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Modelling and Analysis of the Spread of Carrier Dependent Infectious Diseases: Effect of Cumulative Density of Infrastructure

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Abstract: In this paper, a four dimensional SIS epidemic non-linear model with immigration is proposed and analyzed to study the effect of infrastructure on the spread of carrier dependent infectious diseases. It is assumed that the density of carrier population follows logistic model and its growth rate and carrying capacity increase with the cumulative density of infrastructures, which depends on population density non-linearly. The model has been analyzed by using stability theory of differential equations and simulation. The model has three equilibria namely, disease free, carrier free and non-trivial endemic equilibrium. It is shown that the disease free and carrier free equilibria are always unstable and the endemic equilibrium, if exists, becomes locally as well as non-linearly stable under certain conditions. This analysis implies that as the cumulative density of infrastructures increases due to increase in human population density, not only the density of carriers increases but, the spread of carrier dependent infectious disease also increases. It is found that the disease becomes more endemic due to immigration. A numerical analysis of the model is also performed which supports the analytical results.

Keywords: Carriers, Infrastructure, Immigration, Stability, Lyapunov's function.

2010 AMS Classification No: 93A30, 34C60, 34D23.

1. Introduction

In general, the spread of infectious diseases in human population depends upon various factors such as the densities of infectives and susceptibles, population migration, modes of transmission, carriers such as flies, mites, ticks etc., socio-economic, environmental, ecological and geographical factors in the habitat, etc. In the case of carrier dependent infectious diseases such as tuberculosis, diarrhoea, cholera, typhoid fever, the spread depends not only on the carrier population density but also on human population density related factors such as infrastructure. These carriers transport agents of infectious disease from the environment to susceptibles, causing spread of the disease. A detailed account of modelling and study of epidemic diseases can be found in literature in the form of lecture notes, monograph, etc.[1-12].

In a habitat, Infrastructure plays a very important role in the spread of the carrier dependent infectious diseases as it provides a good space for growth and survival of carriers. No attention has been paid to study the effects of infrastructure although several models have been proposed and analysed to study the effect of environment on the spread of infectious disease. In particular, Ghosh et. al.[13-15]. presented some mathematical models for carrier dependent infectious diseases by considering environmental effect. They concluded that the spread of the infectious disease increases, when the growth of carriers caused by conducive environmental factors due to population density related factors, increases. Singh et. al.[16, 17] have also studied the effects of environmental and ecological factors on the spread of carrier and vector dependent infectious diseases.

In view of the above, in this paper, therefore, the effect of cumulative density of infrastructure on the spread of carrier dependent infectious diseases is modelled and analyzed by using stability theory of differential equations and numerical simulation.

2. An SIS Model

Let $X(t)$ and $Y(t)$ denote densities of susceptible and infective classes respectively of total human population density $N(t) = X(t) + Y(t)$, in a region under consideration. Let $C(t)$ be the carrier population density which affects all susceptibles and $I(t)$ be the cumulative density of infrastructures. By assuming simple mass action interaction, an SIS model can be written as follows

(2.1) $$\begin{cases} \dfrac{dX}{dt} = A - \gamma(N - N_0) - \beta XY - \lambda XC + \nu Y - dX, \end{cases}$$

$$\begin{cases} \dfrac{dY}{dt} = \beta XY + \lambda XC - (\nu + \alpha + d)Y, \\ \dfrac{dC}{dt} = s_0 C - \dfrac{s_0 C^2}{L} - s_c C + s_1 IC + s_2 C^2 I, \\ \dfrac{dI}{dt} = Q_0 - \theta_0 I + \theta_1 N + \theta_2 NI, \end{cases}$$

where $X + Y = N$ with initial conditions $X(0) > 0, Y(0) \geq 0, C(0) \geq 0, I(0) > 0.$ In the above model (2.1), A is the immigration rate of human population from outside the region, γ is the rate by which the population density $N(t)$ approaches to its equilibrium density $N_0(t),$ in absence of immigration and interactions etc. The coefficient d is the natural death rate, β and λ are the transmission coefficients due to infective and carrier population respectively, α is the disease related death rate, ν is the recovery rate, s_0 is the growth rate of carrier population, L is the carrying capacity of carrier population, s_c is the rate of control of carriers in the habitat, s_1 is the growth rate coefficient of carrier population and s_2 is the growth coefficient of the carrying capacity caused by the growth of cumulative density of infrastructures. Also Q_0 is the growth rate of cumulative density of infrastructures, assumed to be a constant, θ_0 is its depletion rate coefficient, θ_1 is the growth rate coefficient of infrastructural development due to human population density related factors and θ_2 is the growth rate coefficient caused by the bilinear interaction of human population density. All the coefficients in the model (2.1) are assumed to be positive and constant.

