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The Role Of The Incubation Period In A Disease Model*

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Abstract

The incubation period is defined as the time from exposure to onset of disease, i.e., it corresponds to the time from infection with a microorganism to symptom development. In this paper a mathematical model is proposed with three classes of population namely, susceptible, incubated and infected. The stability behavior of the trivial, disease free and endemic equilibrium states are studied and we observe that the instability of disease free state leads to the existence of the endemic state. The possibility of Hopf-bifurcation of the endemic equilibria is studied using the transfer rate from susceptible to incubated population as bifurcation parameter. Finally, a threshold value of bifurcation parameter is determined numerically.

1 Introduction

The mathematical study of epidemics has come up with an astonishing number of models with explanations for the spread and cause of epidemic outbreaks [1-9, 12]. The landmark book [6] has fascinating stories of the relation between diseases and people. It is a well established fact that the order of magnitude of deaths due to socioeconomic disease is more than anything else in the world. In recent years several studies have come up, which have not only explained various diseases due to socioeconomic aspects but gained triumphs for developing medicine [10, 11].

The appearance of new diseases and resurgence of old ones make the case for interdisciplinary involvement more pressing. Modelling the disease infections is gaining great interest in the study of epidemiology. The main object of modelling is to answer the role of infectious disease in regulating natural populations, i.e., decreasing their sizes and either reducing their natural fluctuations or causing destabilization of equilibrium positions into oscillations of the population states. In epidemiology, the population can be classified into two broad classes, viz., susceptible and infected class. The susceptible population is prone to infection and the infected population can transmit the infection to the susceptible one. In the S-I-S Models the total population size at

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any instant is $N = S+I$, where S is susceptible population and I is infected population at that instant.

As the simple $S - I - S$ model suggests, the population from the susceptible class joins or transfers to the infected class continuously. But in practice this process is not regular, in fact, it is in the case of any viral disease and many other disease. The susceptible individual stays for some definite period after leaving the susceptible class and joining the infected class, this intermediate period may be termed as incubation period. The incubation period is defined as the time from exposure to onset of disease and when limited to infectious disease, corresponds to the time from infection with a microorganism to symptom development [8].

During the incubation period of acute infections disease, which is subsequently followed by a symptomatic period, it should be noted that infected host can be infections. The incubation period of infectious disease offers various insights into clinical and public health practices, as well as it is important for epidemiological and ecological studies [8]. The incubation period is useful not only for making rough guesses so as to determine the causes and sources of infection of individual cases [1, 2, 6], but also for developing treatment strategies to extend the incubation period, for performing early projection of disease prognosis and when the incubation period is clearly associated with clinical severity due to dose response mechanism [2, 4, 5, 8].

Keeping in view of the above, in this paper we will study the role of the incubation period in a disease model by assuming as an intermediate class, namely the incubated population class between the susceptible and infected population classes. The organization of the paper is as follows. Section 2, describes a "susceptible $\rightarrow$ incubation $\rightarrow$ infection $\rightarrow$ susceptible" mathematical model. In section 3, we have studied the boundedness of the system. Finally, in section 4, the dynamical behavior (i.e., stability and Hopf-bifurcation) of the model studied both analytically and numerically.

2 The Mathematical Model

We consider the population density at any time t of the susceptible and infected (or diseased) population are $S(t)$ and $D(t)$ respectively. We also assume that there is no vertical transmission of the disease and the susceptible population is logistically growing with intrinsic growth rate r and carrying capacity K. Let b is the disease contact rate and δ is the rate of removal population from disease class and out of which γ fraction of infected population will rejoin in susceptible class. Then the dynamics of the "susceptible-infected" population is governed by following:

$$\frac{dS}{dt} = rS\left(1 - \frac{S}{K}\right) - bSD + \gamma D \tag{1}$$

$$\frac{dD}{dt} = bSD - \delta D \tag{2}$$

In our present study, we have considered that susceptible population instead of joining infected class directly, will now go through an intermediate class termed as incubated class. Keeping in view that the incubation period is defined as the time from exposure

