Mathematical Model of Methamphetamine Epidemics

Theerat Piyaanangul

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บทคัดย่อ

วิทยานิพนธ์นี้สนใจเกี่ยวกับสังคมของการระบาดของยาบ้า เราสร้างระบบสมการเชิงอนุพันธ์สามัญอันดับหนึ่ง เพื่ออธิบายพฤติกรรมของแบบจำลองเชิงคณิตศาสตร์ภายใต้พื้นฐานของแบบจำลองเชิงคณิตศาสตร์ทางระบาดวิทยา ในแบบจำลองนี้ประชากรได้ถูกแบ่งออกเป็น 4 กลุ่ม ได้แก่ กลุ่มที่เสี่ยงต่อการติดยาบ้า กลุ่มที่ลองยาหรือมีการใช้ยาบ้าในปริมาณที่น้อย กลุ่มที่ติดยาบ้าขั้นรุนแรงและกลุ่มที่อยู่ภายใต้การบำบัด จากการศึกษาเราสามารถหาจุดสมดุลได้ 2 จุด คือ จุดที่ไม่มีการระบาดของยาบ้าและจุดที่พบการระบาดของยาบ้า นอกจากนี้ได้มีการพิจารณาหาผลเฉลยที่สมดุลและความเสถียรเฉพาะที่ของผลเฉลยที่สมดุล

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ABSTRACT

This paper focuses on the social implications of the methamphetamine (MA) epidemics. The model is presented by a system of first order ordinary differential equations, based on the principles of mathematical modeling epidemiology. In this model, the human population is divided into four classes: susceptible individuals, light MA users, hard MA users and drug users in treatment. There are two equilibrium states, namely a drug free state and an endemic state. Furthermore, the existence of steady-state solutions are established and the local stability of the steady-state solution is analyzed.

ACKNOWLEDGEMENTS

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CHAPTER 1

Introduction

Methamphetamine (N,α-dimethylphenethylamine) is a component of the phenethylamine family, which includes a range of substances that may be stimulants, entactogens or hallucinogens. The molecular weight of MA is 149.24 g/mol while the molecular formula is $C_{10}H_{15}N$ [6].

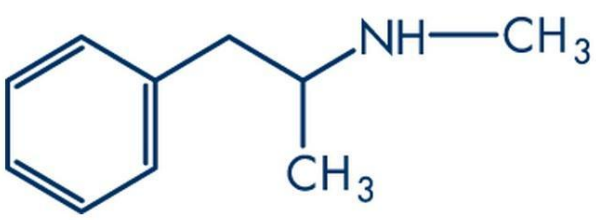

Figure 1.1: The molecular structure of methamphetamine.

Meth, speed, ice, chalk, crank, glass, go, hydro, pervitin, rock candy, crystal meth, whiz (East Europe), yaba, shabu (Southeast Asia), these are all names for methamphetamine (MA) [12]. MA is highly addictive stimulant that affects the central nervous system. MA also speeds up many functions in the body. MA can cause lots of harmful things, including inability to sleep, aggressiveness, hallucinations, paranoia and psychosis [13]. MA can also cause a type of cardiovascular problems, increased blood pressure, including rapid heart rate and irregular heartbeat. Hyperthermia (elevated body temperature) and MA overdose may occur convulsions and, if not treated instantly, can result in death [15].

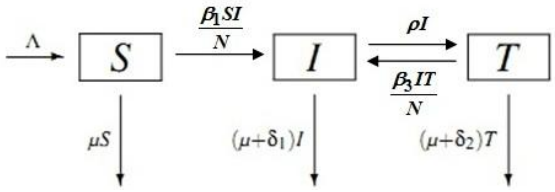

Figure 1.2: A compartmental representation of the epidemic of heroin use.

Recently, two drug models have been proposed. The first research is proposed by White and Comiskey [19]. They have constructed and analyzed a model for heroin users. Later, Mulone and Straughan [11] have investigated the steady-states of White and Comiskey's model. Another is the research about MA problems, proposed by Nyabadza and Hove-Musekwa [16]. In fact, these two models are very similar. Nevertheless, the model of White and Comiskey, as shown in Figure 1.1 divides the population into three classes, namely susceptible individuals (S), heroin users not on treatment (I) and heroin users under treatment (T). While the model of Nyabadza and Hove-Musekwa, as shown in Figure 1.2 classifies the population into five categories, which are susceptible individuals (S), light drug users (I_1) who can still easily stop and recover from drug use, hard drug users (I_2) who are addicted. Moreover, they allow for the recovery of those under treatment (T) into a class of the recovered (R).

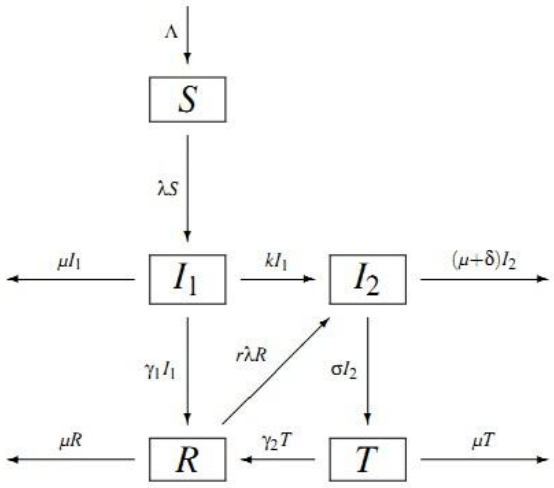

Figure 1.3: A compartmental representation of the epidemic of methamphetamine use.

1.1 Objectives of the Study

The purpose of this thesis is to obtain fundamental mathematical model representing the MA epidemics and analyze the model by studying the stable case in order to obtain condition on the system parameters, which differentiate various dynamic behavior exhibited by the model.

1.2 Expected Benefits

This study is expected to give us a better understanding of the MA epidemics. The resulting model can be used to predict and control the epidemic of MA.

1.3 Organization of the Study

This work will be organized in 5 chapters. An introduction about MA will be given in chapter 1. In chapter 2, we summarize the preliminaries that is necessary for our analysis. Our model will be analyzed in chapter 3 while the numerical simulation of the effects of parameters will be presented in chapter 4. Finally, our conclusions and suggestions for future research are made in chapter 5.

CHAPTER 2

Preliminaries

The mathematical formulation of biological or physical problems results in a set of differential equations, which may be nonlinear. In many cases it is possible to replace the nonlinear equations, by a set of related linear equations that appropriates the actual nonlinear equation closely enough to give useful effects. Such a "linearization"may not always be reasonable. When it is not, the original nonlinear equations must be considered. The study of nonlinear is generally confined to a variety of rather special cases, and one must resort to various method of approximation. In this chapter we shall give an introduction to some of these method [17].

After defining the problem and formulating a consistent set of equations, we turn to the analysis of solutions. The only solutions that can be found and analyzed are the steady state ones. Their stability properties are of particular importance [2]. A steady state is one in which the system does not appear to undergo any further changes.

Definition 2.1. A point $X_e \in \Re^n$ is called an equilibrium point of

$$X' = f(t, X) \tag{2.1}$$

$$\text{if } f(t, X_e) = 0 \text{ for all } t \geqslant t^*.$$

Other names for the equilibrium point are critical point, singular point, rest point

and stationary point. If X_e is an equilibrium point of (2.1) at t^*, then it is an equilibrium point at all $\tau \geq t^*$ [9].

Now if we have 2 steady state solutions (in case of 2 differential equations), it would like to know whether a deviation from steady state will lead to drastic changes or will be damped out.

Definition 2.2. The equilibrium $X = 0$ of (2.1) is stable if for every $\epsilon > 0$ and any $t_0 \in \Re^+$ there exists a $\delta(\epsilon, t_0) > 0$ such that

$$|u(t, t_0, \xi)| < \epsilon \qquad \text{for all } t \geq t_0$$

whenever $|\xi| < \delta(\epsilon, t_0)$ where $u(t, \xi)$ is solution of (2.1) [9].

Definition 2.3. The equilibrium $X = 0$ of (2.1) is is asymptomatically stable if

i) it is stable and

ii) for every $t_0 \geq 0$ there exists an $\eta(t_0) > 0$ such that

$$\lim_{t \to \infty} u(t, t_0, \xi) = 0 \text{ whenever } |\xi| < \eta \text{ [9].}$$

Definition 2.4. The equilibrium X=0 of (2.1) is unstable if it is not stable. In this case, there exists a $t_0 \geq 0$ and a sequence $\xi_n \to 0$ of initial points and a sequence t_m such that $|u(t_0 + t_m, t_0, \xi_m)| \geq \xi$ for all $m, t_m \geq 0$ [9].

Let us look at a more general setting and take the system of ordinary differential equation to be

$$\frac{dX}{dt} = f_1(X, Y) \tag{2.2}$$

$$\frac{dY}{dt} = f_2(X, Y) \tag{2.3}$$

where f_1 and f_2 are nonlinear functions. We assume that $\bar{x}$ and $\bar{y}$ are the steady

state solution, then

$$f_1(\bar{x}, \bar{y}) = f_2(\bar{x}, \bar{y}) = 0. \tag{2.4}$$

Now we set the solution at any time to be in the form

$$X(t) = \bar{x} + x(t) \tag{2.5}$$

and

$$Y(t) = \bar{y} + y(t). \tag{2.6}$$

This method is called a perturbation about the equilibrium point. Substituting (2.5) and (2.6) into (2.2) and(2.3), we get

$$\frac{d}{dt}(\bar{x} + x) = f_1(\bar{x} + x, \bar{y} + y) \tag{2.7}$$

$$\frac{d}{dt}(\bar{y} + y) = f_2(\bar{x} + x, \bar{y} + y). \tag{2.8}$$

On the left-hand side, we expand the derivatives and notice that by definition $\frac{d\bar{x}}{dt}$ and $\frac{d\bar{y}}{dt}$. On the right-hand side, we expand f_1 and f_2 in a Taylor series about the equilibrium point. Moreover, we consider only linear term, obtaining

$$\frac{dx}{dt} = f_{1x}(\bar{x}, \bar{y})x + f_{1y}(\bar{x}, \bar{y})y$$

$$\frac{dy}{dt} = f_{2x}(\bar{x}, \bar{y})x + f_{2y}(\bar{x}, \bar{y})y$$

We get $J(x_0, y_0) = \begin{bmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{bmatrix} = \begin{bmatrix} \frac{\partial f_1}{\partial x} & \frac{\partial f_1}{\partial y} \\ \frac{\partial f_2}{\partial x} & \frac{\partial f_2}{\partial y} \end{bmatrix}_{(x_0, y_0)}$ that is called the Jacobian of the system of equation. Setting

$$\text{a=trace}(J(\bar{x}, \bar{y}))=a_{11} + a_{22}$$

$$\text{b=det}(J(\bar{x}, \bar{y}))=a_{11}a_{22} - a_{12}a_{21}$$

and

$$\text{c = discriminant} = a^2 \text{ - 4b,}$$

the characteristic equation becomes $\lambda^2 + a\lambda + b = 0$ [5].

