Modeling, Control, and Network Dynamics in Epidemiology

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***Abstract*—Epidemic models serve an essential purpose in modeling the spread of a trait throughout a system or collection of systems. To control the spread of this trait, in this study to minimize the infections, the complex dynamics are analyzed via the equilibrium points and linearization. The results of this analysis are then used to construct control methods, in an effort to achieve a target state. This analysis is then extended to populations which interact, and the efficacy of extending the control to an arbitrary amount of regions is discussed.**

I. INTRODUCTION

The epidemic model is defined as such:

$$\frac{dx_1}{dt} = -\frac{V_1 x_1 x_2}{K_1 + x_{2i}} + \alpha x_2 + u_1(t) \tag{1}$$

$$\frac{dx_2}{dt} = \frac{V_1 x_1 x_2}{K_1 + x_2} - \frac{r x_2}{x_2 + K_2} - \alpha x_2 + u_2(t)$$

with parameters:

- $x_1(t)$ is the number of susceptible individuals
- $x_2(t)$ is the number of infected individuals
- V_1 is the infection rate
- K_1/K_2 is the saturation constant for infection/recovery
- r is the recovery rate
- α is the rate of loss of immunity
- $u_1(t)$ and $u_2(t)$ are inputs to the model

This equation will be expanded to the network model, where new terms and coefficients will be defined. This equation is the core of the case study.

It should be noted the infection rate term and the loss of immunity term are added and subtracted from both equations, such that in the zero input case, any amount of population which leaves x_1 will reenter in x_2 and vice versa, not considering the recovery term. The recovery term is the portion of the population which leave the model and, in the infection interpretation of the model, could be seen as people who get infected and become immune or die from the virus.

II. DYNAMICS ANALYSIS

A. Equilibrium Points

Letting $x \triangleq \begin{bmatrix} x_1 \\ x_2 \end{bmatrix}$, the uncontrolled model becomes:

$$\dot{x} = \begin{bmatrix} -\frac{V_1 x_1 x_2}{K_1 + x_2} + \alpha x_2 \\ \frac{V_1 x_1 x_2}{K_1 + x_2} - \frac{r x_2}{x_2 + K_2} - \alpha x_2 \end{bmatrix}$$

At the equilibria of the system $x_e \triangleq \begin{bmatrix} x_{1e} \\ x_{2e} \end{bmatrix}$ we have:

$$\dot{x_e} = \begin{bmatrix} -\frac{V_1 x_{1e} x_{2e}}{K_1 + x_{2e}} + \alpha x_{2e} \\ \frac{V_1 x_{1e} x_{2e}}{K_1 + x_{2e}} - \frac{r x_{2e}}{x_{2e} + K_2} - \alpha x_{2e} \end{bmatrix} = 0$$

Thus, the equilibria must satisfy the following system of equations:

$$-\frac{V_1 x_{1e} x_{2e}}{K_1 + x_{2e}} + \alpha x_{2e} = 0$$

$$\frac{V_1 x_{1e} x_{2e}}{K_1 + x_{2e}} - \frac{r x_{2e}}{x_{2e} + K_2} - \alpha x_{2e} = 0$$

Rearranging the first equation yields:

$$\frac{V_1 x_{1e} x_{2e}}{K_1 + x_{2e}} = \alpha x_{2e}$$

the right side of which can be substituted into the second equation which, when simplified, yields the following:

$$-\frac{r x_{2e}}{x_{2e} + K_2} = 0$$

This implies that $x_{2e} = 0$. This then implies that $x_e = \begin{bmatrix} x_{1e} \\ 0 \end{bmatrix}$ where x_{1e} may be arbitrarily chosen. Notably, this equilibrium point does not depend on any of the parameters. As for a real world interpretation, this equilibrium point may be understood as a disease-free equilibrium that the model may reach following eradication of the disease. At this point, no infectious persons remain in the model, and hence the non-infectious population cannot change according to our model.

