sources/sinks and disease hotspots/non-hotspots, which highlights the significance of the network structures on population persistence and disease invasion in heterogeneous environments.

Mathematically, population and disease control strategies can be modeled via altering certain ecological and epidemiological parameters in the biological processes. To quantitatively measure the scale of the change in need, new indices and methods are introduced and developed to generalize the existing threshold parameters. Properties and implications of these are provided to demonstrate the applicability to infectious disease controls such as anthrax, cholera and Zika virus.

ACKNOWLEDGMENTS

This voyage would not have been possible without the help and support I received from my advisor, mentors, friends and family.

First and foremost, I would like to express my deepest gratitude to my Ph.D. advisor Dr. Zhisheng Shuai, who made this journey possible for me. His vision, guidance and continual support have been a great source of inspiration for me through all these years. He has helped me to develop my critical thinking and research skills. It was such a great privilege to work and study under his supervision. I would also like to thank my committee members, Dr. Joseph Brennan, Dr. Zuhair Nashed, Dr. Andrew Nevai and Dr. David Jenkins, whose kindness and support made my thesis defense smooth and enjoyable. I am grateful for their input and comments.

I would like to extend my appreciation to Dr. Alina Stefanov, Dr. Carlos Borges and Dr. Rachid Ait Maalem Lahcen, for their support and advice when needed the most.

A special thanks to Ms. Doreen Goulding and Ms. Norma Robles for helping me throughout the years.

I would like to take this opportunity to thank my great friends Armina Khajavi Rad (friend of more than 20 years), Farnaz Navid, Thialita Moura do Nascimento, Pan Pan Chen and several others who have brought many joyful moments to my life.

Finally, and most importantly, I would like to thank my amazing family: my wonderful mother, Maryam and my brothers, Arash and Ario for teaching me the power of kindness, forgiveness and courage. I would like to send my special thanks to my supportive husband Lance, whose constant encouragements motivated me to pursue my dreams.

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CHAPTER 1: INTRODUCTION

The network structure is a fundamental tool for understanding complex problems from disciplines like biology, economics, engineering, physics and public health. For this reason, the network structures have attracted a lot of attention over the past two decades. Mathematically, a network is referred to as a graph described as a collection of vertices (nodes) and directed edges. Vertices represent individuals, devices, cities, countries, etc. Directed edges represent connections and relationships between the vertices. Some real world examples of networks include the Internet, airline networks, food webs, and social networks. Due to the size and dynamics of such networks an alternation might not occur simultaneously throughout the network and thus heterogeneity appears. Theoretically, a network is considered strongly connected if there is always a path between any two pair of vertices. This dissertation mainly investigates networks of individual movements in a spatially heterogeneous environment and the impact of their network structures on population persistence in ecological models and disease spread in epidemiological models.

Theoretical foundations for population biology and mathematical epidemiology are rooted from mathematical modelling and their model analyses using theories of differential equations, dynamical systems, matrix and linear algebra. Specifically, the linearization at a trivial (or a semi-trivial) equilibrium for population models in a heterogeneous network often yields a Jacobian matrix in the form of

$$J = Q - \mu L, \tag{1.1}$$

where $Q = \mathrm{diag}\{q_i\}$ is a diagonal matrix encoding within-patch (vertex) population dynamics, $\mu > 0$ is a parameter representing the movement rate in the heterogeneous network, and L is a Laplacian matrix containing all movements in the network. Specifically, L takes the following

form

$$L = \begin{pmatrix} \sum\limits_{j\neq 1} a_{j1} & -a_{12} & \cdots & -a_{1n} \\ -a_{21} & \sum\limits_{j\neq 2} a_{j2} & \cdots & -a_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ -a_{n1} & -a_{n2} & \cdots & \sum\limits_{j\neq n} a_{jn} \end{pmatrix}.$$

The off-diagonal entry (i, j) of L is the opposite of a_{ij}, representing the movement coefficient constant from patch j to patch i. Each diagonal entry of L tracks all the out-moving terms from the patch and thus each column sum of L equals zero. As a consequence, L is singular and has an eigenvalue 0.

The studies for population persistence and disease invasion in heterogeneous networks are often converted to the stability problem of a certain Jacobian matrix in the form of (1.1). That is, if the spectral bound of J, denoted as $r = s(J)$, is negative, then the population (disease) dies out; whereas, if it is positive, then the population (disease) persists.

However, the eigenvalue problems of such a matrix are extremely challenging due to the high dimension, heterogeneity and complex network structures. Prior studies have been focused on some special cases, e.g., for low dimension ($n = 2$ or 3), assuming homogeneity ($q_1 = q_2 = \cdots = q_n$), or symmetric movement in the network ($L = L^\top$).

In this dissertation, we provide a new expansion formula for the spectral bound of the matrix in the form of (1.1) as

$$r = s(J) = \mathcal{A} + \frac{1}{\mu}\mathcal{H} + o\big(\frac{1}{\mu}\big), \tag{1.2}$$

with the *network average*

$$\mathcal{A} := \sum_{i=1}^{n} \theta_i q_i,$$

and the *network heterogeneity index*

$$\mathcal{H} := \sum_{i=1}^{n}\sum_{j=1}^{n} q_i \ell_{ij}^{\#} q_j \theta_j.$$

Here, $\theta = (\theta_1, \ldots, \theta_n)^\top$ is the normalized right eigenvector of L corresponding to eigenvalue 0 and $L^{\#} = [\ell_{ij}^{\#}]$ is the group inverse of L. For the symmetric network (i.e., $L = L^\top$), $\theta = (1, \ldots, 1)^\top$ and thus the network average becomes the normal average. We have also proved the monotonicity and convexity of r in terms of μ. Specifically, the following inequalities hold

$$\mathcal{A} = \sum_{i=1}^{n} q_i \theta_i \leq r = s(J) \leq \max_i\{q_i\},$$

with the upper and lower bounds achieved when $\mu \to 0$ and $\mu \to +\infty$, respectively. For the homogeneous landscape (i.e., $q_i = q$ for all i), the upper bound and lower bound are equal and thus $r = s(J) = q$, irregardless of movement among patches.

When applying these new results to infectious disease models, we have obtained analogous results for the basic reproduction number R_0, which determines whether an infectious disease can invade and spread in a host population. Our results provide answers for several open problems in the field of mathematical epidemiology.

We have demonstrated the applicability of our results to various ecological and epidemiological models, and also to different network structures. In order to control population persistence and disease invasion, we develop new approaches for controlling spectral bounds and R_0, respectively. Applications have been illustrated using well-known biological models in the literature.

Due to the generality and applicability of theoretical results developed in the dissertation, it is highly expected that further applications will likely be seen in ecology, epidemiology, engineering and other science branches.

CHAPTER 2: POPULATION PERSISTENCE AND NETWORK HETEROGENEITY

The objective of this chapter is to provide a new expansion formula for the spectral bound of the matrix $J = Q - \mu L$ as defined in (1.1), which often arises in spatial population models. The main tool to establishing the expansion comes from the analytic perturbation theory (Section 2.2). In the new expansion derived, the first order term can be regarded as the network average while the second order is described as the network heterogeneity index (Section 2.3). Applications to ecological models are illustrated in Section 2.4 and Section 2.5 for single species and two species of predator-prey interactions, respectively. We start this chapter with matrix notation (Section 2.1) that will be used throughout the dissertation.

2.1 Notation

Throughout this dissertation, let n be a given positive integer. Let M be an $n \times n$ matrix, sometimes denoted as $M = [m_{ij}]_{n\times n}$ with m_{ij} representing its (i, j) entry. Let $\sigma(M)$ denote the set of all eigenvalues of M, that is

$$\sigma(M) = \{\lambda \in \mathbb{C} : Mu = \lambda u \quad \text{for some} \quad u \in \mathbb{R}^n \setminus \{0\}\}.$$

Denote the spectral bound of M (also called spectral abscissa) as

$$s(M) = \max\{\mathrm{Re}\lambda : \lambda \in \sigma(M)\},$$

and the spectral radius of M as

$$\rho(M) = \max\{|\lambda| : \lambda \in \sigma(M)\}.$$

For our purpose, we consider a nonnegative matrix $A = [a_{ij}]_{n\times n}$, encoding all movements of population in a heterogeneous network of n nodes (patches). Specifically, $a_{ij} \geq 0, i \neq j$, represents the movement coefficient constant from patch j to patch i. Without loss of generality, we always assume $a_{ii} = 0$ for all i. Customarily, matrix A is called as the movement matrix. In our studies, we also employ the corresponding Laplacian matrix of A, that is,

$$L = \begin{pmatrix} \sum\limits_{j\neq 1} a_{j1} & -a_{12} & \cdots & -a_{1n} \\ -a_{21} & \sum\limits_{j\neq 2} a_{j2} & \cdots & -a_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ -a_{n1} & -a_{n2} & \cdots & \sum\limits_{j\neq n} a_{jn} \end{pmatrix}.$$

As the diagonal entries of L track all the out-moving terms at each node while other entries in the same column track where the movement toward, each column sum of L equals zero. Thus L is singular and has a zero eigenvalue. In fact, $s(-L) = 0$.

It follows from the Perron-Frobenius theory that L has a nonnegative left eigenvector and a nonnegative right eigenvector corresponding to eigenvalue 0. In fact, one can check $\mathbb{1}^\top = (1, \ldots, 1)$ is a left eigenvector of L. Here $\top$ represents the transpose. We often denote $\theta^\top = (\theta_1, \ldots, \theta_n)$ as a normalized right-eigenvector corresponding to eigenvalue 0 such that $L\theta = 0$, $\mathbb{1}^\top L = 0$ and $\mathbb{1}^\top\theta = \sum_{i=1}^n \theta_i = 1$.

Let $L^{\#} = [\ell_{ij}^{\#}]_{n\times n}$ denote the group inverse of L. That is, the following is satisfied:

$$LL^{\#} = L^{\#}L, \quad LL^{\#}L = L \quad \text{and} \quad L^{\#}LL^{\#} = L^{\#}.$$

2.2 Analytic Perturbation of Spectral Bounds

We are now ready to present the main result of the chapter.

Theorem 2.1. *Let $Q = \operatorname{diag}\{q_i\}_{n\times n}$ and L be the Laplacian matrix with the normalized right-eigenvector $\theta = (\theta_1, \ldots, \theta_n)^\top$ corresponding to eigenvalue 0. Let $r = s(Q - \mu L)$. Then, for $\mu > 0$,*

$$r = s(Q - \mu L) = \sum_{i=1}^{n} \theta_i q_i + \frac{1}{\mu} \sum_{i=1}^{n} \sum_{j=1}^{n} q_i \ell_{ij}^{\#} q_j \theta_j + o\Big(\frac{1}{\mu}\Big), \tag{2.1}$$

and

$$\sum_{i=1}^{n} \theta_i q_i \leq r \leq \max_i \{q_i\}, \tag{2.2}$$

with lower and upper bounds achieved as μ approaches to ∞ and 0, respectively.

The following analytic perturbation result is a key to prove Theorem 2.1.

Theorem 2.2 (Analytic Perturbation)**.** *Let $Q = \operatorname{diag}\{q_i\}_{n\times n}$ and L be a Laplacian matrix. Define $M = \epsilon Q - L$, with λ and ν be the Perron eigenvalue and corresponding right-eigenvector of matrix M. Then, the following expansions hold*

$$\lambda = \lambda_0 + \epsilon\lambda_1 + \epsilon^2\lambda_2 + \cdots + \lambda_k\epsilon^k + \cdots \tag{2.3}$$

$$\nu = \nu_0 + \epsilon\nu_1 + \epsilon^2\nu_2 + \cdots + \epsilon^k\nu_k + \cdots \tag{2.4}$$

where $\lambda_0 = 0$, $\lambda_k = \mathbb{1}^\top Q\nu_{k-1}$ for $k \geq 1$, ν_0 is denoted as the normalized right-eigenvector of L

corresponding to eigenvalue 0*,* $\nu_1 = L^{\#}Q\nu_0$*, and* $\nu_k = L^{\#}\Big(Q\nu_{k-1} - \sum_{i=1}^{k-1}\lambda_i\nu_{k-i}\Big)$ *for* $k \geq 2$*.*

Proof. Plugging the expansions (2.3), (2.4) into $(\epsilon Q - L)\nu = \lambda\nu$ yields

$$\begin{aligned} & (\epsilon Q - L)(\nu_0 + \epsilon\nu_1 + \epsilon^2\nu_2 + \cdots + \epsilon^k\nu_k + \cdots) \\ = \quad & (\lambda_0 + \epsilon\lambda_1 + \epsilon^2\lambda_2 + \cdots + \lambda_k\epsilon^k + \cdots)(\nu_0 + \epsilon\nu_1 + \epsilon^2\nu_2 + \cdots + \epsilon^k\nu_k + \cdots). \end{aligned} \tag{2.5}$$

Comparing the ϵ^0-th terms from both sides of (2.5) yields $-L\nu_0 = \lambda_0\nu_0$, thus $\lambda_0 = 0$ and $\nu_0 = \theta$. Multiplying both sides of (2.5) by $L^{\#}$ from the left yields

$$\begin{aligned} & L^{\#}Q(\epsilon\nu_0 + \epsilon^2\nu_1 + \epsilon^3\nu_2 + \cdots + \epsilon^{k+1}\nu_k + \cdots) - L^{\#}L(\nu_0 + \epsilon\nu_1 + \epsilon^2\nu_2 + \cdots + \epsilon^k\nu_k + \cdots) \\ =& (\epsilon\lambda_1 + \epsilon^2\lambda_2 + \cdots + \lambda_k\epsilon^k + \cdots)L^{\#}(\nu_0 + \epsilon\nu_1 + \epsilon^2\nu_2 + \cdots + \epsilon^k\nu_k + \cdots). \end{aligned}$$

It follows from part 2 of Lemma C.1 in Appendix C, $L^{\#}\nu_0 = L\nu_0 = 0$. The above equality can be written as

$$\begin{aligned} & L^{\#}L(\epsilon\nu_1 + \epsilon^2\nu_2 + \cdots + \epsilon^k\nu_k + \cdots) \\ = \; & L^{\#}Q(\epsilon\nu_0 + \epsilon^2\nu_1 + \epsilon^3\nu_2 + \cdots + \epsilon^{k+1}\nu_k + \cdots) \\ & - (\epsilon\lambda_1 + \epsilon^2\lambda_2 + \cdots + \lambda_k\epsilon^k + \cdots)L^{\#}(\epsilon\nu_1 + \epsilon^2\nu_2 + \cdots + \epsilon^k\nu_k + \cdots). \end{aligned}$$

Comparing the ϵ^1-th term and ϵ^k-th terms ($k \geq 2$) yields respectively

$$L^{\#}L\nu_1 = L^{\#}Q\nu_0 \quad \text{and} \quad L^{\#}L\nu_k = L^{\#}Q\nu_{k-1} - L^{\#}\sum_{i=1}^{k-1}\lambda_i\nu_{k-i}\,. \tag{2.6}$$

Straightforward verification shows that $\nu_1 = L^{\#}Q\nu_0$ and $\nu_k = L^{\#}\Big(Q\nu_{k-1} - \sum_{i=1}^{k-1}\lambda_i\nu_{k-i}\Big)$ solve (2.6). In fact, $\nu_k \in \mathrm{range}(L)$ for all $k \geq 1$.

Next, it follows from multiplying both sides of (2.5) by $\mathbb{1}^\top$ from the left that

$$\begin{aligned}&\mathbb{1}^\top Q(\epsilon\nu_0+\epsilon^2\nu_1+\epsilon^3\nu_2+\cdots+\epsilon^{k+1}\nu_k+\cdots)-\mathbb{1}^\top L(\nu_0+\epsilon\nu_1+\epsilon^2\nu_2+\cdots+\epsilon^k\nu_k+\cdots)\\ =&(\epsilon\lambda_1+\epsilon^2\lambda_2+\cdots+\lambda_k\epsilon^k+\cdots)\mathbb{1}^\top(\nu_0+\epsilon\nu_1+\epsilon^2\nu_2+\cdots+\epsilon^k\nu_k+\cdots).\end{aligned}$$

Since $\mathbb{1}^\top L=0$, $\mathbb{1}^\top\nu_0=1$ and $\mathbb{1}^\top\nu_k=0$ for $k\geq 1$ (as $\mathbb{1}^\top L^\#=0$), it follows that

$$\mathbb{1}^\top Q(\epsilon\nu_0+\epsilon^2\nu_1+\epsilon^3\nu_2+\cdots+\epsilon^{k+1}\nu_k+\cdots)=\epsilon\lambda_1+\epsilon^2\lambda_2+\cdots+\lambda_k\epsilon^k+\cdots.$$

Hence $\lambda_k=\mathbb{1}^\top Q\nu_{k-1}$ for $k\geq 1$. □

Remark 1. *Replacing ν_0 with θ in Theorem 2.2 results in $\lambda_1=\mathbb{1}^\top Q\nu_0=\mathbb{1}^\top Q\theta=\sum_{i=1}^n\theta_iq_i$ and $\lambda_2=\mathbb{1}^\top Q\nu_1=\mathbb{1}^\top QL^\#Q\nu_0=\sum_{i=1}^n\sum_{j=1}^nL_{ij}^\#\theta_jq_iq_j$, respectively. Thus, the first two terms in theλ expansion*(2.3) *can be rewritten as*

$$\lambda=s(\epsilon Q-L)=\epsilon\sum_{i=1}^n\theta_iq_i+\epsilon^2\sum_{i=1}^n\sum_{j=1}^nL_{ij}^\#\theta_jq_iq_j+o(\epsilon^2). \tag{2.7}$$

The following lemma, previously proven in [6], is used to establish sharp bounds for λ.

Lemma 2.3 ([6])**.** *Let $Q=\mathrm{diag}\{q_i\}$ and L be a Laplacian matrix. Suppose $r=s(Q-\mu L)$ where $\mu>0$. Then, the following statements hold:*

(a) $\dfrac{dr}{d\mu}\leq 0$*, with equality holding if and only if $q_i=q_j$ for $i,j=1,\cdots,n$.*

(b) $\dfrac{d^2r}{d\mu^2}\geq 0$*, with equality holding if and only if all q_i are equal.*

Proof. (a) Let $w=(w_1,w_2,\ldots,w_n)^\top$ denote the normalized left eigenvector of $Q-\mu L$ corresponding

to r, *i.e.*,

$$w^\top Q - \mu w^\top L = r w^\top, \tag{2.8}$$

or in the component-wise form

$$q_i w_i + \mu \sum_{k \neq i} a_{ki} w_k - \mu \sum_{k \neq i} a_{ki} w_i = r w_i, \qquad i = 1, 2, \ldots, n. \tag{2.9}$$

Dividing w_i on both sides yields

$$r = q_i + \mu \sum_{k \neq i} a_{ki} \frac{w_k}{w_i} - \mu \sum_{k \neq i} a_{ki}. \tag{2.10}$$

Differentiating both sides with respect to μ yields

$$\frac{dr}{d\mu} = \dot{r} = \sum_{k \neq i} a_{ki} \frac{w_k}{w_i} + \mu \sum_{k \neq i} a_{ki} \frac{\dot{w}_k w_i - w_k \dot{w}_i}{w_i^2} - \sum_{k \neq i} a_{ki} = \sum_{k \neq i} a_{ki} \frac{w_k}{w_i} \Big(1 - \frac{w_i}{w_k} + \mu \frac{\dot{w}_k}{w_k} - \mu \frac{\dot{w}_i}{w_i} \Big). \tag{2.11}$$

Set $\tilde{A} = [\tilde{a}_{ki}]$ with $\tilde{a}_{ki} = a_{ki} \frac{w_k}{w_i}$, $\tilde{L}$ be the corresponding Laplacian matrix, and $\tilde{\theta} = (\tilde{\theta}_1 . \tilde{\theta}_2, \ldots, \tilde{\theta}_n)^\top$ be the normalized right-eigenvector of $\tilde{L}$ corresponding to eigenvalue 0. Multiplying $\tilde{\theta}_i$ to (2.11) and summing over all i yield

$$\dot{r} = \sum_i \tilde{\theta}_i \dot{r} = \sum_i \tilde{\theta}_i \sum_{k \neq i} \tilde{a}_{ki} \Big(1 - \frac{w_i}{w_k} + \mu \frac{\dot{w}_k}{w_k} - \mu \frac{\dot{w}_i}{w_i} \Big) \tag{2.12}$$

$$= \sum_i \sum_{k \neq i} \tilde{\theta}_i \tilde{a}_{ki} \Big[1 - \frac{w_i}{w_k} + \mu \Big(\frac{\dot{w}_k}{w_k} - \frac{\dot{w}_i}{w_i} \Big) \Big]. \tag{2.13}$$

It follows from the Tree-Cycle identity (see Appendix A) that

$$\dot{r} = \sum_{\mathcal{Q} \in \mathbb{Q}} w(\mathcal{Q}) \sum_{(r,s) \in E(C_{\mathcal{Q}})} \Big[1 - \frac{w_r}{w_s} + \mu \Big(\frac{\dot{w}_s}{w_s} - \frac{\dot{w}_r}{w_r} \Big) \Big], \tag{2.14}$$

where $\mathbb{Q}$ is the set of all spanning unicycle graphs of $(\mathcal{G}, A)$; $w(\mathcal{Q}) > 0$ is the weight of $\mathbb{Q}$, and

$C_{\mathbb{Q}}$ denotes the directed cycle of $\mathbb{Q}$ with directed edge set $E(C_{\mathbb{Q}})$. Along any directed cycle $C_{\mathbb{Q}}$ of length l,

$$\sum_{(s,r)\in E(C_{\mathbb{Q}})}\Big(1-\frac{w_s}{w_r}\Big)=l-\Big(\sum_{(s,r)\in E(C_{\mathbb{Q}})}\frac{w_s}{w_r}\Big)\le l-l\Big(\prod_{(s,r)\in E(C_{\mathbb{Q}})}\frac{w_s}{w_r}\Big)^{1/l}=l-l=0 \tag{2.15}$$

where the inequality follows from AM-GM inequality $(w_1+\cdots+w_l)/l\ge\sqrt[l]{w_1\cdots w_l}$, and

$$\sum_{(r,s)\in E(C_{\mathcal{Q}})}\Big(\frac{\dot{w}_s}{w_s}-\frac{\dot{w}_r}{w_r}\Big)=0. \tag{2.16}$$

As a consequence, it follows from (2.14), (2.15) and (2.16) that $\dot{r}\le 0$. Notice that $\dot{r}=0$ iff $w_r=w_s$ for every pair (s,r) in (2.15).

(b) Differentiating (2.11) with respect to μ yields

$$\ddot{r}=2\sum_{k\neq i}a_{ki}\Big(\frac{\dot{w}_kw_i-w_k\dot{w}_i}{w_i^2}\Big)+\mu\sum_{k\neq i}a_{ki}\frac{w_k}{w_i}\Big(\frac{\dot{w}_k}{w_k}-\frac{\dot{w}_i}{w_i}\Big)-2\mu\sum_{k\neq i}a_{ki}\frac{w_k}{w_i}\Big[\frac{\ddot{w}_k}{w_k}\frac{\ddot{w}_i}{w_i}-\Big(\frac{\dot{w}_i}{w_i}\Big)^2\Big], \tag{2.17}$$

and

$$\ddot{r}=\sum_{k\neq i}a_{ki}\frac{w_k}{w_i}\Big[2\Big(\frac{\dot{w}_k}{w_k}-\frac{\dot{w}_i}{w_i}\Big)+\mu\Big(\frac{\ddot{w}_k}{w_k}-\frac{\ddot{w}_i}{w_i}\Big)-2\mu\Big(\frac{\dot{w}_k}{w_k}\frac{\dot{w}_i}{w_i}-\Big(\frac{\dot{w}_i}{w_i}\Big)^2\Big)\Big]. \tag{2.18}$$

Recall $\tilde{a_{ki}}=a_{ki}\frac{w_k}{w_i}$, multiplying (2.17) by $\tilde{\theta}_i$ and summing over all i yield

$$\ddot{r}=\sum_i\tilde{\theta}_i\ddot{r}=\sum_{k\neq i}\tilde{\theta}_i\tilde{a_{ki}}\Big[2\Big(\frac{\dot{w}_k}{w_k}-\frac{\dot{w}_i}{w_i}\Big)+\mu\Big(\frac{\ddot{w}_k}{w_k}-\frac{\ddot{w}_i}{w_i}\Big)-2\mu\Big(\frac{\dot{w}_k}{w_k}\frac{\dot{w}_i}{w_i}-\Big(\frac{\dot{w}_i}{w_i}\Big)^2\Big)\Big]. \tag{2.19}$$

It follows from the Tree-Cycle identity (see Appendix A) that

$$\ddot{r}=\sum_{\mathcal{Q}\in\mathbb{Q}}w(\mathcal{Q})\sum_{(s,r)\in E(C_{\mathcal{Q}})}\Big[2\Big(\frac{\dot{w}_s}{w_s}-\frac{\dot{w}_r}{w_r}\Big)+\mu\Big(\frac{\ddot{w}_s}{w_s}-\frac{\ddot{w}_r}{w_r}\Big)-2\mu\Big(\frac{\dot{w}_s}{w_s}\frac{\dot{w}_r}{w_r}-\Big(\frac{\dot{w}_r}{w_r}\Big)^2\Big)\Big]. \tag{2.20}$$

Notice that $2\sum_{(s,r)\in E(C_{\mathcal{Q}})}\left(\frac{\dot{w}_s}{w_s}-\frac{\dot{w}_r}{w_r}\right)=0$ and $\mu\sum_{(s,r)\in E(C_{\mathcal{Q}})}\left(\frac{\ddot{w}_s}{w_s}-\frac{\ddot{w}_r}{w_r}\right)=0$. Hence

$$\begin{aligned}\ddot{r} &= 2\mu\sum_{\mathcal{Q}\in\mathbb{Q}} w(\mathcal{Q})\sum_{(s,r)\in E(C_{\mathcal{Q}})}\Big(\Big(\frac{\dot{w}_r}{w_r}\Big)^2-\frac{\dot{w}_s}{w_s}\frac{\dot{w}_r}{w_r}\Big)\\ &= \mu\sum_{\mathcal{Q}\in\mathbb{Q}} w(\mathcal{Q})\sum_{(s,r)\in E(C_{\mathcal{Q}})}\Big[\Big(\frac{\dot{w}_r}{w_r}\Big)^2-\frac{\dot{w}_s}{w_s}\frac{\dot{w}_r}{w_r}+\Big(\frac{\dot{w}_s}{w_s}\Big)^2-\frac{\dot{w}_s}{w_s}\frac{\dot{w}_r}{w_r}\Big]\\ &= \mu\sum_{\mathcal{Q}\in\mathbb{Q}} w(\mathcal{Q})\sum_{(s,r)\in E(C_{\mathcal{Q}})}\Big(\frac{\dot{w}_r}{w_r}-\frac{\dot{w}_s}{w_s}\Big)^2\geq 0.\end{aligned}$$

Notice that $\ddot{r}=0$ if and only if $\frac{\dot{w}_s}{w_s}=\frac{\dot{w}_r}{w_r}$ for any pair of (s,r) locating in a directed cycle of $(\mathcal{G},L)$. Since $\tilde{A}$ is irreducible, the graph $(\mathcal{G},L)$ is strongly connected. As a consequence, $\frac{\dot{w}_s}{w_s}=\frac{\dot{w}_r}{w_r}$ for any i,j. □

As it is shown below, Theorem 2.1follows immediately from Theorem 2.2 and Lemma 2.3.

Proof. First, we prove the expansion (2.2) in Theorem 2.1. Consider

$$r=s(Q-\mu L)=s(\mu(\frac{1}{\mu}Q-L))=\mu s((\frac{1}{\mu}Q-L)). \tag{2.21}$$

Let $\epsilon=\frac{1}{\mu}$. Thus, (2.21) becomes

$$r=\frac{1}{\epsilon}s(\epsilon Q-L)=\sum_{i=1}^{n}\theta_i q_i+\epsilon\sum_{i=1}^{n}\sum_{j=1}^{n}q_i\ell_{ij}^{\#}q_j\theta_j+o(\epsilon), \tag{2.22}$$

where the last equality follows from (2.7). Thus,

$$r=s(Q-\mu L)=\sum_{i=1}^{n}\theta_i q_i+\frac{1}{\mu}\sum_{i=1}^{n}\sum_{j=1}^{n}q_i\ell_{ij}^{\#}q_j\theta_j+o\Big(\frac{1}{\mu}\Big).$$

follows immediately from Theorem 2.2 and equation (2.7).

Next, we prove the sharp bounds (2.2) for r in Theorem 2.2. From lemma 2.3(a), $r = s(Q-\mu L)$ is decreasing with respect to $\mu > 0$, so the upper bound for r occurs when $\mu \to 0$. Hence, the upper bound for r is

$$\lim_{\mu\to 0} s(Q-\mu L) = s(Q) = \max_{i=1,\cdots,n}\{q_i\}. \tag{2.23}$$

Following above reasoning, the lower bound for r happens as μ approaches ∞.