Theorem 2.1. *The equilibrium $X = 0$ of (2.1) is stable if all eigenvalues of J have non-positive real parts and every eigenvalues of J which has a zero real part is a simple zero of the characteristic polynomial of J*

A line system can have at most one steady state (0, 0) if $det(J) \neq 0$.

The behavior of the steady state solution depends on the eigenvalue of J;

i) Distinct real roots

ii) Repeated real roots

iii) Conjugate complex roots [5].

Case i The eigenvalues of J are real and distinct. There are 3 possible behavior.

a) If both eigenvalues of J are negative, the steady state will be a stable two tangent node.

b) If both eigenvalues of J are positive, the critical point will be an unstable two-tangent node.

c) If there are opposite signs of eigenvalues of J, the equilibrium point will be a saddle point.

Case ii The eigenvalues of J are real and repeated roots. There are 2 possible

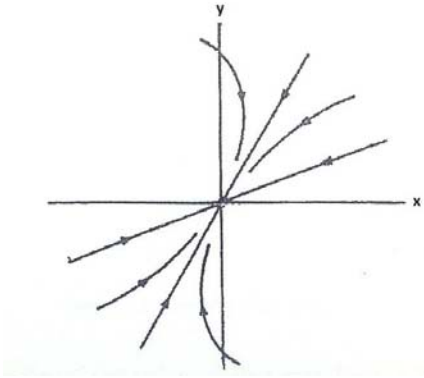

Figure 2.1: A stable two-tangent node [7].

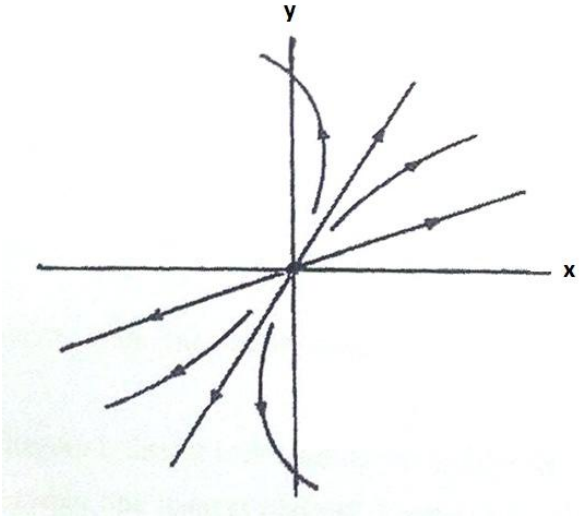

Figure 2.2: An unstable two-tangent node [7].

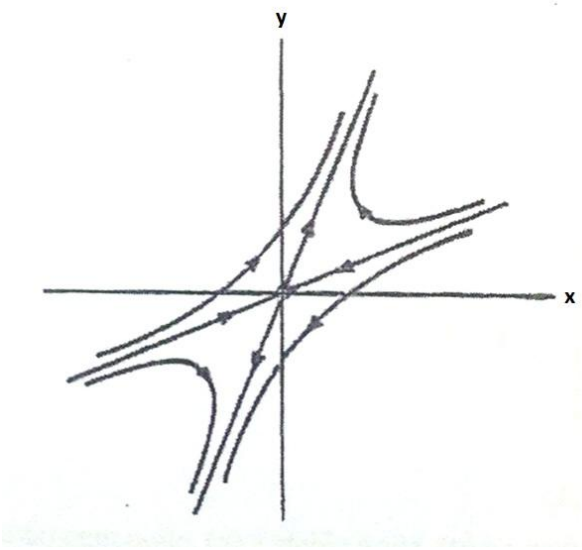

Figure 2.3: A saddle point [7].

cases

a) If is diagonal and J is similar to matrix as $J = \begin{bmatrix} \lambda & 0 \\ 0 & \lambda \end{bmatrix}$, then the critical point is called a stellar node which is stable if $\lambda < 0$ and unstable if $\lambda > 0$.

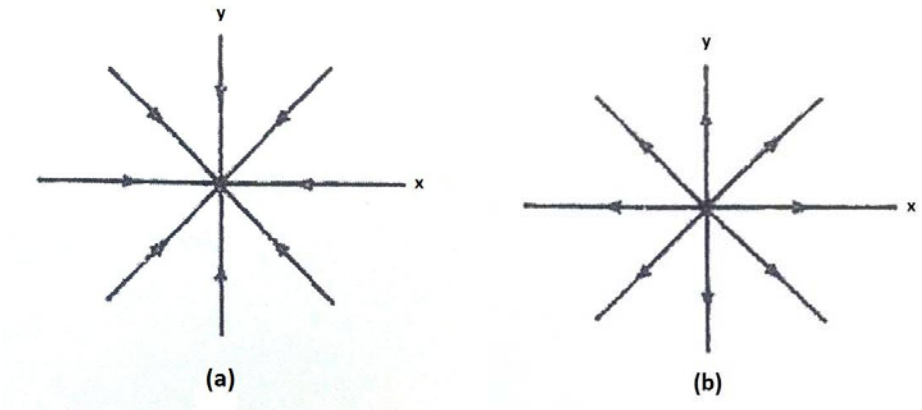

Figure 2.4: A stellar node. (a) a stable node. (b) an unstable node [7].

b) If J is not diagonal, then it is not similar to a diagonal matrix. The critical point is called a stable one-tangent node if $\lambda < 0$ and an unstable one-tangent node if $\lambda > 0$

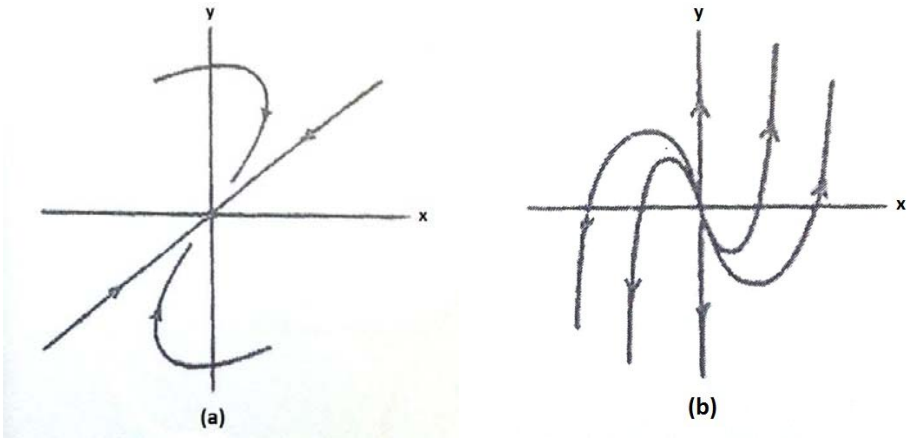

Figure 2.5: The one-tangent node. (a) a stable node. (b) an unstable node [7].

Case iii The eigenvalues of J are conjugate complex.

It is necessary and sufficient that the discriminate term is negative and then

$$\lambda_{1,2} = \frac{a \pm i\sqrt{4b - a^2}}{2}$$

There are three possible behaviors described as follow.

a) If $a^2 < 4b$ and $a > 0$, then the critical point will be an unstable spiral node.

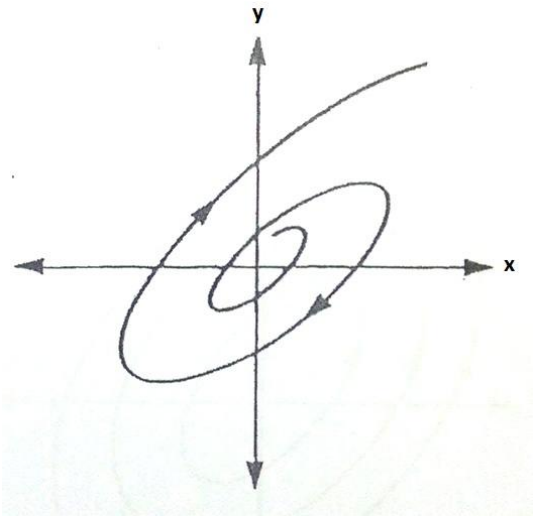

Figure 2.6: An unstable spiral node [7].

b) If $a^2 < 4b$ and $a < 0$, the critical point will be a stable spiral node.

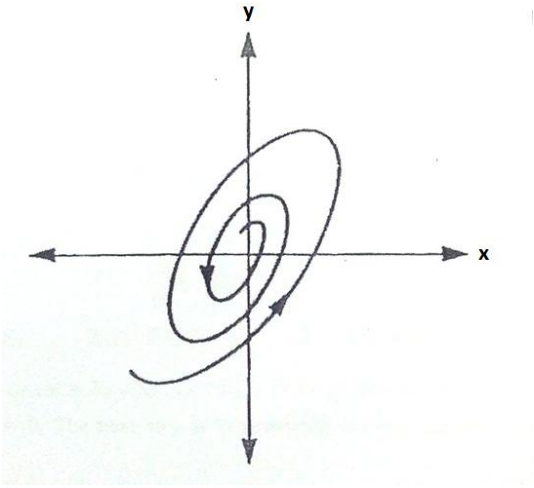

Figure 2.7: A stable spiral node [7].

c) If $a^2 < 4b$ and $a = 0$, which is the eigenvalues of J are purely imaginary, then the critical point will be a center.