Another equilibrium point may be discovered through manipulation of the differential equation relating to x_2 into a single fraction which, when simplified, becomes:

$$\frac{dx_{2e}}{dt} = \frac{x_{2e}[x_{2e}^2 + b x_{2e} + c]}{(K_1 + x_{2e})(x_{2e} + K_2)} = 0$$

where

$$b = (K_1 + K_2) + \frac{r - V_1 x_{1e}}{\alpha}$$

$$c = K_1 K_2 + \frac{r K_1 - V_1 K_2 x_{1e}}{\alpha}$$

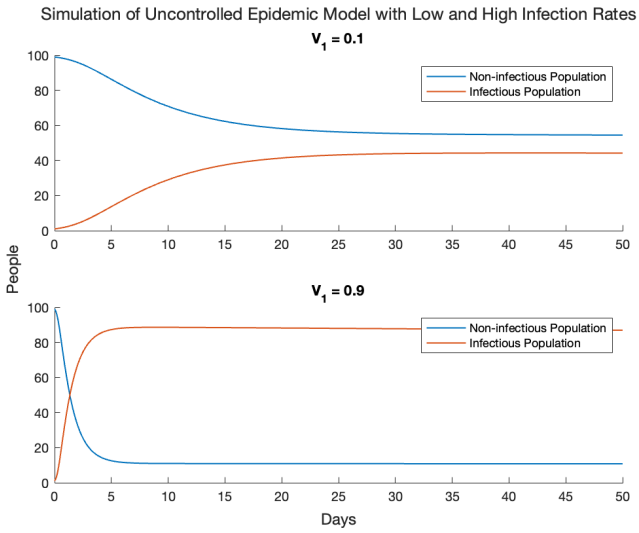

Fig. 1. Simulation of the uncontrolled system using different infection rates $V_1 = 0.1, 0.9$ with $K_1 = 10$, $r = 0.1$, $\alpha = 0.1$, and $K_2 = 100$. Note that the peak number of infected individuals increases with V_1.

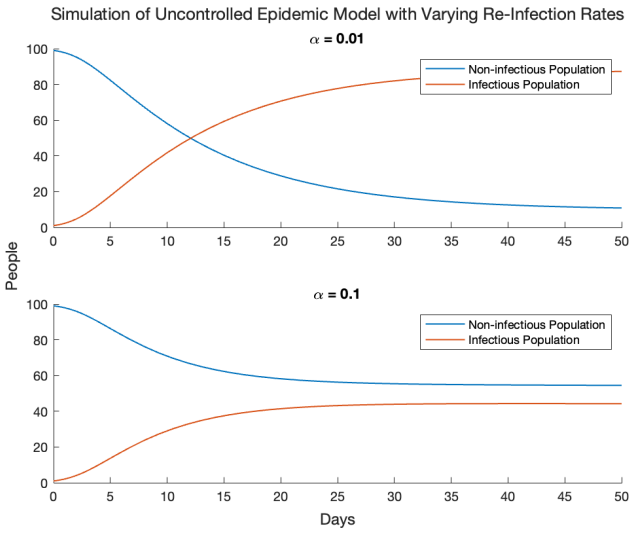

Fig. 2. Simulation of the uncontrolled system using different rates of reinfection $\alpha = 0.1, 0.9$ with $V_1 = 0.1$, $K_1 = 10$, $r = 0.1$, and $K_2 = 100$. The dynamics here are qualitatively similar to those depicted with varying V_1 but with the trend reversed i.e. a larger α or re-infection rate corresponds to a lower peak of infections.

This then yields two possibilities: $x_2 = 0$, as we have considered above, or $x_2^2 + bx_2 + c = 0$. In the second case, there exist two roots:

$$x_{2e} = \frac{-b \pm \sqrt{b^2 - 4c}}{2}$$

Given the extreme complexity of this equilibrium point, its further analysis was considered beyond the scope of this case study, and stability analysis and simulation was considered solely for the disease-free equilibrium point which exists independent of the parameter values chosen.