Taking the limit from (2.2) when $\mu \to \infty$ yields

$$\lim_{\mu\to\infty} s(Q-\mu L) = \lim_{\mu\to\infty}\Big(\sum_{i=1}^{n}\theta_i q_i + \frac{1}{\mu}\sum_{i=1}^{n}\sum_{j=1}^{n} L_{ij}^{\#}\theta_j q_i q_j + o\Big(\frac{1}{\mu}\Big)\Big) = \sum_{i=1}^{n}\theta_i q_i. \tag{2.24}$$

Combining (2.23) and (2.24) yield

$$\sum_{i=1}^{n}\theta_i q_i \le r \le \max_i\{q_i\}.$$

□

Theorem 2.4 (Sharp Bounds)**.** *Let $Q = \mathrm{diag}\{q_i\}_{n\times n}$, L be the Laplacian matrix of digraph $\mathcal{G}_A$ with the normalized right-eigenvector $\theta = (\theta_1, \cdots, \theta_n)$ corresponding to eigenvalue 0, and $\lambda = s(\epsilon Q - L)$. Then, $\frac{\lambda}{\epsilon}$ is monotonically increasing with respect to ϵ for $\epsilon > 0$, and*

$$\sum_{i=1}^{n}\theta_i q_i \le \frac{\lambda}{\epsilon} \le \max_i\{q_i\}, \tag{2.25}$$

with lower and upper bounds achieved as ϵ approaches to 0 and ∞, respectively.

Proof. Set $\mu = \frac{1}{\epsilon}$. Then, $\lambda = s(\epsilon Q - L) = \epsilon s(Q - \frac{1}{\epsilon}L) = \epsilon s(Q-\mu L) = \epsilon r$, where r is defined as in Lemma 2.3. Thus the desired results follow immediately from Theorem 2.1 and Lemma 2.3. □

2.3 Network Average and Network Heterogeneity Index

Let $Q = \mathrm{diag}\{q_i\}$ be a diagonal matrix and let L be a Laplacian matrix with $\theta^\top = (\theta_1, \cdots, \theta_n)$ the normalized right Perron eigenvector of L.

The *network average* $\mathcal{A} = \mathcal{A}(L, Q)$, and *network heterogeneity index* $\mathcal{H} = (L, Q)$ are defined as

$$\mathcal{A} := \sum_{i=1}^{n} q_i \theta_i = \mathbb{1}^\top Q \theta, \tag{2.26}$$

and

$$\mathcal{H} := \sum_{i=1}^{n} \sum_{j=1}^{n} \ell_{ij}^{\#} q_i q_j \theta_j = \mathbb{1}^\top Q L^{\#} Q \theta, \tag{2.27}$$

where $L^{\#} = [\ell_{ij}^{\#}]$ denotes the group inverse of L.

Thus, $r = s(Q - \mu L)$ in expansion (2.2) can be rewritten as

$$r = \mathcal{A} + \frac{1}{\mu}\mathcal{H} + o\Big(\frac{1}{\mu}\Big) \tag{2.28}$$

The following result provides an alternative formulation for $\mathcal{H}$.

Theorem 2.5. *Let $\mathcal{H}$ be the network heterogeneity index as defined in* (2.27)*. Then,*

$$\mathcal{H} = -\frac{1}{2} \sum_{i=1}^{n} \sum_{j \neq i} \ell_{ij}^{\#} (q_i - q_j)^2 \theta_j. \tag{2.29}$$

Proof.

$$\mathcal{H} = \sum_{i=1}^{n} \sum_{j=1}^{n} \ell_{ij}^{\#} q_i q_j \theta_j = \sum_{i=1}^{n} \ell_{ii}^{\#} q_i^2 \theta_i + \sum_{i=1}^{n} \sum_{j \neq i} \ell_{ij}^{\#} q_i q_j \theta_j. \tag{2.30}$$

The column sums of $L^{\#} = [\ell_{ij}^{\#}]$ are zero, i.e. $\ell_{ii}^{\#} = -\sum_{i\neq j} \ell_{ji}^{\#}$. Thus, (2.30) becomes

$$\begin{aligned}\mathcal{H} &= -\sum_{i=1}^{n}\sum_{j\neq i} \ell_{ji}^{\#} q_i^2\theta_i + \sum_{i=1}^{n}\sum_{j\neq i} \ell_{ij}^{\#} q_i q_j \theta_j \\ &= -\sum_{i=1}^{n}\sum_{j\neq i} \ell_{ji}^{\#} q_i^2\theta_i + \frac{1}{2}\sum_{i=1}^{n}\sum_{j\neq i} \ell_{ij}^{\#}[q_i^2 - (q_i-q_j)^2 + q_j^2]\theta_j.\end{aligned}$$

Rearranging the terms on the right hand side yields

$$\begin{aligned}\mathcal{H} &= -\frac{1}{2}\sum_{i=1}^{n}\sum_{j\neq i} \ell_{ij}^{\#}(q_i-q_j)^2\theta_j + \frac{1}{2}\sum_{i=1}^{n}\sum_{i\neq j}[-2\ell_{ji}^{\#}q_i^2\theta_i + \ell_{ij}^{\#}q_i^2\theta_j + \ell_{ij}^{\#}q_j^2\theta_j] \\ &= -\frac{1}{2}\sum_{i=1}^{n}\sum_{j\neq i} \ell_{ij}^{\#}(q_i-q_j)^2\theta_j - \frac{1}{2}\sum_{i=1}^{n}\sum_{j\neq i}[-\ell_{ji}^{\#}q_i^2\theta_i + \ell_{ij}^{\#}q_i^2\theta_j] \\ &= -\frac{1}{2}\sum_{i=1}^{n}\sum_{j\neq i} \ell_{ij}^{\#}(q_i-q_j)^2\theta_j - \frac{1}{2}\sum_{i=1}^{n}\sum_{j\neq i} q_i^2\theta_i\theta_j(\frac{\ell_{ij}^{\#}}{\theta_i} - \frac{\ell_{ji}^{\#}}{\theta_j}).\end{aligned}$$

Using the Tree-Cycle identity (see Appendix A) results in

$$\mathcal{H} = -\frac{1}{2}\sum_{i=1}^{n}\sum_{j\neq i} \ell_{ij}^{\#}(q_i-q_j)^2\theta_j + \sum_{\mathcal{Q}\in\mathbb{Q}} w(\mathcal{Q}) \sum_{(s,r)\in E(\mathcal{C}_{\mathcal{Q}})}(\frac{\ell_{rs}^{\#}}{\theta_r} - \frac{\ell_{sr}^{\#}}{\theta_s}), \tag{2.31}$$

where $\mathcal{Q}$ denotes the set of all spanning unicycle graphs of $(\mathcal{G}, A)$, $w(\mathcal{Q}) > 0$ is the weight of $\mathcal{Q}$, and $\mathcal{C}_{\mathcal{Q}}$ represents the directed cycle of $\mathcal{Q}$ with directed edge set $E(\mathcal{C}_{\mathcal{Q}})$. Notice that

$$\sum_{\mathcal{Q}\in\mathbb{Q}} w(\mathcal{Q}) \sum_{(s,r)\in E(\mathcal{C}_{\mathcal{Q}})}(\frac{\ell_{rs}^{\#}}{\theta_r} - \frac{\ell_{sr}^{\#}}{\theta_s}) = 0.$$

Thus, (2.31) becomes

$$\mathcal{H} = -\frac{1}{2}\sum_{i=1}^{n}\sum_{j\neq i} \ell_{ij}^{\#}(q_i-q_j)^2\theta_j.$$

□

The following result provides necessary and sufficient conditions in determining the order of two different expansions in the form of (2.28) in regards to their corresponding first terms.

Theorem 2.6 (First-Order Determination)**.** *Let Q_1 and Q_2 be two diagonal matrices. Let L_1 and L_2 are two Laplacian matrices. Then, there exists $\eta > 0$ such that $r_1 = s(Q_1 - \mu L_1) > r_2 = s(Q_2 - \mu L_2)$ for all $\mu > \eta$ if and only if $\mathcal{A}_1 > \mathcal{A}_2$.*

Proof. From equation (2.28), the expansions for r_1 and r_2 become

$$r_1 = \mathcal{A}_1 + \frac{1}{\mu}\mathcal{H}_1 + o(\frac{1}{\mu}), \tag{2.32}$$

and

$$r_2 = \mathcal{A}_2 + \frac{1}{\mu}\mathcal{H}_2 + o(\frac{1}{\mu}). \tag{2.33}$$

Let $\mathcal{A}_1 > \mathcal{A}_2$. There exists a fixed $\nu > 0$ in which $\mathcal{A}_1 = \mathcal{A}_2 + \nu$. Choose η such that $\eta < \nu$. Thus,

$$r_1 - r_2 = (\mathcal{A}_1 - \mathcal{A}_2) + \frac{1}{\mu}(\mathcal{H}_1 - \mathcal{H}_2) + o(\frac{1}{\mu}) > \eta + \frac{1}{\mu}(\mathcal{H}_1 - \mathcal{H}_2) + o(\frac{1}{\mu}). \tag{2.34}$$

Then, for all $\mu > \eta$, (2.34) becomes

$$r_1 - r_2 > \frac{1}{\mu}(1 + (\mathcal{H}_1 - \mathcal{H}_2) + o(1)) \tag{2.35}$$

For $\eta > 0$ small enough, the right hand side of (2.35) approaches 0. Thus,

$$r_1 > r_2.$$

Now, let $r_1 > r_2$. It follows from (2.32) and (2.33) that

$$r_1 - r_2 = (\mathcal{A}_1 - \mathcal{A}_2) + \frac{1}{\mu}(\mathcal{H}_1 - \mathcal{H}_2) + o(\frac{1}{\mu}) > 0 \tag{2.36}$$

For $\mu > 0$ large enough, $\mathcal{A}_1 - \mathcal{A}_2 > 0$. Hence, $\mathcal{A}_1 > \mathcal{A}_2$. □

The following result states a sufficient condition in determining the order two different expansions in the form of (2.28) where their corresponding first terms are equal.

Theorem 2.7 (Second-Order Determination)**.** *Let Q_1 and Q_2 be two diagonal matrices. Let L_1 and L_2 be two Laplacian matrices. Suppose that $\mathcal{A}_1 = \mathcal{A}_2$. Then, there exists $\eta > 0$ such that $r_1 = s(Q_1 - \mu L_1) > r_2 = s(Q_2 - \mu L_2)$ holds for all $\mu > \eta$ if $\mathcal{H}_1 > \mathcal{H}_2$.*

Proof. Let $\mathcal{H}_1 > \mathcal{H}_2$, then there exists a fixed $\nu > 0$ such that $\mathcal{H}_1 = \mathcal{H}_2 + \nu$.

Choose η such that $\eta < \nu$. Thus, $\mathcal{H}_1 > \mathcal{H}_2 + \eta$. Using equations (2.32) and (2.33) in Theorem 2.6 result in

$$r_1 - r_2 = (\mathcal{A}_1 - \mathcal{A}_2) + \frac{1}{\mu}(\mathcal{H}_1 - \mathcal{H}_2) + o(\frac{1}{\mu}) > \frac{1}{\mu}(\eta) + o(\frac{1}{\mu}). \tag{2.37}$$

Thus,

$$r_1 - r_2 > \frac{1}{\mu}(\eta + o(1)). \tag{2.38}$$

Letting $\mu \to \infty$ yield $r_1 > r_2$. □

2.4 Application to a Single Species Model

Consider the following single-species model in a heterogeneous landscape of n patches $(n \geq 2)$

$$x_i' = x_i f_i(x_i) + \mu \sum_{j=1}^{n} (a_{ij} x_j - a_{ji} x_i), \quad i = 1, 2, \ldots, n, \tag{2.39}$$

where $x_i \in [0, \infty)$ denotes the population size in patch i and $\mu \geq 0$ represents the movement rate. Function $f_i : [0, \infty) \to \mathbb{R}$ represents the population growth rate in patch i.

$M = [a_{ij}]_{n \times n}$ indicates the movement matrix of the system where $a_{ij} \geq 0$ represents the movement from patch j to patch i. $L = [\ell_{ij}]$ is the Laplacian matrix corresponding to the movement in the system, where $\ell_{ij} = -a_{ij}$ for $i \neq j$ and $\ell_{ii} = -\sum_{j \neq i} a_{ji}$.

The Jacobian matrix of system (2.39) is described as

$$J = \operatorname{diag}\{f_i(x_i) - x_i f'(x_i)\} - \mu L. \tag{2.40}$$

System (3.8) admits a trivial equilibrium point $E_0 = (0, \ldots, 0)$. The stability of E_0 is determined by the sign of the spectral bound of the Jacobian matrix (2.40) evaluated at E_0, i.e.,

$$r(E_0) := s(J_{|E_0}) = s(\operatorname{diag}\{f_i(0)\} - \mu L). \tag{2.41}$$

Thus, E_0 is locally asymptotically stable, if $r(E_0) < 0$, and E_0 is unstable if $r(E_0) > 0$.

The following result is an immediate consequence of Theorem 2.1 for system (2.39), by replacing q_i in expressions (2.7) and (2.2) with $f_i(0)$. Additionally, he monotonically decreasing of $r(E_0)$ is attained from Lemma (2.3).

Theorem 2.8. *Let L be an irreducible Laplacian matrix such that $\theta^\top = (\theta_1, \ldots, \theta_n)$ is the normalized right Perron eigenvector of L. Suppose that* (2.41) *holds. Then, for any $\mu > 0$*

$$r(E_0) = \sum_{i=1}^{n} f_i(0)\theta_i + \frac{1}{\mu}\sum_{i=1}^{n}\sum_{j=1}^{n} f_i(0)\ell_{ij}^{\#} f_j(0)\theta_j + o\big(\frac{1}{\mu}\big), \tag{2.42}$$

where $L_{ij}^{\#} = [\ell_{ij}^{\#}]$ is the group inverse matrix of L.

Furthermore, $r(E_0)$ is strictly decreasing with respect to μ and

$$\sum_{i=1}^{n} f_i(0)\theta_i \leq r(E_0) \leq \max_{1\leq i\leq n}\{f_i(0)\}, \tag{2.43}$$

with lower and upper bounds achieved when $\mu \to \infty$ and $\mu \to 0$, respectively.

The following result describes that $r(E_0)$ is a threshold parameter which determines the global stability of E_0 under certain assumptions.

Proposition 2.9. *Let $f_i(x_i)$ be the function defined in system* (3.8) *such that $f_i'(x_i) \leq 0$ for all $x_i \geq 0$. Then, the following statements hold*

(i) If $r(E_0) \leq 0$, then E_0 is globally asymptotically stable in $\mathbb{R}_+^n$.

(ii) If $r(E_0) \geq 0$, then E_0 is unstable. Furthermore, there exists a unique positive equilibrium $\bar{E} = (\bar{x}_1, \ldots, \bar{x}_n)$ which is globally asymptotically stable in $\mathbb{R}_+^n$.

The Jacobian matrix (2.40) of system (3.8) at $\bar{E}$ is given by

$$J|_{\bar{E}} = \mathrm{diag}\{f_i(\bar{x}_i) + \bar{x}_i f_i'(\bar{x}_i)\} - \mu L. \tag{2.44}$$

The following result discusses the conditions in which $\bar{E}$ is stable. Biologically, it means that the

population survives.

Corollary 2.10. *Assume* $r(E_0) > 0$ *and* $f_i'(x_i) \leq 0$ *for all* x_i. *Then,* $s(J_{|\bar{E}}) < 0$.

2.5 Application to a Predator-Prey Model

Consider the following predator–prey model in a heterogeneous network of n patches $(n \geq 2)$

$$\begin{cases} x_i' &= x_i f_i(x) - g_i(x_i)y_i + \mu_x \sum_{j=1}^{n}(a_{ij}x_j - a_{ji}x_i), \qquad i = 1, 2, \ldots, n, \\ y_i' &= \epsilon_i g_i(x_i)y_i - h_i(y_i) + \mu_y \sum_{j=1}^{n}(m_{ij}y_j - m_{ji}y_i), \qquad i = 1, 2, \ldots, n, \end{cases} \tag{2.45}$$

where $x_i \in [0, \infty)$ and $y_i \in [0, \infty)$ denote the population of the prey and predators in patch i, respectively; $\epsilon_i > 0$ is the conversion rate of the predation. Parameters $\mu_x \geq 0$ and $\mu_y \geq 0$ represent movement rates of prey and predator, respectively. Functions f_i, g_i and h_i are continuous functions that are satisfied in the following assumptions:

(A_1) $f_i : \mathbb{R}_+ \to \mathbb{R}$ denotes the prey growth rate in patch i in which $f_i'(x_i) \leq 0$ and $f_i(x_i) \leq f_i(0)x_i$ for all $x_i \geq 0$.

(A_2) $g_i : \mathbb{R}_+ \to \mathbb{R}_+$ indicates the search efficiency where $g'(x_i) \geq 0$ and $g_i(0) = 0$ for all $x_i \geq 0$.

(A_3) $h_i : \mathbb{R}_+ \to \mathbb{R}_+$ represents the decay rate of predators in patch i in the absence of the prey where $h_i'(x_i) \leq 0$ for all $x_i \geq 0$.

Parameters $a_{ij} \geq 0$ and $b_{ij} \geq 0$ describe the dispersal of the prey and predators from patch i to patch j, respectively, where $a_{ij} \neq a_{ji}$ and $m_{ij} \neq b_{ji}$ for $i \neq j$.

Assume that L_A and L_B denote the Laplacian matrices correspond to the dispersal of the prey and

predators among patches, respectively.

The Jacobian matrix of system (2.45) is described as

$$\tilde{J} = \begin{pmatrix} \mathrm{diag}\{f_i(x_i) + x_i f_i'(x_i)\} - \mu_x L_A & -\mathrm{diag}\{g_i(x_i)\} \\ \mathrm{diag}\{\epsilon_i g_i'(x_i) y_i\} & \mathrm{diag}\{\epsilon_i g_i(x_i) - h_i'(y_i)\} - \mu_y L_B \end{pmatrix}. \tag{2.46}$$

Generally, system (2.45) admits 3 equilibria:

(i) trivial equilibrium point $P_0 = (0, \ldots, 0, \ldots, 0)$ denoting the extinction of both the prey and predators species,

(ii) semi-positive equilibrium point $\bar{P} = (\bar{x}_1, \ldots, \bar{x}_n, 0, \ldots, 0)$, representing the survival of the prey species only, and

(iii) positive equilibrium point $P^* = (x_1^*, \ldots, x_n^*, y_1^*, \ldots, y_n^*)$, indicating the coexistence of the prey and predators species.

For our purpose, it is more insightful to assume that

$$r(E_0) = s(J|_{E_0}) = s(\mathrm{diag}\{f_i(0)\} - \mu_x L_A) > 0, \tag{2.47}$$

where E_0 denotes the trivial equilibrium point of the prey population as discussed in Proposition 2.9. Equation (2.47) states that the prey population survives in the absence of the predator population.

The coexistence of the prey and predators population is dependent on the stability of $\bar{P}$.

The stability of $\bar{P}$ is determined by the sign of the spectral bound of the Jacobian matrix (2.48)

evaluated at $\bar{P}$. That is,

$$s(\tilde{J}|_{\bar{P}}) = s(\begin{pmatrix} \text{diag}\{f_i(\bar{x}_i) + \bar{x}_i f_i'(\bar{x}_i)\} - \mu_x L_A & -\text{diag}\{g_i(\bar{x}_i)\} \\ 0 & \text{diag}\{\epsilon_i g_i(\bar{x}_i) - h_i'(0)\} - \mu_y L_B \end{pmatrix}). \quad (2.48)$$

Denote $r(\bar{P}) = s(\tilde{J}|_{\bar{P}})$. As shown in (2.48), the sign of $r(\bar{P})$ depends on the sign of $s(\text{diag}\{f_i(\bar{x}_i) + \bar{x}_i f_i'(\bar{x}_i)\} - \mu_x L_A)$ and $s(\text{diag}\{\epsilon_i g_i(\bar{x}_i) - h_i'(0)\} - \mu_y L_B)$.

Since $f_i'(x_i) \leq 0$ and equation (2.47) holds, it follow from Corollary 2.10 that $s(J_{|\bar{E}}) = s(\text{diag}\{f_i(\bar{x}_i) + \bar{x}_i f_i'(\bar{x}_i)\} - \mu_x L_A) < 0$.

Theorem 2.11. *Suppose that L_B is irreducible Laplacian matrix such that $(\eta_1, \ldots, \eta_n)$ is corresponding the normalized right Perron eigenvector. Assume that (A_1) and* (2.47) *hold. Then, for any $\mu_y > 0$*

$$\begin{aligned} r(\bar{P}) &= s(\text{diag}\{\epsilon_i g_i(\bar{x}_i) - h_i'(0)\} - \mu_y L_B) \\ &= \sum_{i=1}^{n} (\epsilon_i g_i(\bar{x}_i) - h_i'(0))\eta_i + \frac{1}{\mu_y} \sum_{i=1}^{n} \sum_{j \neq i} (\epsilon_i g_i(\bar{x}_i) - h_i'(0))\tilde{\ell}_{ij}^{\#} (\epsilon_j g_j(\bar{x}_j) - h_j'(0))\eta_j, \end{aligned}$$

where $L_B^{\#} = [\tilde{\ell}_{ij}^{\#}]$ is the group inverse of L_B.

Furthermore, $r(\bar{P})$ is strictly decreasing with respect to μ_y and

$$\sum_{i=1}^{n} (\epsilon_i g_i(\bar{x}_i) - h_i'(0))\eta_i \leq r(E_0) \leq \max_{1 \leq i \leq n} \{\epsilon_i g_i(\bar{x}_i) - h_i'(0)\}, \quad (2.49)$$

with lower and upper bounds achieved when $\mu_y \to \infty$ and $\mu_y \to 0$, respectively.

The following result, discussed in [12], investigates the conditions in which $\bar{P}$ is stable. Biologically, this implies that the prey and predators coexist.

Proposition 2.12. *Let $r(E_0) > 0$ and $f_i'(x_i) \leq 0$. Then, the following statements hold*

(i) If $r(\bar{P}) < 0$*, then* $\bar{P}$ *is globally asymptotically stable in* $\mathbb{R}^n_+$.

(ii) If $r(\bar{P}) > 0$*, then* $\bar{P}$ *is unstable. Furthermore, there exists a unique positive equilibrium point* $P^* = (x_1^*, \ldots, x_n^*, y_1^*, \ldots, y_n^*)$ *in which it is globally asymptotically stable in* $\mathbb{R}^n_+$.

CHAPTER 3: DISEASE INVASION AND R_0 IN HETEROGENEOUS NETWORKS

The objective of this chapter is to examine the disease invisibility, which is associated to the basic reproduction R_0 on multi-patch infectious disease models with movements among the patches. In particular, the computation of the basic reproduction number is defined as the spectral radius of matrix $B(P + \mu L)^{-1}$, that is $R_0 := \rho(B(P + \mu L)^{-1})$, where B and P are diagonal matrices with positive and non-negative elements on the diagonals, respectively; parameter μ denotes the movement rate among patches, and L is the Laplacian matrix of the movements among the patches in the network.

Our motivation comes from calculating R_0 for the multi-patch cholera disease model with water movement among the patches as described in [16], where the recovery rates of all the patches are assumed to be equal. In this chapter, we formulate R_0 for the generalized case when the recovery rates in the patches are not necessarily the same.

The structure of this chapter is as follows: providing several formulations for R_0 on multi-patch infectious disease models with movement among the patches, (re)stating some properties of R_0 including monotonicity, convexity as well as the upper and lower bounds, and finally applying our findings on multi-patch SIS disease model and multi-patch cholera disease model.

3.1 An Expansion for the Reciprocal of R_0

The following Theorem provides an expansion for $\dfrac{1}{R_0}$ on multi-patch disease models by applying the result of Theorem 2.1 and using the group inverse of Laplacian matrix LB^{-1}.

Theorem 3.1. *Let* $B = \mathrm{diag}\{b_i\}$ *and* $P = \mathrm{diag}\{p_i\}$ *where* $b_i > 0$, $p_i \geq 0$ *and* $P \neq 0$. *Suppose that* L *is a Laplacian matrix such that* $\theta^\top = (\theta_1, \ldots, \theta_n)$ *is the corresponding normalized right Perron-eigenvector. Let* $R_0 = \rho(B(P + \mu L)^{-1})$. *Then, for any* $\mu > 0$

$$\frac{1}{R_0} = \frac{1}{\hat{R}_0} - \frac{1}{\hat{R}_0 \mu}\Big(\frac{\mathbb{1}^\top P B^{-1} \tilde{L}^{\#} P \theta}{\mathbb{1}^\top P \theta}\Big) + o(\frac{1}{\mu}), \tag{3.1}$$

where $\hat{R}_0 := \dfrac{\sum_i b_i \theta_i}{\sum_i p_i \theta_i}$ *, and* $\tilde{L}^{\#}$ *is the group inverse of the Laplacian matrix* $\tilde{L} := LB^{-1}$.

Proof. Since B is a positive diagonal matrix, B^{-1} exists. Thus,

$$R_0 = \rho(B(P + \mu L)^{-1}) = \rho((PB^{-1} + \mu L B^{-1})^{-1}) =: \rho((PB^{-1} + \mu \tilde{L})^{-1}),$$

where $\tilde{L} = LB^{-1}$ is a Laplacian matrix and $B\theta$ denotes the Perron right-eigenvector of $\tilde{L}$. Define $\tilde{\theta} = \dfrac{B\theta}{\sum_i b_i \theta_i}$ as the normalized Perron right-eigenvector of $\tilde{L}$.

Following the assumption $(PB^{-1} + \mu\tilde{L})$ is a non-singular M-matrix. Thus, $(PB^{-1} + \mu\tilde{L})^{-1}$ is a non-negative and irreducible matrix. Hence, by the Perron-Frobenius Theorem, R_0 is the Perron eigenvalue of $(PB^{-1} + \mu\tilde{L})^{-1}$. Denote $\mathbb{x}$ as the right Perron-eigenvector of R_0. Thus,

$$R_0 \mathbb{x} = (PB^{-1} + \mu\tilde{L})^{-1}\mathbb{x}.$$

Multiplying both sides by $(PB^{-1} + \mu\tilde{L})$ and $\dfrac{1}{R_0}$ yield

$$(PB^{-1} + \mu\tilde{L})\mathbb{x} = \frac{1}{R_0}\mathbb{x}.$$

Collecting all the terms on one side results in

$$(\frac{1}{R_0}I - PB^{-1} - \mu\tilde{L})\mathbb{x} = 0,$$

where $(\frac{1}{R_0}I - PB^{-1} - \mu\tilde{L})$ is essentially non-negative and irreducible. Thus, by the Perron-Frobenius theory

$$s(\frac{1}{R_0}I - PB^{-1} - \mu\tilde{L}) = 0 \quad \text{and} \quad \frac{1}{R_0} + s(-PB^{-1} - \mu\tilde{L}) = 0.$$

Equivalently,

$$-\frac{1}{R_0} = s(-PB^{-1} - \mu\tilde{L}).$$

Applying the result of Theorem 2.1 to $s(-PB^{-1} - \mu\tilde{L})$ results in

$$-\frac{1}{R_0} = \mathbb{1}^\top(-PB^{-1})\tilde{\theta} + \frac{1}{\mu}\mathbb{1}^\top(-PB^{-1})\tilde{L}^{\#}(-PB^{-1})\tilde{\theta} + o(\frac{1}{\mu}).$$

Replacing $\tilde{\theta}$ with $\frac{B\theta}{\sum_i b_i\theta_i}$ yields

$$\begin{aligned}
\frac{1}{R_0} &= \frac{\mathbb{1}^\top PB^{-1}B\theta}{\sum_i b_i\theta_i} - \frac{1}{\mu}(\frac{\mathbb{1}^\top PB^{-1}\tilde{L}^{\#}PB^{-1}B\theta}{\sum_i b_i\theta_i}) + o(\frac{1}{\mu}) \\
&= \frac{\mathbb{1}^\top P\theta}{\sum_i b_i\theta_i} - \frac{1}{\mu}(\frac{\mathbb{1}^\top PB^{-1}\tilde{L}^{\#}P\theta}{\sum_i b_i\theta_i}) + o(\frac{1}{\mu}) \\
&= \frac{\sum_i p_i\theta_i}{\sum_i b_i\theta_i} - \frac{1}{\mu}(\frac{\mathbb{1}^\top PB^{-1}\tilde{L}^{\#}P\theta}{\sum_i b_i\theta_i}) + o(\frac{1}{\mu}).
\end{aligned}$$

Denote $\hat{R}_0 = \frac{\sum_i b_i\theta_i}{\sum_i p_i\theta_i}$. Thus,

$$\frac{1}{R_0} = \frac{1}{\hat{R}_0} - \frac{1}{\hat{R}_0\mu}\big(\frac{\mathbb{1}^\top PB^{-1}\tilde{L}^{\#}P\theta}{\mathbb{1}^\top P\theta}\big) + o(\frac{1}{\mu}).$$

□

3.2 Expansions for R_0

In this Section we provide two expansions for $R_0 = \rho(B(P+\mu L)^{-1})$, where the first expansion uses the group inverse of the Laplacian matrix LB^{-1} and the second one focuses on the group inverse of the Laplacian matrix L.

The following result is a pivotal tool to provide an expansion for $R_0 = \rho(B(P+\mu L)^{-1})$ in terms of the group inverse of LB^{-1}.

Lemma 3.2. *Let $\mathbb{Q}$ be a non-negative diagonal matrix where $\mathbb{Q} \neq 0$. Suppose that L is a Laplacian matrix where $\mathbb{1}^T$ and θ are the corresponding left and normalized right Perron-eigenvectors such that $\mathbb{1}^T\theta = 1$. Then for any $\mu > 0$,*

$$\rho((\mathbb{Q}+\mu L)^{-1}) = \frac{1}{\mathbb{1}^\top \mathbb{Q}\theta} + \frac{1}{\mu}\Big(\frac{\mathbb{1}^\top \mathbb{Q} L^{\#}\mathbb{Q}\theta}{(\mathbb{1}^\top \mathbb{Q}\theta)^2}\Big) + o(\frac{1}{\mu}). \tag{3.2}$$

Proof. Note that $\rho((\mathbb{Q}+\mu L)^{-1}) = \rho((\mu(\frac{\mathbb{Q}}{\mu}+L))^{-1}) = \frac{1}{\mu}\rho((\frac{\mathbb{Q}}{\mu}+L)^{-1}) =: \epsilon\rho((\epsilon\mathbb{Q}+L)^{-1})$.