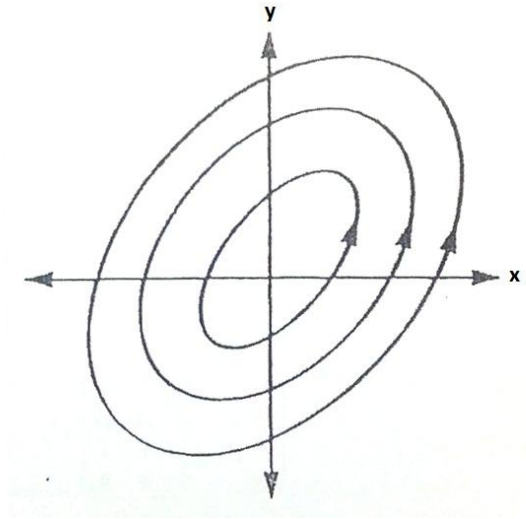

Figure 2.8: A neutral center [7].

In this section we apply some of the above ideas to systems of $n(> 2)$ equations.

Consider $\frac{dX_i}{dt} = f_i(X_1, X_2, ..., X_3)$ where $(i = 1, 2, ..., k)$ or, better still, the vector notation

$$\frac{dX}{dt} = F(X) \tag{2.9}$$

for $X = (X1, X2, ..., X_k); F = (f_1, f_2, ..., f_k)$ where each of the function f_i may depend on all or some $X_1, X_2, ..., X_k$. The equilibrium state, $\bar{X}$, is obtained by solving $F(X) = 0$. The next step is to determine stability properties of this steady solution;

In linearizing equation (2.9) we find the Jacobian of F(X), obtaining

$$J = \frac{\partial}{\partial X} F(X) \tag{2.10}$$

where J is now a $k \times k$ matrix. The eigenvalues λ of the matrix now satisfy

$\det(J - \lambda I) = 0$ [5]. We obtain a characteristic equation in the form

$$\lambda^k + a_1\lambda^{k-1} + \cdots + a_k = 0. \tag{2.11}$$

Theorem 2.2. *(Routh-Hurwitz criteria for local asymptotic stability)*

Given the characteristic equation (2.11), where the coefficients a_i are real constants, i=1, 2, 3, ..., k, define the n Hurwitz matrices using the coefficients a_i of the characteristic equation:

$$H_1 = (a_1), H_2 = \begin{pmatrix} a_1 & 1 \\ a_3 & a_2 \end{pmatrix}, H_3 = \begin{pmatrix} a_1 & 1 & 0 \\ a_3 & a_2 & a_1 \\ a_5 & a_4 & a_3 \end{pmatrix},$$

$$H_k = \begin{pmatrix} a_1 & 1 & 0 & 0 & \cdots & 0 \\ a_3 & a_2 & a_1 & 1 & \cdots & 0 \\ a_5 & a_4 & a_3 & a_2 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \cdots & \vdots \\ 0 & 0 & 0 & 0 & \cdots & a_k \end{pmatrix},$$

where $a_j = 0$ if $j > k$. Then all eigenvalues have negative real part: that is, the steady state $\bar{N}$ is stable if and only if the determinant of all H are positive [2]:

$$\det H_j > 0, j = 1, 2, ..., k.$$

When $k = 2$, Routh-Hurwitz criteria simplify to $\det H_1 = a_1 > 0$ and

$$\det H_2 = det \begin{pmatrix} a_1 & 1 \\ 0 & a_2 \end{pmatrix} = a_1 a_2 > 0$$

or $a_1 > 0$ and $a_2 > 0$. For polynomials of degree $k = 2, 3, 4$ and 5, the Routh-Hurwitz criteria are summarized.

Routh-Hurwitz criteria for $k = 2, 3, 4$ and 5,

$k = 2 : a_1 > 0$ and $a_2 > 0$.

$k = 3 : a_1 > 0, a_3 > 0$ and $a_1 a_2 > a_3$.

$k = 4 : a_1 > 0, a_3 > 0, a_4 > 0$ and $a_1 a_2 a_3 > a_3^2 + a_1^2 a_4$.

$k = 5 : a_i > 0, i = 1, 2, 3, 4, 5, a_1 a_2 a_3 > a_3^2 + a_1^2 a_4$ and

$$(a_1 a_4 - a_5)(a_1 a_2 a_3 - a_3^2 - a_1^2 a_4) > a5(a_1 a_2 - a_3)^2 + a_1 a_5^2 \text{ [2]}.$$

In the next chapter, the theorem discussed in this chapter will be applied to our model in order to derive explicit conditions on the system of parameter, which identify different dynamical behavior exhibited by the system.

CHAPTER 3

Model Analysis

In this chapter, we construct the MA model by developing the work of White and Comiskey, Nyabadza and Hove-Musekwa. We begin the formulation of the model by dividing the host population (N) into 4 compartments [3], [16] that contain susceptible individuals (S), light drug users (I_1), hard drug users (I_2) and users under treatment (T). We assume that individuals who are released from treatment centers can be susceptible individuals. Also, light drug users can relapse to the class of susceptible individuals, because the people in I_1 stage can easily stop and recover form drug use without treatment. Since the treatment for drug users is not currently restricted to treatment centers, we assume that users under therapy can relapse to the class of light drug users or hard drug users.

The possible changes in the life of MA users can be tracked by the schematic representation in Figure 3.1

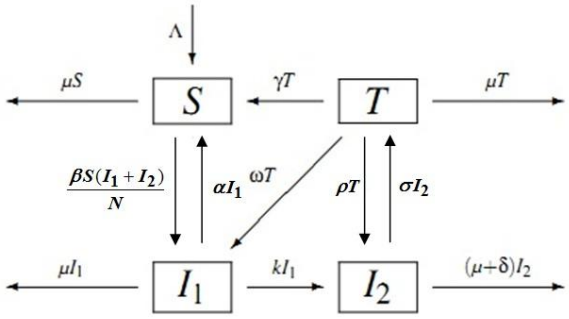

Figure 3.1: A model of methamphetamine epidemics.

Based on Figure 3.1, the time rate of change of any state is equal to the number entering into the state minus the number leaving the state [5]. The model is mathematically described by the following set of equations;

$$\frac{dS}{dt} = \Lambda + \alpha I_1 + \gamma T - \frac{\beta S(I_1 + I_2)}{N} - \mu S \tag{3.1}$$

$$\frac{dI_1}{dt} = \frac{\beta S(I_1 + I_2)}{N} + \omega T - (\alpha + \mu + k)I_1 \tag{3.2}$$

$$\frac{dI_2}{dt} = kI_1 + \rho T - (\mu + \delta + \sigma)I_2 \tag{3.3}$$

$$\frac{dT}{dt} = \sigma I_2 - (\rho + \omega + \gamma + \mu)T, \tag{3.4}$$

where all parameters in the model are assumed to be positive;

Λ is the rate of individuals entering the susceptible population.

μ is the natural death rate of the general population.

α is the rate of light drug user relapsing to the class of susceptible individuals.

k is progression rate to addiction.

δ is the death rate caused by drug use.

σ is the uptake rate into treatment programs.

ρ is the rate of drug users in treatment relapsing to hard MA users.

γ is the rate of drug users in treatment relapsing to susceptible individuals.

ω is the rate of drug users in treatment relapsing to light MA users.

Furthermore, the transmission rate, $\frac{\beta S(I_1 + I_2)}{N}$ is the rate which susceptible individuals become addicted by the inducement from light MA users or hard MA users, where $\beta = \eta\varphi$ [5] and $\frac{\eta}{N}$ is a probability that I_1 and I_2 encounter S and S become I_1 with the rate φ.

In this study, the following assumptions were made to simplify the development of the model:

1. The population is assumed to be of constant size within the modeling time period, that is $N = S + I_1 + I_2 + T$.

Since $\frac{dN}{dt} = \frac{dS}{dt} + \frac{dI_1}{dt} + \frac{dI_2}{dt} + \frac{dT}{dt} = \Lambda - \mu(S + I_1 + I_2 + T) - \delta I_2 = 0$.

Then $\Lambda = \mu(S + I_1 + I_2 + T) + \delta I_2$.

2. A hard MA user must have previously been a light MA user [16].

3. The treatment for drug users is not currently restricted to treatment centers.

4. Users under treatment can relapse to the class of light drug users or hard drug users.

5. All members of the population are assumed to be equally susceptible to drug addiction.

3.1 The Steady State Solutions

A steady state is a situation in which the system does not appear to undergo any change. Since $N = S + I_1 + I_2 + T$ is constant, we introduce the fractions of S, I_1, I_2 and T:

$$\bar{S} = \frac{S}{N},\ \bar{I}_1 = \frac{I_1}{N},\ \bar{I}_2 = \frac{I_2}{N},\ \bar{T} = \frac{T}{N}.$$

The domain of solutions is

$$\Omega = \{(\bar{S}, \bar{I}_1, \bar{I}_2, \bar{T}) | 0 \leq \bar{S} \leq 1, 0 \leq \bar{I}_1 \leq 1, 0 \leq \bar{I}_2 \leq 1, 0 \leq \bar{T} \leq 1\}.$$

Therefore $\bar{S} = 1 - \bar{I}_1 - \bar{I}_2 - \bar{T}$, and hence $\frac{d\bar{S}}{dt} = -\left(\frac{d\bar{I}_1}{dt} + \frac{d\bar{I}_2}{dt} + \frac{d\bar{T}}{dt}\right)$. The set of

dynamic equations is reduced from four equations to three equations

$$\frac{d\bar{I}_1}{dt} = \beta(1 - \bar{I}_1 - \bar{I}_2 - \bar{T})(\bar{I}_1 + \bar{I}_2) + \omega\bar{T} - (\alpha + \mu + k)\bar{I}_1 \tag{3.5}$$

$$\frac{d\bar{I}_2}{dt} = k\bar{I}_1 + \rho\bar{T} - (\mu + \delta + \sigma)\bar{I}_2 \tag{3.6}$$

$$\frac{d\bar{T}}{dt} = \sigma\bar{I}_2 - (\rho + \omega + \gamma + \mu)\bar{T}. \tag{3.7}$$

