Spread of an SIS Epidemic in a Network

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Motivation

- Mathematical models provide an important tool for understanding and controlling the spread of infectious diseases in human populations.
- Certain human diseases such as the common cold and gonorrhea follow the Susceptible-Infective-Susceptible (SIS) pattern.
- When modelling the spread of these diseases in human populations, it is important to consider the structure of the populations.
- People spend much of their time in groups such as workplaces, shopping centers and schools.

Motivation

- An individual's membership in a particular group is not fixed, but rather it changes over time.
- This structure determines the two paths for disease to spread through the population:
  - Disease is spread between individuals in the same group by contact between infected and susceptible individuals.
  - Disease is spread from one group to another by the migration of infected individuals.
- We are primarily interested in determining the conditions under which the disease becomes endemic and the level of endemic infection.

The Model

- This type of population structure can be modeled using a metapopulation network.
- We model the spread of an SIS type epidemic in a metapopulation network using a continuous time Markov chain.
- We consider a population of size N where each individual is located at one of J geographically distinct nodes.
- $m_j(t) :=$ number of infected individuals at node j at time t.
- $n_j(t) :=$ number of susceptible individuals at node j at time t.
- $(\mathbf{m}(t), \mathbf{n}(t)) = (m_1(t), \ldots, m_J(t), n_1(t), \ldots, n_J(t))$

The Model

Transitions (for movement):

- infected individuals move from node j to node k at rate $\eta_{jk} m_j$.
- susceptible individuals move from node j to node k at rate $\lambda_{jk} n_j$.

Transitions (for disease dynamics):

- susceptible individuals are infected at node j at rate $\frac{\beta}{N} m_j n_j$.
- infected individuals recover at node j at rate γm_j.

Long Term Behaviour of the Model

- This Markov chain has an absorbing set:

$$\{(\mathbf{0}, \mathbf{n}) : n_j \geq 0; j = 1, \ldots, J; \Sigma_{j=1}^{J} n_j = N\}.$$

- Any state in the absorbing set is called a disease free state.
- Since the population size is fixed, the population will eventually enter a disease free state with probability one.
- Upon entering the absorbing set, the distribution of susceptible individuals will converge to the stationary distribution of a closed migration processes.

Objectives

- The time taken to reach a disease free state may be very long, so that the number of infectives in the population may tend to a quasi-equilibrium before the population enters a disease free state.
- I am interested in determining a quasi-equilibrium distribution of the Markov chain as it describes the behaviour of the population at an endemic level.
- Previous analyses of the SIS epidemic model for an unstructured population have used the equilibrium distribution of an approximating stochastic model to approximate the quasi-equilibrium.
- Due to the complexity of the model, I will use an approximating ODE to study the quasi-equilibrium behaviour.

