MATHEMATICALLY MODELING THE SPREAD

OF METHAMPHETAMINE USE

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ABSTRACT

The use of methamphetamine is rising faster than most other hard drugs such as cocaine and heroine. To date, mathematical models have not been used to explore the dynamics of methamphetamine use in a population. We propose five mathematical models that can predict and evaluate methamphetamine use: a compartmental model for rural areas, a compartmental model for urban areas, an optimal control model for rural areas, an optimal control model for urban areas, and a metapopulation model. Both the optimal control and metapopulation models are built by extending the proposed compartmental structures. We separate models for urban and rural regions due to differing community characteristics that effect the manner in which methamphetamine is brought into and distributed throughout populations.

Similar to models for the spread of infectious diseases, the interaction between susceptible, using, dealing, and recovered individuals in our illicit drug using population acts as a mechanism for the spread of methamphetamine use in each of our models. Thus, we use many techniques from infectious disease modeling literature in the analysis of our models. We also consider several applications of our models to data on methamphetamine use from Hawaii and Missouri. Our models give several important insights to previously observed yet unexplained characteristics regarding the dynamics of methamphetamine spread and the distribution of its use throughout the United States.

LIST OF ABBREVIATIONS AND SYMBOLS

S percent of drug-using population in susceptible class

D size of dealing class in terms of percent of drug-using population

U percent of drug-using population in user class

R percent of drug-using population in recovered class

x average number of users to which each dealer deals

β rate of population movement from susceptible to user class

α rate of population movement from user to recovered class

γ rate of population movement from recovered to user class

u_1 cost of treatment programs

u_2 increase in cost of law enforcement

T optimal time over which to spend control budgets

χ_R indicator function for rural node

χ_D indicator function for urban node

ζ_{ij} rate of travel from node i to node j

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CHAPTER 1

Introduction

Methamphetamine abuse is rising at an alarming rate throughout the United States of America, surpassing the abuse growth rates of other illicit drugs such as heroin and cocaine [1] [2] [3]. Methamphetamine use is appealing due to the pleasurable rush, increase of awareness, and energy given by the drug. However, these effects cause violent behavior, brain damage, and harmful prenatal effects that make the prevalence of this illicit drug in our society an immediate issue that requires further review [4].

While many statistical studies have been performed to analyze trends in methamphetamine use [5] [6], mathematical models were not available to model the behavior of the spread of use previous to this work. Mathematical models are important because the basic statistical studies provide inaccurate and oversimplified forecasts. This previous work primarily focused on discovering correlations between methamphetamine use and other behaviors such as other illegal drug use and risky sexual activity [7]. It also looked to track past trends as well as investigate correlation or causation with various health issues [8].

In addition to their forecasting ability, mathematical models give us the ability to investigate the dynamics of the spread of methamphetamine. We can quantitatively determine the equilibrium amount of use in populations given different sets of initial

conditions and observe factors or control measures that can change that equilibrium. We can also determine the time period over which these changes in the equilibria will last. These abilities of mathematical models studying the spread of methamphetamine use, in particular, the ones we propose here, allow policy makers to predict and determine effective measures to prevent "outbreaks" of methamphetamine use in communities that would be damaging to society.

We begin by noting that the models we propose only serve to model the spread of methamphetamine use within the United States. The societal characteristics governing the interactions that drive the dynamics of our models are specific to the United States because they are based off of and driven by the laws and community structure of the country. Similar models may be used to study the spread of methamphetamine in other parts of the world, but the patterns of acquisition and use need to be examined to determine whether or not the same characteristics of spread apply.

To model methamphetamine use, we adopt techniques commonly used in infectious disease modeling due to the manner in which interactions between groups of people in a population act as a mechanism for the spread of methamphetamine use. We can compartmentalize a population into groups and use the interaction of these groups to calculate the spread of usage. Analogous compartmental models have been used for infectious disease modeling since the Kermack-McKendrick model in 1927 [9]. For infectious diseases, the interaction between infected members of society with members of society that have yet to contract the disease causes the disease to

spread. We treat current users of methamphetamine use as "infected" and observe that a very similar structure for spread applies.

With this similar mathematical structure, we can also borrow analysis techniques from infectious disease modeling to observe meaningful properties of our models for methamphetamine use. We relate "disease-free" and "endemic" equilibria concepts to the cases in our models when methamphetamine use dies out and when it reaches the maximum sustainable level respectively. Furthermore, we can determine the initial rate of spread when a single user is placed into a population of individuals who have never before used methamphetamine by using computation techniques for the basic reproductive number, R_0. The basic reproductive number yields the same qualitative information for infectious disease models when we relate users to infected individuals. We compute R_0 and our equilibria using the methodology originally proposed in [**10**].

Compartmental models have been significantly expanded since their initial introduction in 1927. Some reviews of the current possibilities of compartmental models by researchers who contributed significantly to the development of these mathematical possibilities include [**11**] and [**12**]. However, while compartmental models can be extended by introducing more complexity to the original system in order to more fully describe the single population spread as done in this previous literature, they can also be used in different, more complicated models to find further information than just single population spread. For example, optimal control models have been developed off of previous compartmental structures to determine effective control measures for disease outbreaks and disease spread within the body. In [**13**], Kirschner, et al. use

an optimal control model to find the optimal chemotherapy treatment for HIV, and, in [14], Tuite, et al. determined optimal control strategies to limit the outbreak of cholera in Haiti.

In addition, spatial considerations are taken into account in metapopulation and network models that frequently use compartmental models to determine disease spread at each patch or node of the larger model. These models take into account that a larger population may have smaller population groupings. In compartmental models for infectious diseases, every person is assumed to have equal probability of interacting with an infected person. However, we consider the case in which there are two large cities separated by a very large rural area. If a disease begins in one city, a person in the other city does not have a very high chance of coming in contact with the infected person. Thus, treating both cities and the rural area in between as one population would not be appropriate because it would create a larger than accurate susceptible class and disease spread would appear to be uniform within the larger population. Metapopulation and network models allow the populations to be considered as separate but connected. Frequently, the connection will be mathematically represented by some rate or probability function representing the chance an individual from one population will travel to the other population and contract the disease. Some examples of metapopulation and network models in infectious disease literature include the work by Fulford, et al. on tuberculosis in [15] and the work by Rohani, et al. on measles in [16].

We choose to extend our compartment models with an optimal control structure and by including them in a metapopulation model. The optimal control model allows us to analyze the effect of government measures in controlling the spread of methamphetamine use. The metapopulation model allows us to observe and analyze the dynamics of the spread of methamphetamine use as use moves between different population groupings.

We note that we are not the first to apply infectious disease modeling to model the spread of illicit drug use, though we are the first to model the spread of methamphetamine use. White, et al. developed a compartmental model to analyze the dynamics of the spread of heroin use and observe the effects of treatment programs in [17]. A compartmental model was also developed to study the spread of cocaine use in [18] by Burattini, et al. We further note that previous authors in this literature of illicit drug use modeling, including the given examples, also borrowed the analysis techniques we described for infectious disease modeling to determine equilibria and initial speed of spread.

Thus, far we have described our use of compartmental, optimal control, and metapopulation models throughout this work. We note that for each population we choose to model, we classify the region as either urban or rural. For each classification, we have a separate compartmental and optimal control model. Each partition of the metapopulation model is classified as urban or rural, allowing mathematical modeling of the interaction between these two population groupings. This model separation is necessary due to the differing methods of obtaining methamphetamine in urban and

rural regions of the United States. The dynamics in each region will be discussed more thoroughly in Chapter 2. We distinguish urban regions as geographical areas with a population density of 1000 people or more per square mile. Consequently, rural populations have a population density of 999 people or less per square mile [19].

We proceed as follows. We begin by presenting and analyzing our rural and urban compartmental models in Chapter 2. Our analysis includes analytical computation of the equilibria, basic reproductive number, and nullclines. We then fit data for Hawaii methamphetamine use to our rural model. We move onto our presentation of our optimal control model and solve analytically for the implying optimal controls in Chapter 3. We fit our rural optimal control model to data for Missouri methamphetamine users and draw conclusions regarding their budget decisions. For the purpose of comparison, we take initial conditions from the Missouri data and perform a simulation with our rural compartmental model to predict the outbreak of methaphetamine over the same time period without the inclusion of control measures to observe the true impact our controls. The last model we present is our metapopulation model in Chapter 4 for which each partition is modeled with our urban or rural compartmental model, depending on its classification. For the application of our model, we partition Missouri into nine groupings of counties, each of which we classify as urban or rural, and collect county data for 2004 to find aggregate data for each partition. We simulate our metapopulation model using this data organized in the described structure. We make a comparison of our metapopulation model to our

simulated compartmental model from statewide aggregated data as well as our optimal control model in the previous chapter. In Chapter 5, we discuss the implications of our analysis for all of the models.

CHAPTER 2

Compartmental Models

We begin by describing the compartmental structure of our models. We consider a population of people living in some geographical region. We can separate this population into three different groups of people: susceptibles, users, and recovered. Susceptibles are people that have never used methamphetamine. Users are people who have used methamphetamine within the past three months. Recovered individuals include any person who has ever used methamphetamine in their lifetime. When separating a population of people in this manner, we will obviously have a very large group of susceptible people in comparison to the using and recovered classes. This size difference will create a significant computational issue when numerically analyzing any kind of mathematical model, so we consider meaningful ways to restrict the size of the susceptible class. Clearly, there are large numbers of people in most populations that would never consider trying methamphetamine. Since methamphetamine is a hard drug with strong and lasting health consequences, it is normally not the first illegal drug attempted by users. Normally, "gateway" drugs such as marijuana and abused use of prescription drugs are attempted before use of methamphetamine [20]. Thus, we only consider individuals "susceptible" to methamphetamine use if they are already a part of the illegal drug community either through using or dealing. Our

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model entirely removes individuals outside the illicit drug using community from its analysis.

We make several further critical assumptions for the compartmental models to describe methamphetamine use in rural and urban populations. We first assume the need for separate models for urban and rural areas because the distribution methods and dynamics of spread differ significantly in rural and urban areas. Secondly, when a susceptible individual initially tries methamphetamine and moves into the user class, their brain chemistry is permanently altered [4] [3]. Thus, they will never again be susceptible in the same way as an individual who has never before used the drug, and we assume that they will permanently remain in a "recovered" state that essentially acts a class of people not currently using methamphetamine but at a high risk to begin. This risk to begin is much higher than the chance that a user of another drug would begin using methamphetamine. In our model, this assumption implies that once methamphetamine has been used, the individual user will only be able to move between the using and recovered classes.