Let $E^* = (I_1^*, I_2^*, T^*)$ be an equilibrium point of the system $(3.5) - (3.7)$. Then setting the left hand side of the equations to zero

$$\beta(1 - I_1^* - I_2^* - T^*)(I_1^* + I_2^*) + \omega T^* - (\alpha + \mu + k)I_1^* = 0 \tag{3.8}$$

$$kI_1^* + \rho T^* - (\mu + \delta + \sigma)I_2^* = 0 \tag{3.9}$$

$$\sigma I_2^* - (\rho + \omega + \gamma + \mu)T^* = 0, \tag{3.10}$$

we obtain

$$I_2^* = \frac{(\rho + \omega + \gamma + \mu)T^*}{\sigma}.$$

For I_1^*, we have

$$I_1^* = \frac{[(\mu + \delta + \sigma)(\rho + \omega + \gamma + \mu) - \sigma\rho]\, T^*}{k\sigma}.$$

Let $m = \mu + \delta + \sigma, n = \rho + \omega + \gamma + \mu$ and $q = \alpha + \mu + k$.

T^* is calculated by

$$\left[\beta\left[1 - \frac{(mn - \sigma\rho)T^*}{k\sigma} - \frac{nT^*}{\sigma} - T^*\right]\left[\frac{(mn - \sigma\rho)}{k\sigma} + \frac{n}{\sigma}\right] + \omega - \left[\frac{q(mn - \sigma\rho)}{k\sigma}\right]\right] T^* = 0. \tag{3.11}$$

In order to simplify (3.11), we let $v = \dfrac{(mn - \sigma\rho)}{k\sigma}$.

One of the solutions from equation (3.11) is $T^* = 0$. This solution yields the drug free state (0, 0, 0) which is labeled as E_0^*. If $T^* \neq 0$, we have

$$T^* = \frac{[\beta(v\sigma + n) - (qv - \omega)\sigma]\,\sigma}{(v\sigma + n)(v\sigma - n - \sigma)\beta}.$$

For our convenience, we set $x = \dfrac{\beta(v\sigma + n) - (qv - \omega)\sigma}{(v\sigma + n)(v\sigma - n - \sigma)\beta}$.

Thus, we have

$$I_2^* = \frac{(\rho + \omega + \gamma + \mu)T^*}{\sigma} = \frac{nT^*}{\sigma} = nx,$$
$$I_1^* = \frac{[(\mu + \delta + \sigma)(\rho + \omega + \gamma + \mu) - \sigma\rho]\,T^*}{k\sigma} = vT^* = \sigma vx.$$

Hence, there are two equilibrium points for this system, namely:

1) Drug Free Equilibrium: $E_0^* = (I_1^*, I_2^*, T^*) = (0, 0, 0)$.

2) Endemic Equilibrium: $E_1^* = (I_1^*, I_2^*, T^*) = (\sigma vx, nx, \sigma x)$.

3.2 Stability of the Drug Free Equilibrium

For the linearized system of (3.5) − (3.7), we obtain the following Jacobian matrix at an equilibrium point

$$J(I_1^*, I_2^*, T^*) = \begin{pmatrix} \beta(1 - 2I_1^* - 2I_2^* - T^*) - q & \beta(1 - 2I_1^* - 2I_2^* - T^*) & -\beta(I_1^* + I_2^*) + \omega \\ k & -m & \rho \\ 0 & \sigma & -n \end{pmatrix}.$$

At the drug free state $E_0^* = (0, 0, 0)$, we obtian

$$J(0,0,0) = \begin{pmatrix} \beta - q & \beta & \omega \\ k & -m & \rho \\ 0 & \sigma & -n \end{pmatrix}.$$

The characteristic equation is $\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$, where

$$a_1 = -\text{trace}(J(0,0,0)) = q - \beta + m + n,$$

$$a_2 = \begin{vmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{vmatrix} + \begin{vmatrix} a_{11} & a_{13} \\ a_{31} & a_{33} \end{vmatrix} + \begin{vmatrix} a_{22} & a_{23} \\ a_{32} & a_{33} \end{vmatrix} = q(m+n) + mn - \beta(m+n+k) - \sigma\rho,$$

$$a_3 = -\det(J(0,0,0)) = \beta(\sigma\rho - mn - kn) + mnq - k\sigma\omega - \sigma\rho q.$$

From Routh-Hurwitz criteria, see [2], for $k = 3$: we need $a_1 > 0, a_3 > 0$ and $a_1 a_2 > a_3$, so

$a_1 > 0;\ q - \beta + m + n > 0,$

$a_3 > 0;\ \beta(\sigma\rho - mn - kn) + mnq - k\sigma\omega - \sigma\rho q > 0$ and

$a_1 a_2 > a_3;\ (q-\beta+m+n)[q(m+n)-\beta(m+n+k)+mn-\sigma\rho] > \beta(\sigma\rho-mn-kn)+$

$mnq - k\sigma\omega - \sigma\rho q.$

If a_1, a_2 and a_3 satisfy the Routh-Hurwitz criteria, the steady state will be stable.

3.3 The Basic Reproduction Number for the Model

A value for R_0, the basic reproduction number, is then proposed for this system. This number tells us how many secondary infections will result from

the introduction of one infected individual into a susceptible population. Usually, if $R_0 < 1$, then each infected individual in its entire period of infectivity will produce less than one infected individual on average. The drug free equilibrium is locally asymptotically stable, thus an epidemic will not result from the introduction of one infected individual in this case. On the other hand $R_0 > 1$ implies that each infected individual, who has contact with susceptible individuals, in its entire infective period will produce more than one infected individual on average, thus epidemic will occur. The final case, $R_0 = 1$ means that each infected person will infect one susceptible person [18].

We use the fact that $R_0 < 1$ is equivalent to the condition that the real parts of all eigenvalues of the Jacobian at the drug-free equilibrium (0, 0, 0) must be negative, and that $R_0 > 1$ is equivalent to the condition that the real part of at least one eigenvalue is positive.

The relationship with the characteristic polynomial $p(\lambda) = \det(\lambda I - J(0, 0, 0))$ is that

$$p(\lambda) = (\lambda - \lambda_1)(\lambda - \lambda_2)(\lambda - \lambda_3).$$

Expanding out, we found that

1. trace$(J) = \lambda_1 + \lambda_2 + \lambda_3$ and therefore stability requires trace$(J) < 0$. Since trace(J) is the sum of diagonal elements of J, this gives the condition $\beta < q+m+n$, which is the first Routh-Hurwitz condition for asymptotic stability.

2. -det$(J) = \lambda_1\lambda_2\lambda_3 = \beta(\sigma\rho - mn - kn) + mnq - k\sigma\omega - \sigma\rho q > 0$. This is equivalent to the second Routh Hurwitz condition for local stability.

This last condition can then be rewritten in the form

$$\begin{aligned}\beta\sigma\rho + mnq &> \beta n(k+m) + \sigma\rho q + k\sigma\omega \\ 1 &> \frac{\beta n(k+m) + \sigma\rho q + k\sigma\omega}{\beta\sigma\rho + mnq} \\ R_0 &= \frac{\beta n(k+m) + \sigma\rho q + k\sigma\omega}{\beta\sigma\rho + mnq}\end{aligned}$$

and the determinant is

$$\det(J) = (\beta\sigma\rho + qmn)(R_0 - 1).$$

3.4 Endemic Equilibrium

At the endemic state $E_1^* = (\sigma vx, nx, \sigma x)$

$$J(\sigma vx, nx, \sigma x) = \begin{pmatrix} \beta(1-2\sigma vx - 2nx - \sigma x) - q & \beta(1-2\sigma vx - 2nx - \sigma x) & -\beta(\sigma vx + nx) + \omega \\ k & -m & \rho \\ 0 & \sigma & -n \end{pmatrix}.$$

The characteristic equation is $\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$, where

$$a_1 = -\text{trace}(J(\sigma vx, nx, \sigma x)) = q + m + n - \beta(1 - 2\sigma vx - 2nx - \sigma x),$$

$$a_2 = \begin{vmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{vmatrix} + \begin{vmatrix} a_{11} & a_{13} \\ a_{31} & a_{33} \end{vmatrix} + \begin{vmatrix} a_{22} & a_{23} \\ a_{32} & a_{33} \end{vmatrix}$$

$$= q(m+n) - \beta\left(1 - 2\sigma vx - 2nx - \sigma x\right)(m+n+k) + mn - \sigma\rho,$$

$$a_3 = -\det(J(\sigma vx, nx, \sigma x)) = \beta\,(1 - 2\sigma vx - 2nx - \sigma x)\,(\sigma\rho - mn - kn) + mnq - k\sigma\omega - \sigma\rho q.$$

From Routh-Hurwitz criteria, for $k = 3$: we need $a_1 > 0, a_3 > 0$ and $a_1 a_2 > a_3$, so

$a_1 > 0;\ q - \beta\,(1 - 2\sigma vx - 2nx - \sigma x) + m + n > 0,$

$a_3 > 0;\ \beta\,(1 - 2\sigma vx - 2nx - \sigma x)\,(\sigma\rho - mn - kn) + mnq - k\sigma\omega - \sigma\rho q > 0$ and

$a_1 a_2 > a_3;\ \ [q - \beta\,(1 - 2\sigma vx - 2nx - \sigma x) + m + n]$

$$[q(m+n) - \beta\,(1 - 2\sigma vx - 2nx - \sigma x)\,(m + n + k) + mn - \sigma\rho] >$$

$$\beta(\sigma\rho - mn - kn)\,(1 - 2\sigma vx - 2nx - \sigma x) + mnq - k\sigma\omega - \sigma\rho q.$$

Since R_0 is a unique threshold parameter, which use to determine the behaviors of the system. Therefore, if $R_0 < 1$; it means that the drug free equilibrium point is stable. On the other hand, if $R_0 > 1$; the endemic equilibrium point occurs and is stable.