Simulation of the process for $J = 2$

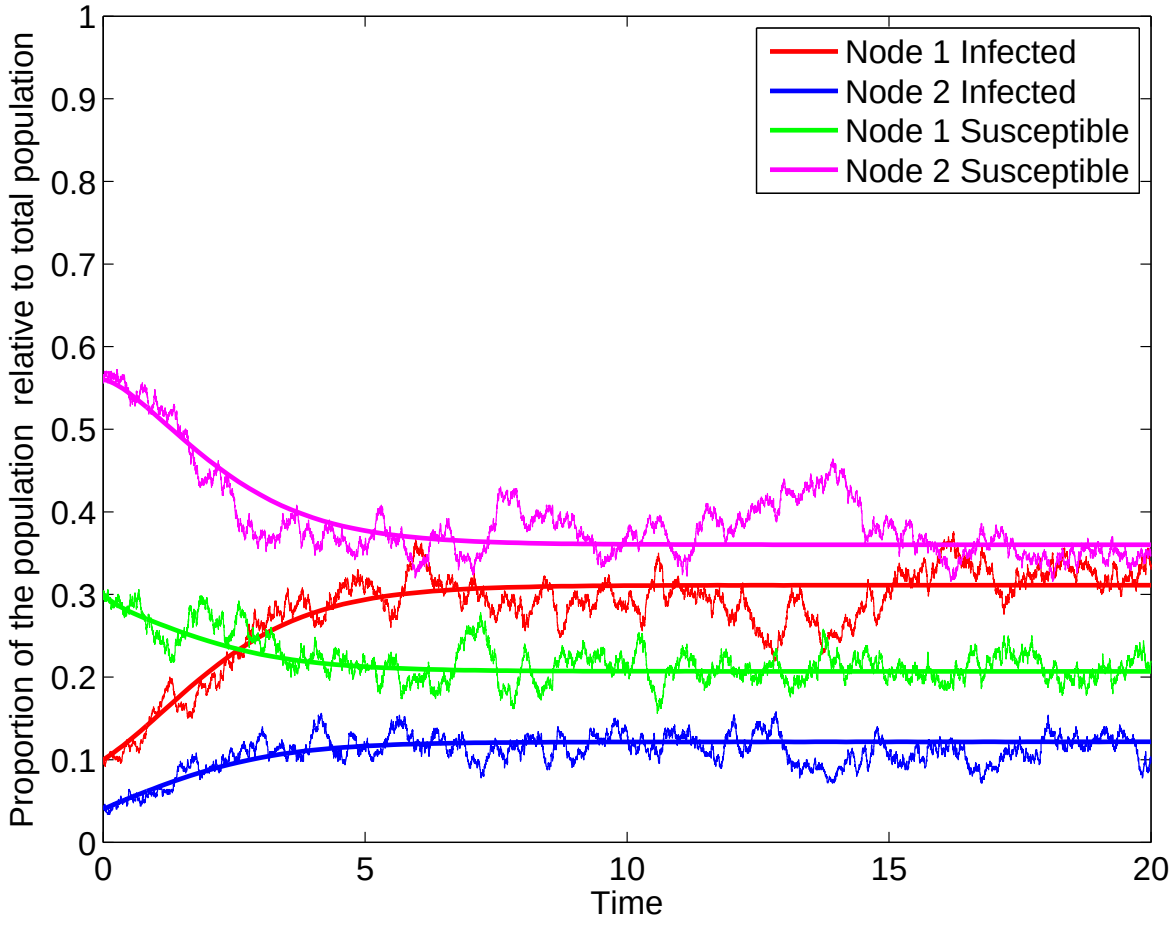

Figure: $N = 500$, $\beta = 4$, $\gamma = 1$, $\lambda_{12} = 2$ $\lambda_{21} = 1$, $\eta_{12} = 1$, $\eta_{21} = 3$