Furthermore, since we work solely with the illicit drug-using community, we make an assumption for each of our data sets regarding the size of the illicit drug community. The National Institute on Drug Abuse (NIDA) reports that around 8.7% of the population is part of this community [2]. We assume this figure is actually 10% of the population because NIDA data does not account for unreported cases. Thus, we take this percentage of the total population of a region for which we are analyzing data to study dynamics in our model. When we consider applications of our models

to data, we note that we normalize our data based on this drug using population size. As our fourth and last assumption, we disregard births and deaths over each analyzed time period. We made this decision due to initial exploratory analysis of our data that indicated outbreaks of methamphetamine use occur within the span of a generation. Therefore, the inclusion of demography is not necessary to gain an accurate picture and will most likely distort our results by creating more complexity in our model than our data can accurately describe. We note that since we normalize our data, this construction implies that $S + U + R = 1$ where S denotes susceptibles, U denotes users, and R denotes recovered individuals.

2.1. Rural Model

We begin by presenting our compartmental model for rural regions. In rural areas, law enforcement is relatively minimal, and population density is low. In addition, large areas of land between residences allow a great degree of privacy to individual properties. These characteristics create the distinguishing motives for the type of acquisition of methamphetamine popular in rural areas.

First, dealers do not have a financial incentive to deal methamphetamine in rural areas due to the low population density. Most individuals in rural areas would be restricted by time and finances to manage traveling to an urban area to obtain methamphetamine. However, a distinguishing trait of methamphetamine that has played a strong factor in its popularity is how easy it is to make. Though some states restrict the allowed quantity of purchase of over-the-counter drugs that are used in

methamphetamine production, all the ingredients are legal and readily available at most drug stores and supermarkets. The primary difficulty for many individuals desiring to make methamphetamine is the strong smell associated with its production. The smell causes neighbors and police to notice the activity and investigate. When police presence is minimal and neighbors do not live close enough to notice the smell, there is almost no barrier for an individual to create their own methamphetamine. As these community characteristics are very common in rural areas, production of methamphetamine frequently goes unnoticed which has led to a growth in popularity of home or local labs. These labs are operated by a user or group of users that produce methamphetamine for the primary purpose of personal drug use [21].

From this information regarding the production and acquisition of methamphetamine in rural areas, we make a hypothesis regarding the structure of population movement between different groups of people involved in illegal drug use. We note that our hypothesis is supported by numerous reports regarding individual cases. Since users in rural areas tend to produce their own methamphetamine, we hypothesize that for susceptible individuals to begin using methamphetamine, they must interact with a user. This interaction is necessary because the user initiates an interest in trying the drug, allows them to attempt using the drug before deciding to produce, and gives them information on how to produce. Though the information and interest could be provided though other sources such as the internet, surveys from hospitals and treatment centers dealing with methamphetamine abuse cases support our claim that the vast majority of use is initiated through contact at some point

with another user. As previously mentioned, we also assume that after a susceptible person becomes a user, they will only move between the user and recovered classes as they move on and off of the drug due to their permanently altered brain chemistry. We present the diagram in Figure 2.1 to visually represent the pattern of movement between classes that we propose.
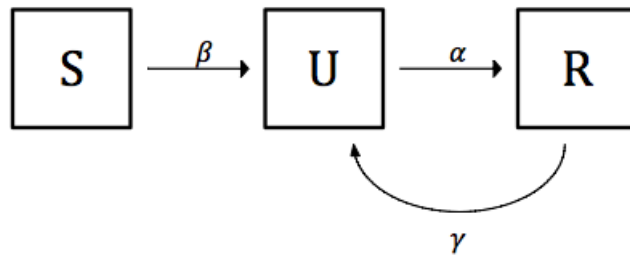
FIGURE 2.1. SUR Diagram

From the above diagram, we can create a system of differential equations to represent the rate of change of each group: susceptibles (S), users (U), and recovered individuals (R). We include the interaction terms SU and RU due to our assumption that use is initiated or reinitiated through contact with a current user and build the system,

$$\frac{dS}{dt} = -\beta SU$$

$$\frac{dU}{dt} = \beta SU - \alpha U + \gamma RU$$

$$\frac{dR}{dt} = \alpha U - \gamma RU.$$

Now that we have presented our rural compartmental model, we perform some analysis regarding its implied population dynamics. We begin by determining the basic reproductive number, R_0, to yield the initial rate of spread when one user is introduced into a completely susceptible population. We use the FV^{-1} methodology from [10] to compute R_0. In this method, we create a matrix, F, to represent the total rate at which secondary "infections", which we treat as methamphetamine usage, arise in all non-disease compartments. Since we are computing an initial "outbreak" case, our only compartment with individuals not "infected" is our susceptible class. The rate users arise from this class is β, so $F = \beta$. We also create a matrix, V, to represent the total rate at which users decrease from any factors. Since individuals only leave the user class to enter the recovered class at a rate α, $V = \alpha$. Thus, we compute

$$R_0 = FV^{-1} = \frac{\beta}{\alpha}.$$

We note that our matrices will always be one dimensional when there is only one user class.

We move onto the analysis of equilibria. We begin by solving for the model equilibria simply by setting each differential equation equal to zero. We immediately see that any equilibria requires either the number of users or the number of susceptibles to be equal to zero. We refer to the equilibria where $U = 0$ as our "disease-free" equilibria, and we begin our equilibria analysis with this case. If $U = 0$, movement between the susceptible and recovered classes is impossible. Thus, denoting S_0 as our

initial number of susceptibles and recalling that $S + U + R = 1$, we find our disease free equilibrium to be

$$(S, U, R) = (S_0, 0, 1 - S_0).$$

We observe that this equilibrium is a collection of points, not a single point, for all possible values of S_0. Our next concern is determining the stability of this equilibrium. To determine the stability, we need to find the sign of our eignevalues of the Jacobian associated with our rural system of equations evaluated at this equilibrium. We set up the matrix

$$J - \lambda I = \begin{pmatrix} -\lambda & -\beta S_0 & 0 \\ 0 & \beta S_0 - \alpha + \gamma(1 - S_0) - \lambda & 0 \\ 0 & \alpha - \gamma(1 - S_0) & -\lambda \end{pmatrix},$$

and find the eigenvalues

$$\lambda = 0, 0, -\alpha + \gamma(1 - S_0) + \beta S_0.$$

Our equilibrium is stable when all of the eigenvalues are non-positive and at least one is strictly negative. Thus, our disease-free equilibrium is stable when

$$R_0 = \frac{\beta}{\alpha} < \frac{\gamma}{\alpha} < 1.$$

If some but not all of these conditions are not met, then the stability of the disease-free equilibrium is dependent on the magnitude of the difference between the relative sizes of α, β, γ, and, consequently, R_0. By some of the conditions, we mean a case such as $\alpha < \gamma$ but $R_0 < 1$. If all of these conditions are not met, then the disease-free equilibrium is unstable. This mathematical analysis qualitatively matches our problem. When $\alpha > \gamma$, less people are moving into the user class from the recovered class than moving to the recovered class from the user class. When $R_0 < 1$, each user is creating less than one more new user. Thus, the number of users will always revert to zero. In contrast, if each user creates more than one new user ($R_0 > 1$) or people are leaving the recovered class at a higher rate than they enter ($\gamma > \alpha$), then the user class could grow depending on the relative size of these rates. Clearly, if each user creates more than one new user and people leave the recovered class at a higher rate than they enter, then the user class will continue to grow.

We recall that we only considered the case for which $U = 0$ in our solution for our equilibria. We determined that another equilibrium could occur where $S = 0$. We refer to this equilibrium as the "endemic" equilibrium, by which we mean the state at which the system attains the largest sustainable number of users. Again recalling that $S + U + R = 1$, we find our endemic equilibrium to be

$$(S, U, R) = (0, 1 - \frac{\alpha}{\gamma}, \frac{\alpha}{\gamma})$$

We proceed again with stability analysis, and find the sign of our eigenvalues of the Jacobian associated with our rural system of equations evaluated at the endemic equilibrium. We set up the matrix

$$
J - \lambda I =
\begin{pmatrix}
-\beta(1 - \frac{\alpha}{\gamma}) - \lambda & 0 & 0 \\
\beta(1 - \frac{\alpha}{\gamma}) & -\lambda & \gamma - \alpha \\
0 & 0 & \alpha - \gamma - \lambda
\end{pmatrix},
$$

and find the eigenvalues

$$
\lambda = 0, \alpha - \gamma, \beta \left(\frac{\alpha}{\gamma} - 1 \right).
$$

To determine the sign of our eigenvalues, we need to compare $\frac{\alpha}{\gamma}$ to 1. However, we recall that the number of users in our endemic equilibrium is given by $1 - \frac{\alpha}{\gamma}$. Clearly, our analysis is not meaningful if we allow numbers of people to take on negative values. Thus, $\frac{\alpha}{\gamma} < 1$ which implies that our two non-zero eigenvalues are always negative. Therefore, our endemic equilibrium is always stable.