CHAPTER 4

Numerical Results and Discussion

In this chapter, we present the numerical results from solving equation (3.5) to (3.7) for some sets of the parameter values in order to verify the theorems presented in the previous chapters. We use MATLAB program to determine the behavior of the solutions. Moreover, the Runge-Kutta 4th order is used in order to obtain the solutions.

Figures 4.1 – 4.5 illustrate the typical behavior of the susceptible individuals, light drug users, hard drug users and users under treatment when $R_0 < 1$. As we see, the drug free state occurs when the rate which susceptible individuals become addicted by the inducement from light MA users or hard MA users ($\beta = 0.00005$) is small. We observe in this case that light drug users, hard drug users and users under treatment proportions decline exponentially to zero.

Figures 4.8 – 4.12 illustrate the typical behavior of the susceptible individuals, light drug users, hard drug users and users under treatment when $R_0 < 1$. The endemic state occurs when the rate which susceptible individuals become addicted by the inducement from light MA users or hard MA users ($\beta = 0.05$) is high. We approach the endemic equilibrium point $I_1^* = 0.256$, $I_2^* = 0.307$ and $T^* = 0.304$.

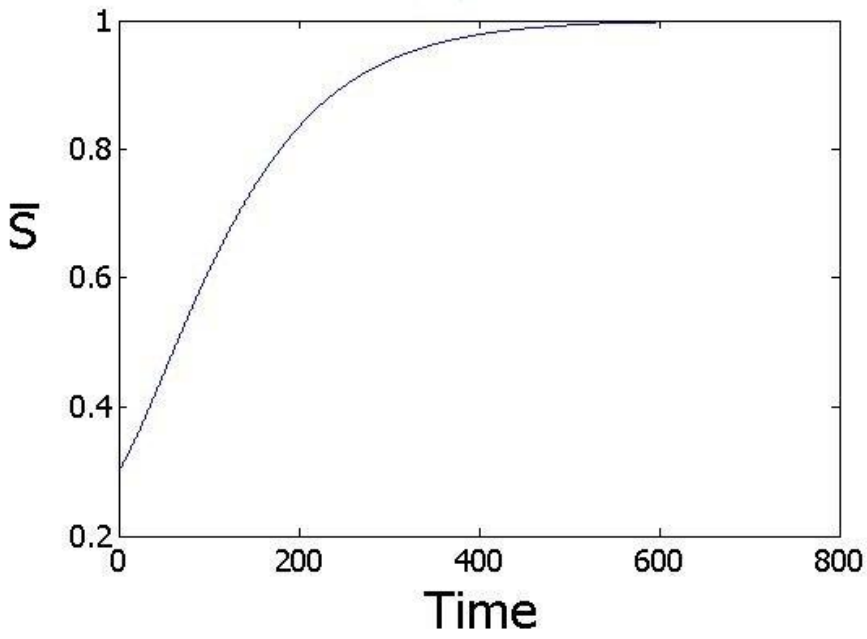

Figure 4.1: Numerical solution of model (3.5) – (3.7) demonstrates the time series of $\bar{S}$ where the parameters are: $\beta = 0.00005$, $\alpha = 0.005$, $\mu = 0.00023$, $k = 0.0095$, $\delta = 0.0006$, $\sigma = 0.0153$, $\rho = 0.0083$, $\gamma = 0.00425$, $\omega = 0.00011$. The proportion of susceptible individuals approach to drug free state.

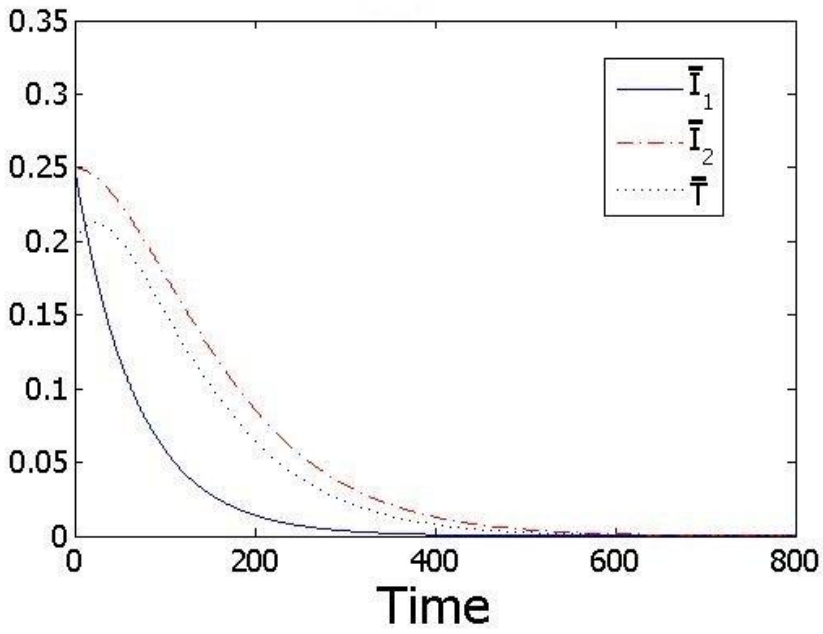

Figure 4.2: Numerical solution of model (3.5) – (3.7) demonstrates the time series of $\bar{I}_1$, $\bar{I}_2$ and $\bar{T}$ where the parameters are: $\beta = 0.00005$, $\alpha = 0.005$, $\mu = 0.00023$, $k = 0.0095$, $\delta = 0.0006$, $\sigma = 0.0153$, $\rho = 0.0083$, $\gamma = 0.00425$, $\omega = 0.00011$. The proportion of light drug users, hard drug users and users under treatment approach to drug free state.

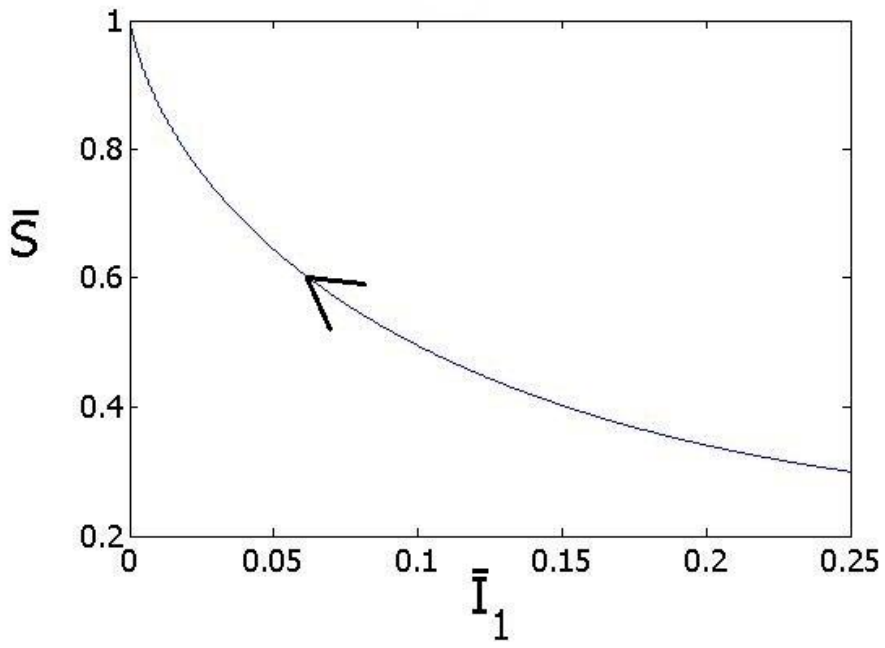

Figure 4.3: Numerical solution of model (3.5) – (3.7) demonstrates the solution trajectory, projected onto the ($\bar{I}_1$, $\bar{S}$) – plane where the parameters are: $\beta = 0.00005$, $\alpha = 0.005$, $\mu = 0.00023$, $k = 0.0095$, $\delta = 0.0006$, $\sigma = 0.0153$, $\rho = 0.0083$, $\gamma = 0.00425$, $\omega = 0.00011$.

From this figure, we consider the phase plane plot of susceptible individuals and light MA users proportions. We found that susceptible individuals proportion is increase to one. Conversely, light MA users proportion decline exponentially to zero, since the drug free state occur.

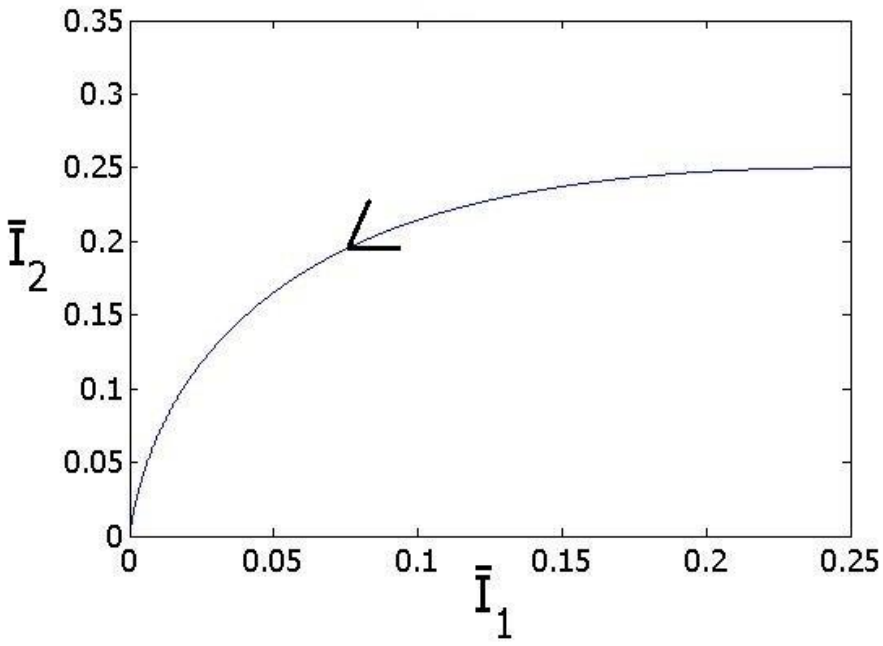

Figure 4.4: Numerical solution of model (3.5) – (3.7) demonstrates the solution trajectory, projected onto the $(\bar{I}_1,\ \bar{I}_2)$ – plane where the parameters are: $\beta = 0.00005$, $\alpha = 0.005$, $\mu = 0.00023$, $k = 0.0095$, $\delta = 0.0006$, $\sigma = 0.0153$, $\rho = 0.0083$, $\gamma = 0.00425$, $\omega = 0.00011$.