Simulation of the process for $J = 2$

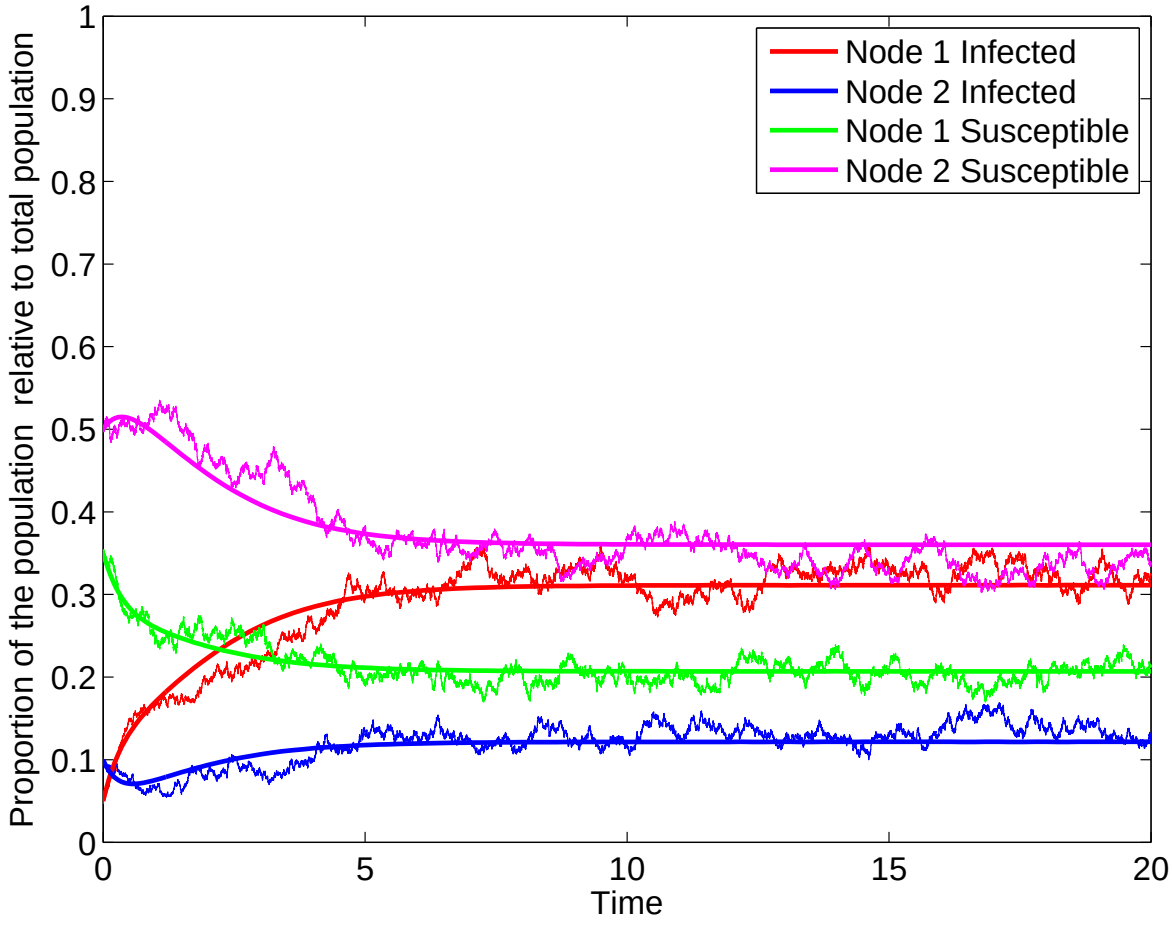

Figure: $N = 1000$, $\beta = 4$, $\gamma = 1$, $\lambda_{12} = 2$ $\lambda_{21} = 1$, $\eta_{12} = 1$, $\eta_{21} = 3$