3. Equilibrium Analysis

Since $X + Y = N$, the model (2.1) can be written as follows

(3.1)
$$\begin{cases} \dfrac{dY}{dt} = \beta(N - Y)Y + \lambda(N - Y)C - (\nu + \alpha + d)Y, \\ \dfrac{dN}{dt} = A_1 - d_1 N - \alpha Y, \\ \dfrac{dC}{dt} = sC - \dfrac{s_0 C^2}{L} + s_1 IC + s_2 C^2 I, \\ \dfrac{dI}{dt} = Q_0 - \theta_0 I + \theta_1 N + \theta_2 NI, \end{cases}$$

where $A_1 = A + \gamma N_0$, $d_1 = d + \gamma$, $s = s_0 - s_c > 0$.

The following lemma establishes region of attraction for the system (3.1)[18].

Lemma 3.1: *The set*

$$\Omega = \left\{ (Y,N,C,I) : 0 \le Y \le N \le \frac{A_1}{d_1},\ \frac{\mathrm{A}_1}{\alpha + \mathrm{d}_1} \le \mathrm{N} \le \frac{A_1}{d_1}, 0 \le C \le C_m, 0 \le I \le I_m \right\},$$

attracts all the solutions initiating in the positive orthant, where

$$C_m = \frac{s + s_1 I_m}{\dfrac{s_0}{L} - s_2 I_m}, \qquad I_m = \frac{Q_0 + \theta_1 \dfrac{A_1}{d_1}}{\theta_0 - \theta_2 \dfrac{A_1}{d_1}}, \tag{3.2}$$

provided

$$\frac{s_0}{s_2 L} > I_m, \qquad \theta_0 > \theta_2 \frac{A_1}{d_1}. \tag{3.3}$$

The proof of the lemma is given in appendix A.

We analyze the model (3.1), under the conditions (3.3).

Theorem 3.1: *The system (3.1) has following three equilibria*

(i) $E_0 (0, \frac{A_1}{d_1}, 0, I_m)$, *the disease free equilibrium,*

where $I_m = \dfrac{Q_0 + \theta_1 \frac{A_1}{d_1}}{\theta_0 - \theta_2 \frac{A_1}{d_1}}$ *which exists if* $\theta_0 - \theta_2 \frac{A_1}{d_1} > 0$, *as assumed in (3.3).*

(ii) $E_1 (\bar{Y}, \bar{N}, 0, \bar{I})$, *the carrier free equilibrium,*

where $\bar{N} = \dfrac{\beta A_1 + \alpha(\nu + \alpha + d)}{\beta(\alpha + d_1)}$, $\bar{Y} = \dfrac{\beta A_1 - d_1(\nu + \alpha + d)}{\beta(\alpha + d_1)}$, $\bar{I} = \dfrac{Q_0 + \theta_1 \bar{N}}{\theta_0 - \theta_2 \bar{N}}$ *and* $\bar{Y}$ *exists if* $R_0 = \dfrac{\beta A_1}{d_1(\nu + \alpha + d)} > 1$. *Here* R_0 *is the basic reproduction number.*

(iii) $E^*\left(Y^*, N^*, C^*, I^*\right)$ *, the endemic equilibrium.*

The proof of the theorem is given in appendix B.

The existence of E_0 or E_1 is obvious. We prove the existence of E^*.

The equilibrium point E^* is given as the solutions of system of following equations, which are obtained after some simplification from (3.1) by putting left hand sides to zero

$$\beta Y^2 + Y\left[(\nu+\alpha+d) - \beta N + \lambda C\right] - \lambda NC = 0, \tag{3.4}$$

$$Y = \frac{A_1 - d_1 N}{\alpha}, \tag{3.5}$$

$$C = \frac{s + s_1 I}{\frac{s_0}{L} - s_2 I}, \tag{3.6}$$

where $s_0 > s_2 IL$.

$$I = \frac{Q_0 + \theta_1 N}{\theta_0 - \theta_2 N}, \tag{3.7}$$

where $\theta_0 - \theta_2 N > 0$.