Define $\Upsilon := \epsilon\rho((\epsilon\mathbb{Q}+L)^{-1})$. Since $\epsilon\mathbb{Q}+L$ is a non-singular M-matrix matrix, $(\epsilon\mathbb{Q}+L)^{-1}$ exists and is a positive matrix. By the Perron-Frobenius Theorem there exists a right Perron-eigenvector $\wp >> 0$ such that

$$\Upsilon\wp = \epsilon(\epsilon\mathbb{Q}+L)^{-1}\wp.$$

Multiplying both sides by $\epsilon\mathbb{Q}+L$ and ϵ^{-1} result in

$$\epsilon^{-1}\Upsilon(\epsilon\mathbb{Q}+L)\wp = \wp. \tag{3.3}$$

Define

$$\left\{ \begin{array}{llll} (a) & \Upsilon & := & r_0 + r_1\epsilon + o(\epsilon), \quad r_0 \neq 0 \\ (b) & \wp & := & v_0 + v_1\epsilon + o(\epsilon), \quad v_0 \neq 0 \end{array} \right\} \tag{3.4}$$

as the perturbation expansions with respect to parameter ϵ. Replacing the expansion corresponding to υ and $\wp$ in equation (3.3) result in

$$\epsilon^{-1}(r_0 + r_1\epsilon + o(\epsilon))(\epsilon\mathbb{Q} + L)(v_0 + v_1\epsilon + o(\epsilon)) = v_0 + v_1\epsilon + o(\epsilon). \tag{3.5}$$

Setting ϵ^{-1}th terms on both sides of (3.5) results in $r_0 L v_0 = 0$. This gives $Lv_0 = 0$ as $r_0 \neq 0$. Hence, v_0 is the right Perron eigenvector of L. For simplicity, we assume that v_0 is the normalized right Perron eigenvector of L. That is,

$$v_0 = \theta. \tag{3.6}$$

Comparing ϵ^0th terms on both sides of (3.5) results in

$$r_0\mathbb{Q}v_0 + r_1 L v_0 + r_0 L v_1 = v_0.$$

Applying (3.6) to the equation above yields

$$r_0\mathbb{Q}\theta + r_1 L\theta + r_0 L v_1 = \theta. \tag{3.7}$$

Since $L\theta = 0$, (3.7) becomes

$$r_0\mathbb{Q}\theta + r_0 L v_1 = \theta. \tag{3.8}$$

Since $\mathbb{1}^\top L = 0$ and $\mathbb{1}^\top\theta = 1$, multiplying both sides of (3.8) from the left side by $\mathbb{1}^\top$ results in

$$r_0 = \frac{1}{\mathbb{1}^\top\mathbb{Q}\theta}. \tag{3.9}$$

Now, to find v_1 multiply both sides of (3.8) by $L^{\#}$ from the left side. Thus (3.8) becomes

$$r_0 L^{\#}\mathbb{Q}\theta + r_0 L^{\#} L v_1 = L^{\#}\theta. \tag{3.10}$$

Since $L^{\#}\theta = 0$ and $L^{\#}Lv_1 = v_1$ (See parts 2 and 3 of Lemma C.1 in Appendix C), (3.10) becomes

$$v_1 = -L^{\#}\mathbb{Q}\theta. \tag{3.11}$$

Comparing ϵ^1th terms of (3.5) from both sides yields

$$r_0\mathbb{Q}v_1 + r_1\mathbb{Q}v_0 + r_0 L v_2 + r_1 L v_1 + r_2 L v_0 = v_1. \tag{3.12}$$

Given $\mathbb{1}^\top L = 0$, multiplying both sides of (3.12) by $\mathbb{1}^\top$ results in

$$r_0\mathbb{1}^\top\mathbb{Q}v_1 + r_1\mathbb{1}^\top\mathbb{Q}v_0 = \mathbb{1}^\top v_1.$$

Applying (3.6), (3.9) and (3.11) to the equation above yield

$$r_1 = \frac{\mathbb{1}^\top\mathbb{Q}L^{\#}\mathbb{Q}\theta}{(\mathbb{1}^\top\mathbb{Q}\theta)^2}. \tag{3.13}$$

Replacing ϵ with $\frac{1}{\mu}$ and applying (3.22) and (3.13) to (3.4) conclude

$$\begin{aligned} R_0 &= r_0 + r_1\epsilon + o(\epsilon) \\ &= \frac{1}{\mathbb{1}^\top\mathbb{Q}\theta} + \frac{1}{\mu}\Big(\frac{\mathbb{1}^\top\mathbb{Q}L^{\#}\mathbb{Q}\theta}{(\mathbb{1}^\top\mathbb{Q}\theta)^2}\Big) + o(\frac{1}{\mu}). \end{aligned}$$

□

The following Theorem generalizes the result of Lemma 3.2 to formulate $R_0 = \rho(B(P+\mu L)^{-1})$ for any positive diagonal matrix B.

Theorem 3.3. *Let B be a positive diagonal matrix and P be a non-negative diagonal matrix where $P \neq 0$. Suppose that L is a Laplacian matrix in which $\mathbb{1}^\top$ and θ are the corresponding left and normalized right Perron-eigenvectors such that $\mathbb{1}^\top\theta = 1$. Let $R_0 = \rho(B(P+\mu L)^{-1})$. Then for any $\mu > 0$*

$$R_0 = \hat{R}_0 + \frac{\hat{R}_0}{\mu}\Big(\frac{\mathbb{1}^\top PB^{-1}\tilde{L}^{\#}P\theta}{\mathbb{1}^\top P\theta}\Big) + o(\frac{1}{\mu}), \tag{3.14}$$

where $\hat{R}_0 = \dfrac{\mathbb{1}^\top B\theta}{\mathbb{1}^\top P\theta}$ and $\tilde{L}^{\#}$ denotes the group inverse matrix of the Laplacian matrix LB^{-1}.

Proof. Since B is a positive diagonal matrix, B^{-1} exists. Thus,

$$R_0 = \rho(B(P+\mu L)^{-1}) = \rho((PB^{-1}+\mu LB^{-1})^{-1}) =: \rho((\tilde{Q}+\mu\tilde{L})^{-1}),$$

where $\tilde{Q} = PB^{-1}$ and $\tilde{L} = LB^{-1}$ is a Laplacian matrix. Denote $\tilde{\theta} = \dfrac{B\theta}{\mathbb{1}^\top B\theta}$ and $\tilde{L}^{\#}$ as the normalized right Perron-eigenvector and the group inverse of $\tilde{L}$, respectively.

Substituting $\tilde{Q}$, $\tilde{L}^{\#}$ and $\tilde{\theta}$ into (3.2) of Lemma 3.2 yields

$$\begin{aligned}
R_0 &= \frac{1}{\mathbb{1}^\top\tilde{Q}\tilde{\theta}} + \frac{1}{\mu}\Big(\frac{\mathbb{1}^\top\tilde{Q}\tilde{L}^{\#}\tilde{Q}\theta}{(\mathbb{1}^\top\tilde{Q}\tilde{\theta})^2}\Big) + o(\frac{1}{\mu}) \\
&= \frac{1}{\mathbb{1}^\top PB^{-1}(\frac{B\theta}{\mathbb{1}^\top B\theta})} + \frac{1}{\mu}\frac{\mathbb{1}^\top PB^{-1}\tilde{L}^{\#}PB^{-1}\frac{B\theta}{\mathbb{1}^\top B\theta}}{(\mathbb{1}^\top PB^{-1}(\frac{B\theta}{\mathbb{1}^\top B\theta})^2)} + o(\frac{1}{\mu}) \\
&= \frac{\mathbb{1}^\top B\theta}{\mathbb{1}^\top P\theta} + (\frac{1}{\mu})(\frac{\mathbb{1}^\top B\theta}{\mathbb{1}^\top P\theta})(\frac{\mathbb{1}^\top PB^{-1}\tilde{L}^{\#}P\theta}{\mathbb{1}^\top P\theta}) + o(\frac{1}{\mu}) \\
&= \hat{R}_0 + \frac{\hat{R}_0}{\mu}\frac{\mathbb{1}^\top PB^{-1}\tilde{L}^{\#}P\theta}{\mathbb{1}^\top P\theta} + o(\frac{1}{\mu}),
\end{aligned}$$

where $\hat{R}_0 = \dfrac{\mathbb{1}^\top B\theta}{\mathbb{1}^\top P\theta}$. □

The following result examines Theorem 3.3 by looking at $R_0 = \rho(B(P+\mu L)^{-1})$ from a different angle. In particular, rather than considering the group inverse $\tilde{L}^{\#}$ of the Laplacian matrix LB^{-1}, the following expansion takes the group inverse $L^{\#}$ of the Laplacian matrix L into consideration.

Theorem 3.4. *Let B be a positive diagonal matrix and P be a non-negative diagonal matrix where $P \neq 0$. Suppose that L is a Laplacian matrix in which $\mathbb{1}^\top$ and θ are the corresponding left and normalized right Perron-eigenvectors such that $\mathbb{1}^\top\theta = 1$. Let $R_0 = \rho(B(P+\mu L)^{-1})$. Then for any $\mu > 0$*

$$R_0 = \hat{R}_0 + \frac{\hat{R}_0}{\mu}\Big(\frac{\mathbb{1}^\top(\frac{B}{\hat{R}_0} - P)L^{\#}(\frac{B}{\hat{R}_0} - P)\theta}{\mathbb{1}^\top P\theta}\Big) + o(\frac{1}{\mu}), \tag{3.15}$$

where $\hat{R}_0 = \dfrac{\mathbb{1}^\top B\theta}{\mathbb{1}^\top P\theta}$ and $L^{\#}$ is the group inverse of L.

Proof. To acquire the expansion, it is convenient to work with $R_0 = \rho((P+\mu L)^{-1}B)$. Note that $B(P+\mu L)^{-1}$ and $(P+\mu L)^{-1}B$ are similar matrices, thus $\rho(B(P+\mu L)^{-1}) = \rho((P+\mu L)^{-1}B)$.

$$R_0 = \rho((P+\mu L)^{-1}B) = \rho((\frac{P}{\mu} + L)^{-1}\frac{B}{\mu}) =: \rho((\epsilon P + L)^{-1}\epsilon B).$$

As all the off diagonal entries of $\epsilon P + L$ are non-positive and the sum of the entries of each column is positive, $\epsilon P + L$ is a non-singular M-matrix, thus $(\epsilon P + L)^{-1}$ exists and is a positive matrix[4]. By the Perron-Frobenius Theorem there exists a right Perron-eigenvector v such that

$$R_0 v = (\epsilon P + L)^{-1}(\epsilon B)v.$$

Multiplying both sides by $(\epsilon P + L)\dfrac{1}{\mathbb{1}^\top v}$ yields

$$R_0(\epsilon P + L)\tilde{v} = (\epsilon B)\tilde{v}, \tag{3.16}$$

where $\tilde{v} := \dfrac{v}{\mathbb{1}^\top v}$ denotes the normalized right Perron-eigenvector. Rewriting R_0 and $\tilde{v}$ as the perturbation expansions with respect to parameter ϵ are given by

$$\left\{ \begin{array}{rcll} R_0 & := & r_0 + r_1\epsilon + o(\epsilon), & r_0 \neq 0 \\ \tilde{v} & := & \tilde{v}_0 + \tilde{v}_1\epsilon + o(\epsilon), & \tilde{v}_0 \neq 0. \end{array} \right\} \tag{3.17}$$

Replacing R_0 and $\tilde{v}$ with the perturbation expansion from (3.17) into (3.16) result in

$$(r_0 + r_1\epsilon + r_2\epsilon^2 + \dots)(\epsilon P + L)(\tilde{v}_0 + \tilde{v}_1\epsilon + \tilde{v}_2\epsilon^2 + \dots) = (\epsilon B)(\tilde{v}_0 + \tilde{v}_1\epsilon + \tilde{v}_2\epsilon^2 + \dots).$$

Setting the powers of ϵ equal to each other gives the following equations

$$\left\{ \begin{array}{lcl} (\epsilon^0) & r_0 L\tilde{v}_0 & = 0, \\ (\epsilon^1) & r_0 P\tilde{v}_0 + r_1 L\tilde{v}_0 + r_0 L\tilde{v}_1 & = B\tilde{v}_0, \\ (\epsilon^2) & r_0 P\tilde{v}_1 + r_1 P\tilde{v}_0 + r_0 L\tilde{v}_2 + r_1 L\tilde{v}_1 + r_2 L\tilde{v}_0 & = B\tilde{v}_1, \\ & \vdots & \end{array} \right\} \tag{3.18}$$

Comparing ϵ^0th terms from both sides of (3.18) yields $r_0 L\tilde{v}_0 = 0$. Equivalently, $L\tilde{v}_0 = 0$, which implies that $\tilde{v}_0$ is the normalized right Perron-eigenvector of L. Thus,

$$\tilde{v}_0 = \theta. \tag{3.19}$$

Comparing ϵ^0th terms from both sides and substituting $\tilde{v_0}$ with θ result in

$$r_0 P\theta + r_1 L\theta + r_0 L\tilde{v}_1 = B\theta. \tag{3.20}$$

Since $L\theta = 0$, (3.20) becomes

$$r_0 P\theta + r_0 L\tilde{v}_1 = B\theta. \tag{3.21}$$

Multiplying both sides of (3.21) by $\mathbb{1}^\top$ from the left side yields

$$r_0\mathbb{1}^\top P\theta + r_0\mathbb{1}^\top L\tilde{v}_1 = \mathbb{1}^\top B\theta$$
$$r_0\mathbb{1}^\top P\theta = \mathbb{1}^\top B\theta,$$

where the last equation is obtained from the assumption that $\mathbb{1}^\top$ is the left Perron eigenvector of L, thus $\mathbb{1}^\top L = 0$ (Lemma C.1 in Appendix C). Hence,

$$r_0 = \frac{\mathbb{1}^\top B\theta}{\mathbb{1}^\top P\theta}. \tag{3.22}$$

Multiplying both sides of (3.21) by $L^\#$ from the left side yields $r_0 L^\# P\theta + r_0 L^\# L\tilde{v}_1 = L^\# B\theta$. It follows from Lemma C.1 in Appendix C that $L^\# L\tilde{v}_1 = \tilde{v}_1$. Hence,

$$\tilde{v}_1 = L^\#(\frac{B}{r_0} - P)\theta. \tag{3.23}$$

Since $\mathbb{1}^\top L = 0$, multiplying both sides of equation (ϵ^2) in (3.18) from the left hand side by $\mathbb{1}^\top$ results in

$$r_0\mathbb{1}^\top P\tilde{v}_1 + r_1\mathbb{1}^\top P\tilde{v}_0 = \mathbb{1}^\top B\tilde{v}_1. \tag{3.24}$$

Applying (3.19) and (3.23) to (3.24) give

$$r_1 = \frac{r_0}{\mathbb{1}^\top P\theta}\mathbb{1}^\top(\frac{B}{r_0} - P)L^\#(\frac{B}{r_0} - P)\theta. \tag{3.25}$$

The proof is complete by substituting $\epsilon = \frac{1}{\mu}$ and applying (3.22) and (3.24) to R_0 in (3.17). □

The following result evaluates R_0 for the special case when P is a nonnegative multiple of the identity matrix. That is, $P = \mathrm{diag}\{p_i\} = \tilde{p}I$ for some $\tilde{p} \geq 0$. In fact, the following result is the direct implication of Theorem 3.4 by replacing P with $\tilde{p}I$ in (3.15).

Corollary 3.5. *Let $B = \mathrm{diag}\{b_i\} > 0$ and $P = \mathrm{diag}\{p_i\} = \tilde{p}I$ for some $\tilde{p} \geq 0$. Suppose that L is a Laplacian matrix in which $\mathbb{1}^\top$ and θ are the corresponding left and normalized right Perron-eigenvectors such that $\mathbb{1}^\top\theta = 1$. Let $R_0 = \rho(B(P+\mu L)^{-1})$. Then for any $\mu > 0$*

$$R_0 = \frac{\sum_i b_i\theta_i}{\tilde{p}} + \frac{1}{\mu}\Big(\frac{\sum_i\sum_j b_i\ell_{ij}^{\#}b_j\theta_j}{\sum_i b_i\theta_i}\Big) + o\Big(\frac{1}{\mu}\Big). \tag{3.26}$$

3.3 Monotonicity of R_0

The following result examines the monotonicity and convexity of the basic reproduction number $R_0 = \rho(B(P+\mu L)^{-1})$ by applying the graph-theoretic approach.

Proposition 3.6. *Let $B = \mathrm{diag}\{b_i\}$ and $P = \mathrm{diag}\{p_i\}$ be diagonal matrices such that $b_i > 0, p_i \geq 0$ and $P \neq 0$. Suppose L is an irreducible Laplacian matrix. Denote $R_0 = \rho(B(P+\mu L)^{-1})$ where $\mu > 0$. Then, the following statements hold:*

(a) $\dfrac{dR_0}{d\mu} \leq 0$*, with equality holding if and only if $b_i = b_j$ and $p_i = p_j$ for $i, j = 1, \cdots, n$.*

(b) $\dfrac{d^2R_0}{d\mu^2} \geq 0$*, with equality holding if and only if $b_i = b_j$ and $p_i = p_j$ for $i, j = 1, \cdots, n$.*

Proof. (a) Let $w = (w_1, \ldots, w_n)$ be the normalized left eigenvector of $B(P+\mu L)^{-1}$ corresponding to R_0, *i.e.*,

$$R_0 w = wB(P+\mu L)^{-1} \iff R_0 w(P+\mu L) = wB \iff w(P+\mu L) = \frac{wB}{R_0},$$

or in the component-wise form

$$p_i w_i - \mu\sum_{k\neq i} a_{ki}w_k + \mu\sum_{k\neq i} a_{ki}w_i = \frac{b_i w_i}{R_0}, \qquad i = 1, 2, \ldots, n. \tag{3.27}$$

Dividing w_i on both sides yields

$$\frac{b_i}{R_0} = p_i - \mu \sum_{k \neq i} a_{ki} \frac{w_k}{w_i} + \mu \sum_{k \neq i} a_{ki}. \tag{3.28}$$

Differentiating both sides with respect to μ yields

$$\begin{aligned}\frac{-b_i}{R_0^2} \frac{dR_0}{d\mu} = \frac{-b_i \dot{R}_0}{R_0^2} &= -\sum_{k \neq i} a_{ki} \frac{w_k}{w_i} - \mu \sum_{k \neq i} a_{ki} \frac{\dot{w}_k w_i - w_k \dot{w}_i}{w_i^2} + \sum_{k \neq i} a_{ki} \\ &= -\sum_{k \neq i} a_{ki} \frac{w_k}{w_i} \Big(1 - \frac{w_i}{w_k} + \mu \frac{\dot{w}_k}{w_k} - \mu \frac{\dot{w}_i}{w_i}\Big),\end{aligned}$$

Thus,

$$\dot{R}_0 = \frac{R_0^2}{b_i} \sum_{k \neq i} a_{ki} \frac{w_k}{w_i} \Big(1 - \frac{w_i}{w_k} + \mu \frac{\dot{w}_k}{w_k} - \mu \frac{\dot{w}_i}{w_i}\Big). \tag{3.29}$$

Setting $\tilde{a}_{ki} = a_{ki} \frac{w_k}{w_i}$ and summing over all i yield

$$\begin{aligned}\dot{R}_0 =& R_0^2 \sum_i \frac{1}{b_i} \sum_{k \neq i} \tilde{a}_{ki} \Big(1 - \frac{w_i}{w_k} + \mu \frac{\dot{w}_k}{w_k} - \mu \frac{\dot{w}_i}{w_i}\Big) \\ =& R_0^2 \sum_i \sum_{k \neq i} \frac{\tilde{a}_{ki}}{b_i} \Big[1 - \frac{w_i}{w_k} + \mu \Big(\frac{\dot{w}_k}{w_k} - \frac{\dot{w}_i}{w_i}\Big)\Big] \\ =& R_0^2 \sum_{\mathcal{Q} \in \mathbb{Q}} w(\mathcal{Q}) \sum_{(r,s) \in E(C_{\mathcal{Q}})} \Big[1 - \frac{w_r}{w_s} + \mu \Big(\frac{\dot{w}_s}{w_s} - \frac{\dot{w}_r}{w_r}\Big)\Big].\end{aligned}$$

The last equality follows from the Tree-Cycle identity (see Appendix A). Applying the AM-GM inequality, $(w_1 + \cdots + w_l)/l \geq \sqrt[l]{w_1 \cdots w_l}$ yields

$$\sum_{(s,r) \in E(C_{\mathbb{Q}})} \Big(1 - \frac{w_s}{w_r}\Big) = l - \Big(\sum_{(s,r) \in E(C_{\mathbb{Q}})} \frac{w_s}{w_r}\Big) \leq l - l\Big(\prod_{(s,r) \in E(C_{\mathbb{Q}})} \frac{w_s}{w_r}\Big)^{1/l} = l - l = 0. \tag{3.30}$$

Furthermore,

$$\sum_{(r,s) \in E(C_{\mathcal{Q}})} \Big(\frac{\dot{w}_s}{w_s} - \frac{\dot{w}_r}{w_r}\Big) = 0. \tag{3.31}$$

Inequality (3.30) together with equation (3.31) result in $\dot{R}_0 \leq 0$. Notice that $\dot{R}_0 = 0$ if and only if $w_r = w_s$ for every pair (s, r) in (2.15).

(b) Differentiating (3.29) with respect to μ yields

$$\ddot{R}_0 = \frac{R_0^2}{b_i} \sum_{k \neq i} a_{ki} \frac{w_k}{w_i} \Big[2\Big(\frac{\dot{w}_k}{w_k} - \frac{\dot{w}_i}{w_i} \Big) + \mu \Big(\frac{\ddot{w}_k}{w_k} - \frac{\ddot{w}_i}{w_i} \Big) - 2\mu \Big(\frac{\dot{w}_k}{w_k} \frac{\dot{w}_i}{w_i} - \Big(\frac{\dot{w}_i}{w_i} \Big)^2 \Big) \Big]. \tag{3.32}$$

Summing over all i yields

$$\ddot{R}_0 = R_0^2 \sum_i \sum_{k \neq i} \frac{\tilde{a_{ki}}}{b_i} \Big[2\Big(\frac{\dot{w}_k}{w_k} - \frac{\dot{w}_i}{w_i} \Big) + \mu \Big(\frac{\ddot{w}_k}{w_k} - \frac{\ddot{w}_i}{w_i} \Big) - 2\mu \Big(\frac{\dot{w}_k}{w_k} \frac{\dot{w}_i}{w_i} - \Big(\frac{\dot{w}_i}{w_i} \Big)^2 \Big) \Big], \tag{3.33}$$

where $\tilde{a_{ki}} = a_{ki} \frac{w_k}{w_i}$. It follows from the Tree-Cycle identity (see Appendix A) that

$$\ddot{R}_0 = R_0^2 \sum_{\mathcal{Q} \in \mathbb{Q}} w(\mathcal{Q}) \sum_{(s,r) \in E(C_{\mathcal{Q}})} \Big[2\Big(\frac{\dot{w}_s}{w_s} - \frac{\dot{w}_r}{w_r} \Big) + \mu \Big(\frac{\ddot{w}_s}{w_s} - \frac{\ddot{w}_r}{w_r} \Big) - 2\mu \Big(\frac{\dot{w}_s}{w_s} \frac{\dot{w}_r}{w_r} - \Big(\frac{\dot{w}_r}{w_r} \Big)^2 \Big) \Big]. \tag{3.34}$$

Note that $\sum_{(s,r) \in E(C_{\mathcal{Q}})} \Big(\frac{\dot{w}_s}{w_s} - \frac{\dot{w}_r}{w_r} \Big) = 0$. Thus, (3.34) becomes

$$\begin{aligned}
\ddot{R}_0 &= R_0^2 2\mu \sum_{\mathcal{Q} \in \mathbb{Q}} w(\mathcal{Q}) \sum_{(s,r) \in E(C_{\mathcal{Q}})} \Big(\Big(\frac{\dot{w}_r}{w_r} \Big)^2 - \frac{\dot{w}_s}{w_s} \frac{\dot{w}_r}{w_r} \Big) \\
&= R_0^2 \mu \sum_{\mathcal{Q} \in \mathbb{Q}} w(\mathcal{Q}) \sum_{(s,r) \in E(C_{\mathcal{Q}})} \Big[\Big(\frac{\dot{w}_r}{w_r} \Big)^2 - \frac{\dot{w}_s}{w_s} \frac{\dot{w}_r}{w_r} + \Big(\frac{\dot{w}_s}{w_s} \Big)^2 - \frac{\dot{w}_s}{w_s} \frac{\dot{w}_r}{w_r} \Big] \\
&= R_0^2 \mu \sum_{\mathcal{Q} \in \mathbb{Q}} w(\mathcal{Q}) \sum_{(s,r) \in E(C_{\mathcal{Q}})} \Big(\frac{\dot{w}_r}{w_r} - \frac{\dot{w}_s}{w_s} \Big)^2 \geq 0.
\end{aligned}$$

Notice that $\ddot{R}_0 = 0$ if and only if $\frac{\dot{w}_s}{w_s} = \frac{\dot{w}_r}{w_r}$ for any pair of (s, r) locating in a directed cycle of $(\mathcal{G}, L)$. □

The following result states the upper and lower bounds for $R_0 = \rho(B(P + \mu L)^{-1})$ by applying

Proposition 3.6.

Theorem 3.7. *Let $B = \mathrm{diag}\{b_i\}$ and $P = \mathrm{diag}\{p_i\}$ be two diagonal matrices such that $b_i > 0$ and $p_i \geq 0$. Suppose L is an irreducible Laplacian matrix where θ is the normalized right Perron-eigenvector. Let $R_0 = \rho(B(P+\mu L)^{-1})$. Then, for any $\mu > 0$*

$$\frac{\sum_{i=1}^{n} b_i\theta_i}{\sum_{i=1}^{n} p_i\theta_i} \leq R_0 \leq \max_{1\leq i\leq n}\Big\{\frac{b_i}{p_i}\Big\}. \tag{3.35}$$

Proof. It follows from Proposition 3.6 that R_0 is decreasing with respect to μ. Thus, the upper bound for R_0 occurs when $\mu \to 0$,

$$\lim_{\mu\to 0} \rho(B(P+\mu L)^{-1}) = \rho(BP^{-1}) = \max_{1\leq i\leq n}\{\frac{b_i}{p_i}\}. \tag{3.36}$$

Similarly, the lower bound for R_0 happens when $\mu \to \infty$. Letting μ approach ∞ in (3.14) yield

$$\lim_{\mu\to\infty} \rho(B(P+\mu L)^{-1}) = \lim_{\mu\to\infty} (\hat{R}_0 + \frac{\hat{R}_0}{\mu}\big(\frac{\mathbb{1}^\top PB^{-1}\tilde{L}^{\#}P\theta}{\mathbb{1}^\top P\theta}\big) + o(\frac{1}{\mu})) = \hat{R}_0 = \frac{\sum_{i=1}^{n} b_i\theta_i}{\sum_{i=1}^{n} p_i\theta_i}. \tag{3.37}$$

Combining (3.36) and (3.37) yields the result desired. □

3.4 Application to an Airborne Disease Model

Consider the following multi-patch SIS epidemiological model in a heterogeneous network of n patches $(n \geq 0)$ [1]

$$\begin{cases} S_i' &= -\dfrac{\beta_i S_i I_i}{S_i + I_i} + \gamma_i I_i + \mu_S \displaystyle\sum_{j=1}^{n} (a_{ij}S_j - a_{ji}S_i), \\ I_i' &= \dfrac{\beta_i S_i I_i}{S_i + I_i} - \gamma_i I_i + \mu_I \displaystyle\sum_{j=1}^{n} (a_{ij}I_j - a_{ji}I_i), \end{cases} \qquad i = 1, 2, \ldots, n, \tag{3.38}$$

where S_i and I_i denote the number of susceptible and infected individuals in patch i, respectively. $\gamma_i > 0$ is the recover rate of the infected individuals in patch i, and $\beta_i > 0$ represents the contact rate between susceptible and infected individuals in patch i.

Parameters $\mu_S > 0$ and $\mu_I > 0$ denote the dispersal rate of the susceptible and infected individuals.

The Jacobian matrix of system (3.38) at the the disease-free equilibrium E_0 becomes

$$J|_{E_0} = \mathrm{diag}\{\beta_i - \gamma_i\} - \mu_I L. \tag{3.39}$$

The disease growth rate is computed as the spectral bound of the Jacobian matrix at the disease free equilibrium, i.e. $s(J|_{E_0})$.

The following result, which is an immediate consequence of Theorem 2.1, provides an expansion for the disease growth rate for system (3.38) by replacing q_i in expressions (2.7) and (2.2) with $\beta_i - \gamma_i$. Additionally, the monotonically decreasing of $r(E_0)$ is attained from Lemma 2.3.

Theorem 3.8. *Let L be an irreducible Laplacian matrix such that $\theta^\top = (\theta_1, \ldots, \theta_n)$ is the normalized right Perron eigenvector of L. Suppose that* (2.41) *holds. Then, for any $\mu > 0$*

$$r(E_0) = \sum_{i=1}^{n}(\beta_i - \gamma_i)\theta_i + \frac{1}{\mu}\sum_{i=1}^{n}\sum_{j=1}^{n}(\beta_i - \gamma_i)\ell_{ij}^{\#}(\beta_j - \gamma_j)\theta_j + o\big(\frac{1}{\mu}\big), \tag{3.40}$$

where $L_{ij}^{\#} = [\ell_{ij}^{\#}]$ is the group inverse matrix of L.