Simulation of the process for $J = 2$

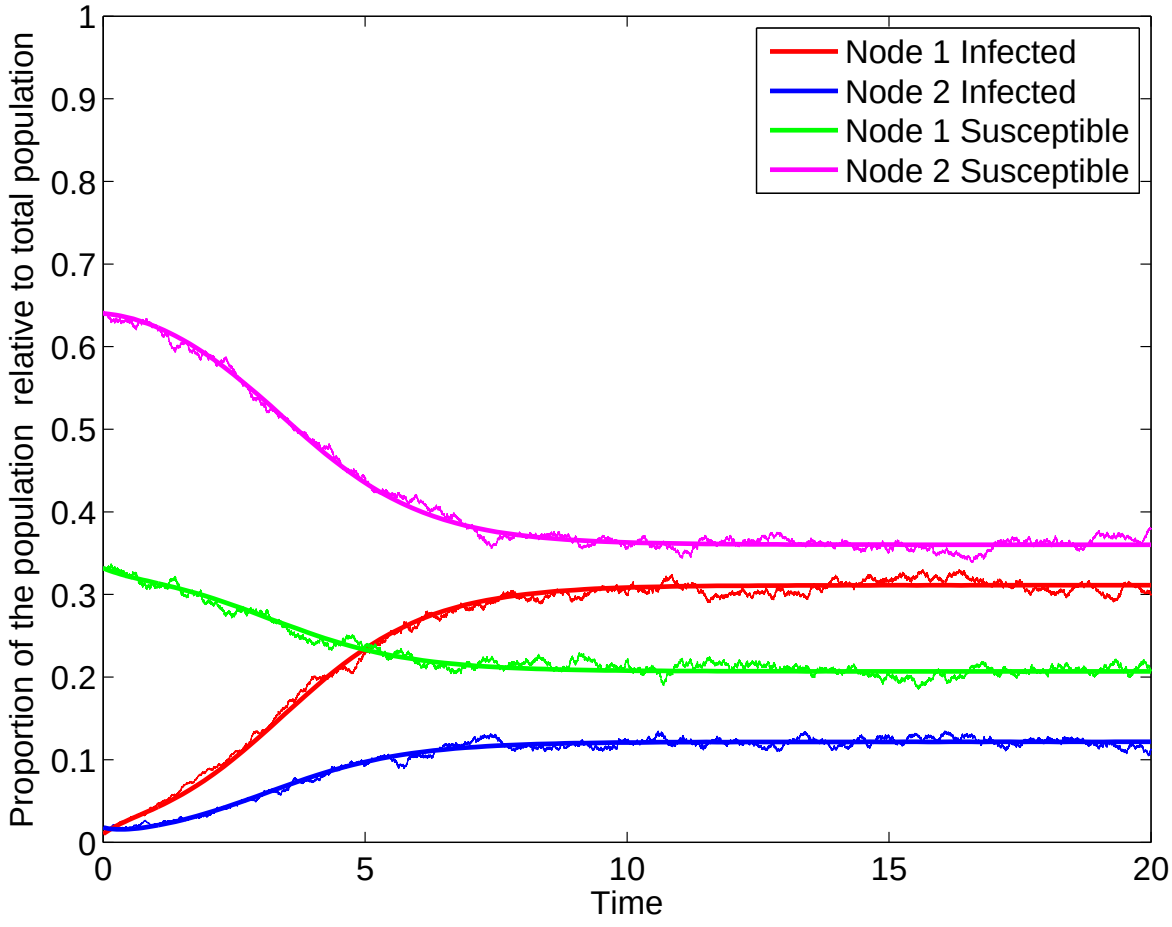

Figure: $N = 5000$, $\beta = 4$, $\gamma = 1$, $\lambda_{12} = 2$ $\lambda_{21} = 1$, $\eta_{12} = 1$, $\eta_{21} = 3$

ODE Approximation

Let $((\mathbf{u}_N(t), \mathbf{v}_N(t)), t \geq 0) := ((N^{-1}\mathbf{m}(t), N^{-1}\mathbf{n}(t)), t \geq 0)$.

Theorem

Suppose $\lim_{N\to\infty}(\mathbf{u}_N(0), \mathbf{v}_N(0)) = (\mathbf{u}^0, \mathbf{v}^0)$. *Then, for each* $T > 0$ *and for all* $\epsilon > 0$,

$$\lim_{N\to\infty} \mathbb{P}\left(\sup_{t\leq T} |(\mathbf{u}_N(t), \mathbf{v}_N(t)) - (\mathbf{u}(t), \mathbf{v}(t))| > \epsilon\right) = 0,$$

where $(\mathbf{u}(t), \mathbf{v}(t))$ *is the unique solution of*

$$\begin{aligned}
\frac{du_j}{dt} &= -\Sigma_{k\neq j}^{J}\eta_{jk}u_j + \beta u_j v_j - \gamma u_j + \Sigma_{k\neq j}^{J}\eta_{kj}u_k, \\
\frac{dv_j}{dt} &= -\Sigma_{k\neq j}^{J}\lambda_{jk}v_j - \beta u_j v_j + \gamma u_j + \Sigma_{k\neq j}^{J}\lambda_{kj}v_k,
\end{aligned}$$

for $j = 1, \ldots, J$, *subject to* $(\mathbf{u}(0), \mathbf{v}(0)) = (\mathbf{u}^0, \mathbf{v}^0)$.

Definitions and Assumptions

- $$\Lambda_{jk} := \begin{cases} \lambda_{kj}, & j \neq k \\ -\Sigma_{l \neq j}^{J} \lambda_{jl}, & j = k, \end{cases} \qquad H_{jk} := \begin{cases} \eta_{kj}, & j \neq k \\ -\Sigma_{l \neq j}^{J} \eta_{jl}, & j = k. \end{cases}$$
- Note that Λ^T and H^T are Q-matrices for migrating individuals.
- The matrices Λ and H are irreducible.
- This implies that the J nodes of the network cannot be separated into two distinct populations such that there is no migration of susceptible or infected individuals from one population to the other.
- This assumption is taken to hold throughout our analysis.

Definitions and Assumptions

- $\Lambda \mathbf{1} = \mathbf{0}$.
- This assumption implies that for each node, the total rate of susceptible individuals leaving a node is equal to the total rate of susceptible individuals entering that.
- $H \mathbf{1} = \mathbf{0}$.
- This assumption has a similar interpretation as above for the migration rates of infected individuals.

Existence of the Disease Free Equilibrium (DFE)

Theorem

The ODE has a unique DFE given by $(\mathbf{0}, \mathbf{v}^*)$ *where* $\Lambda \mathbf{v}^* = \mathbf{0}$ *and* $\mathbf{1}^T \mathbf{v}^* = 1$.