We can observe the discussed equilibria stability switching points in the nullcline plot in Figure 2.2. We reduce our system into that of two variables for clarity purposes by making the substitution $R = 1 - S - U$ in our system. In our plot, we consider the case in which $\alpha < \gamma$ and $R_0 < 1$.
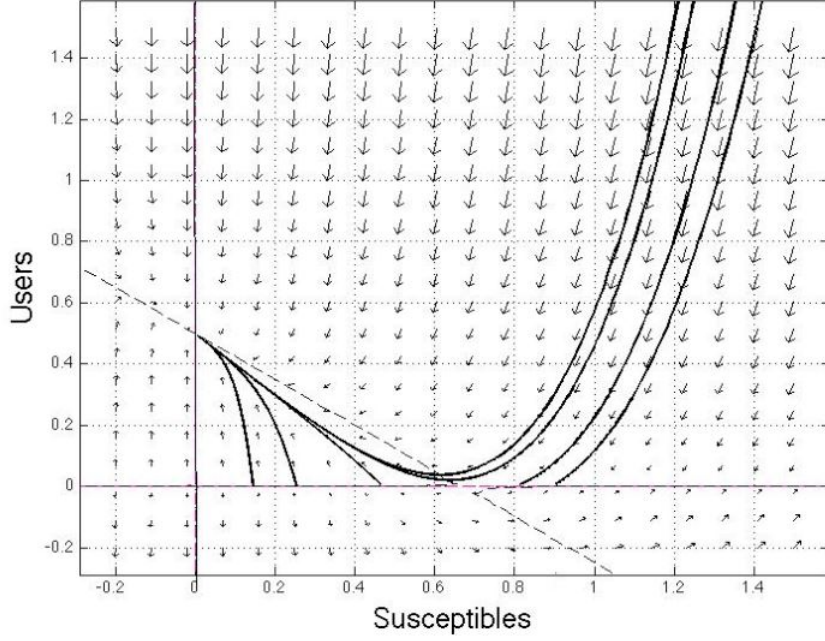
FIGURE 2.2. Rural Nullclines when $\alpha < \gamma$ and $R_0 < 1$

Our nullclines associated with $\frac{dS}{dt} = 0$ form the axes in Figure 2.2. The remaining two curves are given by the nullclines associated with $\frac{dU}{dt} = 0$. We find that the stability behavior of our system changes at the S-intercept,

$$(S, U) = \left(\frac{\alpha - \gamma}{\beta - \gamma}, 0 \right) = \left(\frac{1 - \frac{\gamma}{\alpha}}{R_0 - \frac{\gamma}{\alpha}}, 0 \right).$$

We can determine that, in this case for which $\alpha > \gamma$ and $R_0 < 1$, the stability of our equilibria is dependent on the size of the susceptible population. If we denote the S-axis intercept as S^*, on $[0, S^*]$ the disease-free equilibrium is unstable and on $(S^*, 1]$ the disease-free equilibrium is stable. When the disease-free equilibrium is unstable, the system reverts to the stable endemic equilibrium. When the disease-free equilibrium is stable, the system reverts to the disease-free equilibrium.

Similar analysis can explore the remainder of cases in which stability is determined by the relative sizes of parameters. However, this case study gives a sufficient picture of the typical dynamics of our model.

2.2. Urban Model

In this section, we present our compartmental model for urban regions. In contrast to rural areas, urban areas have a high population density, allowing little privacy for individual residences. Additionally, police presence is high. From these characteristics and supporting case observations, we find a structure for the spread of methamphetamine use in urban regions.

Due to the high population density, dealers have a much greater financial incentive to deal methamphetamine in urban areas. However, drug dealers could choose to deal a variety illicit drug from which they would profit. Thus, we question why would they choose to deal methamphetamine. We hypothesize that it is unlikely that a dealer would choose to start dealing methamphetamine unless there was already a population of methamphetamine users in the area, considering the prevalent drug use in urban areas. The next question that arises naturally becomes how an individual can acquire methamphetamine to use before a dealer enters the situation. Initially, it appears that they would choose to make methamphetamine themselves as was common in rural areas, but urban areas do not afford the privacy of rural regions. Users cannot make their own methamphetamine without immediately alerting both surrounding properties and the local police presence due to the strong and distinct smell. Thus,

we assume either that the initial group of users in an urban area is required to travel to a nearby population where they can acquire methamphetamine until a dealer enters or that the group of users moved from another population grouping where they did have access to methamphetamine [3].

We present the structure of our model dynamics in Figure 2.3. We note that we retain the assumption from our rural compartmental model that after a susceptible individual becomes a user, they will only move between the user and recovered classes as they move on and off of methamphetamine due to their permanently altered brain chemistry.
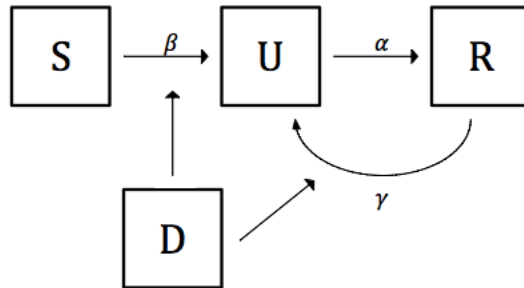
FIGURE 2.3. SDUR Diagram

Before explicitly writing down our system associated with the proposed structure in Figure 2.3, we make several more observation. Since we have established that users cannot make their own methamphetamine in urban areas and must buy it from dealers instead, the question arises of how dealers acquire methamphetamine. We recall that we are modeling regions in the United States. Methamphetamine dealt in urban areas is brought in by dealers from Mexico [22]. Mexican drug cartels dominate the methamphetamine trade in United States cities, and, due to dealers

entering a region to deal from a different population, we do not include them in our drug-using population. Since dealers are not a part of our total population, we cannot estimate their size and accurately model them without greatly increasing the span of our compartmental structure. Thus, in our urban system, we choose to make an estimate of the size of the dealer class by finding an approximate number of users to which each dealer deals [**23**]. We denote this value x. We further extend our previous assumption that a dealer will not enter into a population until a group of users is already present. We now also claim that an additional dealer will not enter the population until there is a market available for him. For example, if each dealer deals to five users on average, another dealer will not begin dealing in the population until the user class grows by an additional five users. We approximate this behavior by replacing our interaction terms with the dealers by a scaled user term, specifically $\frac{U}{x}$. We can now write our urban compartmental systems as

$$\frac{dS}{dt} = -\beta S \frac{U}{x}$$
$$\frac{dU}{dt} = \beta S \frac{U}{x} - \alpha U + \gamma R \frac{U}{x}$$
$$\frac{dR}{dt} = \alpha U - \gamma R \frac{U}{x}.$$

We note that from our assumption that dealers are not a part of the measured drug-using population, we again have $S + U + R = 1$.

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We now proceed with our analysis of our urban compartmental model which exhibits several key differences from our rural compartmental model due to our scaling term. However, we do note that much of the behavior is similar.

We begin by computing the basic reproductive number, R_0. We again apply the methodology in [**10**], and find $F = \beta$ and $V = \alpha$. Thus, we find the same basic reproductive number as in our rural compartmental model in our computation

$$R_0 = FV^{-1} = \frac{\beta}{\alpha}.$$

We now proceed with our analysis of equilibria. Setting each differential equation equal to zero again yields two possibilities: $S = 0$ or $U = 0$. We refer to the equilibrium in which $U = 0$ as our disease-free equilibrium and the equilibrium in which $S = 0$ as our endemic equilibrium as we did in our rural compartmental model. These equilibria each convey the same qualitative ideas as in the rural case.

Setting $U = 0$ yields the same disease-free equilibrium as in the rural case,

$$(S, U, R) = (S_0, 0, 1 - S_0),$$

where S_0 indicates the initial number of susceptible individuals and $1 - S_0$ arises from the relation $S + U + R = 1$. We again recall that this equilibrium is a collection of points, not a single point, for all possible values of S_0.

Despite the identical form of the disease-free equilibrium, the stability analysis differs from the rural case. We set up the matrix

$$J - \lambda I = \begin{pmatrix} -\lambda & -\beta\frac{S_0}{x} & 0 \\ & & \\ 0 & \beta\frac{S_0}{x} - \alpha + \gamma\frac{(1-S_0)}{x} - \lambda & 0 \\ & & \\ 0 & \alpha - \gamma\frac{(1-S_0)}{x} & -\lambda \end{pmatrix},$$

and find the eigenvalues

$$\lambda = 0, 0, \frac{\gamma + \beta S_0 - \gamma S_0 - \alpha x}{x}.$$

Again, when our non-zero eigenvalue is negative, our system is stable. We then determine that when

$$R_0 = \frac{\beta}{\alpha} < \frac{\gamma}{\alpha} < x, \tag{2.2.1}$$

our disease-free equilibrium is stable. This relationship highlights an interesting and highly significant aspect of our urban model. Instead of comparing our basic reproductive number and relative rates of recovery and relapse into methamphetamine use to one, we compare them to x, the average number of users to which each dealer deals. We clearly except this number to be greater than one. In fact, national averages predict that $x = 5$ [23]. Thus, we need a much larger value of R_0 and much higher rate of recovery compared to the rate of relapse in an urban population to

escape the disease-free equilibrium. In other words, our model implies that it is extremely difficult for a methamphetamine outbreak to occur from an initial state with no methamphetamine users in an urban region.

We note that our disease-free equilibrium is not stable when none of the previous conditions hold. When some but not all of the given conditions hold, the stability is determined by the magnitude of the difference between the relative sizes of α, β, γ, and, consequently, R_0.

We now return to our second equilibrium case: the endemic equilibrium. We determined that another equilibrium could occur where $S = 0$, and, thus far, we have only considered the case in which $U = 0$. Again recalling that $S + U + R = 1$, we find our endemic equilibrium to be

$$(S, U, R) = (0, 1 - \frac{\alpha x}{\gamma}, \frac{\alpha x}{\gamma}).$$

We analyze the stability of this equilibrium by finding the sign of the eigenvalues of the Jacobian associated with our urban system of equations evaluated at the endemic equilibrium. We set up the matrix

$$J - \lambda I = \begin{pmatrix} -\frac{\beta}{x} + \frac{\beta\alpha}{\gamma} - \lambda & 0 & 0 \\ & & \\ \frac{\beta}{x} + \frac{\beta\alpha}{\gamma} & -\lambda & \frac{\gamma}{x} - \alpha \\ & & \\ 0 & 0 & -\frac{\gamma}{x} + \alpha - \lambda \end{pmatrix},$$

and find the eigenvalues

$$\lambda = 0, \frac{\beta}{x}\left(\frac{\alpha x}{\gamma} - 1\right), \alpha - \frac{\gamma}{x}.$$

From the form of our endemic equilibrium, if $\frac{\alpha x}{\gamma} > 1$, the number of users in our system will be negative. Clearly, our analysis is not meaningful if we allow numbers of people to take on negative values. Therefore, we must have $\frac{\alpha x}{\gamma} < 1$ which implies that both of our two non-zero eigenvalues are always negative. Thus, our endemic equilibrium is always stable.