Furthermore, $r(E_0)$ is strictly decreasing with respect to μ and

$$\sum_{i=1}^{n}(\beta_i - \gamma_i)\theta_i \leq r(E_0) \leq \max_{1\leq i\leq n}\{\beta_i - \gamma_i\}, \tag{3.41}$$

with lower and upper bounds achieved when $\mu \to \infty$ and $\mu \to 0$, respectively.

In addition to the expansion for the disease growth rate $r(E_0)$, an expansion for the network basic reproduction number for system (3.14) is accessible.

The basic reproduction number of system (3.38) at the the disease-free equilibrium E_0 is given by

$$R_0 = \rho(\tilde{B}(\tilde{P} + \mu L)^{-1}), \tag{3.42}$$

where $\tilde{B} = \mathrm{diag}\{\beta_i\}$ and $\tilde{P} = \mathrm{diag}\{\gamma_i\}$.

The following result describes the expansion for R_0 by replacing b_i with β_i and g_i with γ_i in (3.14) of Theorem 3.9, respectively.

Furthermore, the upper and lower bounds for R_0 is attained from Theorem 3.7.

Theorem 3.9. *Let $\tilde{B} = \mathrm{diag}\{\beta_i\}$ and $\tilde{P} = \mathrm{diag}\{\gamma_i\}$ be two positive diagonal matrices. Suppose that L is an irreducible Laplacian matrix in which $\theta^\top = (\theta_1, \ldots, \theta_n)$ is the normalized right-Perron eigenvector. Let $R_0 = \rho(\tilde{B}(\tilde{P} + \mu L)^{-1})$. Then, for any $\mu > 0$*

$$R_0 = \hat{R}_0 + \frac{\hat{R}_0}{\mu}\Big(\frac{\mathbb{1}^\top \tilde{P}\tilde{B}^{-1}\tilde{L}^{\#}\tilde{P}\theta}{\mathbb{1}^\top \tilde{P}\theta}\Big) + o(\frac{1}{\mu}), \tag{3.43}$$

where $\hat{R}_0 = \dfrac{\sum_i \beta_i\theta_i}{\sum_i \gamma_i\theta_i}$ and $\tilde{L}^{\#}$ denotes the group inverse matrix of the Laplacian matrix $\tilde{L} = L\tilde{B}^{-1}$.

Furthermore, R_0 is strictly decreasing with respect to μ and

$$\frac{\sum_i \beta_i\theta_i}{\sum_i \gamma_i\theta_i} \leq R_0 \leq \max_{1\leq i\leq n}\{\frac{\beta_i}{\gamma_i}\}, \tag{3.44}$$

with lower and upper bounds achieved when $\mu \to \infty$ and $\mu \to 0$, respectively.

3.5 Application to a Waterborne Disease Model

Consider the following multi-patch SIR waterborne disease (e.g., cholera) model in a heterogeneous network of n patches $(n \geq 0)$ [8]

$$\begin{cases} S_i' &= \Lambda_i - \beta_i S_i \dfrac{B_i}{\eta_i + B_i} - d_i S_i + \sigma_i R_i, \\ I_i' &= \beta_i S_i \dfrac{B_i}{\eta_i + B_i} - (d_i + \alpha_i + \gamma_i) I_i, \\ R_i' &= \gamma_i I_i - (d_i + \sigma_i) R_i, \\ B_i' &= \xi_i I_i - \delta_i B_i + \mu \displaystyle\sum_{j=1}^{n} (a_{ij} B_j - a_{ji} B_i), \end{cases} \qquad i = 1, 2, \ldots, n. \tag{3.45}$$

Notice that $\dfrac{\beta_i S_i B_i}{\eta_i + B_i}$ is incidence saturating with constant η_i representing the 50% transmission efficacy, and $\mu > 0$ is the movement rate parameter with a_{ij} is the movement rate from patch j to patch i. In this case we assume that the movement is asymmetric, that is $a_{ji} \neq a_{ij}$.

The Jacobian matrix of system (3.45) at the disease-free equilibrium $E_0 = (S_i^0, \ldots, S_n^0)$ is given by

$$J|_{E_0} = F - V = \begin{pmatrix} 0 & D_2 \\ 0 & 0 \end{pmatrix} - \begin{pmatrix} D_1 & 0 \\ -D_3 & (D_4 + \mu L) \end{pmatrix}, \tag{3.46}$$

where $D_1 = \operatorname{diag}\{d_i + \alpha_i + \gamma_i\}$, $D_2 = \operatorname{diag}\{\frac{\beta_i S_i^0}{\eta_i}\}$, $D_3 = \operatorname{diag}\{\xi_i\}$, and $D_4 = \operatorname{diag}\{\delta_i\}$. Matrix L denotes the Laplacian matrix associated to the movement matrix $[a_{ij}]$.

Notice that the the Jacobian matrix J at E_0 in (3.46) does not follow the same structure as its counterpart in (3.39). Thus, unlike Section 3.4, the disease growth of system (3.45) cannot be determined from the disease the expansion for the disease growth rate, i.e., $r(E_0) = s(J|_{E_0})$, of Theorem 2.1.

However, Theorem 3.9 enables us to investigate the disease growth of the system by computing the basic reproduction number R_0 of the system.

Note that matrix block $D_4+\mu L$ in (3.46) is a Z-matrix, i.e. all off-diagonal entries are non-positive, and the sum of the entries of each column is positive, which means $(D_4 + \mu L)^{-1} \geq 0$. Following the next generation matrix approach, $R_0 = \rho(FV^{-1}) = \rho(V^{-1}F)$. Thus,

$$R_0 = \rho(V^{-1}F) = \rho((D_4 + \mu L)^{-1}D_1^{-1}D_2D_3) =: \rho((D_4 + \mu L)^{-1}D_5),$$

where $D_5 = \mathrm{diag}\{\dfrac{\beta_i S_i^0 \psi_i}{\eta_i(d_i + \alpha_i + \gamma_i)}\}$. Our expansion results of R_0 in Section 3.2 and monotone /convexity/upper bound/lower bound results in Section 3.3 can be applied immediately to produce similar results as those in the previous Section for the SIS disease model, which are thus omitted.

CHAPTER 4: POPULATION PERSISTENCE AND DISEASE INVASION ON SPECIFIC NETWORKS

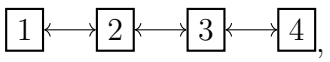
In this chapter, we numerically analyze the main results of Chapters 2 and 3 in epidemiology and ecology models over strongly connected heterogeneous networks. We design a different network structure for each model. We assume the movement between the regions in the network. Depending on the model and network dynamic, the regions might be human-made or created by nature, and the movement between the regions can be humans, animals or water.

An ecological model that describes a population dynamics in two regions, both occupied by the same species is called the sink-source model. In one region the population is sustainable (source), whereas in the other one the population cannot survive when they are isolated from other habitats (sink). Denote $f(0)$ as the population growth. A patch is called a source (sink), if $f(0) > 0$ ($f(0) < 0$).

In infectious disease models, the term hotspot is referred to areas with elevated transmission efficiency. Generally, a region is considered as a hostspot (non-hotspot) if the basic reproduction number $R_0 > 1$ ($R_0 < 1$). Throughout this Chapter $\overline{R}$ and $\underline{r}$ denote the hotspot and non-hotspot regions.

4.1 Population Persistence on a Path Network

Consider the following single species model as described in Section 2.4 on a path network of four regions shown as



where the movement between the patches is assumed to be symmetric with the assigned weight of 1. The Laplacian matrix L corresponding to the movement in the network is given by

$$L = \begin{pmatrix} 1 & -1 & 0 & 0 \\ -1 & 2 & -1 & 0 \\ 0 & -1 & 2 & -1 \\ 0 & 0 & -1 & 1 \end{pmatrix}, \tag{4.1}$$

where $\theta^\top = (\theta_1, \theta_2, \theta_3, \theta_4) = (\frac{1}{4}, \frac{1}{4}, \frac{1}{4}, \frac{1}{4})$ is the normalized right Perron-eigenvector. Denote $L^\#$ as the group inverse matrix of L, and is given by

$$L^\# := [\ell_{ij}^\#]_{4\times 4} = \frac{1}{8}\begin{pmatrix} 7 & 1 & -3 & -5 \\ 1 & 3 & -1 & -3 \\ -3 & -1 & 3 & 1 \\ -5 & -3 & 1 & 7 \end{pmatrix}. \tag{4.2}$$

For details of deriving the group inverse $L^\#$ from L, see C.3 from Appendix C.

Following Theorem 3.8, the population growth $r(E_0)$ of the single species model over 4 patches is described as

$$r(E_0) = \frac{1}{4}\sum_{i=1}^{4} f_i(0) + \frac{1}{4\mu}\sum_{i=1}^{4}\sum_{j=1}^{4} f_i(0)\ell_{ij}^\# f_j(0) + o\big(\frac{1}{\mu}\big) = \mathcal{A} + \frac{1}{\mu}\mathcal{H} + o(\frac{1}{\mu}). \tag{4.3}$$

where $\frac{1}{4}$ denotes the ith, $1 \le i \le 4$, element of the normalized right Perron-eigenvector θ, and $\ell_{ij}^\#$ for $1 \le i, j \le 4$ is the ijth element of $L^\#$. Function $f_i(0)$ corresponds to the population growth rate of patch i.

From (2.26), the first term in (4.3) denoted as $\mathcal{A}$ represents the network average, and from (2.27),

the coefficient of $\frac{1}{\mu}$ in (4.3) denoted as $\mathcal{H}$ represents the network heterogeneity.

Plugging $\ell_{ij}^{\#}$ from (4.2) result in

$$\mathcal{H} = \frac{1}{32}[5(f_1(0)-f_4(0))^2+3(f_1(0)-f_3(0))^2-(f_1(0)-f_2(0))^2+(f_2(0)-f_3(0))^2+3(f_2(0)-f_4(0))^2-(f_3(0)-f_4(0))^2]. \tag{4.4}$$

Given that the movement is assumed to symmetric, the value of $\mathcal{A}$ is independent of arrangement of the population growth rate $f_i(0)$ on each patch. Unlike $\mathcal{A}$, the value of $\mathcal{H}$ varies in regards to different arrangements of $f_i(0)$ on each patch. This implies that $\mathcal{H}$ carries the information that enables us understand the population persistent or extinction in the network.

In what follows, we investigate different sink-source scenarios on a 4-patch path network by calculating the network heterogeneity value $\mathcal{H}$ to understand the population dynamics in the network.

In all the scenarios, we denote $\overline{f(0)} > 0$ as the source patch and $\underline{f(0)} < 0$ as the sink patch.

One-source scenario

In this scenario we assume to have one source patch $\overline{f(0)}$ and three sink patches $\underline{f(0)}$. Since the movement between the patches is symmetric, there are two possible cases for this scenario:

1) $f_1(0) = \overline{f(0)} > f_2(0) = f_3(0) = f_4(0) = \underline{f(0)}$. The network heterogeneity index in (4.4) becomes $\mathcal{H}_1 = \frac{7}{32}(\overline{f(0)} - \underline{f(0)})^2$.

2) $f_2(0) = \overline{f(0)} > f_1(0) = f_3(0) = f_4(0) = \underline{f(0)}$. The network heterogeneity index in (4.4) becomes $\mathcal{H}_2 = \frac{3}{32}(\overline{f(0)} - \underline{f(0)})^2$.

It can be seen that $\mathcal{H}_1 > \mathcal{H}_2$, which implies that locating the source on patch 1 will result in a bigger population growth in the network.

Two-source scenario

In this scenario we assume to have two source patches and two sink patches. The symmetric movement between the patches in the network results in four possible cases as follow:

1) $f_1(0) = f_2(0) = \overline{f(0)} > f_3(0) = f_4(0) = \underline{f(0)}$. The network heterogeneity index become $\mathcal{H}_{12} = \frac{12}{32}(\overline{f(0)} - \underline{f(0)})^2$.

2) $f_1(0) = f_3(0) = \underline{f(0)} > f_2(0) = f_4(0) = \overline{f(0)}$. The network heterogeneity index become $\mathcal{H}_{13} = \frac{4}{32}(\overline{f(0)} - \underline{f(0)})^2$

3) $f_1(0) = f_4(0) = \overline{f(0)} > f_2(0) = f_3(0) = \underline{f(0)}$. The network heterogeneity index become $\mathcal{H}_{14} = \frac{4}{32}(\overline{f(0)} - \underline{f(0)})^2$.

4) $f_2(0) = f_3(0) = \overline{f(0)} > f_1(0) = f_4(0) = \underline{f(0)}$. The network heterogeneity index become $\mathcal{H}_{23} = \frac{4}{32}(\overline{f(0)} - \underline{f(0)})^2$.

The calculations above demonstrate that $\mathcal{H}_{12} > \mathcal{H}_{13} = \mathcal{H}_{14} = \mathcal{H}_{23}$. This implies that locating the sources on patches 1 and 2 will lead to the highest population growth compared to the two other scenarios.

Three-source scenario

For this scenario, we assume to have three source patches $\overline{f(0)}$ and one sink patch $\underline{f(0)}$. Due to the symmetry movement in the network, there are two cases:

1) $f_1(0) = f_2(0) = f_3(0) = \overline{f(0)} > f_4(0) = \underline{f(0)}$. The network heterogeneity index become $\mathcal{H}_{123} = \frac{7}{32}(\overline{f(0)} - \underline{f(0)})^2$.

2) $f_1(0) = f_2(0) = f_4(0) = \overline{f(0)} > f_3(0) = \underline{f(0)}$. The network heterogeneity index become $\mathcal{H}_{124} = \frac{3}{32}(\overline{f(0)} - \underline{f(0)})^2$.

It can be observed that having three sources on patches 1, 2 and 3 lead to a higher network population growth as $\mathcal{H}_{123} > \mathcal{H}_{124}$.

General scenario: same network average

For this scenario, we consider 8 different distributions of patch growth rates, in which they all have the same network average. All the scenarios (except distribution H) have the same maximum; see Figure 4.1(a). Figure 4.1(b) shows the network heterogeneity index $\mathcal{H}$ (for distribution H, this index value is 0). As shown in Figure 4.1(c), the meta-population growth rate r, corresponding to all except distribution H, has the same limiting values (the maximum of patch growth rates and the network average respectively) as the movement rate parameter μ approaches 0 or ∞.

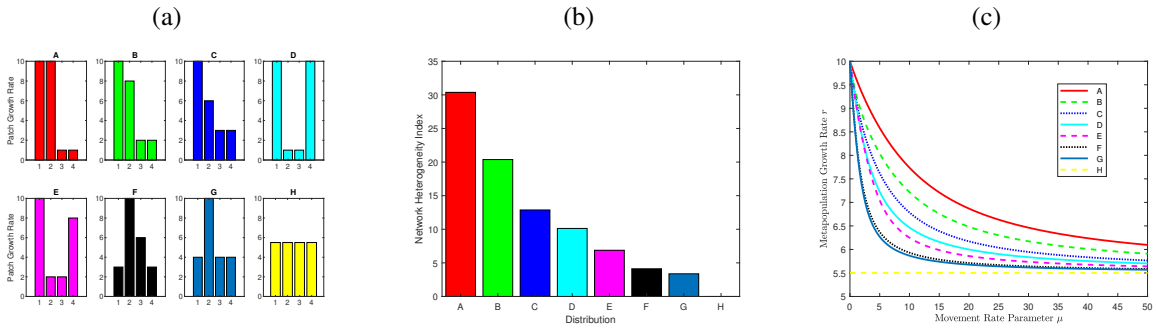
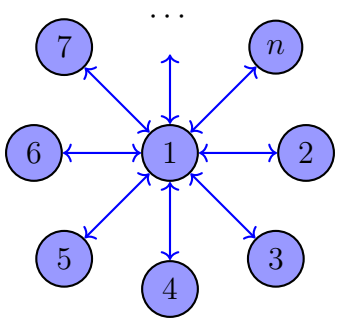


Figure 4.1: Network heterogeneity promotes population persistence.

4.2 Disease Invasion on a Star Network

Consider the SIS model described in Section 3.4 over an n-patch of a star network shown as



Vertex 1 denotes the hub, and vertices $2, 3, \ldots, n$ represent the leaves. All the movements between the hub and each leaf are assumed to be symmetric with the assigned weight of 1. The Laplacian matrix L corresponding to network movement is given by

$$L = \begin{pmatrix} n-1 & -1 & -1 & \cdots & -1 \\ -1 & 1 & 0 & \cdots & 0 \\ -1 & 0 & 1 & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ -1 & 0 & 0 & \cdots & 1 \end{pmatrix}, \tag{4.5}$$

where $\theta^\top = (\frac{1}{n}, \ldots, \frac{1}{n})$ denotes the normalized right Perron-eigenvector of L. The group inverse $L^\#$ of L is given by

$$L^\# = \frac{n-1}{n^2} J + \frac{1}{n} \begin{pmatrix} 0 & -1 & -1 & \cdots & \cdots & \cdots & -1 \\ -1 & n-2 & -2 & \cdots & \cdots & \cdots & -2 \\ -1 & -2 & n-2 & -2 & \cdots & \cdots & -2 \\ -1 & -2 & -2 & n-2 & -2 & \cdots & -2 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ -1 & -2 & -2 & -2 & \cdots & -2 & n-2 \end{pmatrix}, \tag{4.6}$$

where $J = [1]_{n\times n}$. The details of computing $L^{\#}$ over a star network are provided in Section D.1 of Appendix D.

For simplicity, we assume that the recovery rates γ_i, for $1 \leq i \leq n$ of the SIS model are equal. (For parameter details, see Section 3.4). Denote $\tilde{\gamma}$ as the recovery rate for all the patches in the network. Consequently, the basic reproduction number R_0 for the SIS model over an n-patch star network is special case of Theorem 3.4. In particular, the computation of R_0 is followed from equation (3.26) of Corollary 3.5. That is

$$R_0 = \frac{1}{n}\frac{\sum_{i=1}^{n}\beta_i}{\tilde{\gamma}} + \frac{1}{\mu}\frac{\sum_{i=1}^{n}\sum_{j=1}^{n}\beta_i\ell_{ij}^{\#}\beta_j}{\sum_{i=1}^{n}\beta_i} + o\big(\frac{1}{\mu}\big), \tag{4.7}$$

where $\frac{1}{n}$ denotes the ith element $1 \leq i \leq n$ of the normalized right Perron-eigenvector of L and $\ell_{ij}^{\#}$ for $1 \leq i, j \leq n$ is the ijth element of $L^{\#}$. Parameter β_i represents the transmission rate patch i and thus $R^{(i)} := \frac{\beta_i}{\tilde{\gamma}}$ denotes the corresponding basic reproduction number. Expansion (4.7) becomes

$$R_0 = \mathcal{A} + \frac{\tilde{\gamma}}{\mu}\frac{\mathcal{H}}{\mathcal{A}} + o\big(\frac{1}{\mu}\big), \tag{4.8}$$

where $\mathcal{A} := \frac{\sum_{i=1}^{n} R_0^{(i)}}{n}$ represents the average of the basic reproduction numbers of each patch in the network and $\mathcal{H} := \frac{\sum_{i=1}^{n}\sum_{j=1}^{n} R_i^{(0)}\ell_{ij}^{\#}R_j^{(0)}}{n}$ denotes the network heterogeneity index. $\mathcal{A}$ is independent of the arrangements of R_0 in the network, whereas $\mathcal{H}$ is highly dependent of the locations of $R_i^{(0)}$s. Therefore, $\mathcal{H}$ conveys information in regards to the population dynamics of the network.

In the following we investigate 3 scenarios for locating hotspot $\overline{R}$ region(s) and non-hotspot $\underline{r}$ region(s) in the star network.

One-hotspot scenario

In this scenario we consider to have one hotspot patch in the star network. For that, we assume two case: locating source at the hub and at leaf 2. Denote $\mathcal{H}_H$ and $\mathcal{H}_L$ as the network heterogeneity indices corresponding to source at hub and at a leaf, respectively. It follows from the description that

$$\mathcal{H}_H = \frac{n-1}{n^2}(\overline{R} - \underline{r})^2 \quad \text{and} \quad \mathcal{H}_L = \frac{n^2-n-1}{n^2}(\overline{R} - \underline{r})^2.$$

By comparing the values $\mathcal{H}_H$ and $\mathcal{H}_A$ we can state that in a star network of at least 3 regions (a hub and 2 leaves), the network disease invasion occurs more likely when the hotspot is at a leaf.

Two-hotspot scenario

In this scenario we locate two hotspots in the network. This results in 2 cases: hotspots at the hub and a leaf and hotspots at 2 leaves, where $\mathcal{H}_{HL}$ and $\mathcal{H}_{2L}$ denote the corresponding network heterogeneity indices. Thus,

$$\mathcal{H}_{HL} = \frac{n^2-4}{n^2}(\overline{R} - \underline{r})^2 \quad \text{and} \quad \mathcal{H}_{2L} = \frac{2n^2-4n-4}{n^2}(\overline{R} - \underline{r})^2. \tag{4.9}$$

The following observations are made from comparing the values of $\mathcal{H}_{HL}$ and $\mathcal{H}_{2L}$,

- In a star network of at least 5 regions (a hub and 4 leaves), the disease spreads widely when two hotspots are at leaves.
- In a 4-patch star network the disease spread is the same for both instances.
- In a 3-patch star network an outbreak happens more rapidly when one hostpot is at the hub and one at a leaf.

Note that the above results are the direct outcomes of computing network heterogeneity index of the star network for each scenario.

Three-hotspot scenario

In this scenario we assume that there are three hotspots in the star network, which results in two cases: one hotspot at the hub and two at leaves, and three hotspots at leaves, where $\mathcal{H}_{H2L}$ and $\mathcal{H}_{3L}$ denote the respected network heterogeneity indices. It follows from (4.8) that

$$\mathcal{H}_{H2L} = \frac{2n^2 - 3n - 9}{n^2}(\overline{R} - \underline{r})^2 \quad \text{and} \quad \mathcal{H}_{3L} = \frac{3n^2 - 9n - 9}{n^2}(\overline{R} - \underline{r})^2.$$

By comparing $\mathcal{H}_{H2L}$ and $\mathcal{H}_{3L}$, we can deduce that in a star network of

- at least 7 regions (a hub and 6 leaves) an outbreak most likely when all three sources are at leaves.
- 6 regions (a hub and 5 leaves), the disease spread is independent of the location of hotspot and thus it is the same for both cases.
- at most 5 regions (a hub and 4 leaves), the disease spread more widely when one hotspot is at the hub and the other two are at the leaves.

4.3 Cholera Spread on a Stream Network

In this Section, we use the the cholera model in Section 3.5 to demonstrate that the network average (the first order term in the expansion) and the network heterogeneity (the second order term) jointly impact the disease invasion in an asymmetric network.

Consider the spread of a waterborne disease (e.g. cholera) along a river of 4 nodes (as shown in Figure 4.2(a)) with 1 hotspot patch where $R_0^{(k)} = 2.8$ and 3 other patches $R_0^{(k)} = 0.7$. If $b = 2a$, then straightforward calculations yield $\theta_1 = 1/15$, $\theta_2 = 2/15$, $\theta_3 = 4/15$, and $\theta_4 = 8/15$. For large pathogen movement parameter μ, $R_0 \approx \mathcal{A} = \sum_k \theta_k R_0^{(k)}$. If the hotspot is located at patch 1, then $\mathcal{R}_0 \approx (2.8 + 0.7 \times 14)/15 = 0.84$. If the hotspot is at patch 2, then $\mathcal{R}_0 \approx (2.8 \times 2 + 0.7 \times 13)/15 = 0.98$. If the hotspot is at patch 3, then $\mathcal{R}_0 \approx (2.8 \times 4 + 0.7 \times 11)/15 = 1.26$. Lastly, if the hotspot is at patch 4, then $\mathcal{R}_0 \approx (2.8 \times 8 + 0.7 \times 7)/15 = 1.82$.

However, for intermediate values of μ, the network heterogeneity jointly plays an important role, e.g., bring the R_0 value for the case of the hotspot at patch 1 larger than R_0 values for the cases of hotspot at patch 2 or 3 (see Figure 4.2(c)).

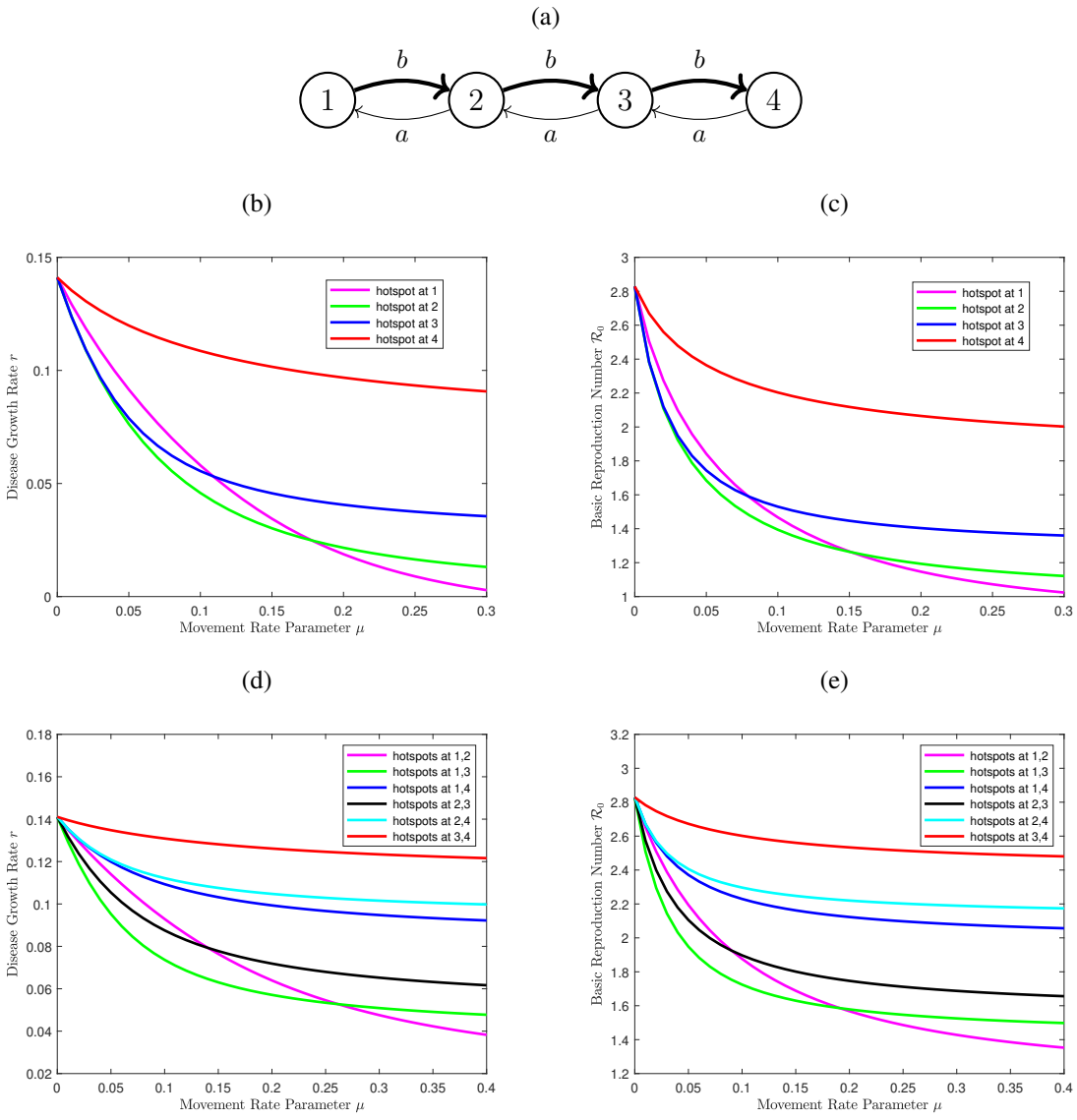


Figure 4.2: Network average and network heterogeneity jointly impact cholera invasion on a stream network: $a = 1$ (upstream movement rate), $b = 2$ (downstream movement rate); patch reproduction number is 2.8 at a hotspot and 0.7 at a non-hotspot; patch disease growth rate is 0.14 at a hotspot and -0.03 at a non-hotspot

CHAPTER 5: A NEW INDEX FOR CONTROLLING R_0

5.1 Motivation

In mathematical epidemiology, the basic reproduction number R_0 is undoubtedly amongst the most crucial threshold quantities, not just for determining whether or not an epidemic or endemic can occur in a host population, but also for providing a measure to guide disease control strategies. For example, the disease can be eradicated if more than a proportion $h = 1 - 1/R_0$ of the host population can be effectively vaccinated, where h is customarily called the herd immunity ratio. For a given infectious disease model of ordinary differential equations, R_0 can be derived as the spectral radius (the largest modulus of its eigenvalues) of a next-generation matrix $K = [k_{ij}]_{n\times n}$ [18], which encodes the disease transmission from one generation to the next; that is, $R_0 = \rho(K) = \max\{|\lambda| : Kx = \lambda x, x \in \mathbb{R}^n \setminus \{0\}\}$.

The herd immunity ratio h indeed measures the number of vaccinations needed to reduce all entries of K simultaneously (in a multiplicative way) to reach the threshold value 1. That is, after effectively vaccinating a proportion h of the host population, each pathway k_{ij} of disease transmission from one generation to another can be reduced by a proportion h, yielding the controlled next-generation matrix $K_c = [k_{ij}(1-h)] = [\frac{k_{ij}}{R_0}] = \frac{K}{R_0}$ and $\rho(K_c) = \rho(\frac{K}{R_0}) = \frac{\rho(K)}{R_0} = 1$.