Existence of an Endemic Equilibrium (EE)

Theorem

Assume $\Lambda \mathbf{1} = \mathbf{0}$.

- *If* $\beta \leq J\gamma$, *then the ODE has no EE.*
- *If* $\beta > J\gamma$, *then the ODE has a unique EE* $(\mathbf{u}^*, \mathbf{v}^*)$ *where* $v_j^* = \gamma/\beta$ *for* $j = 1, \ldots, J$ *and* $\mathbf{u}^*$ *satisfies* $H\mathbf{u}^* = \mathbf{0}$ *and* $\mathbf{1}^T \mathbf{u}^* = (1 - J\gamma/\beta)$.

Some Important Questions

- Can an epidemic take off when the population initially has a small proportion of infected individuals?
  - We may address this question by analysing the local stability of the DFE.
  - If the DFE is unstable, then the trajectory of the ODE starting close to the DFE will be repelled from the DFE. Therefore, an epidemic can take off.
- If the population reaches the EE, can the disease persist at the endemic level?
  - We may address this question by analysing the local stability of the EE.
  - If the EE is locally asymptotically stable, then the disease can persist in the population for a long time.

Next Generation Matrix

- Let R_0 be the spectral radius of the matrix

$$\text{diag}(\beta \mathbf{v}^*) \left(\gamma I - H\right)^{-1},$$

  where v_j^* is the proportion of susceptible individuals at node j at the DFE.

- This matrix is called the next generation matrix.

- Its (j,k)th entry is the expected number of new infections in node j produced by an infected individual originally introduced into node k when the population is disease free.

Stability of the DFE

Theorem

Assume Λ is diagonalizable. The DFE equilibrium is locally asymptotically stable if $R_0 < 1$, but unstable if $R_0 > 1$.

- If $\Lambda \mathbf{1} = \mathbf{0}$, then $R_0 = \beta/(J\gamma)$.
- So, under the assumption $\Lambda \mathbf{1} = \mathbf{0}$, the DFE is
  - unstable if $\beta > J\gamma$ and
  - locally asymptotically stable if $\beta < J\gamma$.

Stability of the EE

- Let ρ^H and ρ^Λ denote eigenvalues of H and Λ.

Theorem

Assume Λ and H are diagonalizable and $\Lambda\mathbf{1} = H\mathbf{1} = \mathbf{0}$. Assume also that $\rho^H \neq \rho^\Lambda - (\beta - J\gamma)/J$. If $\beta > J\gamma$, then the EE is locally asymptotically stable.

- This result requires a number of assumptions on the migration rates which are not needed for the EE to exist.

Result for the Two Node System

- Assume $\Lambda \mathbf{1} = \mathbf{0}$ and $\beta > 2\gamma$. Then, the unique EE of the ODE is

$$(u_1^*, u_2^*, v_1^*, v_2^*) = \left(\zeta_1(1 - \frac{2\gamma}{\beta}), \zeta_2(1 - \frac{2\gamma}{\beta}), \frac{\gamma}{\beta}, \frac{\gamma}{\beta} \right),$$

  where $\zeta_1 = \eta_{21}/(\eta_{21} + \eta_{12})$, $\zeta_2 = \eta_{12}/(\eta_{21} + \eta_{12})$

- This EE is locally asymptotically stable.

- This analysis did not use the assumption $H\mathbf{1} = \mathbf{0}$ or the condition concerning the relationship between eigenvalues of Λ and H.

- A different method of proof may be required to relax these two assumptions in the J node case.