to onset of disease, let us assume that the population density in that class is $I(t)$ at any instant of time t. Let α be the disease contact rate. γ_1 is the fraction of the diseased population recovery from disease that will again join to the susceptible class and β_1 is the fraction of incubated class population that will go to the diseased class. Again, let δ and β be the total removable population from diseased class and incubated class, which include death due to disease and natural death of incubated population respectively. Keeping in view of these assumptions, our population dynamic, i.e., "susceptible-incubated-infected-susceptible" is governed by the following set of differential equations:

$$\frac{dS}{dt} = rS\left(1 - \frac{S}{K}\right) - \alpha SD + \gamma_1 D \tag{3}$$

$$\frac{dI}{dt} = \alpha SD - \beta I \tag{4}$$

$$\frac{dD}{dt} = \beta_1 I - \delta D \tag{5}$$

where initial population, i.e., $S(0) > 0$, $I(0) > 0$ and $D(0) > 0$ and total population at any instant t is $N(t) = S(t) + I(t) + D(t)$.

Now, in the above system (3)-(5), use the following:

$$x = \frac{S}{K};\ y = \frac{I}{K};\ z = \frac{D}{K};\ \tau = rt,$$

to get the following re-scaled system:

$$\frac{dx}{d\tau} = x(1-x) - axz + cz \tag{6}$$

$$\frac{dy}{d\tau} = axz - dy \tag{7}$$

$$\frac{dz}{d\tau} = d_1 y - ez \tag{8}$$

where

$$a = \frac{\alpha K}{r};\ c = \frac{\gamma_1}{r};\ d = \frac{\beta}{r};\ d_1 = \frac{\beta_1}{r};\ e = \frac{\delta}{r}$$

and $x(0) > 0$, $y(0) > 0$ and $z(0) > 0$.

In the next section, we will study the existence of all possible steady states of the system and the boundedness of the solutions.

3 Existence of Equilibrium Points and Boundedness

There are three biologically feasible equilibria for the system (6)-(8), namely, (i) $E_0 = (0, 0, 0)$ is the trivial steady state; (ii) $E_1 = (1, 0, 0)$ is the disease free steady state and (iii) $E^* = (x^*, y^*, z^*)$ is endemic equilibrium state, where

$$x^* = \frac{de}{d_1 a};\ y^* = \frac{de^2(d_1 a - de)}{d_1^2 a^2 (de - d_1 c)} \text{ and } z^* = \frac{de(d_1 a - de)}{d_1 a^2 (de - d_1 c)}.$$

Further, it is clear form the above expression that $E^* \in R^3_+$, if $a > \frac{de}{d_1} > c$. Now we will show that all the solutions of the system (6)-(8) are bounded in a region $B \subset R^3_+$. We consider the following function

$$w(\tau) = x(\tau) + y(\tau) + z(\tau) \tag{9}$$

Then differentiating (6) with respect to τ and substituting the values from (6)-(8), we get

$$\frac{dw}{d\tau} = x(1-x) - (d-d_1)y - (e-c)z$$

If we choose a positive real number $\eta = \min\{d-d_1, e-c\}$, then

$$\frac{dw(\tau)}{d\tau} + \eta w(\tau) \leq x(1+\eta) - x^2 = f(x)$$

Again $f(x)$ is maximum at $x = (1+\eta)/2$ and hence $f(x) \leq M := (1+\eta)^2/4$. Hence

$$\dot{w}(\tau) + \eta w(\tau) \leq M.$$

Now, using comparison theorem, as $\tau \to \infty$, then

$$sup\ w(\tau) \leq \frac{M}{\eta}$$

Therefore,

$$0 \leq x(\tau) + y(\tau) + z(\tau) \leq \frac{M}{\eta}$$

and let us consider the set $B = \{(x,y,z) \in R^3_+ : 0 \leq x(\tau) + y(\tau) + z(\tau) \leq M/\eta\}$, hence we can state the following lemma:

LEMMA 1. The system (6)-(8) is uniformly bounded in the region $B \subset R^3_+$.