Now eliminating Y between equations (3.4) and (3.5) we get

$$F(N) = \left(\frac{\beta}{\alpha^2}\right)(A_1 - d_1 N)^2 + \left(\frac{A_1 - d_1 N}{\alpha}\right)\left[\left(\nu+\alpha+d\right) - \beta N + \lambda C\right] - \lambda NC = 0, \tag{3.8}$$

where C is given in terms of N by using (3.6) and (3.7). From equation (3.8) we note the following

$$F\left(\frac{A_1}{\alpha + d_1}\right) = \frac{A_1}{\alpha + d_1}(\nu+\alpha+d) > 0, \tag{3.9}$$

(3.10) $$F\left(\frac{A_1}{d_1}\right) = -\frac{\lambda A_1}{d_1} C < 0 .$$

Thus, it is clear that there exists a root N^* of $F(N)=0$ in the interval $\frac{A_1}{\alpha+d_1} \le N \le \frac{A_1}{d_1}$. Further, this root will be unique if $F^{'}(N)<0$ for $\frac{A_1}{a+d_1} \le N \le \frac{A_1}{d_1}$. To show this, we differentiate (3.8) to get

(3.11) $$F^{'}(N) = -\frac{2\beta d_1}{\alpha^2}(A_1 - d_1 N) - \frac{d_1}{\alpha}\left[(\nu+\alpha+d) - \beta N + \lambda C\right]$$

$$-\frac{\beta}{\alpha}(A_1 - d_1 N) - \lambda C - \frac{\lambda}{a}\left[N(a+d_1) - A_1\right]C^{'}.$$

Using (3.8) in (3.11), we get on simplification,

(3.12) $$F^{'}(N) = -\frac{\beta d_1}{\alpha^2}(A_1 - d_1 N) - \frac{d_1}{(A_1 - d_1 N)}\lambda NC$$

$$-\frac{\beta}{\alpha}(A_1 - d_1 N) - \lambda C - \frac{\lambda}{\alpha}\left[N(\alpha+d_1) - A_1\right]C^{'} ,$$

which is negative in $\frac{A_1}{\alpha+d_1} \le N \le \frac{A_1}{d_1}$ as $C^{'} = \left[\frac{\frac{s_0 s_1}{L} + s s_2}{\left(\frac{s_0}{L} - s_2 I\right)^2}\right] I^{'}$ and $I^{'} = \frac{\theta_1\theta_0 + \theta_2 Q_0}{(\theta_0 - \theta_2 N)^2}$ are positive.

Now, knowing the value of N^*, the value of Y^*, C^*, I^* can be uniquely determined from (3.5), (3.6), (3.7).

Remark: Using (3.4), (3.5), (3.6), (3.7), we can check that $\frac{dY}{d\theta_0} < 0$, $\frac{dY}{d\theta_1} > 0$ and $\frac{dY}{d\theta_2} > 0$. These conditions imply that as the cumulative density of infrastructures increases (decreases), the density of infectives increases (decreases).

4. Stability Analysis

Now we shall study the stability behavior of above equilibria. The local stability result of equilibria E_0, E_1 and E^* are given in the following theorem

Theorem 4.1: *The equilibria* E_0 *and* E_1 *are locally unstable and the equilibrium* E^* *is locally asymptotically stable provided the following conditions are satisfied,*

(4.1) $$\alpha\lambda^2 C^{*2} < d_1\beta^2 Y^{*2},$$

(4.2) $$\alpha\lambda^2 (N^* - Y^*)^2 < \frac{d_1\beta^2 Y^{*2}\left(\frac{s_0}{L} - s_2 I^*\right)^2 \left(\theta_0 - \theta_2 N^*\right)^2}{2\left(s_1 + s_2 C^*\right)^2 \left(\theta_1 + \theta_2 I^*\right)^2}.$$

The proof of the theorem is given in appendix C.

The nonlinear stability results for E^* are given by the following theorem

Theorem 4.2: *The equilibrium point* E^* *is nonlinearly asymptotically stable in* Ω *provided the following inequalities are satisfied:*

(4.3) $$\alpha\lambda^2 C_m{}^2 < d_1\beta^2 Y^{*2},$$

(4.4) $$\alpha\lambda^2 (N^* - Y^*)^2 < \frac{d_1\beta^2 Y^{*2}\left(\frac{s_0}{L} - s_2 I^*\right)^2 \left(\theta_0 - \theta_2 N^*\right)^2}{2\left(s_1 + s_2 C_m\right)^2 \left(\theta_1 + \theta_2 I_m\right)^2}.$$

The proof of the theorem is given in appendix D.

Remark: It is noted here that if $\lambda = 0$ or $\alpha = 0$, the above inequalities are satisfied automatically, which shows that λ and α have destabilizing effects on the system.