From this figure, we consider the phase plane plot of light MA users and hard MA users proportions. We observe that the light MA users and hard MA users proportions tend toward to zero, since the drug free state occur.

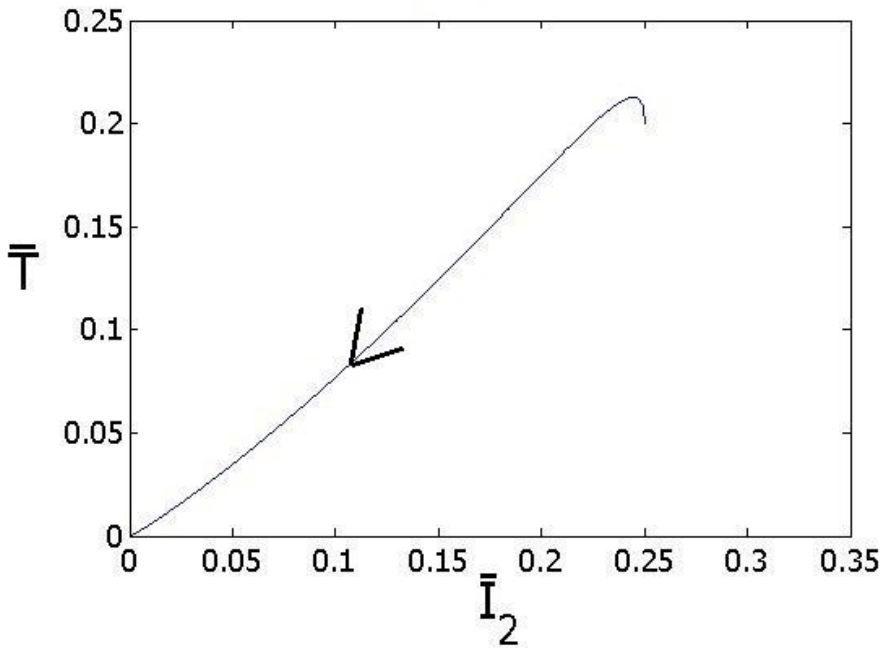

Figure 4.5: Numerical solution of model (3.5) – (3.7) demonstrates the solution trajectory, projected onto the $(\bar{I}_2, \bar{T})$ – plane where the parameters are: $\beta = 0.00005$, $\alpha = 0.005$, $\mu = 0.00023$, $k = 0.0095$, $\delta = 0.0006$, $\sigma = 0.0153$, $\rho = 0.0083$, $\gamma = 0.00425$, $\omega = 0.00011$.

From this figure, we consider the phase plane plot of hard MA users and users under treatment proportions. We observe that the hard MA users and users under treatment proportions decline exponentially to zero, since the drug free state occur.

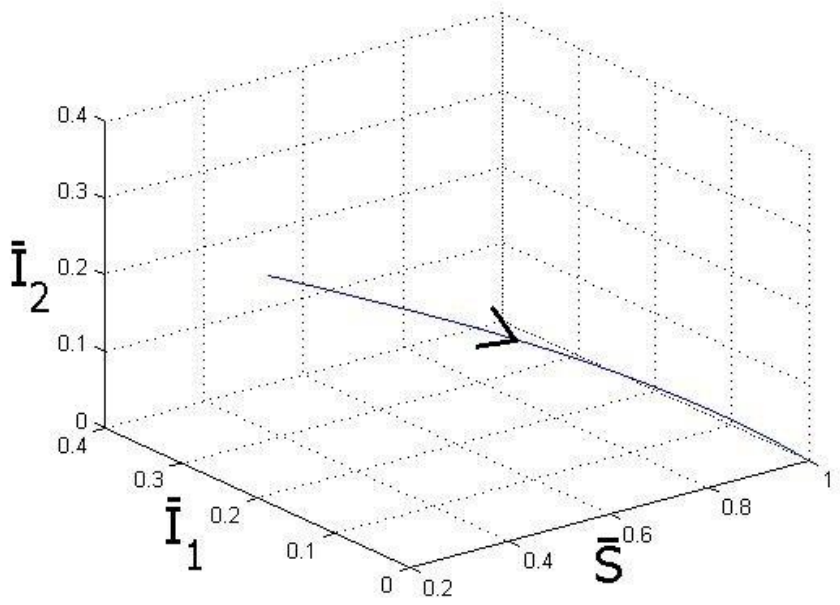

Figure 4.6: Computer simulation of model system (3.5) – (3.7) with parametric values as Figure (4.1) – (4.5). The solution trajectory, projected onto the ($\bar{S}$, $\bar{I}_1$, $\bar{I}_2$) – plane.

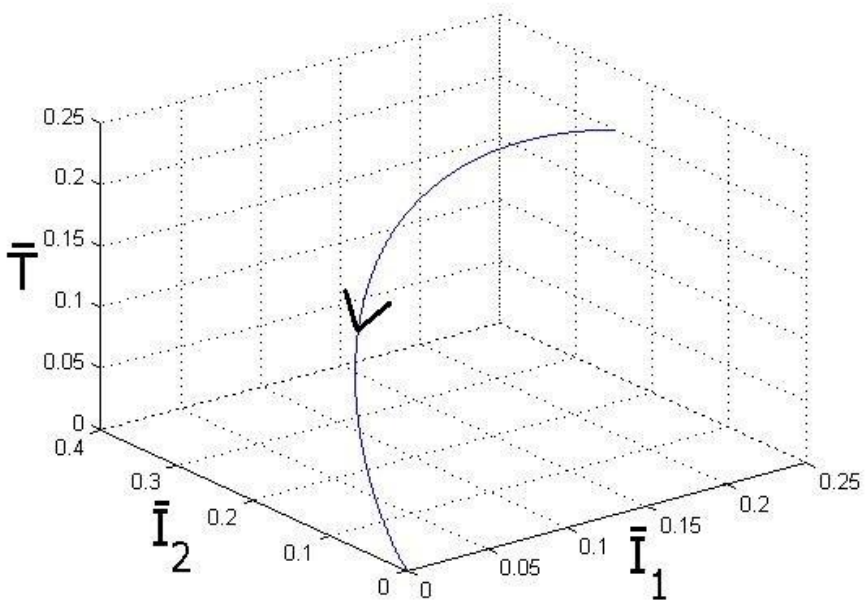

Figure 4.7: Computer simulation of model system (3.5) – (3.7) with parametric values as Figure (4.1) – (4.5). The solution trajectory, projected onto the ($\bar{I}_1$, $\bar{I}_2$, $\bar{T}$) – plane.

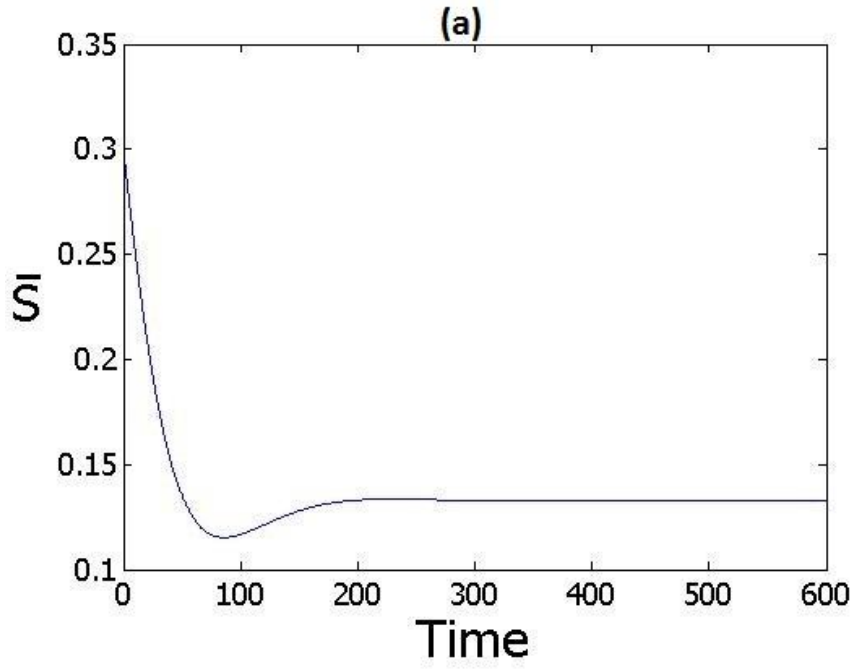

Figure 4.8: Numerical solution of model (3.5) – (3.7) demonstrates the time series of $\bar{S}$ where the parameters are: $\beta = 0.05$, $\alpha = 0.005$, $\mu = 0.00023$, $k = 0.0095$, $\delta = 0.0006$, $\sigma = 0.0153$, $\rho = 0.0083$, $\gamma = 0.00425$, $\omega = 0.00011$. The proportion of susceptible individuals approach to endemic state.