B. MATLAB Simulation for Varying Parameter Values

To substantiate these analytical results, MATLAB simulations were run of the nonlinear model using `ode45` with initial conditions $x_0 = \begin{bmatrix} 99 \\ 1 \end{bmatrix}$ close to the equilibrium point found in part A. We begin by manipulating the infection rate V_1 while keeping other parameters constant. Looking at the differential equations governing the model, mathematically, we expect the rate of change in both populations to have greater magnitude. Indeed, as V_1 increases, the infectious population grows more rapidly, experiencing an initial spike before the recovery term dominates and the infectious population tends toward the equilibrium point of zero (Fig. 1). We find also that there exists a threshold for V_1 at which the infectious population exceeds the non-infectious population, illustrating the case where all people in the model eventually become infected, occurring at α. This phenomenon is of course reflected within the model. The differential equation modeling the infected population can be rewritten as follows:

$$\frac{dx_2}{dt} = \frac{(V_1 - \alpha)x_1x_2}{K_1 + x_2} - \frac{\alpha K_1 x_2}{K_1 + x_2} - \frac{rx_2}{x_2 + K_2}$$

In the case that $V_1 = \alpha$, the rate of the change is negative, and we observe a leveling off of the infectious population. In the case that V_1 is significantly greater than α, the positive term dominates and the infectious population rapidly takes over. This is reflected also in the case that α is varied with all other parameters constant, as shown in Fig. 2. The other two parameters K_1 and r, when solely adjusted, did not have such drastic effects in dynamics as did V_1 and α. For K_1, the other parameters were set such that the infectious population dominates, and it can be seen that the rate at which the infectious population increases is slower. In Fig. 3 this can be understood as the intersection of the two populations occurring at a later point. Thus, we see that an increase in the saturation constant of infection leads to a slower stabilization of the respective populations to their non-zero, steady-state levels. The recovery rate r variable acts similarly but affecting behavior following this stabilization. Notably, in all cases, due to the recovery term in the dynamics, both infectious and non-infectious populations tend toward zero in the limit. And as r increases, the $\frac{dx_2}{dt}$ term becomes increasingly negative in the recovery phase, causing a steeper decrease to zero (Fig. 4). A greater r can thus be used to model a disease that persists only for a short time where the infectious population very quickly moves into the recovered stage.

C. Linearizing About the Disease-Free Equilibrium

In order to gain some more insight about the dynamics around the equilibrium point, we can linearize the model by letting f be defined as follows:

$$f(x) = \begin{bmatrix} -\frac{V_1 x_1 x_2}{K_1 + x_2} + \alpha x_2 \\ \frac{V_1 x_1 x_2}{K_1 + x_2} - \frac{r x_2}{x_2 + K_2} - \alpha x_2 \end{bmatrix}$$

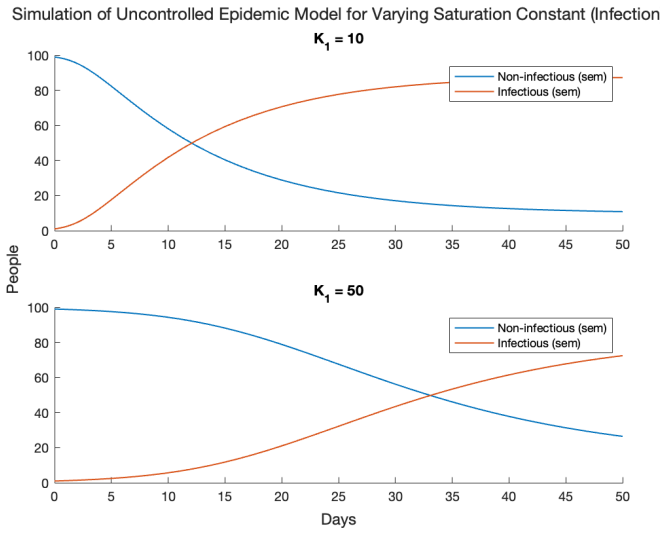

Fig. 3. Simulation of the uncontrolled system using different saturation constants for infection $K_1 = 10, 50$ with $V_1 = 0.1$, $r = 0.1$, $\alpha = 0.1$, and $K_2 = 100$. Although the peak number of infections is unaffected, the rate at which the population reaches this peak seems to increase as K_1 decreases.