5. Numerical Simulation

Here we discuss the existence and stability of the nontrivial equilibrium point E^* by taking the following set of parameter values and using the MAPLE:

$$A_1 = 504, d_1 = 0.0202, d = 0.02, \alpha = 0.03, \beta = 0.000005,$$
$$\lambda = 0.000001, \nu = 0.05, s = 0.899, s_0 = 0.9, L = 100000,$$
$$s_1 = 0.002, s_2 = 0.00000001, Q_0 = 1, \theta_0 = 0.1, \theta_1 = 0.002,$$
$$\theta_2 = 0.00000001$$

For these values of parameters, the value of nontrivial equilibrium point E^* corresponding to (3.3) is obtained as follows

$$N(t) = 12042.07659,\ Y(t) = 8691.668429, C(t) = 215962.8391,\ E(t) = 251.1439613.$$

The variational matrix corresponding to the equilibrium point E^* is obtained as

$$M^* = \begin{bmatrix} -.3426691404 & 0.2594211812 & 0.003350408161 & 0 \\ -0.03 & -0.0202 & 0 & 0 \\ 0 & 0 & -1.401287923 & 898.3251569 \\ 0 & 0.00200251144 & 0 & -0.09987957923 \end{bmatrix}$$

The eigen values of this matrix are

- 0.3191874820, -0.05944515925, -0.08421062520, -1.401193376

which are all negative. Hence $E^*\left(Y^*, N^*, C^*, I^*\right)$ is locally stable. Now numerical simulation is performed for Y vs. N for the different initial starts in the following four cases and displayed in the fig.1 which indicates nonlinear stability of the point $\left(Y^*, N^*\right)$ in $N - Y$ plane.

(i) $N_1(0) = 12500, Y_1(0) = 9200, C_1(0) = 215500, I_1(0) = 250$

(ii) $N_2(0) = 11500, Y_2(0) = 9200, C_2(0) = 215500, I_2(0) = 250$

(iii) $N_3(0)=11500, Y_3(0)=8000, C_3(0)=215500, I_3(0)=250$

(iv) $N_4(0)=12500, Y_4(0)=8000, C_4(0)=215500, I_4(0)=250$

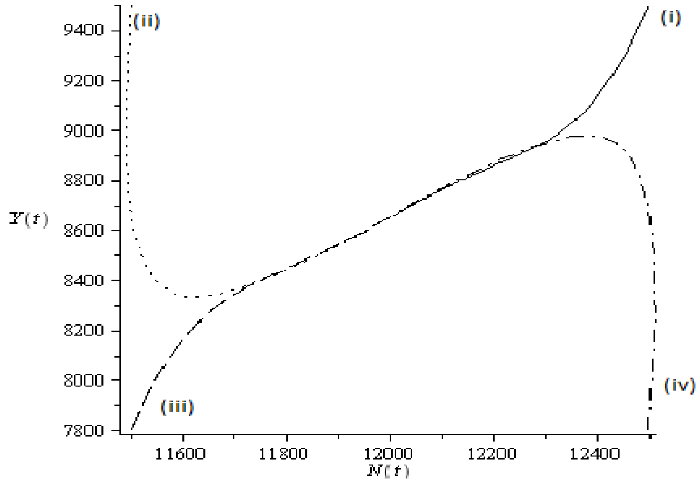

Figure 1: Phase plot between Y and N

The model (3.1) has also been solved by using MAPPLE and the graphs of the variable Y with respect to t for various values of different parameters have been plotted in Figure 2 – Figure 8.From Figure 2, it is noted that $Y(t)$ increases as $s = s_0 - s_c$ increases, ie. s_0 increases or s_c decreases.From Figure 3, it is seen that $Y(t)$ increases as s_1 increases.From Figure 4, we note that $Y(t)$ increases as s_2 increases.The above results are expected, as the carrier population increases with the parameters s_0, s_1, s_2 but it decreases with s_c. Further from Figure 5, it is seen that $Y(t)$ increases as Q_0 increases.From Figure 6, we note that $Y(t)$ increases as θ_0 decreases.From Figure 7, it is seen that $Y(t)$ increases as θ_1 increases.From Figure 8, it is seen that $Y(t)$ increases as θ_2 increases.These results are again expected as increase (decrease) in the cumulative density of infrastructure

causes increase (decrease) in the density of carrier population, resulting increase (decrease) of the density of infectives.