EE of the ODE when $\Lambda \mathbf{1} \neq \mathbf{0}$

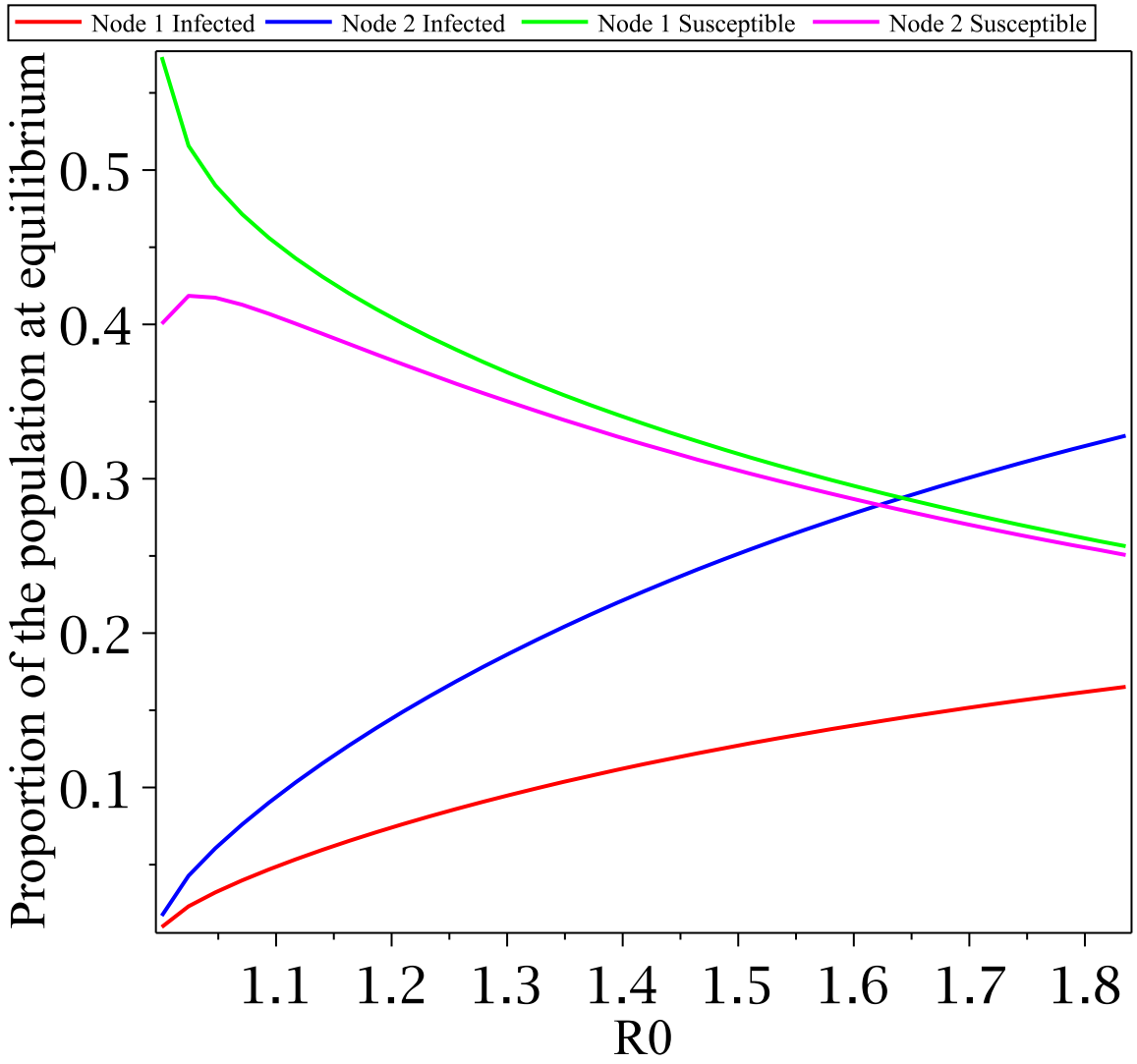

Figure: $J = 2$, $\lambda_{12} = 0.01$, $\lambda_{21} = 0.02$, $\eta_{12} = 2$, $\eta_{21} = 1$, $\gamma = 1$, $\beta \in [1, 4]$