We now explore the stability switching points and dynamics between our two equilibria for a specific case in which relative differences between our parameters are pivotal in stability. Similar to the rural model, we consider the case in which $\alpha < \gamma$ and $R_0 < 1$. We recall that the stability behavior of our rural system switched at the S-intercept of the non-zero nullcline associated with $\frac{dU}{dt} = 0$. We find analogous behavior of our urban nullclines to that shown in Figure 2.2 for our rural system.

However, the S-intercept at which stability of the system switches now occurs at the point

$$(S, U) = \left(\frac{\alpha x - \gamma}{\beta - \gamma}, 0 \right) = \left(\frac{x - \frac{\gamma}{\alpha}}{R_0 - \frac{\gamma}{\alpha}}, 0 \right).$$

Denoting the S value in this intercept as S^*, we observe that on $[0, S^*]$ the disease-free equilibrium is unstable and on $(S^*, 1]$ the disease-free equilibrium is stable. When the disease-free equilibrium is unstable, the system reverts to the stable endemic equilibrium. However, when the disease-free equilibrium is stable, the system reverts to the disease-free equilibrium.

2.3. Application of the Rural Model

Throughout Chapter 2, we have given strong justification for the structure and assumptions of our models. In addition, we have found reasonable implications regarding the dynamics of methamphetamine users from our proposed models. We further support the validity of our compartmental structure by demonstrating both that we can fit our rural model well to data and that the fit of our rural model to data yields realistic parameter choices.

For our application, we use use a data set with the number of users in Hawaii over the years 1968 to 1990. We classify Hawaii as a rural region because the population density of Hawaii is 200.56 people per square mile. We recall that we classify any region as rural with a population density under 999 people per square mile, so Hawaii falls well into the category of rural.

Our data set comes from a survey performed through a partnership of the National Institute on Drug Abuse with the Alcohol and Drug Abuse Branch of the Hawaii Department of Health [24]. We find this data set particularly interesting because it catches the outbreak of a methamphetamine use "epidemic." The popularity of methamphetamine began to become a serious issue in the continental United States before it became an issue at all in Hawaii. Due to the past trends in illegal drug problems throughout the United States, both organizations involved in the survey anticipated an imminent issue in Hawaii. Thus, they kept track of the number of incidents for 22 years. However, for approximately the first 15 years of the study, the reports only found less than 10 methamphetamine users in Hawaii every year. Consequently, the funding for the study was discontinued four years before the end. The last data points were unofficially collected and were not verified for accuracy though the study included them as "estimates." Incidentally, the last decade of the study, the long-anticipated outbreak of methamphetamine use in Hawaii occurred. We discard the first 12 years of data points in which consistently less than 10 users each year were found in Hawaii and fit our model to the "outbreak" data in the last decade of the study in Figure 2.4.

The best-fit parameters for our rural model to this data are $\beta = 0.8599$, $\alpha = 0.1691$, and $\gamma = 0.4428$. Reports on numbers of users, recovery rates, and relapse rates suggest that these parameters are reasonable [23].
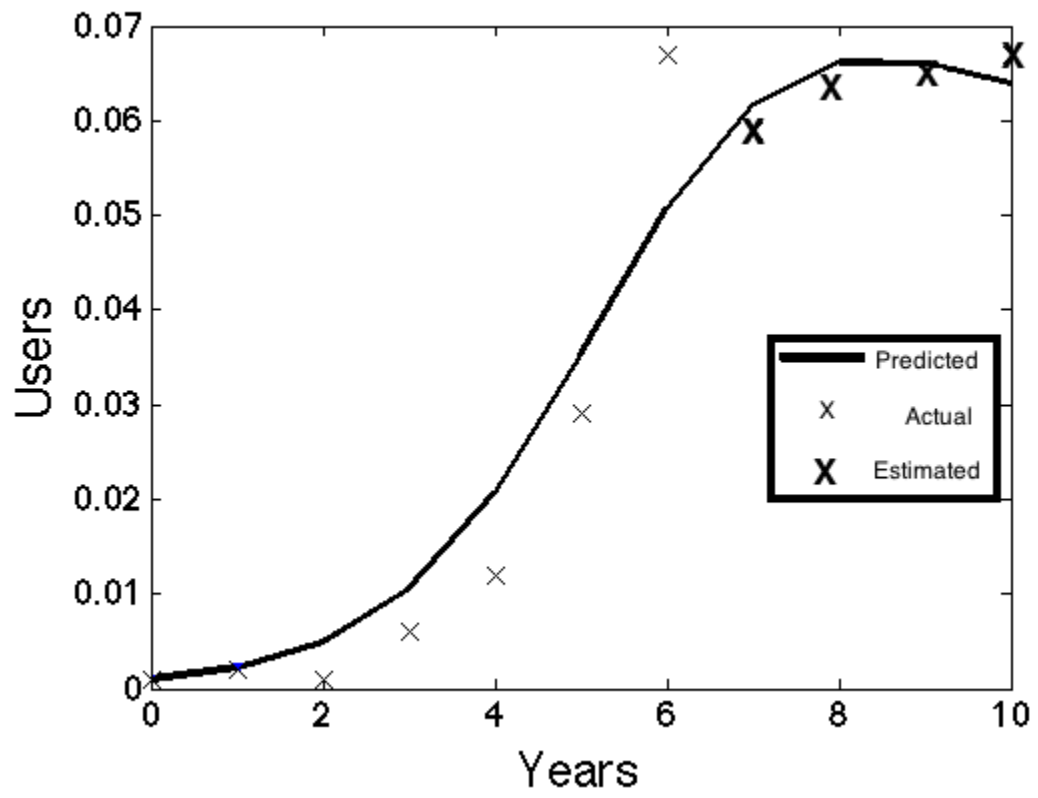
FIGURE 2.4. Hawaii Methamphetamine Users: 1980 to 1990

CHAPTER 3

Optimal Control Models

With our proposed compartmental models, we observed many important characteristics of the dynamics of the spread of methamphetamine use. However, the primary motivation in understanding the dynamics and gaining predictive ability of the spread of methamphetamine use is to control the use in order to end the problems it creates in society. In this chapter, we propose an optimal control structure to impose on our rural and urban compartmental models in order to develop and evaluate strategies to minimize the number of methamphetamine users in a single population.

3.1. The Model

We introduce two different control functions, $u_1(t)$ and $u_2(t)$. We let $u_1(t)$ represent the cost of law enforcement and $u_2(t)$ represent the cost of treatment programs. We briefly discuss what we include in each measure of cost. The cost of treatment programs is fairly straightforward.

We note that the cost of law enforcement includes the increase in both jail and police force costs associated with implementing new laws controlling the distribution and use of methamphetamine.

Each control measure acts on our system by removing users from our user class and putting them in our recovered class at a rate proportional to the number of users in the population. We specifically rewrite our rural system with these control effects,

$$\frac{dS}{dt} = -\beta SU$$

$$\frac{dU}{dt} = \beta SU - \alpha U + \gamma RU - (u_1(t) + u_2(t))U$$

$$\frac{dR}{dt} = \alpha U - \gamma RU + (u_1(t) + u_2(t))U.$$

Similarly, we rewrite our urban system with our control effects,

$$\frac{dS}{dt} = -\beta SD$$

$$\frac{dU}{dt} = \beta SD - \alpha U + \gamma RD - (u_1(t) + u_2(t))U$$

$$\frac{dR}{dt} = \alpha U - \gamma RD + (u_1(t) + u_2(t))U,$$

where $D = \frac{U}{x}$.

As each control appears to act in the same manner on our system, it may seem that our controls can be combined into one control and our problem simplified significantly. However, each of these controls are subject to different constraints which are quite unrelated to each other. Treatment and law enforcement budgets are allocated completely separately and spent by different organizations within different

government systems. Furthermore, our controls have different levels of effects on the reduction of users in our populations under consideration implying that their associated weights in our proposed objective functions 3.1.1 and 3.1.2 will be different. Thus, we analyze our controls separately and write the isoperimetric constraints implied by the qualitative meaning of our controls as

$$\int_0^T u_1(t)\, dt = B_1,$$

$$\int_0^T u_2(t)\, dt = B_2.$$

We denote our law enforcement budget as B_1 and our treatment budget as B_2. We note that each budget is the current total budget available for each control.

Our overall goal with each control is minimizing the total number of people using methamphetamine in our population under consideration. Thus, in our optimal control problem, we look to find an optimal spending plan for each control over a given period of time to minimize users as represented in our following objective function.

$$\min_{u_1,\, u_2} \left(\int_0^T U(t) + A_1 u_1^2(t) + A_2 u_2^2(t)\, dt \right) \tag{3.1.1}$$

Our above objective function can give us information regarding how to spend current budget allocations which is useful information for organizations making decisions with already allocated money between our two controls. However, we can take

our model much further. If we take our budget as fixed and solve for an optimal time period over which we should spend the budget with regard to an optimal spending schedule, we find much more information. One of our hypotheses regarding the United States government's spending on treatment programs is that it is too little to make a difference. If we solve for an optimal time period over which to spend the treatment budget and it is very short, but it was allocated for a much longer period of time, our model would imply that too little money is being spent on treatment programs. On the other hand, if we solve for an optimal time over which to spend a budget and it is longer than the time allocated for that budget to be spent, then we can conclude that too much money is begin allocated to that control measure, and the additional money is not having a significant effect on reducing the methamphetamine using population. Thus, we introduce this free time component into our previous objective function giving us the new minimization problem stated below.

$$\min_{u_1,\, u_2,\, T} \left(\Phi(T) + \int_0^T U(t) + A_1 u_1^2(t) + A_2 u_2^2(t)\, dt \right) \qquad (3.1.2)$$

We continue our analysis of both the problem in which an optimal time is solved for and that in which it is not. We see the usefullness of including free time into our analysis, but we also wish to observe the behavior of our model in which we take all the relevant initial conditions of our system that we have as given.

We observe that each objective function can be paired with either our rural or urban system to form different optimal control problems for our two different systems.