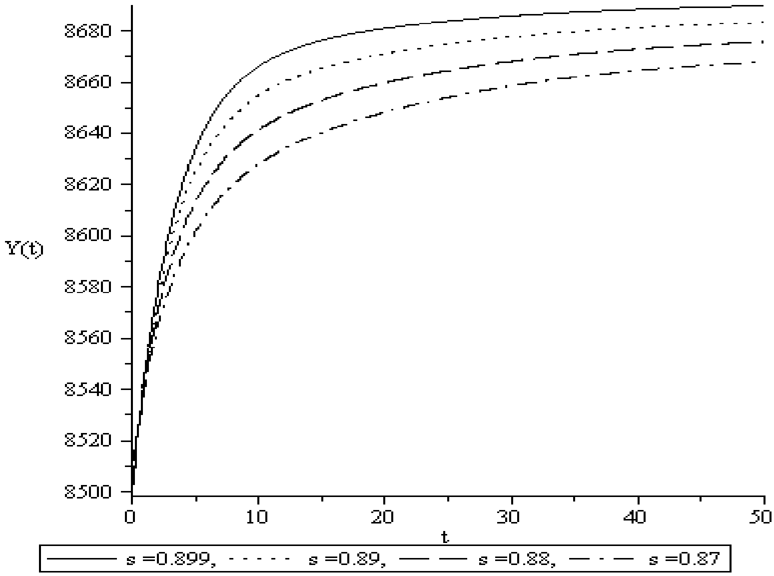

Figure 2: Plot between Y and t for different values of $s = s_0 - s_c$

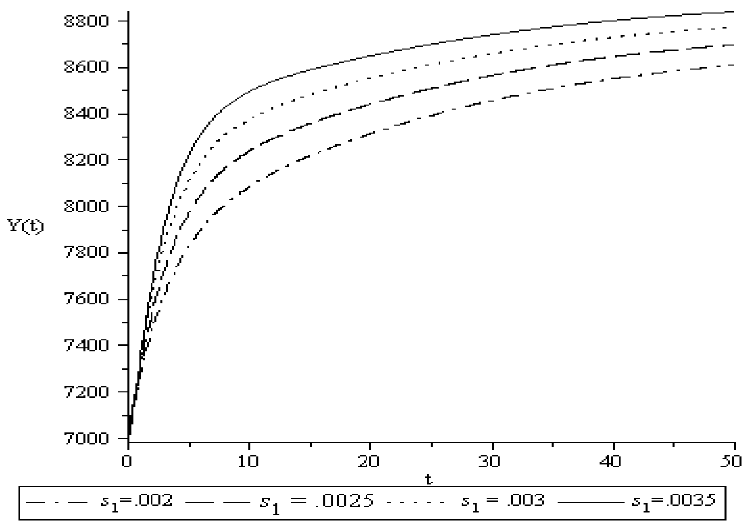

Figure 3: Plot between Y and t for different values of s_1

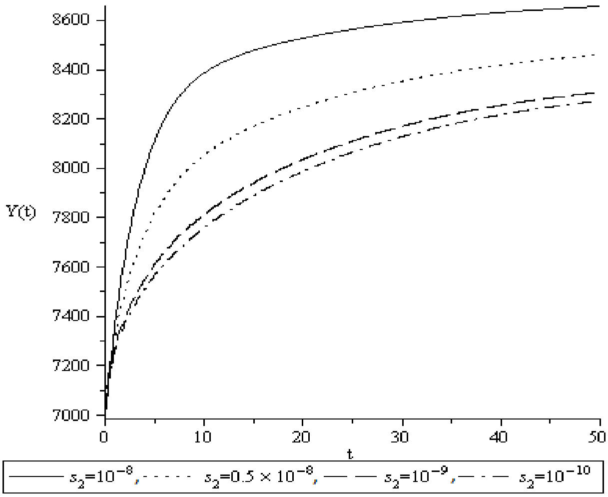

Figure 4: Plot between Y and t for different values of s_2

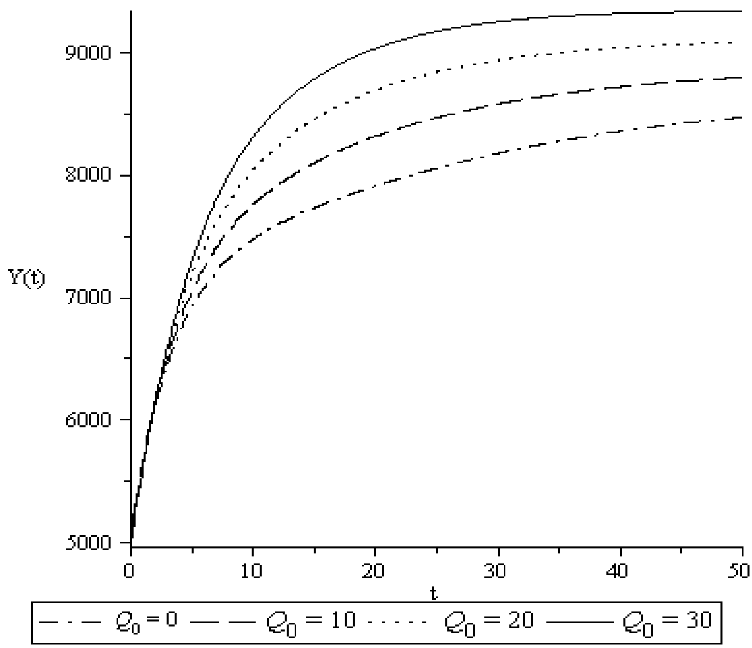

Figure 5: Plot between Y and t for different values of Q_0

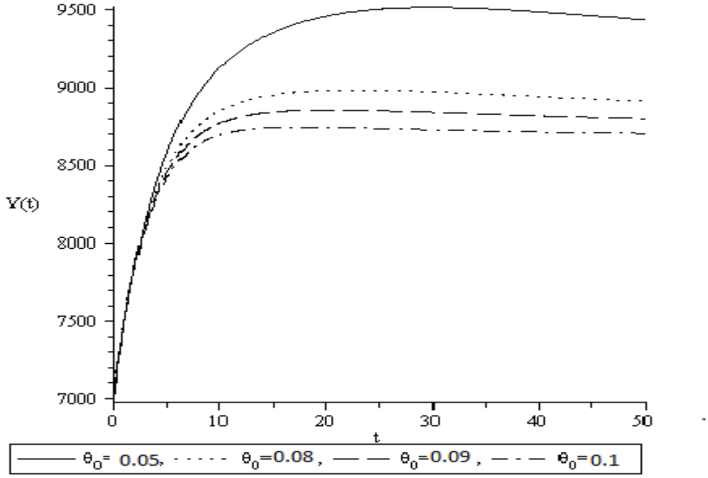

Figure 6: Plot between Y and t for different values of θ_0

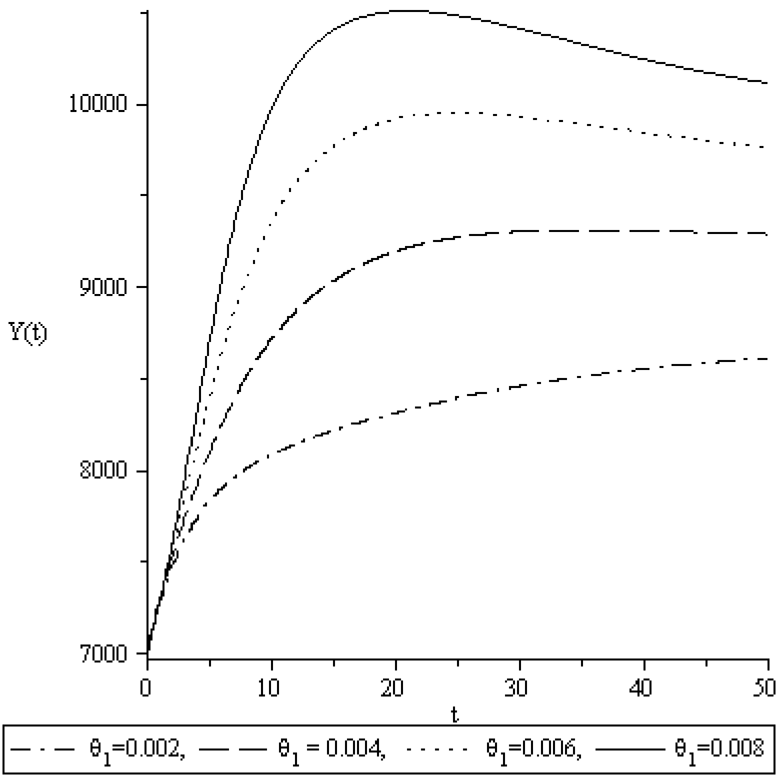

Figure 7: Plot between Y and t for different values of θ_1

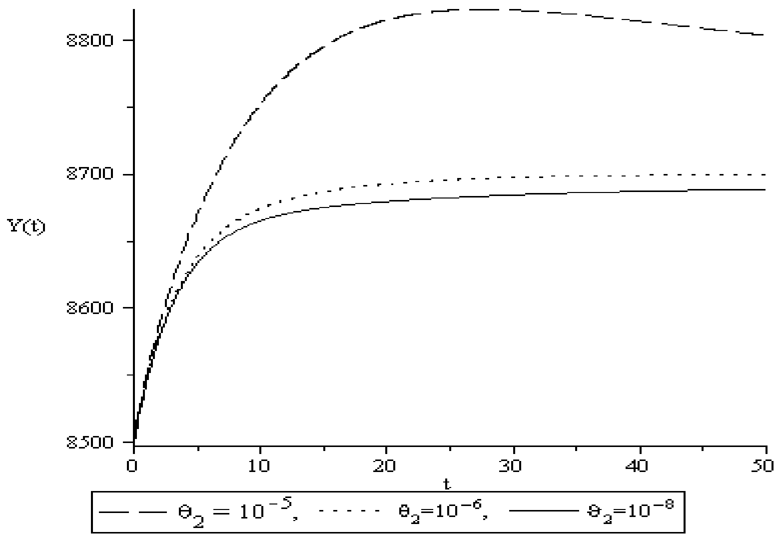

Figure 8: Plot between Y and t for different values of θ_2

6. Conclusions

In this paper, a four dimensional SIS non-linear model with immigration has been proposed and analyzed to study the spread of infectious diseases, which is dependent on the density of the carriers, affected by human made infrastructure. The density of carriers has been assumed to be governed by a logistic model, with prescribed intrinsic growth rate and carrying capacity, which depend on the cumulative density of infrastructures. It is further assumed that the carrier population in the habitat can be controlled by using some insecticide.

In the modeling process, the cumulative density of infrastructure has been assumed to grow with a constant rate, and it is depleted with a rate, which is proportional to cumulative density of infrastructures. In a realistic situation this cumulative density must depend upon human population