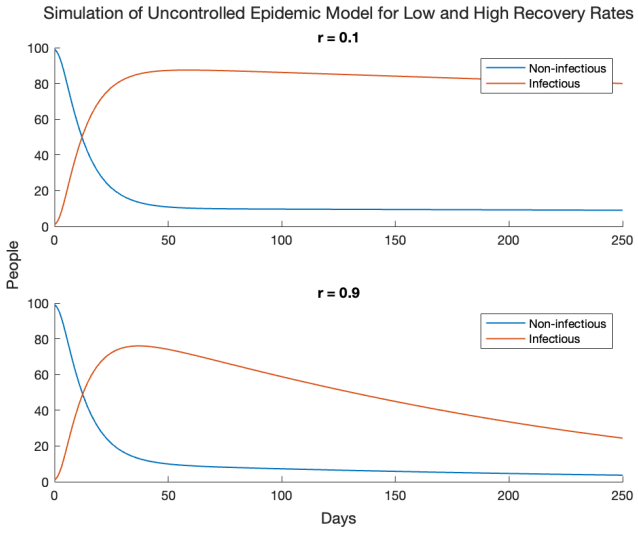

Fig. 4. Simulation of the uncontrolled system using different recovery rates $r = 0.1, 0.9$ with $V_1 = 0.1$, $K_1 = 10$, $\alpha = 0.1$, and $K_2 = 100$. As the recovery rate is increased, the infectious population, which dominates for the V_1 and α chosen, more quickly tends toward zero.

and taking the Jacobian:

$$J_f(x) = \begin{bmatrix} -\frac{V_1 x_2}{K_1 + x_2} & \alpha - \frac{K_1}{(K_1+x_2)^2} \\ \frac{V_1 x_2}{K_1 + x_2} & \frac{K_1}{(K_1+x_2)^2} - \frac{rK_2}{(x_2+K_2)^2} - \alpha \end{bmatrix}$$

Computing the Jacobian at the equilibrium point $x_e = \begin{bmatrix} x_{1e} \\ 0 \end{bmatrix}$ yields:

$$J_f(x_e) = \begin{bmatrix} 0 & \alpha - \frac{1}{K_1} \\ 0 & \frac{1}{K_1} - \frac{r}{K_2} - \alpha \end{bmatrix} \tag{2}$$

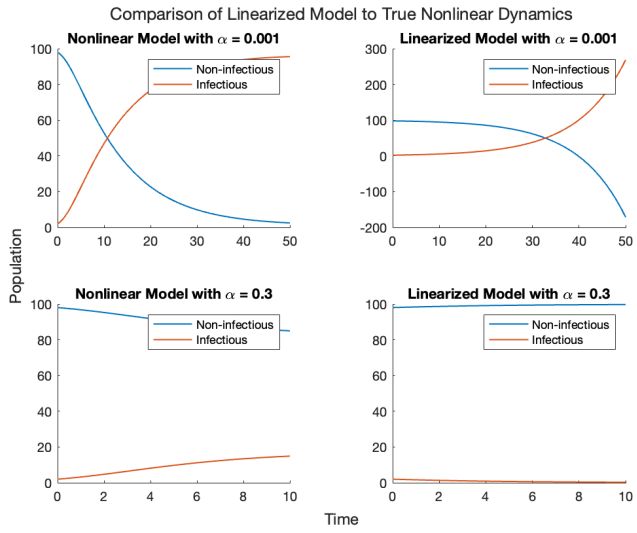

Fig. 5. Comparison of the simulated nonlinear dynamics to the linearized model about the disease-free equilibrium point. α's were selected such that the equilibrium point is unstable (upper right) and stable (lower right) for the linearization.