The analytical solution our optimal control problem yields the following two optimal controls,

$$u_1^* = \frac{(\lambda_2 - \lambda_3)U - \lambda_4}{2A_1},$$

$$u_2^* = \frac{(\lambda_2 - \lambda_3)U - \lambda_5}{2A_2}.$$

We note that these two controls are optimal for the rural optimal control problem as well as the urban optimal control problem. However, as our system of differential equations behave differently for each problem, our numerical solutions for each problem are different. Also, whether or not we choose to solve for an optimal time over which to implement our controls will not effect the analytical solution of our controls. It will only effect our numerical solution of the problem which we discuss in Section 3.2.

3.2. Application to Missouri

We apply our optimal control model to data from Missouri over the years 2002 to 2012. The population density of Missouri is 85.82 people per square mile, so we classify Missouri as a rural region. For our weights, we estimate law enforcement to be approximately four times more effective than treatment programs in stopping users from continuing methamphetamine use. We consider the given budgets for spending as a percent of the total state budget. Figure 3.1 shows the projected behavior of our population of users over time compared to our data. We found the best-fit

parameters for our model without the free-time optimization with this data set to be $\beta = 0.1760$, $\alpha = 0.4626$, and $\gamma = 0.4349$. All these values are reasonable and qualitatively appropriate, implying that our our model is applicable to this data set.
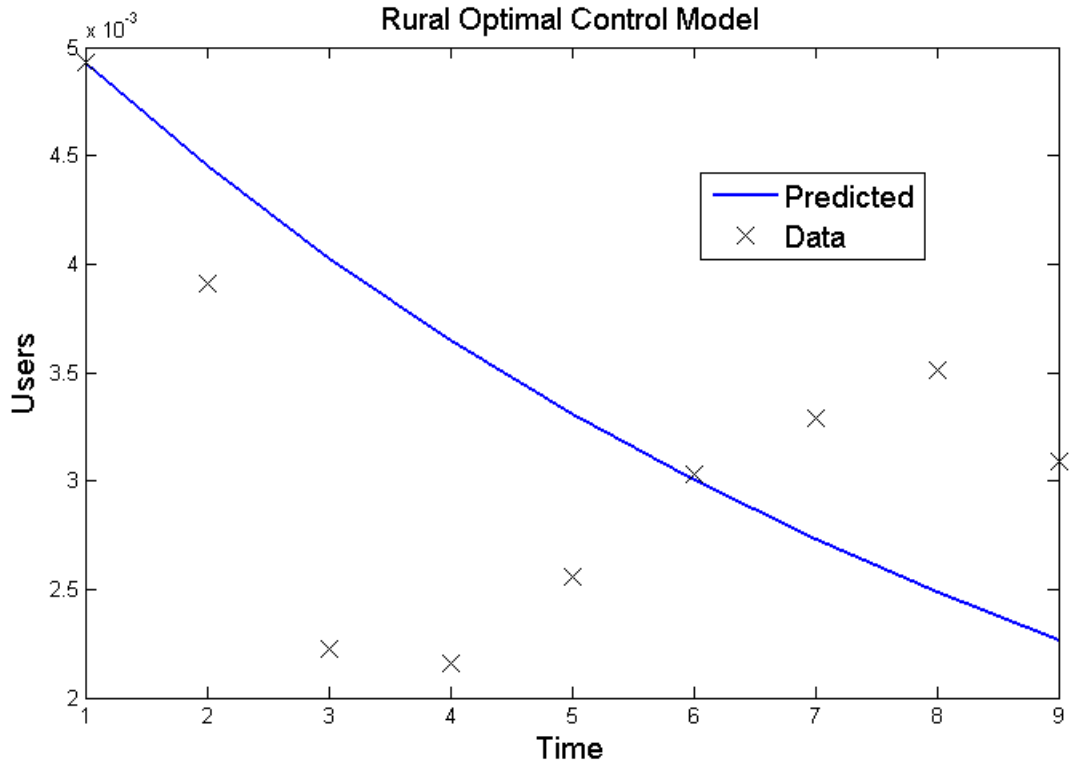

FIGURE 3.1. Missouri Methamphetamine Use From 2002 to 2012

We observe that our optimal control model appears to match the general decreasing trend of the data. However, the fit does not look very accurate. We consider three possible explanations for our lack of fit.

(1) Policies regarding spending for the controls changed significantly enough throughout our modeled time span to effect the system, creating the oscillatory behavior of the data. Our model does not take into account these changing policies.

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(2) We do not have very much data for which to make a comparison between our simulation and actual occurrences. If we had more data, we may observe a closer fit and more obvious trends.

(3) The controls implemented in Missouri were not optimal. Though we fit our parameters to the data, we solve for an optimal spending plan for the system. If their spending decisions were not close to optimal, our model will not fit the system regardless of the parameters.

We anticipate that all three explanations play a role in the difference between our data and projected behavior. Though the actual implemented controls may not be optimal, the overall decreasing trend in the data indicates that the controls may still be effective. We explore this question further in Section 3.3.

In regards to the behavior of our controls, we see very similar trends in both optimal treatment and law enforcement spending. Both require high initial spending which decreases quickly at first before leveling out until the budget is spent. We observe this behavior in Figures 5.1, 5.2, 5.4, and 5.3, all of which we include in our appendix.

3.3. Comparison to the Unconstrained Case

To more clearly observe the effects that each control has upon the final state of our system, we create an estimate of the unconstrained case. We use the first point from our data set as our initial point in our unconstrained model. We then numerically solve our unconstrained model. The graph of simulated data over the same time

period of the optimal control model analysis is presented in Figure 3.2. We make

parameter estimates close to the found values in Section 2.3 which we believe match

qualitative information from the region. In particular, we let $\beta = 0.75$, $\alpha = 0.30$, and
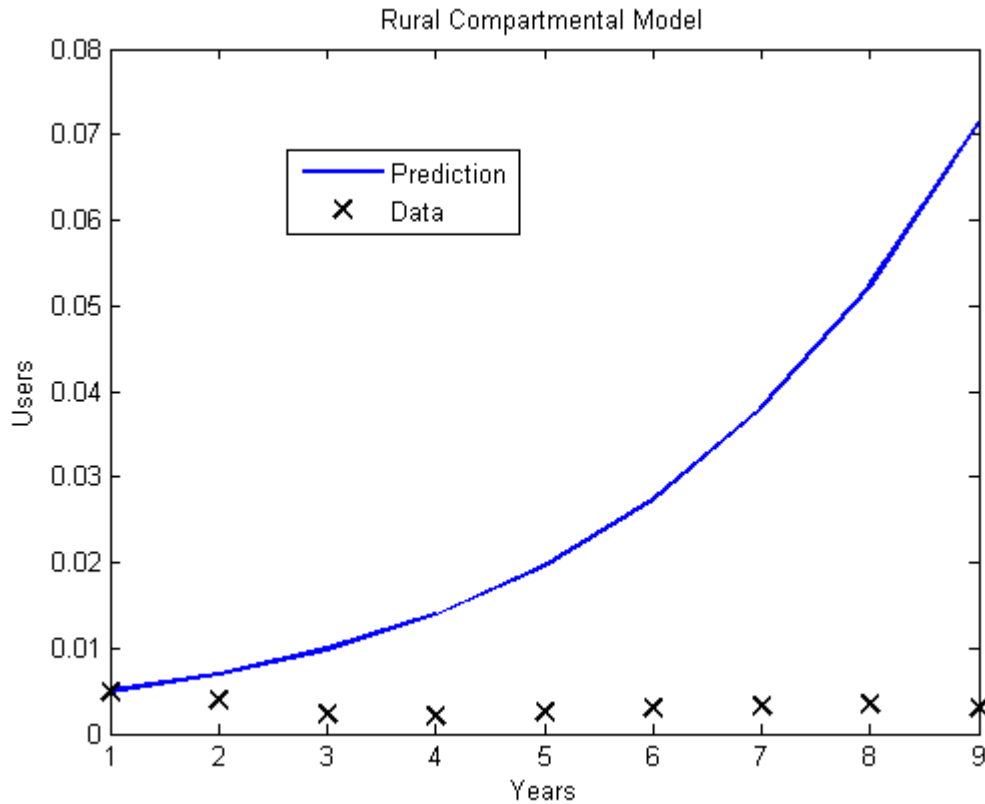
$\gamma = 0.35$.

FIGURE 3.2. Projected Unconstrained Methamphetamine Use in Missouri

Without the controls restraining the growth of our user class, we observe a pre-

dicted 1300 % increase in the number of users in our unconstrained model compared

to our control model by the end of the same time period over which the controls

were implemented. We can thus conclude that the government controls on metham-

phetamine use are indeed effective in decreasing the user class. However, further

analysis and consideration is needed to determine whether the level to which they were effective given the budget spent is optimal for the state of Missouri. Though the percent increase in use is large, the difference in terms of numbers of users may not be so much as to create a drastic difference in damage and danger to society. The Missouri government ought to determine if the level of spending on treatment programs and law enforcement is sustainable, and, if it is not, consider if they can spend less on the programs but allow them to be sustained.

We note that the programs will need to be sustained since they did not significantly decrease the number of users to a point which the system would revert to the disease-free equilibrium; they simply prevented the number from growing. Thus, if we considered a simulation from a later year, we could anticipated the same degree of growth as that given in Figure 3.2 being at the point which the controls ended.

In our last justification of our optimal control model, we make a final application of our unconstrained rural compartmental model to the data set from Missouri. When we observed the drastic difference between the prediction in Figure 3.2 and the data, we picked our own parameters instead of fitting the compartmental model to the data. To observe that our compartmental models are not appropriate for modeling the spread of methamphetamine when controls are introduced and, consequently, that our optimal control model is necessary, we attempt to fit our rural compartmental model to the data set from Missouri. We observe the result in Figure 3.3.