density in the habitat and therefore this aspect has been taken into account by considering its non-linear interaction with population density. The model has been analyzed analytically as well as by computer simulation. It has been found that the density of infectives increases, as the parameters related to increase in infrastructural development due to human population density related factors, increases. It may then be concluded that the spread of carrier dependent infectious diseases increases due to increase in infrastructures in the habitat.

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Appendix A

Proof of lemma 3.1: Here we give only a brief outline of the proof, the detail proof can be seen in Freedman and So (1985). From the first equation of model (3.1),we have

$$\frac{dN}{dt} = A_1 - d_1 N - \alpha Y \le A_1 - d_1 N$$

and

$$\frac{dN}{dt} = A_1 - d_1 N - \alpha Y \ge A_1 - \left(\alpha + d_1\right) N,$$

which give $0 \le Y \le N \le \frac{A_1}{d_1}, \ \frac{\mathrm{A}_1}{\alpha + \mathrm{d}_1} \le \mathrm{N} \le \frac{A_1}{d_1}.$

From the last equation of model (3.1), we have

$$\frac{dI}{dt} \le Q_0 - \theta_0 I + \theta_1 \frac{A_1}{d_1} + \theta_2 \frac{A_1}{d_1} I = Q_0 + \theta_1 \frac{A_1}{d_1} - (\theta_0 - \theta_2 \frac{A_1}{d_1}) I,$$

which gives $0 < I \le I_m = \dfrac{Q_0 + \theta_1 \frac{A_1}{d_1}}{\theta_0 - \theta_2 \frac{A_1}{d_1}}$, which is positive provided $\theta_0 > \theta_2 \frac{A_1}{d_1}$.

Similarly from the equation for carrier population density in (3.1), we have $0 \le C \le C_m = \dfrac{s + s_1 I_m}{\frac{s_0}{L} - s_2 I_m}$, which is positive provided $\frac{s_0}{L} > s_2 I_m$.