Thus, the linearized dynamics about x_e become:

$$\dot{x} = \begin{bmatrix} 0 & \alpha - \frac{1}{K_1} \\ 0 & \frac{1}{K_1} - \frac{r}{K_2} - \alpha \end{bmatrix} x$$

As the above matrix is upper-triangular, the eigenvalues can be identified easily as $\lambda_1 = 0$ and $\lambda_2 = \frac{1}{K_1} - \frac{r}{K_2} - \alpha$. Hence, for this linearized model, we find that the stability of the equilibrium point x_e depends on the sign of λ_2. In the case that $\frac{1}{K_1} < \frac{r}{K_2} + \alpha$, λ_2 is negative, and the equilibrium point is said to be stable. Conversely, this means that $\frac{1}{K_1} < \frac{r}{K_2} + \alpha$ implies an unstable equilibrium point. Note that the existence of a zero eigenvalue implies that there are infinite eigenvectors for this linearization along which the system will converge or diverge, depending on λ_2, to the corresponding equilibrium point along the x_2 axis in the phase portrait representation, equivalent to the states where the disease is eradicated i.e. the infectious population is zero. This behavior is reflected in numerical simulation as well (Fig. 5). The general trend is similar between the nonlinear model and the linearization with an $\alpha = 0.001 < \frac{1}{K_1} - \frac{r}{K_2}$ leading to a spike in the infectious population while $\alpha = 0.3 > \frac{1}{K_1} - \frac{r}{K_2}$ leads to a relatively quick eradication in both models.

III. CONTROL DESIGN AND INTERVENTIONS

A. Control Interpretations

Being that $u_1(t)$ and $u_2(t)$ are independent of one another, the control inputs can be interpreted different ways.

In some methods, perhaps with the control being medicine, some proportion of x_2 is subtracted and added back to the pool of susceptible people x_1. The control would then act functionally like the α term.

Another interpretation would be purely preventative, like a vaccine, subtracting directly from x_1 so there are less people to infect instead of curing already infected people.

Finally, to explore a method like isolation, the control could be the negative of the linearization at the current state for x_2, so the control could attempt to predict the spread of the epidemic, isolating most of the people infected. This would better simulate a real world scenario with some noise, instead of just the negative of the autonomous component of the model.

As the inputs cannot directly interact with x, using a function of x for the input approximates, but does not fully capture the effect of certain methods of intervention. For example, assuming some differentiable closed form $\Delta x(t)$ exists for the autonomous response, for the vaccine method:

$$x(t) = \Delta x(t) + \begin{pmatrix} -10 \\ 0 \end{pmatrix} t$$

Where $x(t)$ is the susceptible and infected populations, ten people are vaccinated every day, and t is in days. Then, to find the vector field:

$$\frac{dx}{dt} = \frac{d\Delta x}{dt} + \begin{pmatrix} -10 \\ 0 \end{pmatrix}$$

Then based on this analysis, an input $u_1 = -10$ and $u_2 = 0$ should be applied to simulate this. However, this approach does not take into account different population sizes, and cannot predict real world scenarios (shortages, larger amounts of vaccines given in the beginning of the epidemic, etc.). These could be circumvented with different choices of inputs, but in general, because the dynamics are non-linear, its controllability cannot be determined, so the efficacy of the inputs cannot be determined without simulation.