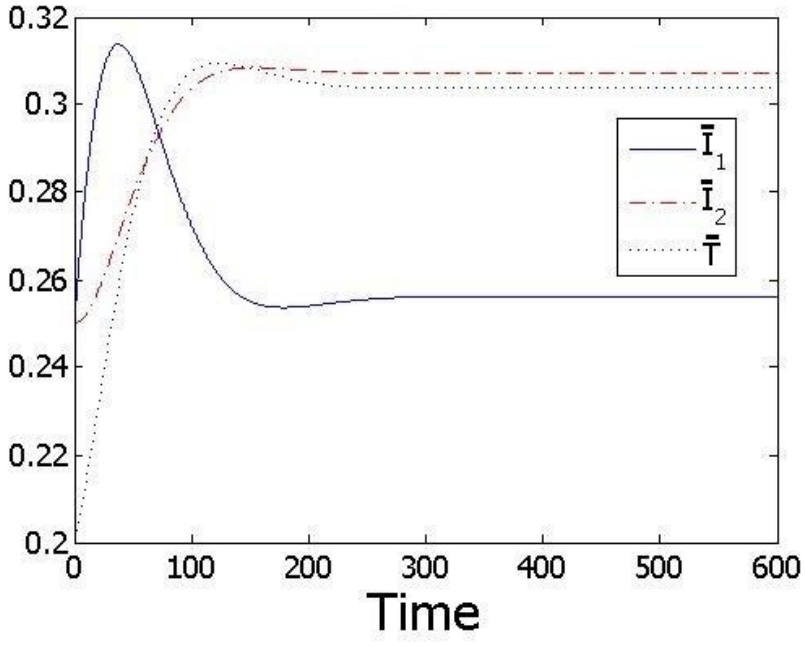

Figure 4.9: Numerical solution of model (3.5) – (3.7) demonstrates the time series of $\bar{I}_1$, $\bar{I}_2$ and $\bar{T}$ where the parameters are: $\beta = 0.05$, $\alpha = 0.005$, $\mu = 0.00023$, $k = 0.0095$, $\delta = 0.0006$, $\sigma = 0.0153$, $\rho = 0.0083$, $\gamma = 0.00425$, $\omega = 0.00011$. The proportion of light drug users, hard drug users and users under treatment approach to endemic state.

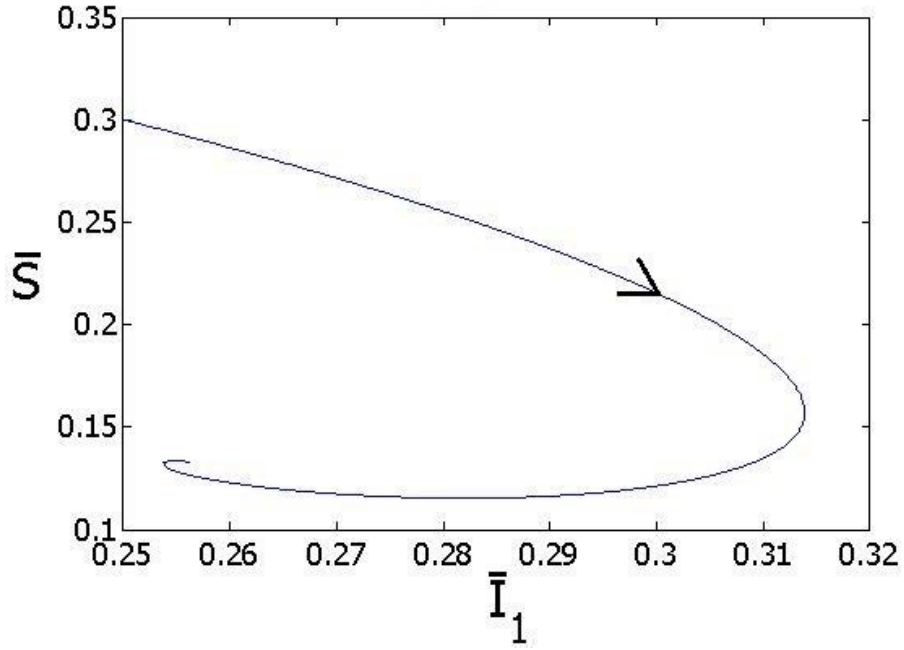

Figure 4.10: Numerical solution of model (3.5) – (3.7) demonstrates the solution trajectory, projected onto the $(\bar{I}_1, \bar{S})$ – plane where the parameters are: $\beta = 0.05$, $\alpha = 0.005$, $\mu = 0.00023$, $k = 0.0095$, $\delta = 0.0006$, $\sigma = 0.0153$, $\rho = 0.0083$, $\gamma = 0.00425$, $\omega = 0.00011$.

From this figure, we consider the phase plane plot of susceptible individuals and light MA users proportions in endemic state. We found that susceptible individuals proportion is decrease since they become addiction and reach to I_1 state. While the light MA users proportion is increase in first interval of time, and decrease in next interval of time because the light MA users progress addiction and become to I_2 state. Finally, we can see that both proportions tend toward the equilibrium point $\bar{S} = 0.133$ and $\bar{I}_1 = 0.256$.

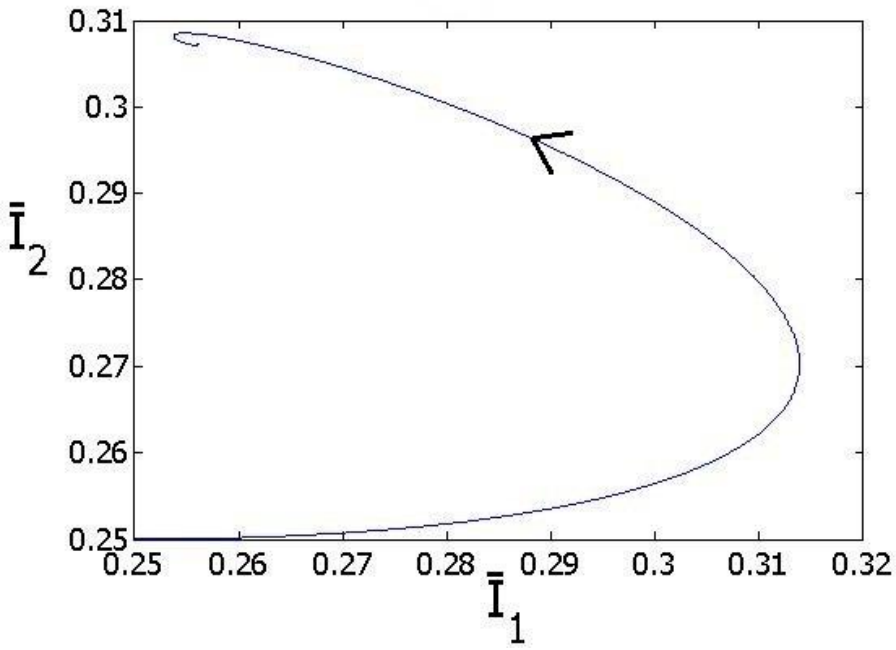

Figure 4.11: Numerical solution of model (3.5) – (3.7) demonstrates the solution trajectory, projected onto the $(\bar{I}_1, \bar{I}_2)$ – plane where the parameters are: $\beta = 0.05$, $\alpha = 0.005$, $\mu = 0.00023$, $k = 0.0095$, $\delta = 0.0006$, $\sigma = 0.0153$, $\rho = 0.0083$, $\gamma = 0.00425$, $\omega = 0.00011$.

From this figure, we consider the phase plane plot of light MA users and hard MA users proportions in endemic state. We observe that in this case the light drug users proportion is increase in first interval of time, and decrease in next interval of time since light MA users progress addiction and become to I_2 state. As the hard drug users proportion is increase because I_1 entering I_2 state and the users under therapy relapse to I_2 state. Finally, we can see that both proportions tend toward the equilibrium point $\bar{I}_1 = 0.256$ and $\bar{I}_2 = 0.307$.

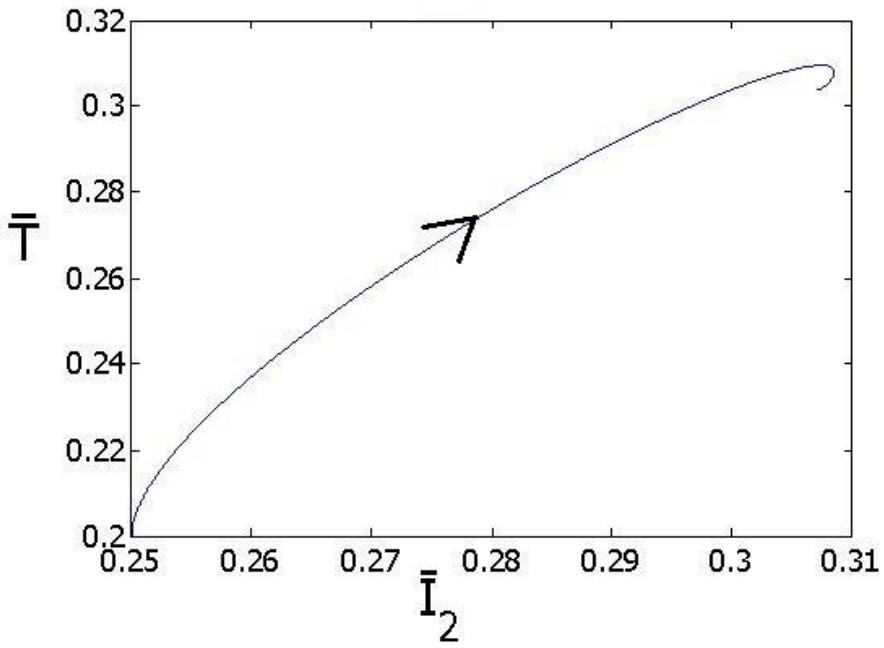

Figure 4.12: Numerical solution of model (3.5) – (3.7) demonstrates the solution trajectory, projected onto the $(\bar{I}_2, \bar{T})$ – plane where the parameters are: $\beta = 0.05$, $\alpha = 0.005$, $\mu = 0.00023$, $k = 0.0095$, $\delta = 0.0006$, $\sigma = 0.0153$, $\rho = 0.0083$, $\gamma = 0.00425$, $\omega = 0.00011$.