However, the concept of R_0 is less useful when control efforts target a specific group, or if the infection includes another host type, i.e., a vector, intermediate host, or reservoir host. To overcome the problem, [13, 9] defined the type-reproduction number $\mathcal{T}_i$ for an infectious disease, and showed that $\mathcal{T}_i$ not only has the required threshold behavior, but also correctly determines the critical control effort for heterogeneous populations. For example, if sub-population i of the host population is to be vaccinated, then the type reproduction number $\mathcal{T}_i$ [13, 9] measures the required

vaccine coverage for the group, and $1 - \frac{1}{T_i}$ indicates the proportion of vaccination coverage in group i to have the disease under the control among all the host population groups.

In [15] the target reproduction number method was presented as an extension to the type reproduction number, allowing us to estimate disease control measurements targeting not just specific host types, but also transition terms between them. The method description in [11] concentrated on the decomposition of the next generation matrix K into nonnegative target matrix C and nonnegative residual matrix B with $\rho(B) < 1$, that is $K = B + C$. Then, the target reproduction number is defined as $T_C = \rho(C(I - B)^{-1})$ and the controlled next generation matrix $K_c = B + \frac{C}{T_C}$ has the spectral radius of 1. The following proposition establishes the relationships among the basic, type, and target reproduction numbers. The computation of the target reproduction number is similar to that of the type reproduction number, where more projection matrices are added to the target reproduction number.

In the applications, A can take the form of projection matrices in ecological models with $r = \rho(A)$ denotes the population growth rate, and next-generation matrices in epidemiological models where $R_0 = \rho(A)$ represents the basic reproduction number.

Let p be a parameter (or a set of parameters) subject to change (due to some population/disease control), where $A = A(p)$ and $r_p = \rho(A(p))$. Set $r_\infty := \lim_{p\to\infty} \rho(A(p))$ and $r_0 := \lim_{p\to 0} \rho(A(p))$ if they exist and could be ∞.

Lemma 5.1. *Let A be a nonnegative matrix and p be a parameter (set) subject to change. Suppose $r_p = \rho(A(p))$ is strictly monotone and $\min\{r_0, r_\infty\} < 1 < \max\{r_0, r_\infty\}$. Then there exists a unique p^* such that $r_{p^*} = \rho(A(p^*)) = 1$.*

Proof. As $\rho(A(p))$ is a continuous function with respect to p, and $\min\{r_0, r_\infty\} < 1 < \max\{r_0, r_\infty\}$, then by the Intermediate Value Theorem, there exists $p^* \in (0, \infty)$ such that $r_{p^*} = \rho(A(p^*)) = 1$.

The uniqueness of r_{p^*} is determined by strict monotonicity of r_{p^*}.

□

Let A be an irreducible matrix $A = B + C$, where A, B and C are nonnegative matrices. An explicit formula for p^* can be derived under certain circumstances.

- Let $A = B+C$ with $B = [b_{ij}], C = [c_{ij}] \geq 0$. If $p = \{c_{ij} : 1 \leq i \leq n, 1 \leq j \leq n\}$, then $p^* = \frac{p}{T_C}$, where $T_C = \rho(C(I - B)^{-1})$ is the corresponding target reproduction number. Here p^* is uniquely defined provided that $r_0 = \lim_{p\to 0} \rho(A) = \rho(B) < 1$. Note that $r_\infty = \lim_{p\to\infty} \rho(A) = \infty$.

- If $p = a_{ij}$ for some i, j (*i.e.*, the (i, j)-entry of A), then $p^* = \frac{a_{ij}}{\mathcal{T}_{ij}}$ where $\mathcal{T}_{ij}$ is the target reproduction number with the target entry (i, j) of A.

- If $p = \{a_{i1}, a_{i2}, \ldots, a_{in}\}$ for some i (*i.e.*, the i-th row of A), then $p^* = \frac{a_{ij}}{\mathcal{T}_i}$ where $\mathcal{T}_i$ is the target reproduction number with the target i-th row of A.

- If $p = \{a_{ij} : 1 \leq i \leq n, 1 \leq j \leq n\}$ (*i.e.*, all entries of A), then $p^* = \frac{p}{\rho(A)}$.

Proposition 5.2. *All (basic/type/target) reproduction numbers, if they exist, stay at the same side of 1.*

Proof. Let $K = B + C$ be the next generation matrix and $T_C = \rho(C(I - B)^{-1})$ be the target reproduction number corresponding to target matrix C. Assume $T_C > 1$, then from the definition the controlled next generation matrix $K_C = B + \frac{1}{T_C}C$ has the spectral radius of 1, which means $\rho(K_C) = 1$. Furthermore, $K_C = B + \frac{C}{T_C} < B + C = K$, thus $\rho(K_C) < \rho(K)$ [4]. This yields $1 < \rho(K) = R_0$.

Similarly, if $T_C < 1$, then $K_C = B + \frac{C}{T_C} < K$ resulting $R_0 = \rho(K) < 1$. □

5.2 Spectrum Yield Index

In the previous Section we have given an overview of the concept of the target reproduction number which targets parameters that appear (partially or as a whole) in the numerator of the next generation matrix. In this Section, we extend the notion of targeting parameters to a more general setting by proposing a new index. By doing so, we clarify some points of confusions from the literature.

To start, set $A = B + C = B + f(p)D$ where A, B and C are defined above, D is a nonnegative matrix, and independent of p and $f(p)$ is a nonnegative function of p, which is monotone(increasing or decreasing); thus, the inverse f^{-1} exists.

We define the *spectrum yield index* of p as the following:

$$\mathcal{Y}_p = \frac{p}{f^{-1}(\frac{f(p)}{T_C})}, \tag{5.1}$$

where $T_C = \rho(C(I-B)^{-1}) = \rho(f(p)D(I-B)^{-1})$ provided that $\rho(B) < 1$.

Theorem 5.3. *Let A be an irreducible and nonnegative matrix and $A = B + C$ with $C = f(p)D$, where B, D are nonnegative matrices independent of p. If f is strictly monotone and f^{-1} exists, then $p^* = \frac{p}{\mathcal{Y}_p}$ and $r_{p^*} = \rho(A(p^*)) = 1$, where the spectrum yield index $\mathcal{Y}_p$ is defined as in* (5.1)*.*

Proof. Let $x^\top \geq 0$ be a nonnegative left eigenvector of $C(I-B)^{-1} = f(p)D(I-B)^{-1}$ corresponding to the Perron eigenvalue of T_C, then

$$x^\top T_C = x^\top f(p)D(I-B)^{-1} \iff x^\top(I-B) = x^\top \frac{f(p)}{T_C}D \iff x^\top = x^\top(B + \frac{f(p)}{T_C}D).$$

By Perron-Frobenius Theory, the spectral radius of $(B + \frac{f(p)}{T_C}D)$ is the unique largest eigenvalue

with a nonnegative eigenvector. Thus $\rho(B + \frac{f(p)}{T_C}D) = 1$. From (5.1), $\frac{f(p)}{T_C} = f(\frac{p}{\mathcal{Y}_p})$, thus $\rho(B + f(\frac{p}{\mathcal{Y}_p})D) = 1$, which implies $\rho(A(\frac{p}{\mathcal{Y}_p})) = 1$. Following Lemma 5.1, $\rho(A(p^*)) = 1$ where $p^* = \frac{p}{\mathcal{Y}_p}$. □

Theorem 5.4. *Let $\mathcal{Y}_p$ be as defined in* (5.1)*. If $f(p)$ is strictly increasing, then $\mathcal{Y}_p$ and reproduction numbers stay at the same side of 1; if $f(p)$ is strictly decreasing, then $\mathcal{Y}_p$ and reproduction numbers stay at the opposite side of 1.*

Proof. We prove the case when $f(p)$ is increasing. Assume $T_C > 1$, then

$$\frac{f(p)}{T_C} < f(p) \iff f^{-1}(\frac{f(p)}{T_C}) < f^{-1}(f(p)) = p \iff 1 < \frac{p}{f^{-1}(\frac{f(p)}{T_C})} \iff 1 < \mathcal{Y}_p. \quad (5.2)$$

By proposition 5.2, all reproduction numbers stay at one side of 1, hence $\mathcal{Y}_p > 1$ if and only if $\rho(A(p)) > 1$. In similar fashion it can be shown that $T_C < 1$ if and only if $\mathcal{Y}_p < 1$.
The proof when $f(p)$ is decreasing can be performed by reversing all the inequalities above. □

Corollary 5.5. *Let $\mathcal{Y}_p$ be defined as in* (5.1)*, and $f(p)$ be a monotone function (decreasing or increasing). Then $\mathcal{Y}_p = 1$ if and only if $T_C = 1$.*

Proof. Suppose $T_C = 1$, then

$$\frac{f(p)}{T_C} = f(p) \iff f^{-1}(\frac{f(p)}{T_C}) = f^{-1}(f(p)) = p \iff 1 = \frac{p}{f^{-1}(\frac{f(p)}{T_C})} \iff 1 = \mathcal{Y}_p.$$

□

Theorem 5.6. *Let $A = A(p)$ and $\mathcal{Y}_p$ be well-defined, then the following holds.*

(a) If $f(p)$ is increasing, then $\mathcal{Y}_p > 1$ if and only if $\frac{dr}{dp} = \frac{d}{dp}\rho(A(p)) > 0$.

(b) If $f(p)$ is decreasing, then $\mathcal{Y}_p < 1$ if and only if $\frac{dr}{dp} = \frac{d}{dp}\rho(A(p)) > 0$.

Proof. We prove (a) only. The proof of (b) is similar. Assume $\mathcal{Y}_p > 1$, then $p^* = \frac{p}{\mathcal{Y}_p} < p$, which implies $f(p^*) < f(p)$, which follows from $f(p)$ being strictly increasing. Thus,

$$A(p^*) = B + f(p^*)D < B + f(p)D = A(p). \tag{5.3}$$

Since both $A(p^*)$ and $A(p)$ are irreducible, then $\rho(A(p^*)) < \rho(A(p))$ [4] for any $p^* < p$. Now,

$$\begin{aligned}\frac{d}{dp}\rho(A(p)) &= \lim_{\epsilon\to 0}\frac{\rho(A(p)_{|(p^*+\epsilon)} - \rho(A(p)_{|(p^*)}}{\epsilon}\\ &= \lim_{\epsilon\to 0}\frac{\rho(A(p^*+\epsilon)) - \rho(A(p^*))}{\epsilon} > 0.\end{aligned}$$

□

In this section we illustrate three applications in the context of compartmental epidemic models. The first two examples emphasize various control measures for disease elimination. The last one focuses on the different next-generation matrix decompositions to compare their corresponding target reproduction numbers and spectrum yield indices. As computations show, different next generation matrix constructions lead to the same spectrum yield index value, which is thus independent of the next generation matrix decomposition.

Note that in all disease infectious applications the assumption is that the outbreak occurs, that is $R_0 > 1$, leading us to look for effective control strategies to prevent the spread of the disease.

5.3 Application to a Zika Model

Zika virus is a mosquito-borne disease that is primarily transmitted by the bite of an infected mosquito from the *Aedes* genus, mainly *Aedes aegypti*, in tropical and subtropical regions. This is

the same mosquito that transmits dengue, chikungunya and yellow fever. Zika virus can also be transmitted from human to human including mother to fetus during pregnancy, and through sexual contact.

Consider a human-vector population Zika virus model in which the human population is divided into five classes: susceptible S_H, exposed E_H, symptomatic infected I_{HS}, asymptomatic infected I_{HA} and and recovered R_H, while the mosquito population is divided into three classes: susceptible S_V, exposed E_V and infectedI_V as described in [3]. The system has five infected states, E_H, I_{HS}, I_{HA}, E_V and I_V where E_H and E_V are states-at-infection, and I_{HS}, I_{HA} and I_V are states of infectiousness so next generation matrix with the large domain K_L is a 5×5 matrix.

In [7] an approach to derive the next generation matrix K form K_L is introduced, which has the same epidemiological reasoning as K_L, but keeps out irrelevant information, and usually is of lower dimension than K_L. The entry (i, j) of K corresponds to the expected number of new cases at state-at-infection i produced by a single individual who has just entered state-at-infection j in a completely susceptible population. Here we derive K in this manner with states-at-infection E_H and E_V. Thus,

$$K = \begin{pmatrix} \dfrac{\psi_S q + \psi_A(1-q)}{\gamma} & \dfrac{a_H b \beta_V}{(\beta_V + \mu_V)\mu_V} \\ \dfrac{a_V b}{\gamma} & 0 \end{pmatrix},$$

where ψ_A and ψ_S denote humans' asymptomatic and symptomatic sexual transmission rate, respectively for an entire infectious period of $\frac{1}{\gamma}$. Infected individuals become symptomatic infectious with probability q. Parameter $a_H(a_V)$ is the transmission rate from an infectious mosquito(individual) to a susceptible individual(mosquito) per mosquito bite, b is the mosquito's biting rate and β_V^{-1} is the latency period of Zika virus in mosquitoes. Finally, μ_V represents the death rate of mosquitoes.

In the following, we explain the biological description of entries of $K = [k_{ij}]$.

- $k_{11} = \dfrac{\psi_S q + \psi_A(1-q)}{\gamma}$ determines the expected number of exposed cases, generated by one individual who has just entered state E_H during the infectious period. Here, the individual survives the E_H state with probability 1 and moves to one of the two infectious states, I_{HS} or I_{HA} with probability q and $1-q$, respectively. During their stay in I_{HS}, the individual is expected to produce new cases at a rate ψ_S, and to produce new cases at rate ψ_A while they are in state I_{HA} for an expected time $\frac{1}{\gamma}$.

- $k_{12} = \dfrac{a_H b \beta_V}{(\beta_V + \mu_V)\mu_V}$ corresponds to the expected number of new cases of exposed humans by one mosquito that has just entered state E_V for the infectious life. For the mosquito to be infectious, it needs to survive the E_V state and moves to infectious state I_V with probability $\dfrac{\beta_V}{\beta_V + \mu_V}$. While in the I_V state, the infectious vector is expected to produce new cases of exposed humans at a rate $a_H b$, for an expected time $\frac{1}{\mu_V}$.

- $k_{21} = \dfrac{a_V b}{\gamma}$ indicates the expected number of new cases of exposed mosquitoes produced by one human who just entered state E_H during the infectious time. The exposed human moves to states I_{HS} and I_{HA} with probability q and $1-q$, respectively. While in infectious state, I_{HS} or I_{HA}, they are expected to produce new cases of exposed vectors with rate $a_V b$, for an expected time $\dfrac{1}{\gamma}$.

- $k_{22} = 0$ because Zika virus is spread mainly by mosquito bites, thus there is no transmission between mosquitoes.

As there is no vaccine or antiviral treatment available for Zika virus infection, the following disease control measurements are recommended.

Reducing the infectious mosquitoes to individuals transmission

One method to prevent the spread of Zika virus is to decrease the encounter between the infectious mosquitoes and susceptible individuals. To achieve it, the *Wolbachia* bacterium is introduced into the mosquito population by breeding and releasing Wolbachia-carrying mosquitoes into the disease affected areas. From mathematical point of view, these strategies target parameter a_H where it appears in entry $(1,2)$ of K. Then, the target matrix is $C = \begin{pmatrix} 0 & \frac{a_H b \beta_V}{(\beta_V+\mu_V)\mu_V} \\ 0 & 0 \end{pmatrix}$ and the residual matrix is $B = \begin{pmatrix} \frac{\psi_S q+\psi_A(1-q)}{\gamma} & 0 \\ \frac{a_V b}{\gamma} & 0 \end{pmatrix}$, with the controllability condition

$$\rho(B) < 1 \iff \frac{\psi_S q + \psi_A(1-q)}{\gamma} < 1,$$

where it leads to $\gamma - (\psi_S q + \psi_A(1-q)) > 0$. Thus, the target reproduction number

$$\begin{aligned} T_C &= \rho(C(I-B)^{-1}) \\ &= \rho\left(\begin{pmatrix} 0 & \frac{a_H b \beta_V}{(\beta_V+\mu_V)\mu_V} \\ 0 & 0 \end{pmatrix} \begin{pmatrix} 1 - \frac{\psi_S q + \psi_A(1-q)}{\gamma} & 0 \\ -\frac{a_V b}{\gamma} & 1 \end{pmatrix}^{-1} \right) \\ &= \rho\left(\begin{pmatrix} \frac{a_H \beta_V a_V b}{\mu_V(\beta_V+\mu_V)(\gamma-(\psi_S q+\psi_A(1-q)))} & \frac{a_H \beta_V}{(\mu_V+\beta_V)} \\ 0 & 0 \end{pmatrix} \right) \\ &= \frac{a_H \beta_V a_V b}{\mu_V(\beta_V+\mu_V)(\gamma-(\psi_S q+\psi_A(1-q)))}. \end{aligned}$$

T_C is meaningful as $\gamma - (\psi_S q + \psi_A(1-q)) > 0$. This implies that the transmission rate from

infectious mosquitoes to susceptible individuals is successfully reduced as every entry c_{ij} of target matrix C becomes $\frac{c_{ij}}{T_C}$. That means, the dominant eigenvalue of the controlled matrix $K_C = B + \frac{1}{T_C}C$ is 1, i.e. $\rho(K_C) = 1$.

Reduction in mosquito bites

One way to control the spread of Zika virus is to prevent the mosquito bites by using screens on the windows or air conditioner to keep mosquitoes from entering. Individuals are recommended to stay indoors during the peak of biting time of vectors, which are early morning and late afternoon/evening. If individuals can't avoid being outdoors, they are suggested to take some precautions such that wearing light-colored clothing and using insect repellents. Such measurements target parameter "b" in which it appears at entries $(1,2)$ and $(2,1)$ of the next generation matrix. Thus, target matrix is $C = \begin{pmatrix} 0 & \frac{a_H b \beta_V}{(\beta_V+\mu_V)\mu_V} \\ \frac{a_V b}{\gamma} & 0 \end{pmatrix}$, and the residual matrix is $B = \begin{pmatrix} \frac{\psi_S q + \psi_A(1-q)}{\gamma} & 0 \\ 0 & 0 \end{pmatrix}$ with the controlability condition $\rho(B) < 1 \iff 0 < \gamma - (\psi_S q + \psi_A(1-q))$. Following the definition of target reproduction T_C, we have

$$
\begin{aligned}
T_C &= \rho(C(I-B)^{-1}) \\
&= \rho\left(\begin{pmatrix} 0 & \frac{a_H b \beta_V}{(\beta_V+\mu_V)\mu_V} \\ \frac{a_V b}{\gamma} & 0 \end{pmatrix} \begin{pmatrix} 1 - \frac{\psi_S q + \psi_A(1-q)}{\gamma} & 0 \\ 0 & 1 \end{pmatrix}^{-1} \right) \\
&= \rho\left(\begin{pmatrix} 0 & \frac{a_H b \beta_V}{(\beta_V+\mu_V)\mu_V} \\ \frac{a_V b}{\gamma - (\psi_q + \psi_A(1-q))} & 0 \end{pmatrix} \right) \\
&= b\sqrt{\frac{a_V a_H \beta_V}{\psi_S q + \psi_A(1-q) - \gamma}}.
\end{aligned}
$$

Reduction in the latent period

From the model description, β_V^{-1} is the latent period of mosquitoes from the exposed compartment to the infected one. Given the short lifespan of mosquitoes, we assume infectious vectors remain infectious for the rest of their life . Hypothetically, if we are to increase the latency period, there will be less infectious mosquitoes, as the result the spread of Zika virus can be controlled. Such strategies target parameter β_V, where is located both in the numerator and denominator of entry $(1,2)$. From (5.1), to measure such strategies, we are required to calculate the corresponding spectrum yield index $\mathcal{Y}_{\beta_V}$. Note that target matrix C is the same as the one in Section 5.3, so is the associated target reproduction number, hence $T_C = \frac{a_H \beta_V a_V b}{\mu_V(\beta_V+\mu_V)(\gamma-(\psi_S q+\psi_A(1-q)))}$. Following (5.1), the target matrix can be represented $C = \frac{\beta_V}{\beta_V+\mu_V}\begin{pmatrix} 0 & a_H b \\ 0 & 0 \end{pmatrix}$ where $f(\beta_V) = \frac{\beta_V}{\beta_V+\mu_V}$ is a continuous strictly increasing function of β_V as $\beta_V, \mu_V > 0$, so the inverse exists and $f^{-1}(\beta_V) = \frac{\beta_V \mu_V}{1-\beta_V}$. Thus, β_V associated spectrum yield index is

$$\begin{aligned}
\mathcal{Y}_{\beta_V} &= \frac{\beta_V}{f^{-1}(\frac{f(\beta_V)}{T_C})} \\
&= \frac{T_C(\beta_V+\mu_V)-\beta_V}{\mu_V} \\
&= \frac{\beta_V(a_H a_V b-(\gamma-(\psi_S q+\psi_A(1-q))))}{\mu_V^2(\gamma-(\psi_S q+\psi_A(1-q))}.
\end{aligned}$$

Decrease in the symptomatic sexual transmission rate

Zika virus can be passed through sexual intercourse from a person who has Zika to their sex partners. To control the spread of Zika virus, individuals must be informed about the correct and consistent use of condoms or abstinence during infectious period. Such interventions target parameter ψ_S where it appears as part of entry $(1,1)$. Target matrix C and residual matrix B are

defined as

$$C = \begin{pmatrix} \frac{\psi_S q}{\gamma} & 0 \\ \\ 0 & 0 \end{pmatrix} \quad \text{and} \quad B = \begin{pmatrix} \frac{\psi_A(1-q)}{\gamma} & \frac{a_H b \beta_V}{(\beta_V+\mu_V)\mu_V} \\ \\ \frac{a_V b}{\gamma} & 0 \end{pmatrix},$$

with the controllability condition

$$\begin{aligned}
&\rho(B) < 1 \\
&\quad \frac{1}{2}\left(\frac{\psi_A(1-q)}{\gamma} + \sqrt{\left(\frac{\psi_A(1-q)}{\gamma}\right)^2 + 4\left(\frac{a_V a_H b^2 \beta_V}{(\beta_V+\mu_V)\mu_V}\right)}\right) < 1 \\
&\quad \iff \left(\frac{\psi_A(1-q)}{\gamma}\right)^2 + 4\left(\frac{a_V a_H b^2 \beta_V}{(\beta_V+\mu_V)\mu_V}\right) < \left(2 - \frac{\psi_A(1-q)}{\gamma}\right)^2 \\
&\quad \iff \frac{a_V a_H b^2 \beta_V}{(\beta_V+\mu_V)\mu_V} < \frac{\gamma - \psi_A(1-q)}{\gamma} \\
&\quad \iff 0 < \frac{\mu_V(\gamma - \psi_A(1-q))(\beta_V+\mu_V) - a_V a_H \beta_V b^2}{\gamma \mu_V(\beta_V+\mu_V)}.
\end{aligned}$$

Following the definition of the target reproduction number, T_C is given by

$$T_C = \rho\left(\begin{pmatrix} \frac{\psi_S q}{\gamma\Omega} & \frac{a_H b \beta_V \psi_S q}{\gamma \mu_V(\mu_V+\beta_V)\Omega} \\ \\ 0 & 0 \end{pmatrix}\right),$$

where $\Omega = \dfrac{\gamma\mu_V(\beta_V+\mu_V)}{\mu_V(\gamma - \psi_A(1-q))(\beta_V+\mu_V) - a_V a_H \beta_V b^2}$.

Hence ,

$$T_C = \frac{\psi_S q \mu_V(\beta_V+\mu_V)}{\mu_V(\gamma - \psi_A(1-q))(\beta_V+\mu_V) - a_V a_H \beta_V b^2}.$$

T_C is well defined as the condition for controllability, $\rho(B) < 1$, holds. One can check that the

controlled matrix $K_C = B + \frac{1}{T_C}C$ corresponds to the control measures reducing ψ_S has dominant eigenvalue 1.

Increase in the death rate of mosquitoes

Another Zika virus prevention strategy is to spray *Permethrin* on the clothes treating clothes to increase the death rate of mosquitoes. Such control strategies effect parameter μ_V where it appears in the quadratic form in the denominator of entry $(1, 2)$ of K. Following (5.1), the effort required to increase the death rate of mosquitoes can be estimated using the spectrum yield index associated to parameter μ_V.

Note that the target matrix C and residual matrix B are the same as the ones described in Section 5.3, so is the target reproduction number. Thus, $T_C = \rho(C(I - B)^{-1}) = \frac{a_H\beta_V a_V b^2}{\mu_V(\beta_V+\mu_V)(\gamma-\psi_s q-\psi_A(1-q))}$. Note that the target matrix can be represented as $C = \frac{1}{(\beta_V+\mu_V)\mu_V}\begin{pmatrix} 0 & a_H b\beta_V \\ 0 & 0 \end{pmatrix}$, where $f(\mu_v) = \frac{1}{(\beta_V + \mu_V)\mu_V}$ is decreasing and continuous everywhere as $\beta_V > 0$ and $\mu_V > 0$. Thus, the inverse exists and $f^{-1}(\mu_V) = \sqrt{\frac{\beta_V^2}{4} + \frac{1}{\mu_V}} - \frac{\beta_V}{2}$. From (5.1), the spectrum yield index corresponding to parameter μ_V is

$$\begin{aligned} \mathcal{Y}_{\mu_V} &= \frac{\mu_V}{f^{-1}(\frac{f(\mu_V)}{T_C})} \\ &= \frac{\mu_V}{\sqrt{\frac{a_H\beta_V a_V b^2}{\gamma-\psi_s q-\psi_A(1-q)} + \frac{\beta^2}{4}} - \frac{\beta}{2}}. \end{aligned}$$

For effective control strategies μ_V is to be replaced with $\frac{\mu_V}{\mathcal{Y}_{\mu_V}} = \sqrt{\frac{a_H\beta_V a_V b^2}{\gamma-\psi_s q-\psi_A(1-q)} + \frac{\beta^2}{4}} - \frac{\beta}{2}$, thus the spectral radius of the controlled next generation matrix is 1, that is

$$\rho(K_{\mu_V}) = \rho\left(\begin{pmatrix} \frac{\psi_S q + \psi_A(1-q)}{\gamma} & \frac{a_H b\beta_V}{(\beta_V + \frac{\mu_V}{\mathcal{Y}_{\mu_V}})\frac{\mu_V}{\mathcal{Y}_{\mu_V}}} \\ \frac{a_V b}{\gamma} & 0 \end{pmatrix}\right) = 1.$$

5.4 Application to an Anthrax Disease model

Anthrax is a zoonotic infectious disease caused by bacteria called *Bacillus anthracis*. It can be found naturally in soil in dormant form called spores, and mainly affects animals, specially live stock. Humans can also become infected if they come in contact with infected animals, contaminated animal products or inhaling the spores. Usually, the bacteria enters the body through a wound in the skin.

Consider the four-compartment $SIAC_a$ anthrax disease model in animal populations is given in [14], where S and I denote susceptible and infected animals, C_a represents infected carcasses and A denotes the grams of spores in the environment. The dynamics of a special case of the model are described in [17] as

$$\begin{aligned}
\dot{S} &= r(S+I)(1-\frac{S+I}{K}) - \eta_a AS - \eta_c C_a S - mS + \tau I \\
\dot{I} &= \eta_a AS + \eta_c C_a S - (\gamma + m + c)I \\
\dot{A} &= -\alpha A + \beta C_a \\
\dot{C_a} &= (\gamma + m)I - \delta(S+I)C_a - \kappa C_a.
\end{aligned}$$

The animal population is assumed to follow logistic growth with birth rate r and carrying capacity $\mathcal{K}$. η_a is the contact rate between susceptible animals and spores times the probability of transmission

from spores to susceptible animals, η_c is the contact rate between susceptible animals and infected carcasses. β and α denote the spore growth rate and decay rate in the environment on the infected carcasses, κ is the carcasses decay rate, δ is the carcass consumption rate, κ is the decay rate of carcasses, m and γ are the natural and the disease induced death rates, respectively, and τ is the recovery rate of infected animals.

The system has three infected states; S, I and C_a, thus, the next generation matrix around the disease-free equilibrium $(S_0, 0, 0, 0)$ with $S_0 = \mathcal{K}(1 - \frac{m}{r})$ is

$$K = \begin{pmatrix} 0 & \frac{\eta_a S_0}{\alpha} & \frac{\eta_c S_0}{\delta S_0 + \kappa} \\ 0 & 0 & \frac{\beta}{\delta S_0 + \kappa} \\ \frac{\gamma + m}{\gamma + m + \tau} & 0 & 0 \end{pmatrix}. \tag{5.4}$$

Table 5.1: Model parameter values, descriptions and associated units.

Parameter	Baseline value	Unit
$\mathcal{K}$	100	animals
r	$1/300$	day^{-1}
m	$1/600$	day^{-1}
δ	$1/20$	day^{-1}animal^{-1}
α	$1/20$	day^{-1}
η_a	$1/2$	day^{-1}gm spore^{-1}
β	$1/500$	gm spores carcass^{-1} day^{-1}
τ	$1/10$	day^{-1}
γ	$1/7$	day^{-1}
η_c	$1/10$	day^{-1}carcass^{-1}
κ	$1/10$	day^{-1}

Using the table above, the basic reproduction number R_0 is approximated as 1.113.

In what follows we investigate different disease control strategies to calculate the spectrum yield index associated with each strategy in order to have anthrax under control.