B. Controllability of Linearized Models

Equation 2 is the drift of the linearized system. There are two independent inputs $u_1(t)$ and $u_2(t)$, so the input matrix $\mathrm{B} \in \mathbb{R}^{2\times 2}$ is defined as the identity matrix. So the linearized system is written as:

$$\Delta \dot{x} = A\Delta x + Bu = J_f(x)\Delta x + I \begin{pmatrix} u_1(t) \\ u_2(t) \end{pmatrix} \tag{3}$$

With controllability matrix W_c as follows,

$$x \in \mathbb{R}^2 \rightarrow W_c = \begin{bmatrix} B & AB \end{bmatrix} = \begin{bmatrix} I & J_f(x_{eq})I \end{bmatrix}$$

By inspection, W_c has as many linearly independent rows as Δx has elements, or the linearized system is controllable $\forall x \in \mathbb{R}^2$. This is equivalent to claiming the linearized system is controllable independent of the point it is linearized around. This is true as the rows of the B matrix will be linearly independent for any values in the Jacobian.

C. Control Design

The linearized dynamics around any x show the non-linearized system, sufficiently close to the linearized point, is close to if not controllable. The control methodology, then, will be as follows, assuming the linearization analysis will translate well to the non-linear dynamics:

1) The goal is twofold:
   a) force the steady state values for x to zero for infected people (x_2) and some nonzero steady state values for x_1.
   b) make the transient response of the nonlinear system settle more quickly.
2) To these ends, analyze the linearized system around the initial conditions, making the assumption behavior around the initial conditions are close to the linear approximation.
3) Use the input:

$$u = \begin{pmatrix} u_1(t) \\ u_2(t) \end{pmatrix} = -Kx + u^*,\ K \in \mathbb{R}^{2\times 2} \tag{4}$$

   a) The $-Kx$ term reduces the time constant to eliminate the transient response as quickly as possible. K is a diagonal matrix, to simplify calculations.
   b) Let u^* be constant. It is used to inflate the steady state response, such that the transient response dying out only removes all people from the infected populations.

For u^*, since a steady state of 0 is chosen to be desired for the infected population, the model will let $u^* = \begin{pmatrix} 0 \\ \beta \end{pmatrix}$, where β is chosen such that the steady state is farthest from zero without being unreasonable given the real world interpretation of the input (e.g. introducing 1000 people into the susceptible population as the input to have a steady state of 100 is not in the spirit of controlling an epidemic).

The results of controlling the linearized dynamics as well as the results without any control are given in Fig 6. The non-linear counterpart, the result of this control, is shown in Fig. 7.

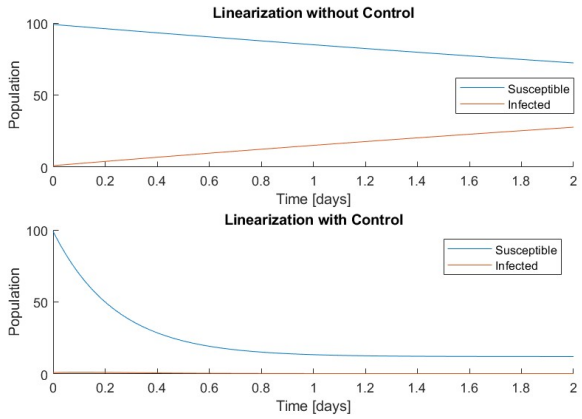

Fig. 6. The linearized dynamics with and without control. The time constant of the system without control is ~ 45, while the time constant with control is ~ 0.6. This is reflected in how quickly both graphs approach their steady state.