While the prediction does not look completely inaccurate, this fit yields parameter values of $\beta = 0.0944$, $\alpha = 0.7564$, and $\gamma = 202.4470$. The value of γ necessary for our
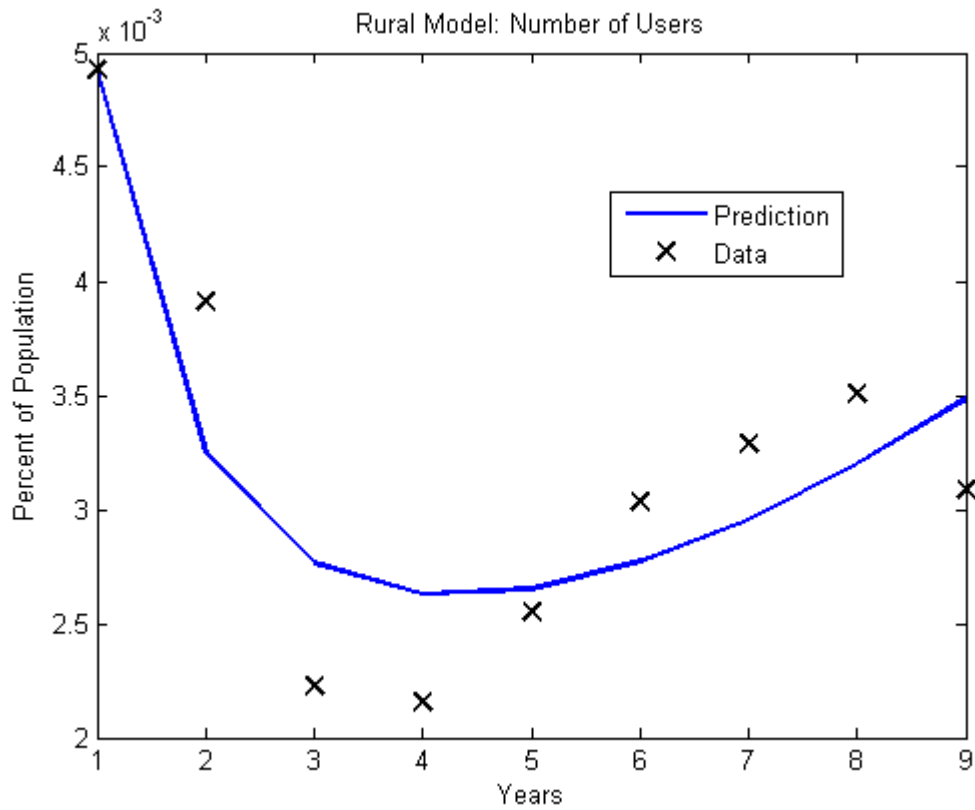
FIGURE 3.3. An Attempt to Fit Parameters From Our Unconstrained Model

model to even come close to fitting the data is entirely impracticle. The qualitative interpretation of such a large value for this rate is meaningless. Therefore, we conclude that our compartmental models are not appropriate for modeling these situations, and our optimal control models are necessary.

CHAPTER 4

Metapopulation Model

Thus far, we have constructed models for the case in which methamphetamine use spreads unconstrained throughout a single population and the case in which the dynamics of the spread are changed and use is controlled by government implemented treatment programs and legal enforcement. However, population groupings are not all adjacent to each other, and the spread of methamphetamine use will certainly be different within a single large population in a small region as opposed to a similar size population separated into clusters throughout a very large region. Our separation between urban and rural regions deals in part with the differing dynamics of spread when populations are distributed differently. With that distinction, we account for the change in the mechanism of spread, but we do not account for the spatial barrier between population clusters. In this section, we account for that change by constructing a metapopulation model.

4.1. The Model

The mathematical formulation of our metapopulation model is a natural extension of our compartmental models. We classify each partition as an urban or rural region and use our urban or rural compartmental model as per the classification to model the behavior within each smaller region. We make only two additions to the

model for each partition. For each model, we must take into account the movement of our drug-using population both in and out of the partition.

We begin taking into account this movement by finding some rate of travel between the two regions. We consider while we are building the model what type of data will be available for an application. Data listing number of cars traveling on regions of highways in the United States is readily available and separates movement in each direction [25]. Thus, we can use this information to determine a rate of movement out of each partition, i, and into each partition, j.

We note the meaning of the following new parameters we will use to construct our system.

- χ_R = indicator function for rural node

- χ_D = indicator function for urban node

- ζ_{ij} = rate of travel from partition i into partition j

We further note that any index j denotes the current node our system is modeling and i denotes an adjacent node. We use this notation to write our metapopulation model as

$$\frac{dS_j}{dt} = -\beta_j S_j(\chi_R U_j + \chi_D \frac{U_j}{x}) - \sum_{i=1}^{n} \zeta_{ji} S_j + \sum_{i=1}^{n} \zeta_{ij} S_i$$

$$\frac{dU_j}{dt} = \beta_j S_j(\chi_R U_j + \chi_D \frac{U_j}{x}) - \alpha_j U + \gamma_j R(\chi_R U_j + \chi_D \frac{U_j}{x}) - \sum_{i=1}^{n} \zeta_{ji} U_j + \sum_{i=1}^{n} \zeta_{ij} U_j$$

$$\frac{dR_j}{dt} = \alpha_j U_j - \gamma_j R_j(\chi_R U_j + \chi_D \frac{U_j}{x}) - \sum_{i=1}^{n} \zeta_{ji} R_j + \sum_{i=1}^{n} \zeta_{ij} R_i.$$

4.2. Application

Given data availability, we can do no meaningful parameter fit of our metapopulation model in this form because we would need data on a large region during the breakout of an epidemic of methamphetamine use due to the fact that the metapopulation model is unconstrained in its current form. Every large region for which data is currently available has an established presence of methamphetamine use with growth and fluctuations taking place as a result of various levels of control measures typically implemented by federal or state governments. An area of future work would include integrating our metapopulation model with our optimal control model to track and analyze these fluctuations. However, we focus our work here on demonstrating the model's behavior through an example simulation using reasonable parameter guesses for a specific area and make a comparison to the simulation for the aggregate case presented in Section 3.3 as well as the data. We use data from methamphetamine use in 2004 in Missouri as an initial point and simulate the spread given by our model.

From our observation in our Chapter 3, we verified that the control measures implemented in Missouri over the years 2004 to 2012 were effective in reducing the spread of methamphetamine use. Thus, for our models to be consistent, simulation of our metapopulation model which does not take the control measures into account should yield aggregate state methamphetamine use higher than the actual use in the data. Furthermore, we should find more information and detail regarding patterns of distribution than previously given from our simulation in Chapter 3.

We begin our application by creating a partition of the state of Missouri and related data demonstrated in Figure 4.1. Now that we have grouped the counties in Missouri into 9 partitions, we classify each partition based on population density as urban or rural. We find that A and C are both urban, and the remaining partitions are rural.

FIGURE 4.1. Missouri Methamphetamine Laboratory Incident Totals 2004

Using this partition, we create Figure 4.2 with the graph of the numerical solution of our model. We input parameters within .1 of the parameters used in our aggregate

simulation in Section 3.3: $\beta = 0.75$, $\alpha = 0.30$, and $\gamma = 0.35$. We want the simulations to be comparable without the parameters in each partition being identical. Our data for the rates of travel between regions were estimated from related data given by the Missouri State Highway Patrol and the Missouri Department of Transportation, Traffic and Highway Safety Division [26]. Furthermore, in the graph of our metapopulation model, we let the percents denote the percent of the population within each partition.

We find a very interesting insight from modeling Missouri methamphetamine use in this manner. We find that the number of users in F, G, and I increase the most drastically. However, the number of users in both of our urban regions, A and C, are actually declining. Considering the location of F, G, and I directly between the two urban locations, our model seems to imply that users in urban regions with immediately adjacent rural regions will tend to leave the urban regions for the urban regions where they have easier availability of methamphetamine. This analysis makes sense because isolated urban regions tend to obtain methamphetamine from nearby rural communities. However, rural producers typically produce for personal use, not for distribution. Thus, users from urban regions would have a motive to move to the rural regions when they are nearby to self-produce methamphetamine, increasing their ability to easy acquire the drug.
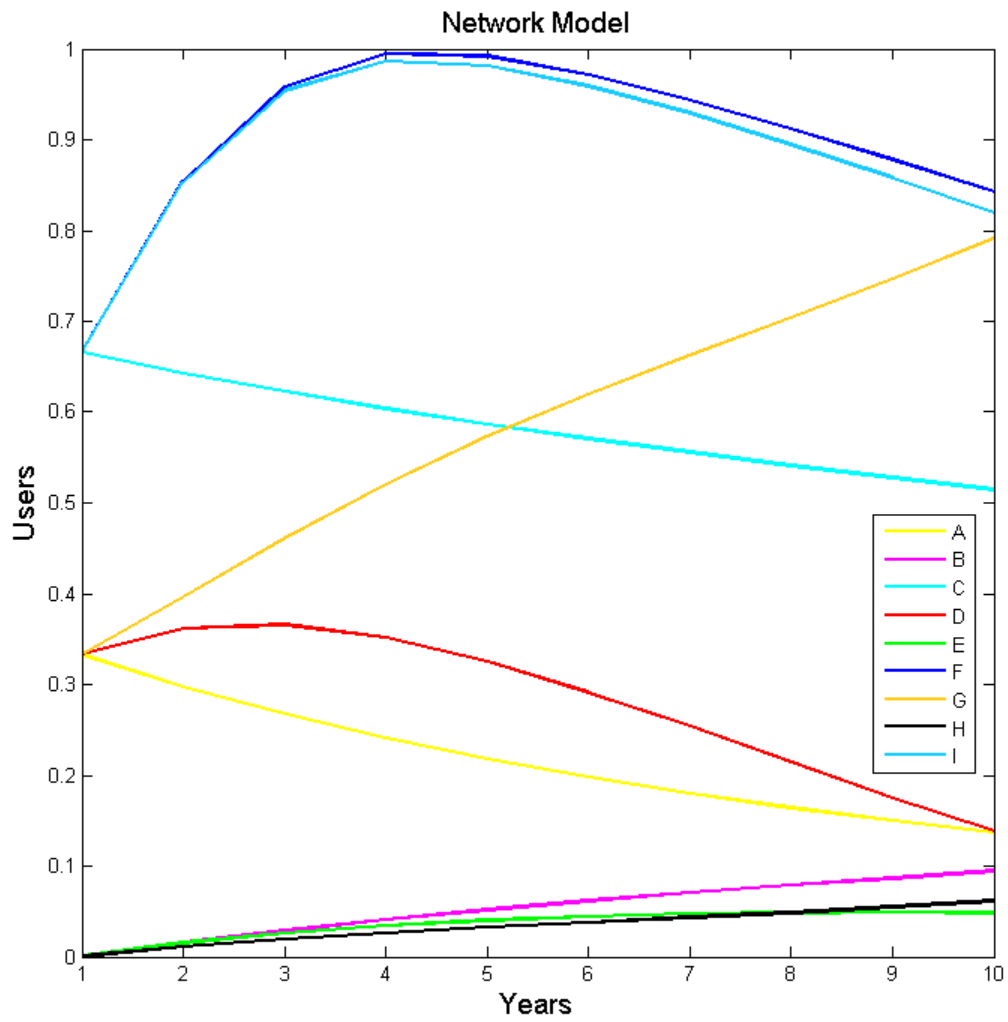
FIGURE 4.2. Metapopulation Simulation of Unconstrained Growth

CHAPTER 5

Conclusion

We believe that our models are very successful in informing us about the dynamics of the spread of methamphetamine use in the United States. We made reasonable assumptions in our models from previously observed and well supported characteristics of methamphetamine use, distribution, relapse, and recovery. We found that our models fit well with reasonable parameter results to data from a variety of regions throughout the country. Furthermore, our analysis yielded several insights to the spread and distribution patterns of methamphetamine use throughout the country that were not obvious before our modeling exercise. We review the main conclusions we found from our models. We begin by reviewing the results from our applications and analyses of our compartmental models and metapopulation model.