Increase in the decay rate of carcasses

In the case of anthrax outbreak, one approach to reduce the spread of anthrax is to increase the decay rate of carcasses. In most countries, the best method of disposal of infected carcasses is incineration. Such control measures target parameter κ, where it happens to appear in the denominator of entries $(1,3)$ and $(2,3)$ of K. Following (5.1), to measure the change in κ, we are required to compute $\mathcal{Y}_\kappa$ with the target matrix $C = \begin{pmatrix} 0 & 0 & \frac{\eta_c S_0}{\delta S_0+\kappa} \\ 0 & 0 & \frac{\beta}{\delta S_0+\kappa} \\ 0 & 0 & 0 \end{pmatrix}$ and residual matrix $B = \begin{pmatrix} 0 & \frac{\eta_a S_0}{\alpha} & 0 \\ 0 & 0 & 0 \\ \frac{\gamma+m}{\gamma+m+\tau} & 0 & 0 \end{pmatrix}$, where $\dfrac{\gamma+m}{\gamma+m+\tau} < 1$, following the controllability condition $\rho(B) < 1$.

The corresponding target reproduction number T_C is

$$T_C = \rho(C(I-B)^{-1}) = \begin{pmatrix} \dfrac{S_0\eta_c(\gamma+m)}{(\delta S_0+\kappa)(\gamma+m+\tau)} & \dfrac{S_0^2\eta_c\eta_a(\gamma+m)}{\alpha(\delta S_0+\kappa)(\gamma+m+\tau)} & \dfrac{S_0\eta_c}{\delta S_0+\kappa} \\ \dfrac{\beta(\gamma+m)}{(\delta S_0+\kappa)(\gamma+m+\tau)} & \dfrac{S_0\beta\eta_a(\gamma+m)}{\alpha(\delta S_0+\kappa)(\gamma+m+\tau)} & \dfrac{\beta}{\delta S_0+\kappa} \\ 0 & 0 & 0 \end{pmatrix}$$

$$= \frac{S_0\eta_c(\gamma+m)}{(\delta S_0+\kappa)(\gamma+m+\tau)} + \frac{S_0\beta\eta_a(\gamma+m)}{\alpha(\delta S_0+\kappa)(\gamma+m+\tau)}.$$

Note that the target matrix C can be represented as

$$C = \frac{1}{\delta S_0 + \kappa} \begin{pmatrix} 0 & 0 & S_0\eta_c \\ 0 & 0 & \beta \\ 0 & 0 & 0 \end{pmatrix},$$

where $f(\kappa) = \dfrac{1}{\delta S_0 + \kappa}$ that is strictly decreasing with respect to κ and continuous everywhere, thus the inverse exits and $f^{-1}(\kappa) = \dfrac{1}{\kappa} - \delta S_0$. Now, we can derive $\mathcal{Y}_\kappa$ from (5.1).

$$\mathcal{Y}_\kappa = \frac{\kappa}{f^{-1}(\frac{f(\kappa)}{T_C})} = \frac{\kappa\alpha(\gamma + m + \tau)}{S_0(\gamma + m)(\beta\eta_\alpha + a\eta_c) - S_0\delta a(\gamma + m + \tau)}.$$

Using the parameter values provided in table (5.1), $\mathcal{Y}_k = 0.133$, which implies that in order to control the spread of anthrax, the decay rate of carcasses must be increased from $\kappa = 0.1$ day^{-1} to $\dfrac{\kappa}{\mathcal{Y}_\kappa} = 0.751$ day^{-1}. This implies that in order to have the spread of anthrax under the control, on average, a carcass must decompose in about 1.331 days rather than 10 days. By doing so, the basic reproduction of the controlled next generation matrix K_κ, which was 1.113 in the outset of anthrax reduces to 1. Thus, $\rho(K_\kappa) = 1$, where $K_\kappa = \begin{pmatrix} 0 & \frac{\eta_a}{\alpha} & \frac{\eta_c}{\delta + \frac{\kappa}{\mathcal{Y}_\kappa}} \\ 0 & 0 & \frac{\beta}{\delta + \frac{\kappa}{\mathcal{Y}_\kappa}} \\ \frac{\gamma+m}{\gamma+m+\tau} & 0 & 0 \end{pmatrix}$.

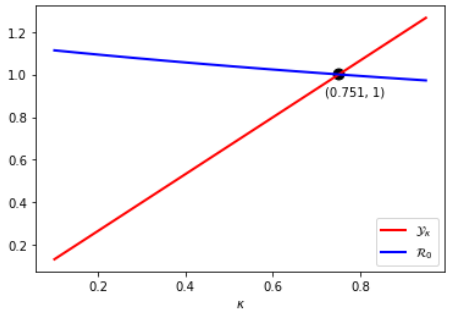


Figure 5.1: The relation between R_0 and spectrum yield index $\mathcal{Y}_\kappa$

Note that both R_0 and $\mathcal{Y}_\kappa$ reach the threshold value 1 simultaneously, which is the direct result of Proposition 5.2 and Corollary 5.5. Additionally, R_0 and $\mathcal{Y}_\kappa$ stay on the opposite side of 1, $R_0 > 1$ whenever $\mathcal{Y}_\kappa < 1$, which is consistent with the result of Theorem 5.4, as $f(\kappa) = \dfrac{1}{\delta S_0 + \kappa}$ is a decreasing function of κ.

Decrease in the anthrax induced mortality rate

During anthrax outbreak, another approach to have the disease under control is to reduce the fatality rate caused by anthrax by treating the infected animals with antibiotics (antibiotics treatments are the most effective if started early). From a mathematical perspective, such measures target parameter m, which appears both in the numerator and denominator of entry $(3,1)$ of K. Hence, the target matrix $C = [c_{ij}]$, $1 \leq i, j \leq 3$ has only one nonzero entry: $c_{31} = \frac{\gamma+m}{\gamma+m+\tau}$, and $c_{ij} = 0$ for $(i,j) \neq (1,3)$. By definition the target reproduction number is given as

$$T_C = \rho(C(I-B)^{-1}) = \frac{S_0(\gamma+m)}{(\delta S_0+\kappa)(\gamma+m+\tau)}(\frac{\eta_a\beta}{a}+\eta_c).$$

Notice that the target matrix can be shown as $C = \frac{\gamma+m}{\gamma+m+\tau}\begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 1 & 0 & 0 \end{pmatrix}$, where $f(\gamma) = \frac{\gamma+m}{\gamma+m+\tau}$ is an increasing and continuous function of γ on its domain, thus, the inverse exists and $f^{-1}(\gamma) = \frac{m-\gamma\tau-\gamma m}{\gamma-1}$.
Following (5.1), the corresponding spectrum yield index $\mathcal{Y}_\gamma$ is

$$\mathcal{Y}_\gamma = \frac{\gamma}{f^{-1}(\frac{f(\gamma)}{T_C})} = \frac{\gamma(a(\delta S_0+\kappa) - S_0(\eta_a\beta+\eta_c\alpha))}{mS_0(\eta_a\beta+\eta_c\alpha) - \alpha(\delta S_0+\kappa)(\tau+m)}.$$

By using the parameter values provided in table (5.1), $\mathcal{Y}_\gamma \approx 1.624$. thus, $\gamma = 1/7$ day^{-1} become $\frac{\gamma}{\mathcal{Y}_\gamma} \approx 0.088$ day^{-1}. This implies after a successful treatment, an infected animal dies on average 11.36 days after being exposed to disease rather than 7 days.

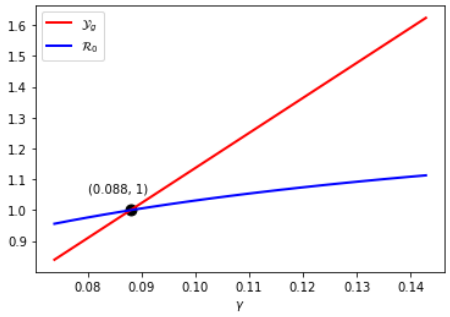


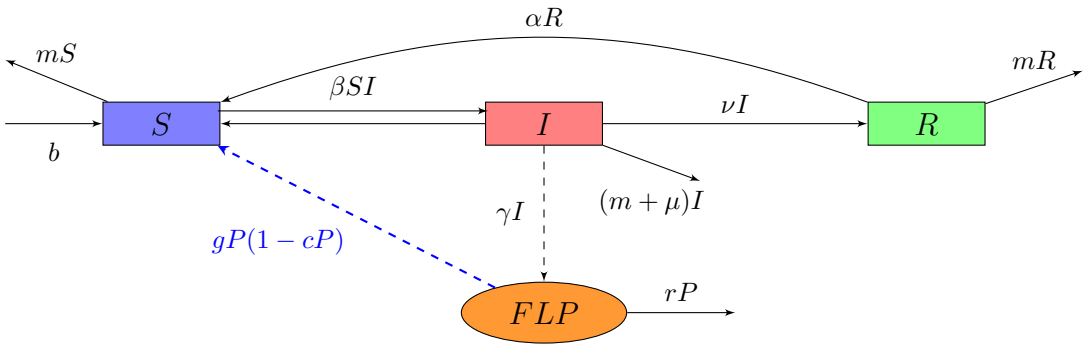
Figure 5.2: The relation between R_0 and spectrum yield index $\mathcal{Y}_\gamma$

Note that both R_0 and $\mathcal{Y}_\gamma$ stay on one side of threshold value 1, as $f(\gamma) = \frac{\gamma+m}{\gamma+m+\tau}$ is an increasing function of γ Theorem 5.4, Furthermore, they reach the threshold value 1 together; Proposition 5.2 and Corollary 5.5.

5.5 Application to a Cholera Model

Cholera is a water-borne infectious disease caused by bacteria called *Vibrio cholerae*. Cholera outbreak occurs primarily in areas with inadequate water treatment and poor sanitation. Individuals become sick by eating food or drinking water contaminated by feces of infected individuals.

Consider the four-class $(SIRSP)$ Cholera model described in [2], where S, I and R denote susceptible, infected and recovered classes, respectively, and P indicates free-living pathogen (FLP) that can grow and survive in the environment, where I and P are states-at-infection.



Thus, the corresponding Jacobian matrix J is

$$J = \begin{pmatrix} \frac{\beta b}{m} - (\mu + m + \nu) & \frac{\delta b}{m} \\ \gamma & g - r \end{pmatrix}, \tag{5.5}$$

where b and m denote the birth and death rate, respectively, μ indicates diseased induced mortality rate. δ and β represent environment to host an host to host transmission rate. Finally, γ, g and r are shedding, growth and decay rate of pathogens in the environment. To ensure stability of the system around the disease free equilibrium we assume $r > g$.

It is worth noting that there are some uncertainties surrounding the role of the contaminated environment in the literature. While some studies highlight the role of the environment as a

reservoir of infectious FLP, other works remark the environment with the less crucial part on disease infections.

In this example, we consider both scenarios to derive next generation matrix from (6.8), and show that the decomposition of the next generation has no impact on the computation of the spectrum yield index.

- *Environment as a reservoir*

  The environment is viewed solely as a reservoir, where both FLP growth rate g and pathogen shedding rate γ are regarded as new infections. Thus, the new infection matrix F and transition matrix V are

$$F = \begin{pmatrix} \frac{\beta b}{m} & \frac{\delta b}{m} \\ \\ \gamma & g \end{pmatrix}, \quad V = \begin{pmatrix} (\mu + m + \nu) & 0 \\ \\ 0 & r \end{pmatrix},$$

  and the NGM K is

$$K = FV^{-1} = \begin{pmatrix} \dfrac{\beta b}{m(\mu + m + \nu)} & \dfrac{\delta b}{mr} \\ \\ \dfrac{\gamma}{\mu + m + \nu} & \dfrac{g}{r} \end{pmatrix}. \tag{5.6}$$

- *Environment as a transition-reservoir*

  Unlike the previous case, the environment is not solely considered as a reservoir. While the pathogen shedding by the infectious host is assumed as transitions, the pathogen growth within the environment is regarded as new infection. Thus, the shedding rate g, and the

growth rate γ are placed into matrices F and V, respectively. Hence,

$$F = \begin{pmatrix} \frac{\beta b}{m} & \frac{\delta b}{m} \\ 0 & g \end{pmatrix}, \quad V = \begin{pmatrix} (\mu + m + \nu) & 0 \\ -\gamma & r \end{pmatrix},$$

where the NGM K is

$$K = FV^{-1} = \begin{pmatrix} \dfrac{\beta b}{m(\mu + m + \nu)} + \dfrac{\delta \gamma b}{m(\mu + m + \nu)r} & \dfrac{\delta b}{mr} \\ \dfrac{\gamma g}{r(\mu + m + \nu)} & \dfrac{g}{r} \end{pmatrix}. \tag{5.7}$$

In the remaining of this example, we implement control measure to target a particular parameter corresponding to NGMs (5.6) and (5.7) to compare the associated spectrum yield index of each scenario.

Reduction in the environment-to-host transmission

As cholera outbreak is mainly associated to inadequate sanitation system, its further spread can be prevented by promoting the hygiene habits including washing hands with soap, and safe food preparations. Such measures tend to reduce the contact between the environment and host, in which they target parameter δ of NGMs (5.6) and (5.7).

Table 5.2: Description of targeting parameter δ.

		Reservoir	Transition-Reservoir
1	NGM	$\begin{pmatrix} \frac{\beta b}{m(\mu+m+\nu)} & \frac{\delta b}{mr} \\ \frac{\gamma}{\mu+m+\nu} & \frac{g}{r} \end{pmatrix}$	$\begin{pmatrix} \frac{\beta br+\delta\gamma b}{mr(\mu+m+\nu)} & \frac{\delta b}{mr} \\ \frac{\gamma g}{r(\mu+m+\nu)} & \frac{g}{r} \end{pmatrix}$
2	Target matrix C	$\frac{\delta}{m}\begin{pmatrix} 0 & \frac{b}{r} \\ 0 & 0 \end{pmatrix}$	$\frac{\delta}{m}\begin{pmatrix} \frac{\gamma b}{(\mu+m+\nu)r} & \frac{b}{r} \\ 0 & 0 \end{pmatrix}$
3	Residual matrix B	$\begin{pmatrix} \frac{\beta b}{m(\mu+m+\nu)} & 0 \\ \frac{\gamma}{\mu+m+\nu} & \frac{g}{r} \end{pmatrix}$	$\begin{pmatrix} \frac{\beta b}{m(\mu+m+\nu)} & 0 \\ \frac{\gamma g}{r(\mu+m+\nu)} & \frac{g}{r} \end{pmatrix}$
4	$C(I-B)^{-1}$	$\frac{\delta b}{r-g}\begin{pmatrix} \frac{\gamma}{m(\mu+m+\nu)-\beta b} & \frac{1}{m} \\ 0 & 0 \end{pmatrix}$	$\frac{\delta b}{r-g}\begin{pmatrix} \frac{\gamma}{m(\mu+m+\nu)-\beta b} & \frac{1}{m} \\ 0 & 0 \end{pmatrix}$
5	$T_C = \rho(C(I-B)^{-1})$	$\frac{\delta\gamma b}{(m(\mu+m+\nu)-\beta b)(r-g)}$	$\frac{\delta\gamma b}{(m(\mu+m+\nu)-\beta b)(r-g)}$
6	$\mathcal{Y}_\delta = \frac{\delta}{f^{-1}(\frac{f(\delta)}{T_C})}$	$\frac{\delta\gamma b}{(m(\mu+m+\nu)-\beta b)(r-g)}$	$\frac{\delta\gamma b}{(m(\mu+m+\nu)-\beta b)(r-g)}$

Note that despite parameter δ having to appear in different entries of the NGM associated to each case, the corresponding target reproduction number T_C (step 5) is the same. Additionally, from (5.1) $f(\delta) = \delta$ and $f^{-1}(\delta) = \delta$. Thus, $\mathcal{Y}_\delta = \dfrac{\delta}{f^{-1}(\frac{f(\delta)}{T_C})} = \dfrac{\delta}{\frac{\delta}{T_C}} = T_C$ (step 6).

Decrease in the cholera induced mortality rate

Cholera may cause severe diarrhea which can lead to the dehydration and eventually death. This can be prevented by simple treatments such as rehydration solution. By doing so, we decrease cholera induced fatality rate. Mathematically, such treatments target parameter μ of NGMs (5.6) and (5.7).

Table 5.3: Description of targeting parameter μ

		Reservoir	Transition-Reservoir
1	NGM	$\begin{pmatrix} \frac{\beta b}{m(\mu+m+\nu)} & \frac{\delta b}{mr} \\ \frac{\gamma}{\mu+m+\nu} & \frac{g}{r} \end{pmatrix}$	$\begin{pmatrix} \frac{\beta br+\delta\gamma b}{m(\mu+m+\nu)} & \frac{\delta b}{mr} \\ \frac{\gamma g}{r(\mu+m+\nu)} & \frac{g}{r} \end{pmatrix}$
2	Target matrix C	$\frac{1}{\mu+m+\nu}\begin{pmatrix} \frac{\beta b}{m} & 0 \\ \gamma & 0 \end{pmatrix}$	$\frac{1}{\mu+m+\nu}\begin{pmatrix} \frac{\beta br+\delta\gamma b}{mr} & 0 \\ \frac{\gamma g}{r} & 0 \end{pmatrix}$
3	Residual matrix B	$\begin{pmatrix} 0 & \frac{\delta b}{mr} \\ 0 & \frac{g}{r} \end{pmatrix}$	$\begin{pmatrix} 0 & \frac{\delta b}{mr} \\ 0 & \frac{g}{r} \end{pmatrix}$
4	$C(I-B)^{-1}$	$\frac{1}{\mu+m+\nu}\begin{pmatrix} \frac{\beta b}{m} & \frac{\delta\beta b^2}{m^2(r-g)} \\ \gamma & \frac{\delta\gamma b}{m(r-g)} \end{pmatrix}$	$\frac{1}{\mu+m+\nu}\begin{pmatrix} \frac{\beta br+\delta\gamma b}{mr} & \frac{\delta b^2(\beta r+\delta\gamma)}{m^2 r(r-g)} \\ \frac{\gamma g}{r} & \frac{\delta\gamma g b}{mr(r-g)} \end{pmatrix}$
5	$T_C = \rho(C(I-B)^{-1})$	$\frac{\beta b(r-g)+\delta\gamma b}{m(r-g)(\mu+m+\nu)}$	$\frac{\beta b(r-g)+\delta\gamma b}{m(r-g)(\mu+m+\nu)}$
6	$\mathcal{Y}_\mu = \frac{\mu}{f^{-1}(\frac{f(\mu)}{T_C})}$	$\frac{m\mu(r-g)}{(r-g)(\beta b-m(m+\nu))+\delta\gamma b}$	$\frac{m\mu(r-g)}{(r-g)(\beta b-m(m+\nu))+\delta\gamma b}$

Note that μ is located in the same entries $(1,1)$ and $(2,1)$ of each scenario's NGMs (step 1). While the associated target matrix is different (step 2), the resulting target matrices is the same (step 5). Furthermore, in both scenarios $f(\mu) = \frac{1}{\mu+m+\nu}$ (step 2) where it is decreasing and continuous everywhere, thus the inverse exists. From (5.1), the spectrum yield index is $\mathcal{Y}_\mu = \dfrac{\mu}{f^{-1}(\frac{f(\mu)}{T_C})} = \dfrac{\mu}{f^{-1}(\frac{m(r-g)}{\beta b(r-g)+\delta\gamma b})} = \dfrac{m\mu(r-g)}{(r-g)(\beta b - m(m+\nu)) + \delta\gamma b}$ (step 6), where $f^{-1}(\mu) = \dfrac{1}{\mu} - (m+\nu)$.

Increase in the pathogen decay rate

As Cholera is mainly an aquatic disease, we can mitigate the spread by providing clean water to drink and use via boiling or using antiseptic, i.e., Chlorine. Such measures increase the decay rate of pathogens which lead to the disease decline where they target parameter r of NGM (5.6) and (5.7).

Table 5.4: Description of targeting parameter r

		Reservoir	Transition-Reservoir
1	NGM	$\begin{pmatrix} \frac{\beta b}{m(\mu+m+\nu)} & \frac{\delta b}{mr} \\ \frac{\gamma}{\mu+m+\nu} & \frac{g}{r} \end{pmatrix}$	$\begin{pmatrix} \frac{\beta br+\delta\gamma b}{m(\mu+m+\nu)r} & \frac{\delta b}{mr} \\ \frac{\gamma g}{r(\mu+m+\nu)} & \frac{g}{r} \end{pmatrix}$
2	Target matrix C	$\frac{1}{r}\begin{pmatrix} 0 & \frac{\delta b}{m} \\ 0 & g \end{pmatrix}$	$\frac{1}{r}\begin{pmatrix} \frac{\delta\gamma b}{m(\mu+m+\nu)} & \frac{\delta b}{m} \\ \frac{\gamma g}{(\mu+m+\nu)} & g \end{pmatrix}$
3	Residual matrix B	$\begin{pmatrix} \frac{\beta b}{m(\mu+m+\nu)} & 0 \\ \frac{\gamma}{\mu+m+\nu} & 0 \end{pmatrix}$	$\begin{pmatrix} \frac{\beta b}{m(\mu+m+\nu)} & 0 \\ 0 & 0 \end{pmatrix}$
4	$C(I-B)^{-1}$	$\frac{1}{r}\begin{pmatrix} \frac{\delta\gamma b}{m(\mu+m+\nu)-\beta b} & \frac{\delta b}{m} \\ \frac{\gamma g m}{m(\mu+m+\nu)-\beta b} & g \end{pmatrix}$	$\frac{1}{r}\begin{pmatrix} \frac{\delta\gamma b}{m(\mu+m+\nu)-\beta b} & \frac{\delta b}{m} \\ \frac{\gamma g m}{m(\mu+m+\nu)-\beta b} & g \end{pmatrix}$
5	$T_C = \rho(C(I-B)^{-1})$	$\frac{g}{r} + \frac{\delta\gamma b}{r[m(\mu+m+\nu)-\beta b]}$	$\frac{g}{r} + \frac{\delta\gamma b}{r[m(\mu+m+\nu)-\beta b]}$
6	$\mathcal{Y}_r = \frac{r}{f^{-1}(\frac{f(r)}{T_C})}$	$\frac{r(m(\mu+m+\nu)-\beta b)}{mg(\mu+m+\nu)-g\beta b+\gamma b\delta}$	$\frac{r(m(\mu+m+\nu)-\beta b)}{mg(\mu+m+\nu)-g\beta b+\gamma b\delta}$

Given targeted parameter r is located in different entries of the corresponding NGM of each scenario (step 1) and leading to different target and residual matrices (step 2 and 3), the target reproduction number in both cases is identical (step 5). Moreover, in both cases, $f(r) = \frac{1}{r}$ (step 2). From (5.1), we have

$\mathcal{Y}_r = \dfrac{r}{f^{-1}(\frac{f(r)}{T_C})} = \dfrac{r}{f^{-1}(\frac{1}{rT_C})} = \dfrac{1}{T_C}$ (step 6), where $f^{-1}(r) = \frac{1}{r}$.

- *A different decomposition for K*

Note that we can consider another decomposition for the Jacobian matrix (6.8), where FLP growth rate g is regarded as transition, whereas the shedding rate γ is assumed to be new infectious. Under these assumptions, matrices F, V and K are defined as

$$F = \begin{pmatrix} \frac{\beta b}{m} & \frac{\delta b}{m} \\ \gamma & 0 \end{pmatrix}, \quad V = \begin{pmatrix} \mu + m + \nu & 0 \\ 0 & r - g \end{pmatrix},$$

and

$$K = \begin{pmatrix} \dfrac{\beta b}{m(\mu + m + \nu)} & \dfrac{\delta b}{m(r - g)} \\ \dfrac{\gamma}{\mu + m + \nu} & 0 \end{pmatrix}.$$

If we target r, then the target matrix C and residual matrix B are

$$C = \frac{1}{r - g} \begin{pmatrix} 0 & \frac{\delta b}{m} \\ 0 & 0 \end{pmatrix} \quad \text{and} \quad B = \begin{pmatrix} \dfrac{\beta b}{m(\mu + m + \nu)} & 0 \\ \dfrac{\gamma}{\mu + m + \nu} & 0 \end{pmatrix}.$$

Thus, the corresponding target reproduction number is

$$T_C = \rho(C(I-B)^{-1}) = \frac{\delta\gamma b}{m(r-g)[m(\mu+m+\nu)-\beta b]}, \tag{5.8}$$

Substituting (5.8), $f(r) = \dfrac{1}{r-g}$ and $f^{-1}(r) = \dfrac{1}{r} + g$ as expressions defined in (5.1), give rise to

$$\mathcal{Y}_r = \frac{r}{f^{-1}\left(\frac{f(r)}{T_C}\right)} = \frac{r(m(\mu+m+\nu)-\beta b)}{mg(\mu+m+\nu)-g\beta b+\gamma b\delta}. \tag{5.9}$$

Notice that while T_C and $f(r)$ provided in (5.8) are not the same as their counterparts in 5.4 (steps 2 and 5), the corresponding $\mathcal{Y}_r$ to all scenarios are the same. This implies that calculating $\mathcal{Y}_r$ is independent of the the decomposition of NGM K.

CHAPTER 6: A NEW METHOD FOR CONTROLLING THE SPECTRAL BOUND

Over the past several years, a substantial amount of work has been done to develop effective disease control strategies on the epidemiological disease models. Generally, such strategies target particular entries of the next generation matrix K of the disease models to bring the basic reproduction number $R_0 = \rho(K)$ to the threshold value 1.

The objective of this work, is to impose disease control strategies directly to the entries of the jacobian matrix J rather than the ones in the next generation matrix K.

As it will be discussed in the next Section, the disease control strategies that determine the efforts to bring R_0 to the threshold value 1, are exactly the ones that make the determinant of the jacobian matrix $|J|$ equal to 0.

6.1 Motivation

Let $A = [a_{ij}]_{n\times n}$ such that $\sigma(A)$ is the set of eigenvalues of A. Let $\rho(A)$ be the spectral radius of A, then

$$\rho(A) = \max\{|\lambda| : \lambda \in \sigma(A)\}.$$

Let $s(A)$ be the spectral bound of A, then

$$s(A) = \max\{\mathrm{Re}\lambda : \lambda \in \sigma(A)\}.$$

Matrix A is called essentially non-negative if A has a non-positive spectral bound, i.e., $s(A) \leq 0$. That is, A is essentially non-negative, if $a_{ij} \geq 0$ for $i \neq j$.

Proposition 6.1. *Let $A = [a_{ij}]$ be an irreducible and essentially non-negative matrix. Then, the spectral bound of A is an eigenvalue of A. That is, $Ax = s(A)x$ for some $x \in \mathbb{C}^n$.*

Proposition 6.2. *Let $J = F - V$ be a jacobian matrix with the non-negative matrix F and the non-singular M-matrix matrix V. Suppose $K = FV^{-1}$ is a non-negative next generation matrix where $R_0 = \rho(K)$. Then,*

$$R_0 = 1 \iff s(J) = 0.$$

The following result, which is the direct implication of Propositions 6.1 and 6.2, highlights the relationship between R_0 and the determinant of J.

Lemma 6.3. *Let $J = F - V$ be a jacobian matrix such that F is a non-negative matrix and V is a non-singular M-matrix matrix. Suppose $K = FV^{-1}$ is a non-negative next generation matrix with $R_0 = \rho(K)$. Then,*

$$R_0 = 1 \iff |J| = 0.$$

Proof. Let $R_0 = 1$. Thus, by Proposition 6.2, $s(J) = 0$. On the other hand, by the assumption J is essentially non-negative. Following Proposition 6.1, this implies that $s(J) = 0$ is an eigenvalue of J. Thus, $|J| = 0$. □

Definition 6.1. *Let $p^* > 0$. Parameter p^* is called the **pivotal index**, if it measures the required effort to bring the value of the determinant of the jacobian matrix J to 0 by targeting a particular parameter in J. That is,*

$$|J(p^*)| = 0,$$

*where $J(p^*)$ is the **controlled jacobian matrix**, and is a function of p^*.*

Remark 2. *The above definition on the pivotal index p^* can be extended to targeting a set of parameters in J.*

Remark 3. *The pivotal index p^* also works for situations where parts of entries of J are targeted.*

Remark 4. *The same effort that makes the determinant of J, is the same effort that bring R_0 to the threshold value 1. Thus,*

$$\frac{R_0}{p^*} = 1 \iff |J(p^*)| = 0.$$

In the following Section, we elaborate the role of p^* in the connection with the jacobian matrix in details. Specifically, we provide a technique to compute p^* from the jacobian matrix.

6.2 Method Description

In this Section, we first describe the general method to calculate the pivotal index p^* that brings the determinant of the jacobian matrix J to 0. Then, we disclose some closed form formulas for a special case.

General technique

Step 1. Decompose the jacobian matrix J as $B + C = B + pD$, where:

- p is the target parameter,
- D is the p correspondence coefficient matrix,
- C is the target matrix, consisting of entries containing p, and
- B is the residual matrix, consisting entries not containing p.

Step 2. Derive the controlled jacobian matrix $J(p^*)$ from J by replacing p with $\frac{p}{p^*}$. Thus,

$$J(p^*) = B + \frac{p}{p^*}D.$$

Step 3. Find p^* by solving $\det(B + \frac{p}{p^*}D) = 0$.

Special case: $\operatorname{rank}(C) = 1$

The method description in 6.2 to derive the pivotal index p^* works for any target matrix C. This Section gives a more explicit expression for the pivotal index p^* for situations when the rank of target matrix C is 1.

Before stating the main result of this Section and its corresponding implications, let us take a look at the following result, which is a powerful tool to prove the primary result of this Section.