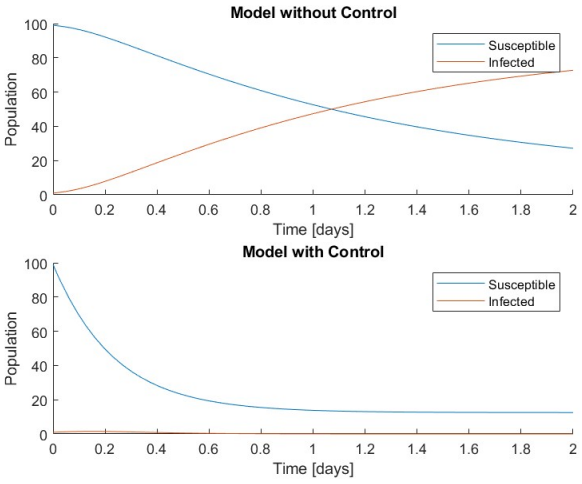

Fig. 7. The non-linear dynamics, with and without control. Without control, the epidemic explodes, and the people infected increases with time. With it, the model's transient response dies out within a day, and the susceptible people's steady state response is zero.

The method described above involves forcibly reducing $\frac{dx_1}{dt}$ by mathematically convenient values, determined by β, and changing the autonomous behavior by some factor of BK. In this case, it would be more like government intervention, removing people for isolation and reintroducing people into the susceptible population.

The magnitude of eigenvalues is the reason the steady state is relatively small for the controlled case. The steady state response, in the linearized case with a step input u^* is a function of two parameters, the eigenvalues and the gain applied to the step input.

Deciding to give the model smaller eigenvalues in exchange for a larger steady state value is feasible, and should be considered from case to case.

IV. GENERALIZATION TO NETWORK SETTING

In a network, the system for each region i for N regions is:

$$\frac{dx_{1i}}{dt} = -\frac{V_1 x_{1i} x_{2i}}{K_1 + x_{2i}} + \alpha x_{2i} + u_{1i}(t) - \sum_{j=1}^{N} c_{ij}(x_{1i} - x_{1j})$$

$$\frac{dx_{2i}}{dt} = \frac{V_1 x_{1i} x_{2i}}{K_1 + x_{2i}} - \frac{r x_{2i}}{x_{2i} + K_2} - \alpha x_{2i} + u_{2i}(t) - \sum_{j=1}^{N} d_{ij}(x_{2i} - x_{2j})$$

This model uses coefficients c_{ij} and d_{ij}, where the difference in populations is multiplied by this term. d_{ij} and c_{ij} could describe the proximity of one region to another, such that the more regions in close proximity to some region there are, the more infected people will spread to that region.

Alternatively, if the assumption is made $c_{ij} = c_{ji}$ and $d_{ij} = d_{ji}$, then the transfer of populations work out, so the population lost by region i is gained by region j. For each term in the summation, that term's contribution to the overall vector field will be positive if population j is larger than population i. This means the terms $c_i j$ and d_{ij} could model the spread of epidemic from larger cities to smaller cities. Large population density tends to result in higher rates of infection, so this could model the trickle down effect as the disease spreads from region to region.

A. Network Model Simulation

To model the network, two assumptions will be made about c_{ij} and d_{ij}, where the ith row and jth element in C and D will correspond to c_{ij} and d_{ij}.

- For all $i = j$, $c_{ij} = d_{ij} = 0$
- For any i, j, $c_{ij} = c_{ji}$ and $d_{ij} = d_{ji}$

With these two assumptions, C and D can contain every value of c_{ij} and d_{ij} as upper triangular matricies, with zeros on the diagonal.

The simulation was evaluated for random values of c_{ij} and d_{ij}, for several iterations. The results are contained in Fig. 8 and show the zero input response of the system.

B. Controlled Network Simulation

The control methodology generalizes fairly well to the network model, and changes in two key ways. K is still diagonal, and for N regions, $K \in \mathbb{R}^{2N \times 2N}$. The second term in the control, u^*, is just N of the control terms from Eq. 4 concatenated. Using this method, the results are shown in Fig. 9. The settling time is quick, the transient response lasting less than two days before the steady state dominates.