Appendix B

Proof of theorem 3.1: In the following, we find the characteristics of E^*.

(i) We show that at E^*, $\frac{dY}{d\theta_0} < 0.$

For equilibrium point E^*, (3.1) can be reduced as

(B.1) $$\beta Y^2 + Y\left[(\nu+\alpha+d) - \beta N + \lambda C\right] - \lambda NC = 0,$$

(B.2) $$N = \frac{A_1 - \alpha Y}{d_1},$$

(B.3) $$C = \frac{s + s_1 I}{\frac{s_0}{L} - s_2 I}, \text{ where } s_0 > s_2 IL,$$

(B.4) $$I = \frac{Q_0 + \theta_1 N}{\theta_0 - \theta_2 N}, \text{ where } \theta_0 - \theta_2 N > 0.$$

From (B.2) we have

(B.5) $$\frac{dN}{d\theta_0} = \frac{-\alpha}{d_1}\frac{dY}{d\theta_0}$$

Now on differentiating (B.1) w. r. t. θ_0 and using (B.1) and (B.2) we get

(B.6) $$\frac{dY}{d\theta_0}\left[\beta Y + \lambda\frac{NC}{Y} + \frac{\alpha\beta}{d_1}Y + \frac{\lambda\alpha}{d_1}C\right] = \lambda\left(N - Y\right)\frac{dC}{d\theta_0}$$

From (B.4), we get

(B.7) $$\frac{dI}{d\theta_0} = \frac{-\frac{\alpha}{d_1}\left(\theta_0\theta_1 + Q_0\theta_2\right)\frac{dY}{d\theta_0} - \left(Q_0 + \theta_1 N\right)}{\left(\theta_0 - \theta_2 N\right)^2}$$

From (B.3), we get

(B.8)
$$\frac{dC}{d\theta_0} = \frac{\left(\frac{s_0 s_1}{L} + s s_2\right)\frac{dI}{d\theta_0}}{\left(\frac{s_0}{L} - s_2 I\right)^2}$$

Using (B.7) and (B.8) in (B.6), we get at $E^* \ \frac{dY}{d\theta_0} < 0$

Thus it is seen here that as the depletion rate coefficient of cumulative density of infrastructures θ_0 increases, the infective human population density decrease at E^*.