Proposition 6.4. *Let A be $n \times n$ matrix, where $\operatorname{rank}(A) = 1$. Then,*

$$\det(A + I) = 1 + \operatorname{tr}(A).$$

Proof. Let $A = \Psi\Delta\Psi^{-1}$, such that $\Delta = \operatorname{diag}\{\upsilon_1, \ldots, \upsilon_n\}$ is the matrix of eigenvalues of A, in which the eigenvalues of A are the diagonal entries of Δ, and Ψ denotes the matrix of eigenvectors of A, in which column i for $1 \leq i \leq n$ is the eigenvector associated to eigenvalue υ_i and Ψ^{-1} exists. Since $\operatorname{rank}(A) = 1$, matrix Δ has only one nonzero eigenvalue, i.e., $\upsilon_1 \neq 0$ and $\upsilon_i = 0$ for

$i = 2, \ldots, n$. Thus,

$$\begin{aligned}
\det(A + I) &= \det(\Psi\Delta\Psi^{-1} + \Psi\Psi^{-1}) \\
&= \det(\Psi)\det(\Delta + I)\det(\Psi^{-1}) \\
&= \det(\mathrm{diag}\{\upsilon_1 + 1, 1, \ldots, 1\}) \\
&= 1 + \upsilon_1 \\
&= 1 + \mathrm{tr}(A).
\end{aligned}$$

□

Theorem 6.5. *Let J be an $n \times n$ jacobian matrix such that $J = B + C = B + pD$, where*

(i) C is the target matrix associated to target parameter p, and $D = [d_{ij}]$ is the p correspondence matrix with $\mathrm{rank}(C) = \mathrm{rank}(D) = 1$, and

(ii) B is the residual matrix, consists of entries not containing parameter p, with $\mathrm{rank}(B) = n$.

Then, the pivotal index p^* is given by

$$p^* = -p\frac{\Sigma_{i,j}(-1)^{i+j}d_{ij}B_{ij}}{det(B)},$$

where B_{ij} is the cofactor element of B obtained from omitting the ith row and jth column of B.

Proof. It follows from Step 3. in the method description of Section 6.2 that in order to compute the pivotal index p^*, it is required to solve $\det(B + \frac{p}{p^*}D) = 0$ for p^*. That is,

$$\det(B + \frac{p}{p^*}D) = \det(B)\det(I + \frac{p}{p^*}B^{-1}D) = 0,$$

where it follows from the fact that $\mathrm{rank}(B) = n$, i.e., B^{-1} exists, and $\det(B) \neq 0$. Thus,

$$\det(I + \frac{p}{p^*}B^{-1}D) = 0. \tag{6.1}$$

On the other hand, as $\mathrm{rank}(D) = 1$, $\mathrm{rank}(B^{-1}D) = 1$. Thus, by Proposition 6.4, equation (6.1) becomes

$$0 = \det(I + \frac{p}{p^*}B^{-1}D) = 1 + \mathrm{tr}(\frac{p}{p^*}B^{-1}D) = 1 + \frac{p}{p^*}\mathrm{tr}(B^{-1}D) = 1 + \frac{p}{p^*}\frac{\Sigma_{i,j}(-1)^{i+j}d_{ij}B_{ij}}{det(B)},$$

where B_{ij} is the cofactor element of B obtained by eliminating the ith row and the jth column of B. Hence,

$$p^* = -p\frac{\Sigma_{i,j}(-1)^{i+j}d_{ij}B_{ij}}{\det(B)}.$$

□

The pivotal index p^* in Theorem 6.5 works for any matrix D of rank 1. The following result provides a derivation for the pivotal index p^* when matrix D of rank 1 with one nonzero row (or column).

Corollary 6.6. *Let J be an $n \times n$ jacobian matrix such that $J = B + C = B + pD$, such that parameter p and matrices C, B and D are satisfied in conditions (i) and (ii) in Theorem 6.5. Assume that D has one nonzero row at j. That is,* $D = [d_{ij}] = \begin{cases} d_{ij} \neq 0 & row \quad j \\ 0 & otherwise. \end{cases}$

Then, the pivotal index p^* is given by

$$p^* = -p\frac{\Sigma_{i}(-1)^{i+j}d_{ij}B_{ij}}{\det(B)}, \tag{6.2}$$

where B_{ij} is the cofactor element of B obtained from removing the ith row and jth column of B.

Proof. From the method description in Section 6.2, to determine p^*, solve $\det(B + \frac{p}{p^*}D) = 0$ for p^*. Applying the Laplacian determinant expansion, the expansion of the determinant of $B + \frac{p}{p^*}D$ along the jth row is as follows:

$$\det(B+\frac{p}{p^*}D) = (\frac{pd_{1j}}{p^*}+b_{1j})B_{1j}(-1)^{1+j}+(\frac{pd_{2j}}{p^*}+b_{2j})B_{2j}(-1)^{2+j}+\cdots+(\frac{pd_{nj}}{p^*}+b_{nj})B_{nj}(-1)^{n+j} = 0.$$

Collecting all the terms with p^* on the left side yields

$$\frac{p}{p^*}\sum_i(-1)^{i+j}d_{ij}B_{ij} = -\sum_i(-1)^{i+j}b_{ij}B_{ij} = -\det(B).$$

Thus,

$$p^* = -\frac{p\sum_i(-1)^{i+j}d_{ij}B_{ij}}{\det(B)}.$$

□

Remark 5. *The result of Corollary 6.6 holds when matrix D has one nonzero column, i.e., column j. In this case, the pivotal index* (6.3) *is an expansion along column j.*

The pivotal index p^* formula in Corollary 6.6 works when matrix D has only one nonzero row (or column). The following result provided a derivation for the pivotal index p^* when matrix D contains only one nonzero entry. Since the following result follows directly from Corollary 6.6, the proof is omitted.

Corollary 6.7. *Let J be an $n \times n$ jacobian matrix such that $J = B + C = B + pD$, such that parameter p and matrices C, B and D are satisfied in conditions (i) and (ii) of Theorem 6.5. Assume that D has one nonzero element at entry (i, j), that is, $D = [d_{ij}] = \begin{cases} d_{ij} \neq 0 & entry \quad (i,j) \\ 0 & otherwise. \end{cases}$*

Then, the pivotal index p^* is given by

$$p^* = -p\frac{(-1)^{i+j}d_{ij}B_{ij}}{\det(B)}, \tag{6.3}$$

where B_{ij} is the cofactor element of B obtained from omitting the ith row and jth column of B.

6.3 Graph-Theoretic Interpretation

The previous Section used the matrix theoretic and linear algebraic results to formulate the pivotal index p^* This Section uses the graph theoretic technique to compute p^*.

We first present the definition of the determinant by using the graph terminology, which is a powerful too to establish the main results of this Section.

Let $A = [a_{ij}]$ be an $n \times n$ matrix. Denote $\mathcal{D} = \mathcal{D}(A)$ as the corresponding weighted digraph of A. Digraph $\mathcal{D}$ consists of n vertices which are labelled as $1, \ldots, n$. An arc from vertex j to vertex i for $1 \leq i, j \leq n$ in $\mathcal{D}$ has a weight of a_{ij}. Note that the weights of arcs in digraph $\mathcal{D}$ are not necessarily positive. An arc is called a target arc, if its weight corresponds to the target parameter in A. A subdigraph $\mathcal{D}$ is a digraph whose set of vertices is a subset of vertices of $\mathcal{D}$, and set of edges is a subset of set of edges of $\mathcal{D}$. A linear-subdigraph $\mathcal{L}$ is a subdigraph of $\mathcal{D}$ that consists of all vertices of $\mathcal{D}$ in which each vertex has in-degree 1 and out-degree 1. That is, linear subdigraph $\mathcal{L}$ consists of all pairwise vertex-disjoint cycles in $\mathcal{D}$. The product of the weights of the edges of $\mathcal{L}$ is the weight $w(\mathcal{L})$ of $\mathcal{L}$. The number of cycles contained in $\mathcal{L}$ is denoted by $c(\mathcal{L})$.

The following definition gives the formulation of the determinant $\det(A)$ of the matrix A using the linear subdigraphs of digraph of $\mathcal{D}(A)$.

Definition 6.2. *Let A be an $n \times n$ matrix. Then*

$$\det(A) = (-1)^n \sum_{\mathcal{L}} (-1)^{c(\mathcal{L})} w(\mathcal{L}), \tag{6.4}$$

where the sum is all over linear subdigraph $\mathcal{L}$ of $\mathcal{D}(A)$.

The following result uses Definition 6.2 to provide an alternative way to compute the pivotal index p^*.

Theorem 6.8. *Let J be an $n \times n$ jacobian matrix such that $J = B + C = B + pD$, where $\mathrm{rank}(B) = n$ and $\mathrm{rank}(C) = \mathrm{rank}(D) = r$ for $r \leq n$. Then, the pivotal index p^* satisfies the following characteristic equation*

$$\frac{\varrho_r}{(p^*)^r} + \frac{\varrho_{r-1}}{(p^*)^{r-1}} + \cdots + \frac{\varrho_1}{p^*} + \varrho_0 = 0, \tag{6.5}$$

with

$$\varrho_i = \sum_{\mathcal{L}^i} (-1)^{c(\mathcal{L}^i)} w(\mathcal{L}^i),$$

where the sum is over all linear subdigraphs $\mathcal{L}^i$ of $\mathcal{D}$ consist of i target arcs of C.

When the rank of target matrix C is 1, an explicit expression for the pivotal index p^* can be derived as follows.

Theorem 6.9. *Let J be an $n \times n$ jacobian matrix such that $J = B + C = B + pD$, where $\mathrm{rank}(B) = n$ and $\mathrm{rank}(C) = \mathrm{rank}(D) = 1$. Then, the pivotal index p^* is given by*

$$p^* = \frac{\Sigma_\zeta (-1)^{1+c(\zeta)} w(\zeta)}{\Sigma_\vartheta (-1)^{c(\vartheta)} w(\vartheta)}, \tag{6.6}$$

where the sums are over all linear subdigraphs ζ and linear subdigraphs ϑ of $\mathcal{D}$ that contain and

do not contain target arc carrying p.

Proof. Since $\mathrm{rank}(C) = 1$, the characteristic equation (6.5) in Theorem 6.8 becomes

$$\frac{\varrho_1}{p^*} + \varrho_0 = 0, \tag{6.7}$$

with

$$\varrho_1 = \sum_{\zeta}(-1)^{c(\zeta)}w(\zeta) \quad \text{and} \quad \varrho_0 = \sum_{\vartheta}(-1)^{c(\vartheta)}w(\vartheta),$$

where linear subdigraphs ζ and ϱ contain and do not contain a target arc in C, respectively. Solving the pivotal index p^* from (6.7) results in

$$p^* = -\frac{\sum_{\zeta}(-1)^{c(\zeta)}w(\zeta)}{\sum_{\vartheta}(-1)^{c(\vartheta)}w(\vartheta)}.$$

□

6.4 Application to a Homogeneous Cholera Model

Consider the following one-patch cholera model described as

$$\begin{aligned}
\dot{S} &= b - \beta SI - \delta SW + \alpha R - mS, \\
\dot{I} &= \beta SI + \delta SW - (\eta + m + \gamma)I, \\
\dot{R} &= \gamma I - (\alpha + m)R, \\
\dot{W} &= \xi I + gW(1 - cW) - \nu W,
\end{aligned}$$

where S, I and R compartments denote the number of susceptible, infectious, and recovered hosts, respectively. The W compartment indicates the free living pathogens (FLP). Parameters b, m and η

denote the birth rate, natural death rate and diseased induced mortality rate, respectively. Parameter γ represents the recover rate. The environment to host and the host to host transmission rates are denoted by δ and β. Parameters ξ, g and ν are the shedding, growth and decay rates of pathogens in the environment, respectively. Assume that the pathogens cannot survive in the absence of the cholera infection, thus, $\nu > g$.

The jacobian matrix J of the system at the disease free equilibrium is given by

$$J = \begin{pmatrix} \frac{\beta b}{m} - (\gamma + m + \eta) & \frac{\delta b}{m} \\ \\ \xi & g - \nu \end{pmatrix}, \tag{6.8}$$

In what follow, we implement different disease control strategies to have the spread of cholera under control. Mathematically, these strategies target a particular parameter (or a set of parameters) in the jacobian matrix in (6.8) to bring the determinant of J to the threshold value 0.

Reduction in the host-to-host contact

The spread of cholera can be controlled by reducing the contact between the susceptible and infected individuals. Mathematically, this practice targets parameter β, which is part of the entry $(1, 1)$ of (6.8).

Following the method description in Section 6.2, the target matrix C and the residual matrix B are given by

$$C = \beta \begin{pmatrix} \frac{b}{m} & 0 \\ \\ 0 & 0 \end{pmatrix} =: \beta D \quad \text{and} \quad B = \begin{pmatrix} -(\gamma + m + \eta) & \frac{\delta b}{m} \\ \\ \xi & g - \nu \end{pmatrix},$$

where D denotes the β correspondence coefficient matrix. The pivotal index p^* measures the

required reduction in the contact rate between susceptible and infected individuals. Since $\mathrm{rank}(D) = 1$ with one nonzero entry, by Corollary 6.7 the pivotal index p^* is given as

$$p^* = -\beta \frac{(-1)^{(1+1)} \frac{b}{m}(g-\nu)}{-(\gamma+m+\eta)(g-\nu) - \frac{\xi\delta b}{m}} = \frac{\beta b(g-\nu)}{m(\gamma+m+\eta)(g-\nu)+\delta b\xi}. \tag{6.9}$$

This implies that the effective quarantine practice decreases the host to host contact by fraction p^* provided in (6.9). Thus, $\dfrac{\beta}{p^*}$ replaces p^* in (6.8).

Reducing both the environment-to-host and the host-to-host transmissions

In areas where cholera outbreak is serious one effective way to have the spread under control is to promote vaccination among newborns. Such control strategy targets parameter b, which appears in entries $(1,1)$ and $(1,2)$ of (6.8). Thus, the target matrix C and the residual matrix B are given as

$$C = b\begin{pmatrix} \frac{\beta}{m} & \frac{\delta}{m} \\ 0 & 0 \end{pmatrix} = bD \quad \text{and} \quad B = \begin{pmatrix} -(\gamma+m+\eta) & 0 \\ \xi & g-\nu \end{pmatrix},$$

where D is the b correspondence coefficient matrix. The pivotal index p^* determines the required vaccine coverage to have cholera under control. Since $\mathrm{rank}(D) = 1$ with a nonzero row, following Corollary 6.6 the pivotal index p^* is

$$p^* = -b\frac{\frac{\beta}{m}(-1)^{(1+1)}(g-\nu) + \frac{\delta}{m}(-1)^{(1+2)}\xi}{-(\gamma+m+\eta)(g-\nu)} = \frac{b[(g-\nu)-\delta\xi]}{m(\gamma+m+\eta)(g-\nu)}.$$

This implies that effective vaccination practices decrease parameter b in (6.8) to $\dfrac{b}{p^*}$.

Reduction in the shedding rate

In addition to the above mentioned strategies, one factor to prevent cholera is to decrease the bacterial shedding. Appropriate antibiotics are recommended to shorten the duration and volume of diarrhoea and reduce the duration of the bacterial shedding. Such prevention strategies target parameter ξ which is located in entry $(2,1)$ of (6.8). Thus, the target matrix C and the residual matrix B are described as

$$C = \xi \begin{pmatrix} 0 & 0 \\ \\ 1 & 0 \end{pmatrix} = \xi D \quad \text{and} \quad B = \begin{pmatrix} \frac{\beta b}{m} - (\gamma + m + \eta) & \frac{\delta b}{m} \\ \\ 0 & g - \nu \end{pmatrix},$$

where D is the ξ correspondence coefficient matrix. The pivotal index p^* determines the effective reduction in bacterial shedding to prevent cholera. Since $\mathrm{rank}(D) = 1$ with one nonzero entry, following Corollary 6.7 the pivotal index is given as

$$p^* = \frac{\xi \beta b}{(\beta b - m(\gamma + m + \nu))(g - \nu)}, \tag{6.10}$$

which implies that the appropriate antibiotics could reduce transmission and interrupt the outbreak by reducing the shedding rate from ξ to $\dfrac{\xi}{p^*} = \dfrac{(g-\nu)[\beta b - m(\gamma + m + \nu)]}{\delta b \xi}$.

6.5 Application to a Heterogeneous SIS Model

Consider the following jacobian matrix of a SIS model as follows

$$J = \text{diag}\{\beta_i - \gamma_i\} - \mu L = \begin{pmatrix} \beta_1 - \gamma_1 - \mu \sum_{i \neq 1} a_{i1} & \mu a_{12} & \dots & \mu a_{1n} \\ \mu a_{21} & \beta_2 - \gamma_2 - \mu \sum_{i \neq 2} a_{i2} & \dots & \mu a_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ \mu a_{n1} & \mu a_{n2} & \dots & \beta_n - \gamma_n - \mu \sum_{i \neq n} a_{in} \end{pmatrix}, \tag{6.11}$$

where $\gamma_i > 0$ denotes the recover rate of the infected individuals in patch i, $\beta_i > 0$ represents the contact rate between susceptible and infected individuals in patch i, and $a_{ij} \geq 0$ is the movement from patch j to patch i for $1 \leq i, j \leq n$ and $i \neq j$. Parameter $\mu > 0$ denotes the dispersal rate of the susceptible and infected individuals.

In the remaining of this Section, we consider different disease control strategies.

Reducing the movement between two particular patches

One way to have the spread of the infectious under control is to reduce the movement from patch l to patch k, for $k > l$, by imposing the practice of social distancing. This strategy targets parameter a_{kl},which is located in entries (k, k) and (k, l) of the jacobian matrix (6.11). The pivotal index p^* determines the effective quarantine practice applied to a_{kl} to control the spread of the infectious. Following the method description in Section 6.2, the target matrix C has two nonzero entries as

follows

$$C = \begin{pmatrix} 0 & \dots & & 0 & & \dots & 0 \\ \vdots & & & & & & \vdots \\ & & & \overbrace{-\mu a_{kl}}^{(l,l)entry} & & & \\ 0 & \dots & 0 & & 0 & \dots & 0 \\ \vdots & & \vdots & & \vdots & & \\ 0 & \dots & 0 & \underbrace{\mu a_{kl}}_{(k,l)entry} & 0 & \dots & 0 \\ & & & & & & \\ \vdots & & \vdots & & \vdots & & \\ 0 & \dots & & 0 & & \dots & 0 \end{pmatrix} = a_{kl} \begin{pmatrix} 0 & \dots & & 0 & & \dots & 0 \\ \vdots & & & & & & \vdots \\ & & & \overbrace{-\mu}^{(l,l)entry} & & & \\ 0 & \dots & 0 & & 0 & \dots & 0 \\ \vdots & & \vdots & & \vdots & & \\ 0 & \dots & 0 & \underbrace{\mu}_{(k,l)entry} & 0 & \dots & 0 \\ & & & & & & \\ \vdots & & \vdots & & \vdots & & \\ 0 & \dots & & 0 & & \dots & 0 \end{pmatrix} =: a_{kl} D,$$

where D is the coefficient matrix associated to a_{kl}. Similarly, by the method description in Section 6.2, the residual matrix B obtained from the jacobian matrix in (6.11) by eliminating parameter a_{ij}. Thus,

$$B = \begin{pmatrix} \beta_1 - \gamma_1 - \mu \sum\limits_{i \neq 1} a_{i1} & \dots & \mu a_{1\ell} & \dots & \mu a_{1n} \\ \vdots & \ddots & \vdots & \dots & \vdots \\ & & \overbrace{\qquad\qquad}^{(\ell,\ell)entry} & & \\ \mu a_{\ell 1} & \dots & \beta_\ell - \gamma_\ell - \mu \sum\limits_{i \neq k,\ell} a_{i\ell} & \dots & \mu a_{\ell n} \\ \vdots & & \vdots & & \vdots \\ \mu a_{k1} & \dots & \underbrace{0}_{(k,\ell)entry} & \ddots & \mu a_{kn} \\ \vdots & \vdots & & & \vdots \\ \mu a_{n1} & \dots & \mu a_{n\ell} & \dots & \beta_n - \gamma_n - \mu \sum\limits_{i \neq n} a_{in} \end{pmatrix}.$$

It can be observed from equation (6.5) that $\mathrm{rank}(D) = 1$ with one nonzero column at column ℓ. Thus, from Corollary 6.6 the pivotal index p^* is given by

$$p^* = \mu a_{k\ell} \frac{(-1)^{\ell+\ell} B_{\ell\ell} + (-1)^{k+\ell} B_{k\ell}}{\det(B)}, \tag{6.12}$$

where $B_{\ell\ell}$ and $B_{k\ell}$ are the co-factor matrices of B. To control the disease spread effectively, the movement from patch ℓ to patch k should be decreased by the pivotal index provided in

equation (6.12).

Reducing transmission rate of a particular patch

One way to reduce the spread of the disease is to bring down the contact between the susceptible and infected individuals in one patch, i.e., patch ℓ. Such control strategies target parameter β_ℓ, which is located partially in entry (ℓ, ℓ) of the jacobian matrix in (6.8). Following the method description in Section 6.2, the residual matrix B is obtained from J in (6.8) by omitting β_ℓ from entry (ℓ, ℓ), and target matrix C only consists of β_ℓ at entry (ℓ, ℓ). Thus,

$$B = \begin{pmatrix} \beta_1 - \gamma_1 - \mu \sum\limits_{i \neq 1} a_{i1} & \dots & \mu a_{1\ell} & \dots & \mu a_{1n} \\ \vdots & \ddots & \vdots & \dots & \vdots \\ \mu a_{\ell 1} & \dots & \overbrace{-\gamma_\ell - \mu \sum\limits_{i \neq k, \ell} a_{i\ell}}^{(\ell,\ell) entry} & \dots & \mu a_{\ell n} \\ \vdots & \vdots & & & \vdots \\ \mu a_{n1} & \dots & \mu a_{n\ell} & \dots & \beta_n - \gamma_n - \mu \sum\limits_{i \neq n} a_{in} \end{pmatrix}$$

and

$$C = \begin{pmatrix} 0 & \dots & 0 & \dots & 0 \\ \vdots & & & & \vdots \\ 0 & \dots & \beta_\ell & \dots & 0 \\ \vdots & & & & \vdots \\ 0 & \dots & 0 & \dots & 0 \end{pmatrix} =: \beta_\ell D,$$

where D is the β_ℓ associated coefficient matrix. The pivotal index p^* determines required reduction in the contact between the susceptible and infected individuals in patch ℓ.

Since D has only one nonzero entry, by Corollary (6.7), p^* is computed as follows

$$p^* = -\frac{\beta_\ell (-1)^{\ell+\ell} B_{\ell\ell}}{\det(B)}, \tag{6.13}$$

where $B_{\ell\ell}$ is the co-factor matrix of B obtained by eliminating row ℓ and column ℓ of B. This implies, to constructively control the spread of the disease β_ℓ becomes $\dfrac{\beta_\ell}{p^*}$ for p^* given as in (6.13).

Reducing the movement rate in all patches

One way to have the disease under control is to reduce the movement rate among all patches. Mathematically, such control strategies target parameter μ in the jacobian matrix J of (6.8), which is located in all entries of J.

To compute the pivotal index p^*, which is the required effort to bring down the movement rate among all patches, we are required to construct the residual matrix B and the target matrix C. Following the method description in Section 6.2, B and C are generated from J by excluding parameter μ and including μ, respectively. Thus,

$$B = \operatorname{diag}\{\beta_i - \gamma_i\}, \quad \text{and} \quad C = -\mu L, \tag{6.14}$$

where L is the Laplacian matrix associated to the movement in the system, and, $\operatorname{rank}(L) = n - 1$. Consequently, the rank of target matrix C is not 1. Thus, to compute the pivotal index p^*, none of the closed form formulas, i.e., Theorem 6.5, Corollary 6.6 and Corollary 6.7 works. However, one can compute p^* by following the general technique in Section 6.2.

In the remaining, we investigate the pivotal index p^* for each disease control strategy described above for the special case of jacobian matrix J in (6.8) with two patches. Additionally,for each scenario the graph theoretic interpretation approach, as described in Section 6.3, is applied to compute the the pivotal index p^*.

Note that both the algebraic formulation and the graph interpretation method lead to the same p^*

value.

Application to a Two-Patch SIS Model: A Special Case

Consider a special case of the jacobian matrix of (6.8) with two patches. That is,

$$J = \begin{pmatrix} \beta_1 - \gamma_1 - \mu a_{21} & \mu a_{12} \\ \mu a_{21} & \beta_2 - \gamma_2 - \mu a_{12} \end{pmatrix}, \tag{6.15}$$

where all the parameter descriptions are exactly the same as the ones in Section 6.5.

Reducing the movement from patch 1 *to patch* 2*: Target* a_{21}

Closed form formula The target parameter a_{21} appears at entries $(1,1)$ and $(2,1)$ of the jacobian matrix in (6.15). By the method description in Section 6.2, the residual matrix B and the target matrix C are given as

$$B = \begin{pmatrix} \beta_1 - \gamma_1 & \mu a_{12} \\ 0 & \beta_2 - \gamma_2 - \mu a_{12} \end{pmatrix} \quad \text{and} \quad C = \begin{pmatrix} -\mu a_{21} & 0 \\ \mu a_{21} & 0 \end{pmatrix} = a_{21} \begin{pmatrix} -\mu & 0 \\ \mu & 0 \end{pmatrix} =: a_{21} D$$

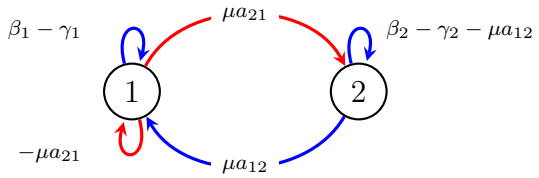
where D is the coefficient matrix associated to a_{21}. It can be observed that $\mathrm{rank}(D) = 1$ with one nonzero column at column 1. Thus, from equation (6.3) in Corollary 6.6 the pivotalindex p^* is given by

$$p^* = -a_{21} \frac{(-1)^{1+1}(-\mu)(\beta_2 - \gamma_2 - \mu a_{12}) + (-1)^{1+2}\mu(\mu a_{12})}{(\beta_1 - \gamma_1)(\beta_2 - \gamma_2 - \mu a_{12})} = \frac{\mu a_{21}(\beta_2 - \gamma_2)}{(\beta_1 - \gamma_1)(\beta_2 - \gamma_2 - \mu a_{12})}. \tag{6.16}$$

This implies that effective quarantine practice reduces the movement from patch 2 to patch 1 by

factor p^*. This implies that a_{21} becomes $\dfrac{a_{21}}{p^*}$.

Graph theoretic interpretation Consider the following weighted digraph corresponding to the jacobian matrix of (6.15) as



where the red arcs correspond to those containing target parameter a_{21}. Following Theorem 6.9, the pivotalindex p^* is given by

$$p^* = \frac{\mu^2 a_{12} a_{21}(-1)^{1+1} + (-\mu a_{21})(\beta_2 - \gamma_2 - \mu a_{12})(-1)^{1+2}}{(\beta_1 - \gamma_1)(\beta_2 - \gamma_2 - \mu a_{12})} = \frac{\mu a_{21}(\beta_2 - \gamma_2)}{(\beta_1 - \gamma_1)(\beta_2 - \gamma_2 - \mu a_{12})} \tag{6.17}$$

where the numerator is the sum over linear subdigraphs consisting target arc a_{21}, and the denominator is the sum over linear subdigraphs not consisting target arc a_{21}.

As it was expected, p^* value from the algebraic formulation, equation (6.16), is equal to the graph interpretation approach, equation (6.17).

Reduction in the transmission rate in patch 1*: Target* β_1

Closed form formula The target parameter β_1 appears only at entry $(1, 1)$ of the jacobian matrix of (6.15). From the method description of Section 6.2, the target matrix C and the residual matrix

B are described as

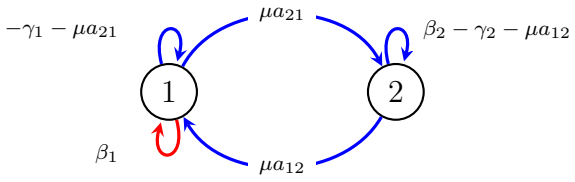
$$C = \begin{pmatrix} \beta_1 & 0 \\ 0 & 0 \end{pmatrix} =: \beta_1 D \quad \text{and} \quad B = \begin{pmatrix} -\gamma_1 - \mu a_{21} & \mu a_{12} \\ \mu a_{21} & \beta_2 - \gamma_2 - \mu a_{12} \end{pmatrix},$$

where D is the coefficient matrix associated to β_1. Since $\text{rank}(D) = 1$ with one nonzero entry, by Corollary 6.7, the pivotalindex p^* is as follows

$$p^* = -\beta_1 \frac{(-1)^{1+1}(\beta_2 - \gamma_2 - \mu a_{12})}{(\beta_2 - \gamma_2 - \mu a_{12})(-\gamma_1 - \mu a_{21}) - \mu^2 a_{12} a_{21}} = \frac{\beta_1(\beta_2 - \gamma_2 - \mu a_{12})}{(\beta_2 - \gamma_2 - \mu a_{12})\gamma_1 + \mu a_{21}(\beta_2 - \gamma_2)}, \tag{6.18}$$

which determines the required decrease in the transmission rate in patch 1. That is, $\frac{\beta_1}{p^*}$ replaces p^* in the jacobian matrix of (6.15).

Graph theoretic interpretation Consider the the following weighted digraph associated to the jacobian matrix of (6.15) given as



where the red arc correspond to the target arc β_1. By Theorem 6.9, the pivotal index p^* is the negative of the sum of all weighted linear sub digraphs that contain β_1 over the sum of all weighted linear sub digraphs that do not contain β_1. That is,

$$p^* = \frac{\beta_1(\beta_2 - \gamma_2 - \mu a_{12})}{(\beta_2 - \gamma_2 - \mu a_{12})\gamma_1 + \mu a_{21}(\beta_2 - \gamma_2)}. \tag{6.19}$$

It can be seen from equations (6.18) and (6.19) that both the graph interpretation approach and the

closed form formula result in the same pivotal index p^* value.