Our urban compartmental model reveals an explanation for the strange pattern of methamphetamine use distribution throughout the continental United States. We see a clear estimate of this distribution through the map of methamphetamine users admitted for drug treatment in each state for the year 2009 in Figure 5.5 from [**27**] included in our appendix. We notice that methamphetamine use is concentrated in California and the Midwest. In contrast, use of the drug is almost nonexistent in the Northeastern states. Since methamphetamine has been an issue for many decades in the United States, this uneven pattern is interesting. Other drugs often have uneven

distribution of use, but typically the concentrations of use are associated with the characteristics of a certain type of region. For example, much other illicit drug use is more heavily observed in urban areas due to the necessity of acquiring the drug through a dealer. For the point of comparison, we consider the distribution of heroin throughout the United States in 2005 represented in the map in Figure 5.6 from [28] in our appendix. Though use is not evenly distributed, heavy areas of use are distinctly focused in urban regions. No such pattern is obvious with methamphetamine.

Our urban compartmental model analysis together with historical information regarding the origins of methamphetamine in the United States give a complete explanation of the strange distribution of use throughout the country. Methamphetamine was not illegal until the passage of the U.S. Drug Abuse Regulation and Control Act of 1970. In fact, use was promoted by both the Axis powers and the Allies in World War II to keep troops awake. In the 1950's, Obetrol Pharmaceuticals patented Obetrol, one of the first pharmaceutical methamphetamine products. Throughout the rest of that decade and into the 1960's, Obetrol was a very popular diet pill sold throughout the United States. Thus, when the harmful effects of methamphetamine were investigated and the drug was outlawed in 1970, large numbers of people were already addicted [29].

Shortly after methamphetamine was outlawed, Mexican drug cartels entered California and profited heavily off of the population of already addicted residents through the continued distribution of methamphetamine. In addition, deserts adjacent to major Southwest cities proved prime locations for nearby community labs. Use in rural

communities continued to spread with the discovery of the ability to self-produce the drug fairly easily. However, use in the Northeast did not prevail to a significant extent past the banning of the pharmaceutical products. The population of the Northeast did not immediately began making methamphetamine because regions were mostly urban. Cartels were located much closer to California, so the Northeast was an inconvenient first market. Our models provide more insight to why no significant growth of methamphetamine use has occurred in the Northeast since the downturn after 1970.

We introduce the idea that a sufficient base of users must first be present for dealers to enter an urban region in our model. This dynamic is made possible by the construction of our metapopulation model as well as the existence of use before the ban of the substance. The combination of these two traits imply that urban areas that transition quickly to very nearby rural areas can gain a using population, but the barriers are large for a population to begin use of methamphetamine when many urban areas are adjacent to each other as is characteristic of the Northeast.

Furthermore, Equation 2.2.1 demonstrates the difficulty of escaping the disease-free equilibrium in our urban compartmental model. Through the relationship given in Equation 2.2.1, we found that the disease-free equilibrium in the rural model is unstable only for the case in which the "infection" rate and relapse rate are both much higher than the "recovery" rate additionally implying that we require a very high basic reproductive number for this equilibrium to be unstable. In our applications, we typically do not see parameter differences of the magnitude necessary for the disease-free equilibrium to be unstable. Thus, we can anticipate that the disease-free

equilibrium in most urban areas is stable, resulting in additional difficulty for an outbreak of methamphetamine use to occur.

We note that the endemic equilibrium in urban areas is also stable, so, given either an existing "epidemic" or a sudden influx of a large number of users, large numbers of methamphetamine users can be sustained in an urban population. We observe the case in which an existing epidemic continued in many Western cities, particularly throughout California. However, neither of these characteristics are applicable to the Northeast.

One question brought to light by this analysis remains. Not all of the Midwest is rural. In particular, Missouri has many urban regions, and those regions appear to have just a large a methamphetamine problem and the rural areas in the Midwest. However, the cartel presence supplying the Western cities with methamphetamine dealers does not exist in these cities. Our metapopulation model allows us to observe a probable dynamic for these regions. While use spreads through the surrounding rural areas in the Midwest, residents of the urban regions interact with rural users. They temporarily become urban users receiving their drugs from rural "dealers" contrary to the general dynamics of our models. However, our metapopulation model shows the tendency of residents of urban areas to move to the immediately adjacent areas to produce their own methamphetamine as their use continues. We see decrease in use only in the urban partitions which corresponds exactly with increases in use in the adjacent rural partitions. This dynamic is again impossible for the Northeast, so

our description of the distribution throughout the United States only becomes more complete.

We move onto review our results given by our optimal control model. Our results from this model are not as general, but its use in continued applications is possibly the most extensive. We found in our application to data from Missouri that the controls attempting to restrict methamphetamine use throughout the state are not the optimal set of controls, but they are definitely effective in decreasing use. We also validated our model by showing that our application to data yielded meaningful parameters. We can continue our use of this model with further data to analyze the effectiveness of control measures and appropriate allocation of budgets for governments of different levels throughout the United States.

Looking ahead, we hope that these models can continue to be used to discover information regarding the use and abuse of methamphetamine throughout the United States to control the harm use and production causes for so many people. To continue their application, the main area of future work in these studies is data collection. In addition, we hope to combine our optimal control model with our metapopulation model. Both the increase in data availability and the combination of these two models would allow an enormous increase in accuracy and power of our model's predictive and explanatory ability.

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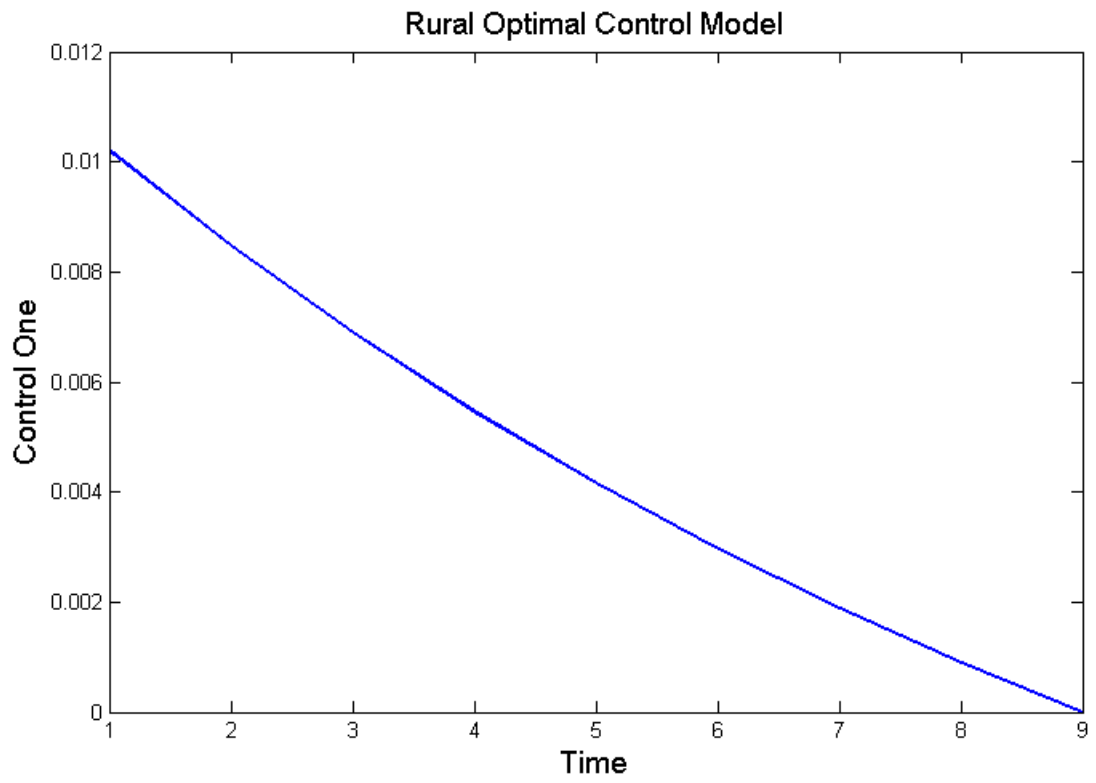
Appendix