From this figure, we consider the phase plane plot of hard MA users and users under treatment proportions in endemic state. We observe that in this case both proportions is increase since the endemic state occur. Finally, $\bar{I}_2$ is decrease since the death caused by drug use and the uptake of them into treatment programs. Similarly, $\bar{T}$ is decrease because the individuals who are released from treatment center can be the susceptible individuals and the users under therapy relapse to I_2 state. We can see that both proportions tend toward the equilibrium point $\bar{I}_2 = 0.307$ and $\bar{T} = 0.304$.

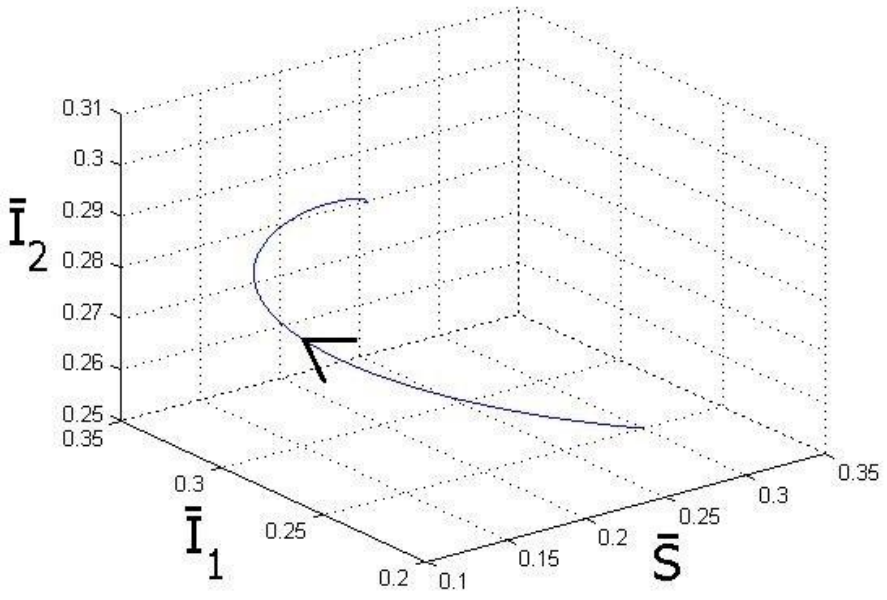

Figure 4.13: Computer simulation of model system (3.5) – (3.7) with parametric values as Figure (4.8) – (4.12). The solution trajectory, projected onto the ($\bar{S}$, $\bar{I}_1$, $\bar{I}_2$) – plane.

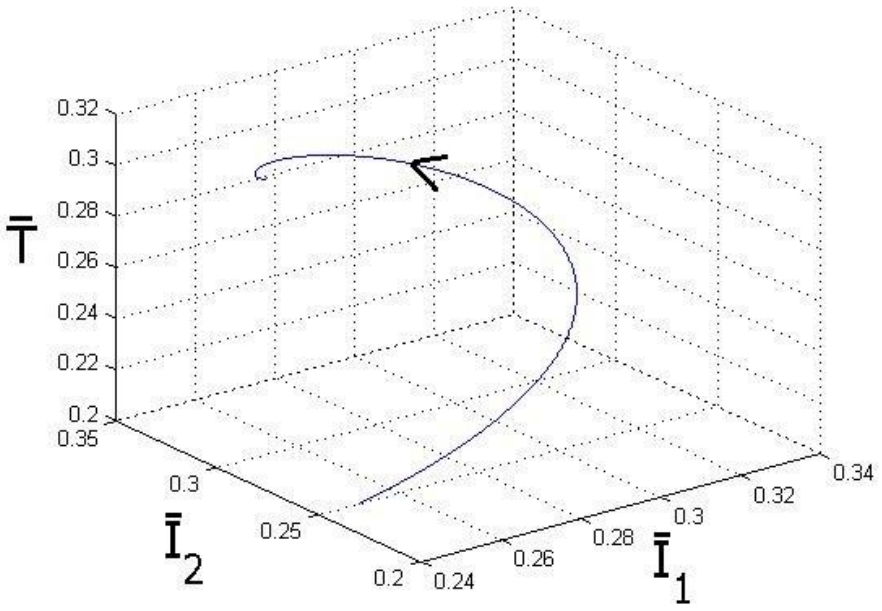

Figure 4.14: Computer simulation of model system (3.5) – (3.7) with parametric values as Figure (4.8) – (4.12). The solution trajectory, projected onto the ($\bar{I}_1$, $\bar{I}_2$, $\bar{T}$) – plane.

CHAPTER 5

Conclusion

We have developed the MA model which is more realistic than the previously studied models. Unlike the work of Nyabadza and Hove-Musekwa, in our model, the light MA users (I_1) can relapse to be susceptible (S) or become hard MA users (I_2). Moreover, the population under therapy (T) can relapse to be in I_1, I_2 or S stages.

We examined the existence of the equilibrium state in the model. There exists a threshold parameter, the basic reproductive number (R_0), for which the drug free will persevere if and only if R_0 exceeds one. The drug free state exists and is locally stable if R_0 is less than one and becomes unstable when $R_0 > 1$. We demonstrate that the drug free state is locally stable when $R_0 \leq 1$ through the use of numerical simulation. As we see, the drug free state occurs when the rate which susceptible individuals become addicted by the inducement from light MA users or hard MA users ($\beta = 0.00005$) is small. We observe in this case that light drug users, hard drug users and users under treatment proportions decline exponentially to zero. For $R_0 > 1$, the endemic state occurs when the rate which susceptible individuals become addicted by the inducement from light MA users or hard MA users ($\beta = 0.05$) is high. We approach the endemic equilibrium point $I_1^* = 0.256$, $I_2^* = 0.307$ and $T^* = 0.304$. We find that there is endemic stable state which is locally and asymptotically stable. Numerical simulation confirmed this

result.

The latter behavior can also be explained in terms of R_0. If this number is less than or equal to one, so that an addiction replace itself with less than one new addiction, the MA users die out. Furthermore, the susceptible individuals proportion approaches one since everyone is susceptible when the MA users has vanished [11]. On the other hand, if $R_0 > 1$, the susceptible population decreases. The normalized MA users and population under treatment however first increase to a peak and then decreases. This subsequent behavior occurs because there are not sufficient enough susceptible population to be addictive and for the MA users to move into the treatment state.

In this research, we assume that the people in a recovery stage are still in a treatment stage, since it is easier to analyze the steady state. In the future work, the recovery stage should be separated from the treatment stage in order to make our to be more accurate.

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APPENDIX

A. Numerical Solution of Differential Equations

Mathematical models have been applied in many fields such as in biology, physics and engineering. They would like to know the relationships that illustrate how both the variables and their rates of change for example derivatives, affect each other.

For an ordinary differential equation involving one or more physical quantities, the problem of interest is to find the relationship it imposes upon the variables themselves for instance to find its solution. Many techniques are available for the approximate solutions of the ordinary differential equation.

Numerical methods for differential equation are of vast importance to many fields of study including physics, chemistry, biology, medicine and economics since practical problems often lead to differential equations that can not be solved by direct method to get analytic solution.

In this thesis we use Runge - Kutta 4^{th} order method which is one of the most popular methods, and is particularly suitable in case when the computation of higher derivatives is complicated. It can be used for equations of arbitrary order by meant for a transformation to a system of first - order equations. We will discuss the solution of a system of 3 first - order equations.

Let this system be

$$\frac{dx}{dt} = f(x, y, t)$$

$$\frac{dy}{dt} = g(x, y, t)$$

$$\frac{dz}{dt} = h(x, y, t)$$

with initial values (x_0, y_0, z_0, t_0) and interval h.

Runge - Kutta 4^{th} order method for finding approximate values of x, y and z at each step is

$$x_{n+1} = x_n + \left(\frac{k_1 + 2k_2 + 2k_3 + k_4}{6}\right)$$
$$y_{n+1} = y_n + \left(\frac{l_1 + 2l_2 + 2l_3 + l_4}{6}\right)$$
$$z_{n+1} = z_n + \left(\frac{m_1 + 2m_2 + 2m_3 + m_4}{6}\right)$$

where

$k_1 = hf(x_n, y_n, z_n, t_n)$

$k_2 = hf(x_n + \frac{k_1}{2}, y_n + \frac{l_1}{2}, z_n + \frac{m_1}{2}, t_n + \frac{h}{2})$

$k_3 = hf(x_n + \frac{k_2}{2}, y_n + \frac{l_2}{2}, z_n + \frac{m_2}{2}, t_n + \frac{h}{2})$

$k_4 = hf(x_n + k_3, y_n + l_3, z_n + m_3, t_n + h).$

Runge - Kutta 4^{th} order method can be applied directly to a system of n first order differential equations.

B. Computer Program

```
function dudt = equ(u,t)
Alpha=0.005;
Gamma=0.00425;
Beta=—; use 0.00005 for Drug free state/use 0.05 for Endemic state
Mu=0.00023;
Omega=0.00011;
k=0.0095;
Rho=0.0083;
Delta=0.0006;
Sigma=0.0153;
dudt = [(Beta*(1-u(1)-u(2)-u(3))*(u(1)+u(2)) + Omega*u(3) - (Alpha+Mu+k)*u(1));
(k*u(1) + Rho*u(3) - (Mu+Delta+Sigma)*u(2));
(Sigma*u(1) - (Rho+Omega+Gamma+Mu)*u(3))];
```

```
function rkorders4
dt = 0.2;
t = 0:dt:800;
u = zeros(3,numel(t));
u(1,1) = 0.25;
u(2,1) = 0.25;
```

u(3,1) = 0.2;

for j = 2:numel(t)

$u\_ = u(:, j-1);$

$t\_ = t(j-1);$

$fa = equ(u\_, t\_);$

$fb = equ(u\_ + dt/2. * fa, t\_ + dt/2);$

$fc = equ(u\_ + dt/2. * fb, t\_ + dt/2);$

$fd = equ(u\_ + dt. * fc, t\_ + dt);$

$u(:, j) = u(:, j-1) + dt/6 * (fa + 2 * fb + 2 * fc + fd);$

end

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