Decrease in the movement rate between both patches: Target μ

Closed form formula The target parameter μ appears in every entry of the jacobian matrix of (6.15). Thus, by the method description in Section 6.2, the residual matrix B and the target matrix C are described as

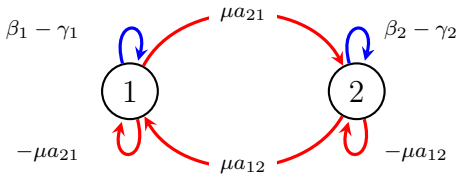
$$B = \begin{pmatrix} \beta_1 - \gamma_1 & 0 \\ 0 & \beta_2 - \gamma_2 \end{pmatrix} \quad \text{and} \quad C = \begin{pmatrix} -\mu a_{21} & \mu a_{12} \\ \mu a_{21} & -\mu a_{12} \end{pmatrix} = \mu \begin{pmatrix} -a_{21} & a_{12} \\ a_{21} & -a_{12} \end{pmatrix} =: \mu D,$$

where D is the μ associated coefficient matrix with $\operatorname{rank}(D) = 1$. Thus, by Theorem 6.5 the pivotal index p^* is as follows

$$p^* = -\frac{-\mu a_{21}(\beta_2 - \gamma_2) - \mu a_{12}(\beta_1 - \gamma_1)}{(\beta_1 - \gamma_1)(\beta_2 - \gamma_2)} = \mu \frac{a_{21}(\beta_2 - \gamma_2) + a_{12}(\beta_1 - \gamma_1)}{(\beta_1 - \gamma_1)(\beta_2 - \gamma_2)}. \tag{6.20}$$

This implies that to successfully have the spread of the disease under control, the movement rate of both patches should be decreased by factor p^*. That is, μ becomes $\dfrac{\mu}{p^*}$ in the jacobian matrix of (6.15).

Graph theoretic interpretation Consider the the following weighted digraph associated to the jacobian matrix of (6.15) given as



where the red arcs corresponds to the the target arc consisting μ. By Theorem 6.9, the pivotal index p^* is described as

$$p^* = -\frac{-\mu a_{12}(\beta_1 - \gamma_1)(-1)^2 - \mu a_{21}(\beta_2 - \gamma_2)(-1)^2}{(\beta_2 - \gamma_2)(\beta_1 - \gamma_1)(-1)^2} = \mu \frac{a_{12}(\beta_1 - \gamma_1) + a_{21}(\beta_2 - \gamma_2)}{(\beta_2 - \gamma_2)(\beta_1 - \gamma_1)}, \quad (6.21)$$

where the numerator consists of the linear subdigraph including target arc μ, and the denominator consists of all linear subdigraphs excluding the target arc μ.

It can be verified from equations (6.20) and (6.21), that the pivotal index p^* is the same for both techniques.

CHAPTER 7: SUMMARY AND FUTURE WORK

This dissertation primarily investigates the architectures of heterogeneous networks and how they impact population and disease dynamics in ecological and epidemiological models. We developed an expansion for the network population growth in ecological models, which can also be applied for the network disease growth rate and the basic reproduction number R_0 in epidemiological models. Notice that two different expansions for the same R_0 are derived, which involve group inverse matrices corresponding to two Laplacian matrices different by a product of a diagonal matrix. A possible future work is to investigate the group inverse of the product matrix of a Laplace matrix and a diagonal matrix as this has potential applications in spatial heterogeneous population dynamics.

We have focused our applications on two specific networks (path and star) due to the time strain, and further studies of other network configurations would be of both practical interests and theoretical needs in order to apply results in the dissertation to real world problems.

Our new indices and methods in controlling the spectral bound and spectral radius of matrices can be further applied to other ecological, epidemiological, engineering and scientific problems.

APPENDIX A: TREE CYCLE IDENTITY

Let $\mathcal{G} = (V, E)$ denote a *weighted digraph* with $V = \{1, 2, \cdots, n\}$ be the set of vertices and E the set of arcs (i, j) with weight $a_{ij} > 0$ from initial vertex j to terminal vertex i. Define the weight matrix $A = [a_{ij}]_{n\times n}$ whose entry a_{ij} equals the weight of arc (i, j) if it exists, and 0 otherwise. We denote a weighted digraph as $\mathcal{G}_A = (\mathcal{G}, A)$. A digraph is strongly connected if, for any pair of distinct vertices, there exists a directed path from one to the other.The Weighted digraph $\mathcal{G}_A$ is strongly connected if and only if A is irreducible. A sub-digraph $\mathcal{H}$ of $\mathcal{G}$ is *spanning* if both $\mathcal{H}$ and $\mathcal{G}$ have the same vertex set. The weight $w(\mathcal{H})$ of $\mathcal{H}$ is the product of the weights of all its arcs. A connected sub-digraph $\mathcal{T}$ is called a *tree*, if it contains no directed cycle. A tree is called *rooted-in*, if there is one vertex, called the *root*, that is not an initial vertex of any arcs while each of the remaining vertices is an initial vertex of exactly one arc. A sub-digraph $\mathcal{Q}$ of G is *unicyclic* ,if it is a disjoint union of rooted-in trees whose roots form a directed cycle. Every vertex of unicyclic $\mathcal{Q}$ is an initial vertex of exactly one arc. The Laplacian matrix of $(\mathcal{G}, A)$ is defined as

$$L = \text{diag}(\sum_{i\neq 1} a_{i1}, \sum_{i\neq 2} a_{i2}, \cdots, \sum_{i\neq n} a_{in}) - A, \tag{A.1}$$

with $\theta = (\theta_1, \cdots, \theta_n)^\top$ be the positive, normalized principal right eigenvector of L. It follows from Kirchhoff's Matrix-Tree Theorem that $\theta_i = \dfrac{C_{ii}}{\sum_{k=1}^n C_{kk}}$; C_{ii} is the cofactor of the i-th diagonal entry of L and is interpreted as $C_{ii} = \sum_{\mathcal{T}\in\mathbb{T}_i} w(\mathcal{T})$ where $\mathbb{T}_i$ is the set of all spanning-in trees rooted at vertex i, and $w(\mathcal{T})$ is the weight of $\mathcal{T}$.

Theorem A.1. *(Tree-Cycle Identity) Let $\mathcal{G}_A$ be a strongly connected weighted digraph, and $L = [a_{ij}]$ be the corresponding Laplacian matrix of $\mathcal{G}_A$ with $\theta = (\theta_1, \cdots, \theta_n)^\top$ be the positive, normalized Perron right eigenvector of L. Then, the following identities holds*

$$\sum_{i,j=1}^n \theta_i a_{ji} F_{ji}(x_i, x_j) = \sum_{\mathcal{Q}\in\mathbb{Q}} w(\mathcal{Q}) \sum_{(s,r)\in E(\mathcal{C}_\mathcal{Q})} F_{rs}(x_s, x_r),$$

where $F_{ji}(x_j, x_i), 1 \leq j, i \leq n$ are arbitrary functions, $\mathbb{Q}$ is the set of all spanning unicycle graphs

of $(\mathcal{G}, A)$, $w(\mathcal{Q}) > 0$ *is the weight of* $\mathcal{Q}$*, and* $\mathcal{C}_{\mathcal{Q}}$ *denotes the directed cycle of* $\mathcal{Q}$ *with arc set* $E(\mathcal{C}_{\mathcal{Q}})$.

Corollary A.2. *Let* θ_j *and* a_{ji} *be given as above, then the following identity holds and*

$$\sum_{i,j=1}^{n} \theta_j a_{ji} G_j(x_j) = \sum_{i,j=1}^{n} \theta_j a_{ji} G_i(x_i),$$

where $G_j(x_j), 1 \leq j \leq n$ *are arbitrary functions.*

APPENDIX B: THE GROUP INVERSE OF LAPLACIAN MATRIX

Preliminaries

Lemma B.1. *[5] Let $M \in \mathbb{R}^n$, then there exists a non-negative integer k such that*

$$\mathbb{R}^n = \ker(M^k) \bigoplus \operatorname{range}(M^k).$$

Proof. By the rank-nullity theorem $\dim(\ker(M^k)) + \dim(\operatorname{range}(M^k)) = n$. To complete the proof we show if $x \in \ker(M^k) \cap \operatorname{range}(M^k)$, then $x = 0$. Let k be the smallest non-negative integer such that $\operatorname{rank}(M) \supset \operatorname{rank}(M^2) \supset \cdots \operatorname{rank}(M^k) = \operatorname{rank}(M^{k+1}) = ...$; equivalently $\ker(M) \subset \ker(M^2) \subset \cdots \ker(M^k) = \ker(M^{k+1}) = ...$ Now suppose $x \in \ker(M^k) \cap \operatorname{range}(M^k)$, then, there exist a $y \in \mathbb{R}^n$ such that $Mx = y$, thus $M^k y = A^{2k}x = 0$, so $y \in \ker(M^{2k}) = \ker(M^k)$, so $x = 0$. □

The smallest non-negative integer k such that $\operatorname{rank}(M^k) = \operatorname{rank}(M^{k+1})$ or equivalently $\mathbb{R}^n = \ker(M^k) \bigoplus \operatorname{range}(M^k)$ is called the *index* of M and denoted by $\operatorname{ind}(M)$.

Let $M \in \mathbb{R}^n$ be a singular matrix of $\operatorname{ind}(M) \leq 1$. Then, the group inverse of M denoted by $M^{\#} \in \mathbb{R}^n$ is a unique matrix satisfying the three equations

$$MM^{\#} = M^{\#}M, \quad M^{\#}MM^{\#} = M^{\#}, \quad \text{and} \quad MM^{\#}M = M.$$

Now, we will proceed to prove some of properties of the group inverse that will be used later.

Lemma B.2. *Let $M \in \mathbb{R}^n$, such that $\operatorname{Ind}(M) = 0$ then the followings hold*
(a) 0 is an eigenvalue of M if and only if it is an eigenvalue of $M^{\#}$.
(b) $\lambda \neq 0$ is an eigenvalue of M if and only if $\dfrac{1}{\lambda}$ it is an eigenvalue of $M^{\#}$.

Proof. (a) Let 0 be the gienvalue of M, and v be its 17 corresponding eigenvector, then $Mv = 0$.

$$0 = Mv = M^{\#}M^{\#}Mv = M^{\#}MM^{\#}v = M^{\#}v.$$

(b) Let $\lambda \neq 0$ and v be the eigenvalue and eigenvector of A. Since $v \in \mathrm{range}(M)$, then there exist $w \in \mathbb{R}^n$ such that $Mw = v$.

$$\begin{aligned} Mv = \lambda v &\iff M^{\#}Mv = \lambda M^{\#}v \iff MM^{\#}v = \lambda M^{\#}v \\ &\iff MM^{\#}Mw = \lambda M^{\#}v \iff \\ Mw = \lambda M^{\#}v &\iff v = \lambda M^{\#}v \iff \frac{1}{\lambda}v = M^{\#}v \end{aligned}$$

□

Theorem B.3. *Let $M \in \mathbb{R}^n$ of $\mathrm{ind}(M) \leq 1$ with $\mathrm{rank}(M) = n - r$, and let P_0 be a projection matrix onto $\ker(M)$ along $\mathrm{range}(M)$ with $\mathrm{rank}(P_0) = r$. Then $(M - P_0)$ is nonsingular and*

$$M^{\#} = P_0 + (M - P_0)^{-1}.$$

In addition, if $\mathrm{rank}(M) = n - 1$, then $P_0 = uv^{\top}$ where $v^{\top}M = Mu = 0$ and $v^{\top}u = 1$.

Proof. We first show $(M - P_0)$ is nonsingular, by showing $MP_0 = 0$ For matrix M of index 1, $\mathrm{range}(A) \cap \ker(M) = 0$. Thus $\mathrm{range}(M)$ and $\ker(M)$ are complementary spaces, and $\mathbb{R}^n = \mathrm{range}(M) \oplus \ker(M)$. Since P_0 is a projecion matrix onto $\mathrm{range}(M)$, it sends $\mathrm{range}(M)$ to 0. In other words p_j denote the jth column of P_0, then $p_j = v_j + w_j$ where $v_j \in \mathrm{range}(M)$ and $w_j \in \ker(M)$, then $P_0(v_j) = 0$ and $P_0(w_j) = w_j$.

Now, let M_j for $j = 1, \cdots, n$ be columns of matrix A. As columns of A are in range of M, $A_j \in \text{range}(M)$, then it follows $P_0(M_j) = 0$ for $j = 1, \cdots, n$, giving $P_0 A = 0$.
Conversely, as P_0 is a projection matrix onto $\text{Ker}(M)$, its columns are in the $\text{Ker}(M)$, i.e. $p_j \in \text{Ker}(M)$, hence $M(p_j) = 0$ for $j = 1, \cdots, n$, thus $MP_0 = 0$.

Now, we show $M - P_0$ is nonsingular. To do so, we we show $(M - P_0)x = 0$ has a solution if and only if $x = 0$. $(M - P_0)x = 0$ if and only if $Mx = P_0 x$. This means $Mx \in \text{range}(M)$ and $Mx \in \text{ker}(M)$(as $P_0 x \in \text{ker}(M)$), hence $Mx = 0$, therefore $x \in \text{ker}(M)$. On the other hand, $P_0 x = 0$, this implies that $x \in \text{range}(M)$, so $x = 0$. So $M - P_0$ is nonsingular, and $M(M - P_0)^{-1} = (M - P_0)^{-1} M$.

For $M^{\#}$ to be the group inverse of M, three properties of group inverse must hold.

- $M^{\#}M = (P_0 + (M - P_0)^{-1})M = P_0 M + (M - P_0)^{-1} M = 0 + M(M - P_0)^{-1} = MP_0 + M(M - P_0)^{-1} = M(P_0 + (M - P_0)^{-1}) = MM^{\#}$
- $MM^{\#}M = M(P_0 + (M - P_0)^{-1})M = M(M - P_0)^{-1} M = (M - P_0)^{-1} M^2 = M$
- $M^{\#}MM^{\#} = (P_0 + (M - P_0)^{-1})M(P_0 + (M - P_0)^{-1}) = (M - P_0)^{-1} M(M - P_0)^{-1} = (M - P_0)^{-1}((M - P_0) + P_0)(M - P_0)^{-1} = (M - P_0)^{-1} + P_0 = M^{\#}$

□

APPENDIX C: FURTHER PROPERTIES OF LAPLACIAN MATRIX

Let L be a Laplacian matrix of a directed graph $\mathcal{G}$ of order n. Suppose that $\mathcal{G}$ is strongly connected; namely, L is irreducible, and $\mathrm{rank}(L) = n - 1$. As a consequence, L has a simple eigenvalue 0, with corresponding left eigenvector $\mathbb{1}$ which is the all ones column vector of dimension n and right (normalized) eigenvector $\theta = (\theta_1, \theta_2, \ldots, \theta_n)^\top$ with $\sum_i \theta_i = 1$. That is, $\mathbb{1}^\top L = 0$, $L\theta = 0$, and $\mathbb{1}^\top \theta = 1$. Thus, L can be be partitioned as $L = P \left(\begin{array}{c|c} 0 & \bar{0}^\top \\ \hline \bar{0} & C \end{array}\right) P^{-1}$, where $P_{n\times n}$ and $C_{(n-1)\times(n-1)}$ are non-singular matrices, and $\bar{0}$ is a zero vector of dimension $n-1$. Simple calculations result in $L^2 = P \left(\begin{array}{c|c} 0 & \bar{0}^\top \\ \hline \bar{0} & C^2 \end{array}\right) P^{-1}$, Hence, $\mathrm{rank}(L) = \mathrm{rank}(L^2) = n - 1$, equivalently, $\mathrm{ind}(L) = 1$, so the group inverse $L^\#$ of L is well-defined and unique. The following lemma provides several related properties of $L^\#$, which will be used throughout the paper.

Lemma C.1. *Let L be an irreducible Laplacian matrix and $L^\#$ be its corresponding group inverse, then*

1. $\mathbb{1}^\top L^\# = \mathbb{1}^\top L = 0$.
2. *If* $u \in \ker(L)$, *then* $L^\# u = Lu = 0$.
3. *If* $u \in \mathrm{range}(L)$, *then* $LL^\# u = L^\# L u = u$.
4. $L^\# = \theta\mathbb{1}^\top + (L - \theta\mathbb{1}^\top)^{-1}$, *where* $\theta \in \ker(L)$ *and* $\mathbb{1}^\top\theta = 1$.
5. $L = \theta\mathbb{1}^\top + (L^\# - \theta\mathbb{1}^\top)^{-1}$.
6. $LL^\# = I - \theta\mathbb{1}^\top$.

Proof. 1. It follows from the properties of the Laplacian matrix that $0 = \mathbb{1}^\top L$. Now,

$$\mathbb{1}^\top L^\# = \mathbb{1}^\top L^\# L L^\# = \mathbb{1}^\top L L^\# L^\# = 0.$$

2. If $u \in \ker(L)$, then $Lu = 0$. Thus $L^{\#}u = L^{\#}LL^{\#}u = L^{\#}L^{\#}Lu = 0$.

3. If $u \in \text{range}(L)$, then there exists $w \in \mathbb{R}^n$ such that $Lw = u$. Hence, $LL^{\#}u = LL^{\#}Lw = Lw = u$.

4. It is the direct result of Theorem B.3 (See Appendix) with $P_0 = \mathbb{1}^\top\theta$ and $M = L$.

5. It follows from part 4. $L^{\#} - \mathbb{1}^\top\theta = (L - \mathbb{1}^\top\theta)^{-1}$. From Theorem B.3, $(L - \mathbb{1}^\top\theta)$ is nonsingular, so $(L^{\#} - \mathbb{1}^\top\theta)^{-1} = L - \mathbb{1}^\top\theta$, and $L = 1^\top\theta + (L^{\#} - \mathbb{1}^\top\theta)$.

□

From the hypotheses on L, it is easy to see that L may be partitioned as

$$L = \left(\begin{array}{c|c} \bar{\mathbb{1}}^\top z & -\bar{\mathbb{1}}^\top B \\ \hline -z & B \end{array}\right), \tag{C.1}$$

where B is an $(n-1)\times(n-1)$ invertible matrix, u_1 is the first entry of u, $\bar{u} = (u_2, \ldots, u_n)^\top$, $z = \frac{1}{u_1}B\bar{u}$, and $\bar{\mathbb{1}}$ is the all ones column vector of dimension $n-1$. It follows from Observation 2.3.4 in [10]: From the hypotheses on L, it is easy to see that L may be partitioned as

$$L = \left(\begin{array}{c|c} \bar{\mathbb{1}}^\top z & -\bar{\mathbb{1}}^\top B \\ \hline -z & B \end{array}\right). \tag{C.2}$$

Thus, the group inverse of L denoted as $L^{\#}$ is as follow:

$$L^{\#} = (\bar{\mathbb{1}}^\top B^{-1}\bar{u})u\mathbb{1}^\top + \left(\begin{array}{c|c} 0 & -u_1\bar{\mathbb{1}}^\top B^{-1} \\ \hline -B^{-1}\bar{u} & B^{-1} - B^{-1}\bar{u}\bar{\mathbb{1}}^\top - \bar{u}\bar{\mathbb{1}}^\top B^{-1} \end{array}\right). \tag{C.3}$$

APPENDIX D: TWO SPECIFIC NETWORKS

D.1 Star Network

Consider a star network with vertex 1 as the hub, and $2, 3, \ldots, n$ as leaf vertices. Assume that all movement coefficients between adjacent vertices are the same and equal to 1, then the resulting Laplacian matrix can be written as the form of

$$L = \begin{pmatrix} n-1 & -1 & -1 & \cdots & -1 \\ -1 & 1 & 0 & \cdots & 0 \\ -1 & 0 & 1 & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ -1 & 0 & 0 & \cdots & 1 \end{pmatrix}_{n\times n}.$$

Following the partition in (C.2), set $B = \mathbf{I}_{n-1}$, i.e., the identity matrix of order $n-1$, $u = (\frac{1}{n}, \frac{1}{n}, \cdots, \frac{1}{n})^\top$, and $z = \bar{\mathbb{1}}$. Straightforward calculations yield $B^{-1} = \mathbf{I}_{n-1}$, $\bar{\mathbb{1}}^\top B^{-1}\bar{u} = \frac{n-1}{n}$, $u\mathbb{1}^\top = \frac{1}{n}\mathbf{J}_n$, and $B^{-1} - B^{-1}\bar{u}\bar{\mathbb{1}}^\top - \bar{u}\bar{\mathbb{1}}^\top B^{-1} = \frac{1}{n}(n\mathbf{I}_{n-1} - 2\mathbf{J}_{n-1})$, where $\mathbf{J}$ is the all ones matrix (i.e., every entry of $\mathbf{J}$ is 1). As a consequence,

$$L^{\#} = \frac{n-1}{n^2}\mathbf{J}_n + \frac{1}{n}\left(\begin{array}{c|c} 0 & -\bar{\mathbb{1}}^\top \\ \hline -\bar{\mathbb{1}} & n\mathbf{I}_{n-1} - 2\mathbf{J}_{n-1} \end{array}\right),$$

that is,

$$L^{\#} = \frac{n-1}{n}u\bar{\mathbb{1}}^\top + \frac{1}{n}\begin{pmatrix} 0 & -1 & -1 & \cdots & \cdots & \cdots & -1 \\ -1 & n-2 & -2 & \cdots & \cdots & \cdots & -2 \\ -1 & -2 & n-2 & -2 & \cdots & \cdots & -2 \\ -1 & -2 & -2 & n-2 & -2 & \cdots & -2 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ -1 & -2 & -2 & -2 & \cdots & -2 & n-2 \end{pmatrix}. \tag{D.1}$$

Note that each column sum of the matrix in the second term has the same value $-n+1$.

When $n=2$, $L=\begin{pmatrix} 1 & -1 \\ -1 & 1 \end{pmatrix}$ and $L^{\#}=\frac{1}{2}\cdot\frac{1}{2}\begin{pmatrix} 1 & 1 \\ 1 & 1 \end{pmatrix}+\frac{1}{2}\begin{pmatrix} 0 & -1 \\ -1 & 0 \end{pmatrix}=\frac{1}{4}\begin{pmatrix} 1 & -1 \\ -1 & 1 \end{pmatrix}$.

When $n=3$, $L=\begin{pmatrix} 2 & -1 & -1 \\ -1 & 1 & 0 \\ -1 & 0 & 1 \end{pmatrix}$ and

$L^{\#}=\frac{2}{3}\cdot\frac{1}{3}\begin{pmatrix} 1 & 1 & 1 \\ 1 & 1 & 1 \\ 1 & 1 & 1 \end{pmatrix}+\frac{1}{3}\begin{pmatrix} 0 & -1 & -1 \\ -1 & 1 & -2 \\ -1 & -2 & 1 \end{pmatrix}=\frac{1}{9}\begin{pmatrix} 2 & -1 & -1 \\ -1 & 5 & -4 \\ -1 & -4 & 5 \end{pmatrix}$.

For $n=4$, $L^{\#}=\frac{1}{16}\begin{pmatrix} 3 & -1 & -1 & -1 \\ -1 & 11 & -5 & -5 \\ -1 & -5 & 11 & -5 \\ -1 & -5 & -5 & 11 \end{pmatrix}$. For $n=5$, $L^{\#}=\frac{1}{25}\begin{pmatrix} 4 & -1 & -1 & -1 & -1 \\ -1 & 19 & -6 & -6 & -6 \\ -1 & -6 & 19 & -6 & -6 \\ -1 & -6 & -6 & 19 & -6 \\ -1 & -6 & -6 & -6 & 19 \end{pmatrix}$.

D.2 Path Network

Consider a path network with vertices labeled $1, 2, 3, ..., n$ consecutively located along a line, and assume that all movement between adjacent vertices are the same and of weight 1. The

corresponding Laplacian matrix takes the form of

$$L = \begin{pmatrix} 1 & -1 & 0 & \cdots & 0 \\ -1 & 2 & -1 & \cdots & 0 \\ 0 & -1 & 2 & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & \cdots & -1 & 2 & -1 \\ 0 & \cdots & 0 & -1 & 1 \end{pmatrix}_{n\times n}.$$

Following the partition (C.2), set $z = \bar{\mathbb{1}}$, $u = (\frac{1}{n}, \cdots, \frac{1}{n})^\top$, and

$$B = \begin{pmatrix} 2 & -1 & \cdots & 0 \\ -1 & 2 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ \cdots & -1 & 2 & -1 \\ \cdots & 0 & -1 & 1 \end{pmatrix}_{(n-1)\times(n-1)}.$$

It can be verified that

$$B^{-1} = \begin{pmatrix} 1 & 1 & 1 & 1 & \cdots & 1 \\ 1 & 2 & 2 & 2 & \cdots & 2 \\ 1 & 2 & 3 & 3 & \cdots & 3 \\ 1 & 2 & 3 & 4 & \cdots & 4 \\ \vdots & \vdots & & & \ddots & \vdots \\ 1 & 2 & 3 & 4 & \cdots & (n-1) \end{pmatrix}_{(n-1)\times(n-1)},$$

$u_1\bar{\mathbb{1}}^\top B^{-1} = \frac{1}{n}(\sum_{i=n-1}^{n-1} i, \sum_{i=n-2}^{n-1} i, \cdots, \sum_{i=1}^{n-1} i)$ and $B^{-1}u = \frac{1}{n}(\sum_{i=n-1}^{n-1} i, \sum_{i=n-2}^{n-1} i, \cdots, \sum_{i=1}^{n-1} i)^\top$. It follows that

$$L^{\#} = \frac{(n-1)(2n-1)}{6} u\mathbb{1}^\top - \frac{1}{n}\begin{pmatrix}
0 & \sum_{i=n-1}^{n-1} i & \sum_{i=n-2}^{n-1} i & \sum_{i=n-3}^{n-1} i & \cdots & \sum_{i=3}^{n-1} i & \sum_{i=2}^{n-1} i & \sum_{i=1}^{n-1} i \\
\sum_{i=n-1}^{n-1} i & \sum_{i=n-1}^{n-1} i - 1 & \sum_{i=n-2}^{n-1} i - 1 & \sum_{i=n-3}^{n-1} i - 1 & \cdots & \sum_{i=3}^{n-1} i - 1 & \sum_{i=2}^{n-1} i - 1 & \sum_{i=2}^{n-1} i \\
\sum_{i=n-2}^{n-1} i & \sum_{i=n-2}^{n-1} i - 1 & (\sum_{i=n-2}^{n-1} i - 1) - 2 & (\sum_{i=n-3}^{n-1} i - 1) - 2 & \cdots & (\sum_{i=3}^{n-1} i - 1) - 2 & \sum_{i=3}^{n-1} i - 1 & \sum_{i=3}^{n-1} i \\
\sum_{i=n-3}^{n-1} i & \sum_{i=n-3}^{n-1} i - 1 & (\sum_{i=n-3}^{n-1} i - 1) - 2 & ((\sum_{i=4}^{n-1} i - 1) - 2) - 3 & \cdots & (\sum_{i=4}^{n-1} i - 1) - 2 & \sum_{i=4}^{n-1} i - 1 & \sum_{i=4}^{n-1} i \\
\vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\
\sum_{i=3}^{n-1} i & \sum_{i=3}^{n-1} i - 1 & (\sum_{i=3}^{n-1} i - 1) - 2 & (\sum_{i=4}^{n-1} i - 1) - 2 & \cdots & (\sum_{i=n-2}^{n-1} i - 1) - 2 & \sum_{i=n-2}^{n-1} i - 1 & \sum_{i=n-2}^{n-2} i \\
\sum_{i=2}^{n-1} i & \sum_{i=2}^{n-1} i - 1 & \sum_{i=3}^{n-1} i - 1 & \sum_{i=4}^{n-1} i - 1 & \cdots & \sum_{i=2}^{n-1} i - 1 & \sum_{i=n-2}^{n-1} i - 1 & \sum_{i=n-1}^{n-1} i \\
\sum_{i=1}^{n-1} i & \sum_{i=2}^{n-1} i & \sum_{i=3}^{n-1} i & \sum_{i=n-2}^{n-1} i & \cdots & \sum_{i=n-1}^{n-1} i & \sum_{i=n-1}^{n-1} i & 0
\end{pmatrix}$$

When $n = 2$, $L^{\#} = \frac{1}{4}\begin{pmatrix} 1 & -1 \\ -1 & 1 \end{pmatrix}$.

When $n = 3$, $L^{\#} = \frac{1}{9}\begin{pmatrix} 5 & -1 & -4 \\ -1 & 2 & -1 \\ -4 & -1 & 5 \end{pmatrix}$.

When $n = 4$, $L^{\#} = \frac{1}{8}\begin{pmatrix} 7 & 1 & -3 & -5 \\ 1 & 3 & -1 & -3 \\ -3 & -1 & 3 & 1 \\ -5 & -3 & 1 & 7 \end{pmatrix} = \frac{1}{16}\begin{pmatrix} 14 & 2 & -6 & -10 \\ 2 & 6 & -2 & -6 \\ -6 & -2 & 6 & 2 \\ -10 & -6 & 2 & 14 \end{pmatrix}$.

When $n = 5$, $L^{\#} = \frac{1}{5}\begin{pmatrix} 6 & 2 & -1 & -3 & -4 \\ 2 & 3 & 0 & -2 & -3 \\ -1 & 0 & 2 & 0 & -1 \\ -3 & -2 & 0 & 3 & 2 \\ -4 & -3 & -1 & 2 & 6 \end{pmatrix} = \frac{1}{25}\begin{pmatrix} 30 & 10 & -5 & -15 & -20 \\ 10 & 15 & 0 & -10 & -15 \\ -5 & 0 & 10 & 0 & -5 \\ -15 & -10 & 0 & 15 & 10 \\ -20 & -15 & -5 & 10 & 30 \end{pmatrix}$.

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