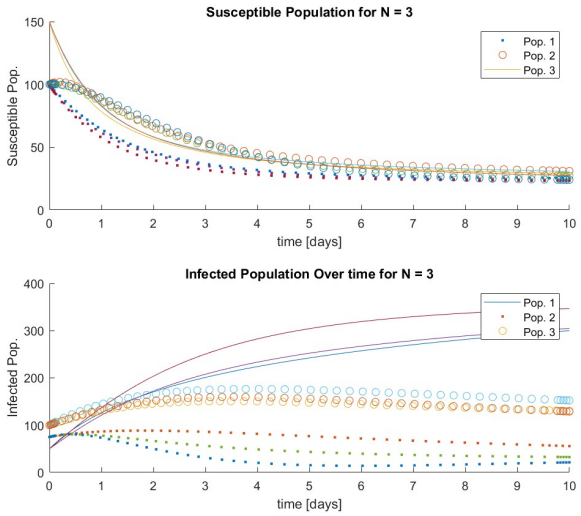

Fig. 8. The autonomous behavior of the network model. The model has three regions, and each of their behaviors for varying C and D matricies are plotted, grouped by their region. The settling time takes few days, and not all states settle by 10 days.

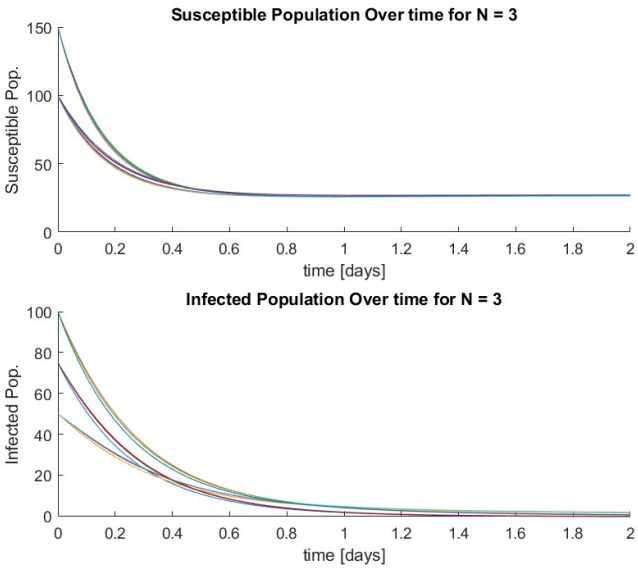

Fig. 9. The network model, with the extended control methodology applied. The graphs are not sorted by region to reduce clutter, as settling time is quick. This brute force method could be applied in regions with virulent, rampant infection to quickly isolate and replace infected persons while they are treated.

V. Conclusion

An analysis of the dynamics revealed both parameter dependent and state dependent equilibria. The state dependent equilibria related to the real world interpetation, and had varying stability dependent on the choice of parameters. The linearization elucidated the behavior of the non-linear system, and allowed for analysis of the system at any point.

Showing the linearized system was controllable meant adopting a methodology as a result of that foothold. By designing control adapted to the linearized model and forcing the transient response to approach zero as quickly as possible, opportunity for the non-linear dynamics to vary far from the linearization is reduced.

Interpreting the characteristics of the model as well as the control allowed for interpretation of the control strategy in terms of the real world. This meant understanding an aggressive strategy such as the control method applied would be reserved for dangerous diseases, ones which would need constant intervention.

In the network setting, the autonomous response of the system is analyzed for differing behaviors. By not varying any parameters but c_{ij} and d_{ij}, the systems can be shown to have different trajectories.

Allowing for negative values in C and D could show the effects of many populations of smaller regions moving to larger regions. For example, that could model how disease spreads from country to country, with portions of the population from different, smaller countries moving or visiting larger countries, and seeing the infection spread from smaller populations to larger populations as people move into bigger cities.

Finally, the control methods were generalized to the network model, in which its efficacy was shown to be largely unperturbed.

Future work could involve linearizing the network model to form better control methods and letting the $-Kx$ term in the input form an optimization problem with the drift of the linearized model to minimize the eigenvalues.