4 Dynamical Behavior of the System

We have already established that the system (6)-(8) has three equilibrium points, namely, $E_0 = (0,0,0)$, $E_1 = (1,0,0)$ and $E^* = (x^*, y^*, z^*)$ in the previous section. Again, the general variational matrix corresponding to the system is given by

$$J = \begin{bmatrix} 1-2x-az & 0 & -ax+c \\ az & -d & ax \\ 0 & d_1 & -e \end{bmatrix}$$

Now, corresponding to the trivial steady state $E_0 = (0,0,0)$ the Jacobian J has the following eigenvalues $\lambda_i = 1,\ -d,\ -e$; hence E_0 is repulsive in x-direction and attracting in $y-z$ plane. Clinically it means when there is no susceptible population then there will be no mass in incubated and in infected class. Hence, E_0 is a saddle point.

Again, corresponding to the disease free equilibrium point $E_1 = (1,0,0)$, the following eigenvalues $\lambda_1 = -1$ and $\lambda_{2,3}$ are the roots of the following quadratic equation:

$$\lambda^2 + (d+e)\lambda + (de - ad_1) = 0$$

when $de > d_1 a$, then the both the roots having negative real part and thus $E_1(1,0,0)$ is a locally stable in this case.

Further, from the existence of E^* and the stability condition of E_1, it is clear that the instability of the disease free equilibrium will lead to the existence of the endemic equilibrium. Now, we will examine the local behavior of the flow of the system around the endemic equilibria E^*. The characteristic equation corresponding to the equilibrium is

$$P(\lambda) = \lambda^3 + A_1\lambda^2 + A_2\lambda + A_3 = 0 \tag{10}$$

where

$$\begin{aligned} A_1 &= 2x^* + az^* + d + e - 1 \\ A_2 &= (d+e)(2x^* + az^* - 1) \\ A_3 &= d_1 az^*(ax^* - c) \end{aligned}$$

on substitution the values of x^* and z^*, it can be easily verified that $A_i > 0$, for $i = 1, 2, 3$. Now, from the Routh-Hurwitz criterion, a set of necessary and sufficient conditions for all the roots of the equation (10) having negative real part are $A_i > 0,\ i = 1, 2, 3$ and $A_1 A_2 > A_3$. Again, solving the last inequality, we get a sufficient condition for stability which is given by $d_1 c(d + e) > 1$. Hence, we can state the following theorem:

THEOREM 1. The system (6)-(8) is locally stable around the endemic equilibrium point E^*, when $d_1 c(d + e) > 1$.

Further, we will study the Hopf-bifurcation of above system, taking "a" (i.e., the rate of transfer from susceptible to incubated population) as the bifurcation parameter. Now, the necessary and sufficient condition for the existence of the Hopf-bifurcation, if there exists $a = a_0$ such that (i) $A_i(a_0) > 0$, $i = 1, 2, 3$, (ii) $A_1(a_0)A_2(a_0) - A_3(a_0) = 0$ and (iii) if we consider the eigen values of the characteristic equation (10) of the form $\lambda_i = u_i + iv_i$, then $Re\frac{d}{da}(u_i) \neq 0$, $i = 1, 2, 3$. After substitution of the values, the condition $A_1 A_2 - A_3 = 0$ becomes

$$\frac{1}{a^2}B_1 + \frac{1}{a}B_2 + B_3 = 0 \tag{11}$$

where

$$\begin{aligned} B_1 &= (d+e)\left[\tfrac{2de}{d_1} - \tfrac{d^2e^2}{d_1(de-d_1c)}\right]^2 \\ B_2 &= (d+e)\left[\tfrac{2de}{d_1} - \tfrac{d^2e^2}{d_1(de-d_1c)}\right]\left[\tfrac{2de}{de-d_1c} + d + e - 2\right] + \tfrac{d^2e^2}{de-d_1c}\left(\tfrac{de}{d_1} - c\right) \\ B_3 &= (d+e)\left[\tfrac{de}{de-d_1c} - 1\right]\left[\tfrac{de}{de-d_1c} + d + e - 1\right] - \tfrac{ded_1}{de-d_1c}\left(\tfrac{de}{d_1} - c\right) \end{aligned}$$

For example, taking a particular set of parameters: $c = 0.01$, $d = 0.11$, $d_1 = 0.1$ and $e = 0.08$, we get a positive root $a = 7.09264$ of the quadratic equation (11). Therefore, the eigen values of the characteristic equation (10) at $a = 7.09264$ are of the form $\lambda_{1,2} = \pm iv$ and $\lambda_3 = -w$, where v and w are positive real number.