EE of the ODE when $\Lambda \mathbf{1} \neq \mathbf{0}$

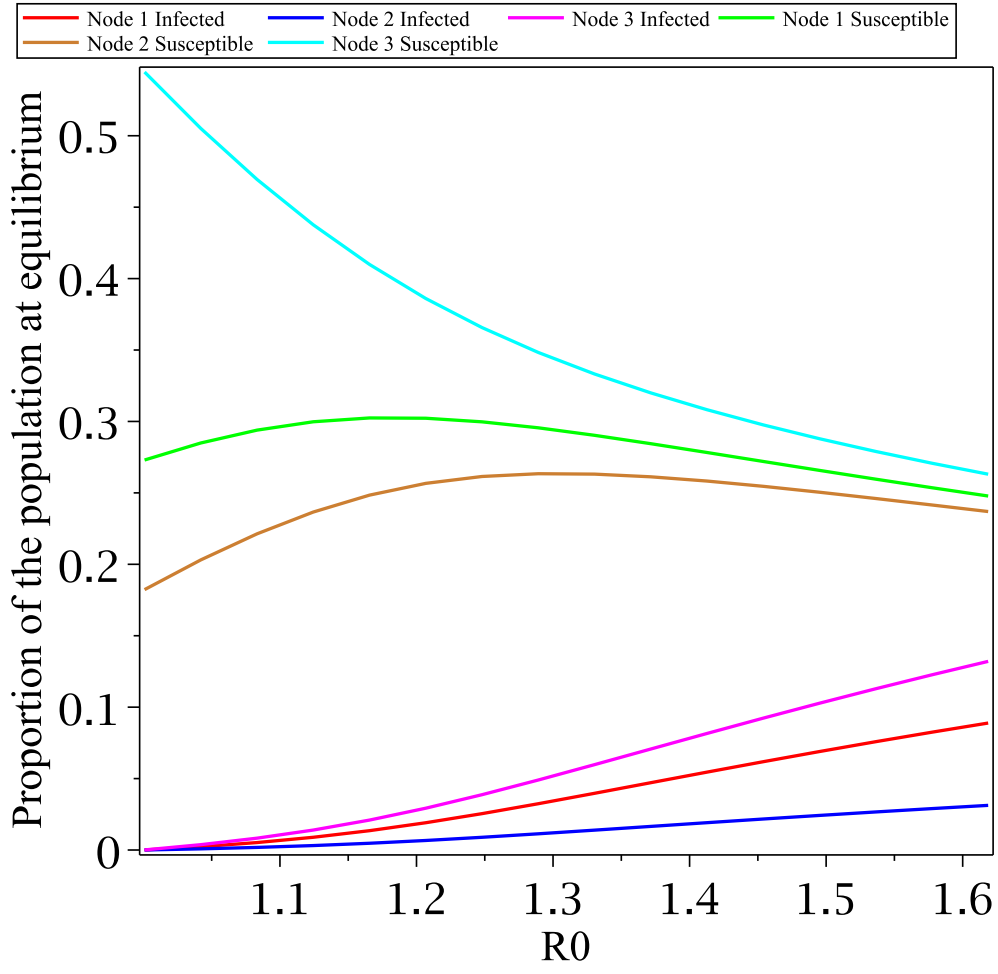

Figure: $J = 3$, $\lambda_{12} = 0.02$, $\lambda_{21} = 0$, $\lambda_{23} = 0.03$, $\lambda_{32} = 0$, $\lambda_{13} = 0$, $\lambda_{31} = 0.01$, $\eta_{12} = 1$, $\eta_{21} = 3$, $\eta_{23} = 4$, $\eta_{32} = 1$, $\eta_{13} = 3$, $\eta_{31} = 2$, $\gamma = 1$, $\beta \in [1, 4]$

Conclusions

- We have shown that, if $\Lambda \mathbf{1} = \mathbf{0}$, then
  - $R_0 = \beta/(J\gamma)$.
  - If $R_0 > 1$, the DFE is unstable and there exists a unique stable EE.
  - If $R_0 \leq 1$, no EE exists and the DFE is stable.
- We note that assumptions $\Lambda \mathbf{1} = \mathbf{0}$ and $H\mathbf{1} = \mathbf{0}$, used in determining the existence of the EE and its stability, are relatively strong and need to be relaxed to broaden the applicability of these results.
- Our analysis of the two node case and numerical results suggest that these assumptions could be dropped, but a different approach may be needed to obtain these results.

Conclusions

- One approach to controlling the spread of a disease is suggested by the stability result concerning the DFE.
- If a small number of infected individuals are introduced into a population with $R_0 < 1$, then the disease should die out quickly as the DFE is stable in that case.
- Since R_0 is given by the spectral radius of the matrix

$$\text{diag}(\beta \mathbf{v}^*) \left(\gamma I - H\right)^{-1},$$

it may be possible to reduce R_0 to less than one by altering the migration rates.

Thank you