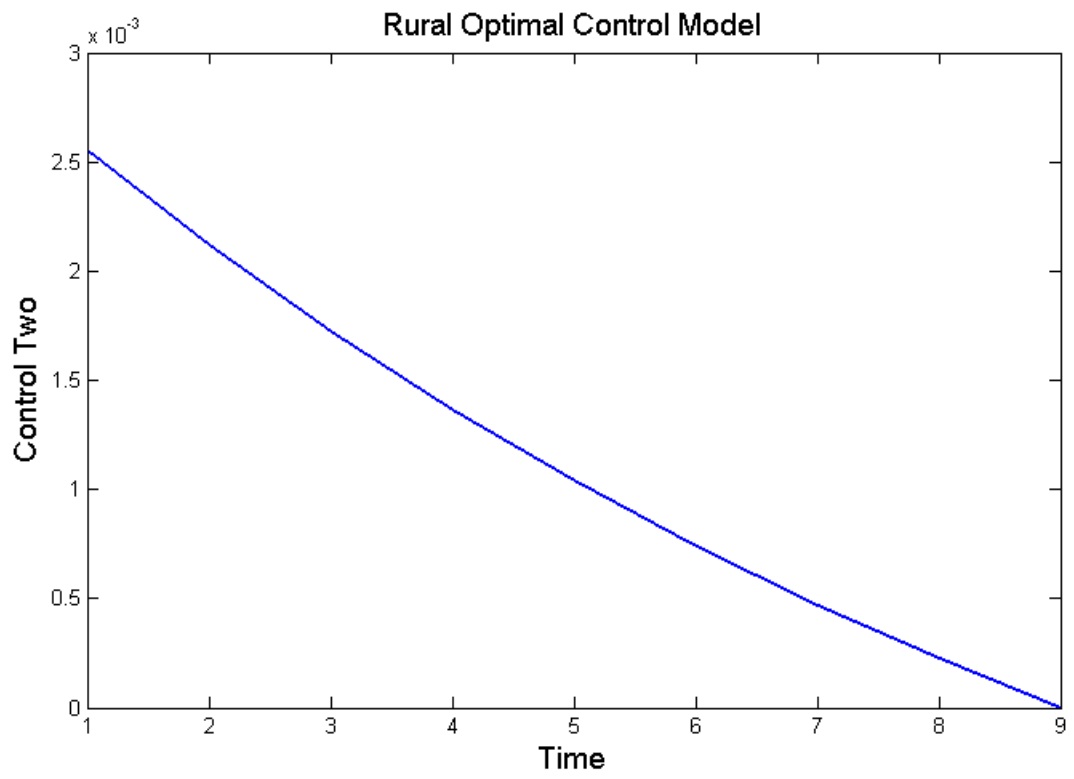FIGURE 5.1. Optimal State Spending on Law Enforcement

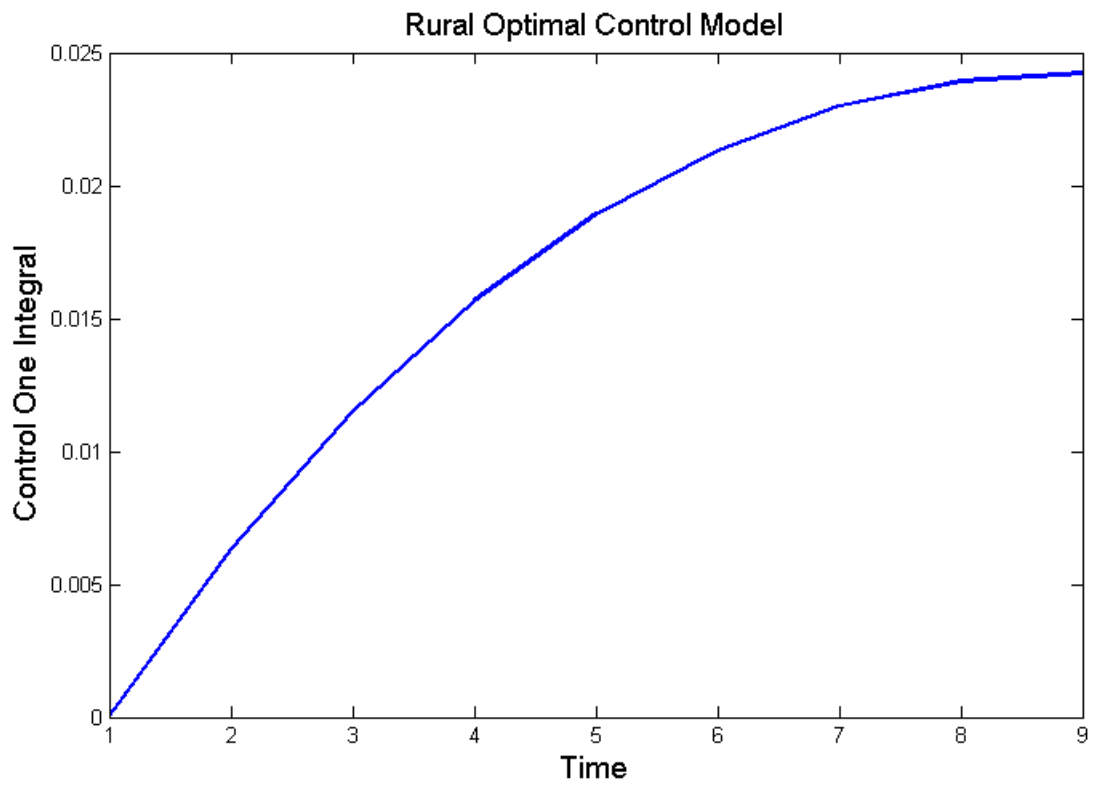FIGURE 5.2. Optimal State Spending on Treatment Programs

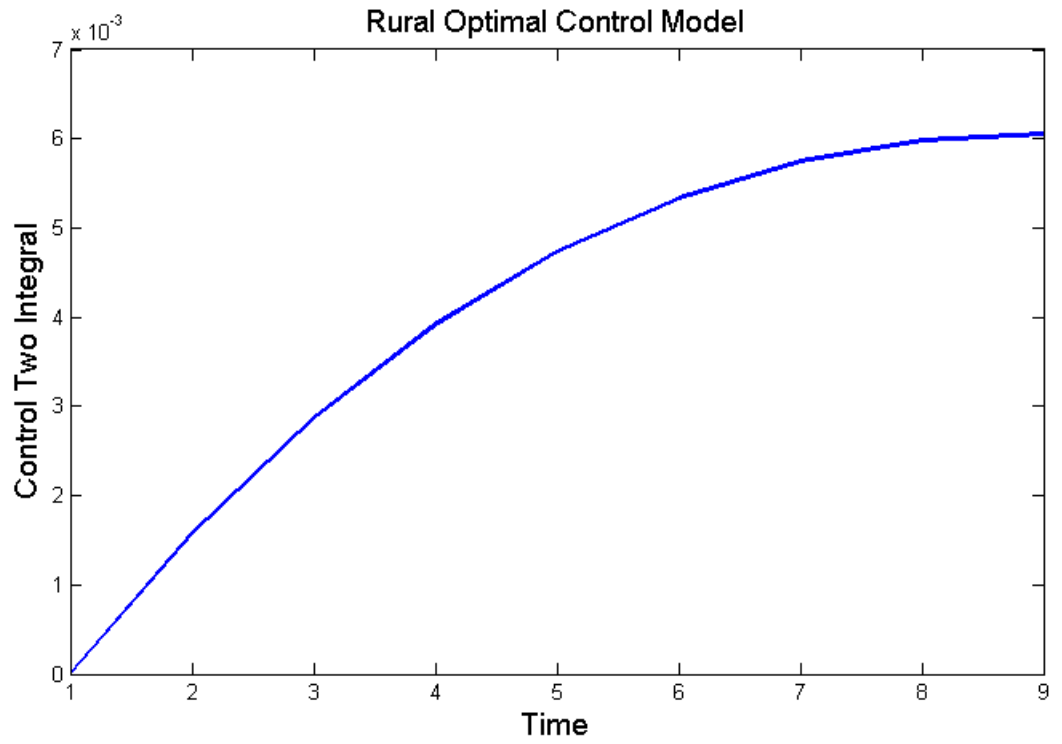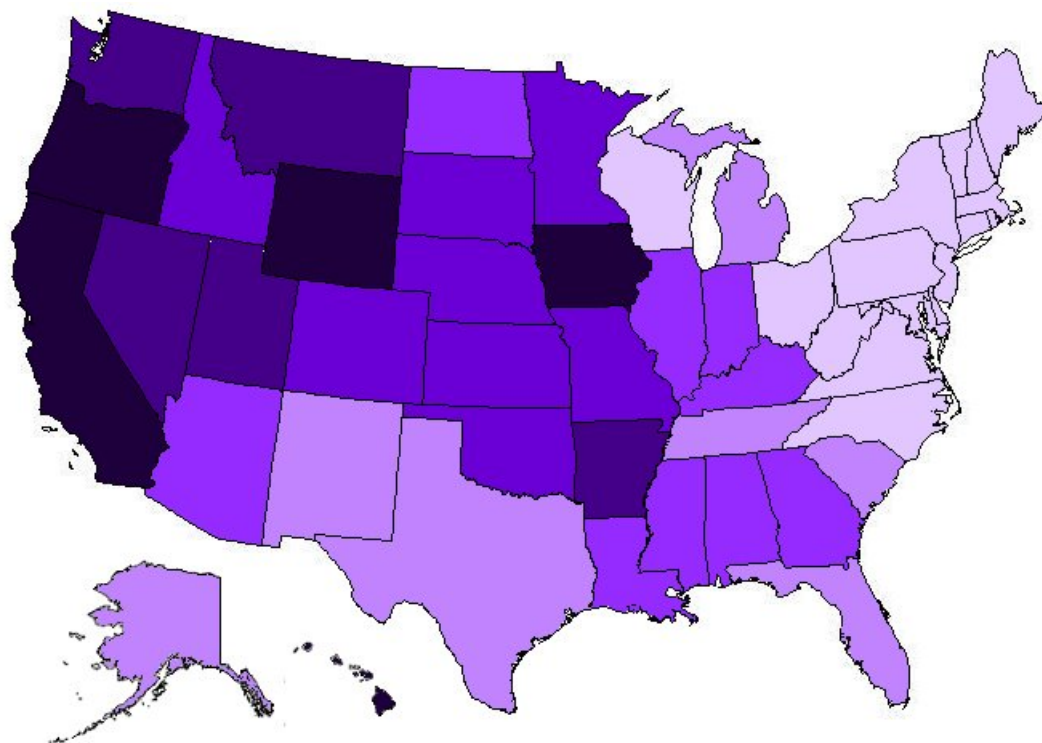FIGURE 5.3. Optimal Aggregate State Spending on Law Enforcement

Figure 5.4. Optimal Aggregate State Spending on Treatment Programs

Meth Users Admitted for Drug Treatment Per 100,000 Residents

☐	<5	■	51-100
☐	5-15	■	101-150
☐	16-50	■	151+

FIGURE 5.5. United States Methamphetamine Use Distribution

FIGURE 5.6. United States Heroin Use Distribution