Now, we will verify the condition (iii) of Hopf-bifurcation. Put $\lambda = u + iv$ in (10), we get

$$(u + iv)^3 + A_1(u + iv)^2 + A_2(u + iv) + A_3 = 0 \tag{12}$$

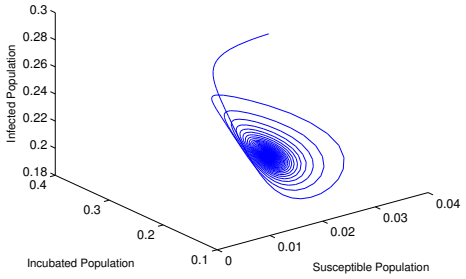

Figure 1: The phase portrait of three species around the endemic equilibrium, taking c =0.01, d=0.11, d1=0.1, e=0.08 and a=5.1

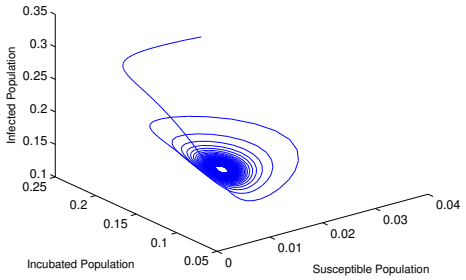

Figure 2: The phase plane representation of three species around the endemic equilibrium, taking c =0.01, d=0.11, d1=0.1, e=0.08 and a=7.15

On separating the real and imaginary part and eliminating v between real and imaginary part, we get

$$8u^3 + 8A_1u^2 + 2(A_1^2 + A_2)u + A_1A_2 - A_3 = 0 \tag{13}$$

It is clear from the above that $u(a_0) = 0$ iff $A_1(a_0)A_2(a_0) - A_3(a_0) = 0$. Further, at $a = a_0$, $u(a_0)$ is the only root, since the discriminant $8u^2 + 8A_1u + 2(A_1^2 + A_2) = 0$ is $64A_1^2 - 64(A_1^2 + A_2) < 0$. Again, differentiating (13) with respect to a, we have

$$\left(24u^2 + 16A_1u + 2(A_1^2 + A_2)\right)\frac{du}{da} + \left(8u^2 + 4A_1u\right)\frac{dA_1}{da} + 2u\frac{dA_2}{da} + \frac{d}{da}(A_1A_2 - A_3) = 0$$

Now, since at $a = a_0$, $u(a_0) = 0$, we get

$$\left[\frac{du}{da}\right]_{a=a_0} = \frac{-\frac{d}{da}(A_1A_2 - A_3)}{2(A_1^2 + A_2)} \neq 0,$$

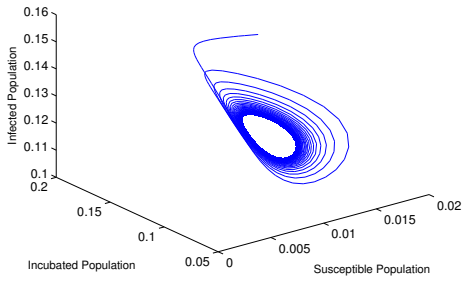

Figure 3: The phase plane representation of three species around the endemic equilibrium, taking c =0.01, d=0.11, d1=0.1, e=0.08 and a=9.1

which will ensure that the above system has a Hopf-bifurcation.

Hence as the rate of transfer from susceptible to incubated population (or the rate of interaction between disease and susceptible class), i.e., a, when crosses it's threshold value, i.e., $a = a_0$, then susceptible, incubated and disease population start oscillating around the endemic equilibrium. The above result is shown numerically in Figures 1-3. In Figure 1, we observed that the endemic equilibrium is stable, when $a < 7.09264$, but when we cross the threshold value of $a = 7.09264$, the above system is showing Hopf-bifurcation, see Figures 2 and 3.

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