(ii) For E^*, $\frac{dY}{d\theta_1} > 0.$

In the similar manner as in (i), we can show that $\frac{dY}{d\theta_1} > 0.$
Thus it is seen here that as the growth rate coefficient of infrastructural development due to human population density related factors θ_1 increases, the infective human population density increases at the equilibrium point E^*.

(iii) Again for E^*, we get, $\frac{dY}{d\theta_2} > 0.$

Thus it is seen here that as the growth rate coefficient caused by the bilinear interaction of human population density θ_2 increases, the infective human population density increases at the equilibrium point E^*.

From the above discussion it may be concluded that the spread of the carrier dependent infectious disease increases as infrastructures increase in a habitat.

Appendix C

Proof of theorem 4.1: The local stability 123ersiste of each of the two equilibria E_0 or E_1 is studied by computing corresponding variational matrices for system (3.1) and for the nontrivial equilibrium point E^* it is studied by using Lyapunov's theory.

The variational matrix M_i corresponding to equilibrium points is given by

$$M_i = \begin{bmatrix} \begin{matrix}\beta N - 2\beta Y - \lambda C \\ -(\nu + \alpha + d)\end{matrix} & \beta Y + \lambda C & \lambda(N - Y) & 0 \\ -\alpha & -d_1 & 0 & 0 \\ 0 & 0 & \begin{matrix} s - \dfrac{2s_0}{L}C \\ + s_1 I + 2s_2 CI \end{matrix} & s_1 C + s_2 C^2 \\ 0 & \theta_1 + \theta_2 I & 0 & -\theta_0 + \theta_2 N \end{bmatrix}$$

Local Stability Behaviour of $E_0\left(0, \frac{A_1}{d_1}, 0, I_m\right)$

The variational matrix corresponding to equilibrium point E_0 is given by

$$M_0 = \begin{bmatrix} \beta\dfrac{A_1}{d_1} - (\nu + \alpha + d) & 0 & \lambda\dfrac{A_1}{d_1} & 0 \\ -\alpha & -d_1 & 0 & 0 \\ 0 & 0 & s + s_1 I_m & 0 \\ 0 & \theta_1 + \theta_2 I_m & 0 & -\theta_0 + \theta_2\dfrac{A_1}{d_1} \end{bmatrix}$$

Here one of the eigen value $s + s_1 I_m$ is positive and hence E_0, if exists, is unstable.

Local Stability Behaviour of $E_1\left(\bar{Y}, \bar{N}, 0, \bar{I}\right)$

In this case the variational matrix will be

$$M_1 = \begin{bmatrix} \beta\bar{N} - 2\beta\bar{Y} \\ -(\nu+\alpha+d) & \beta\bar{Y} & \lambda(\bar{N}-\bar{Y}) & 0 \\ -\alpha & -d_1 & 0 & 0 \\ 0 & 0 & s+s_1\bar{I} & 0 \\ 0 & \theta_1+\theta_2\bar{I} & 0 & -\theta_0+\theta_2\bar{N} \end{bmatrix}$$

This variational matrix has a positive eigen value $s+s_1\bar{I}$ and hence E_1, if exists, is unstable.

Local Stability Behaviour of $E^*\left(Y^*, N^*, C^*, I^*\right)$

We study the stability 125ersiste or E^* by Lyapunov's method. For this we linearize the system (3.1) by using following transformations

$$Y = Y^* + y,\ N = N^* + n, C = C^* + c \text{ and } I = I^* + i$$

and use following positive definite function to use the sufficient condition for stability

(C.1) $$V = \frac{1}{2}y^2 + \frac{k_1}{2}n^2 + \frac{k_2}{2}c^2 + \frac{k_3}{2}i^2,$$

where k_1, k_2 and k_3 are positive constants to be chosen appropriately.

Differentiating (C.1) w.r.t. t and using the linearized version of (3.1), $\frac{dV}{dt}$ can be written as

$$\begin{aligned}\frac{dV}{dt} = &-\left(\beta Y^* + \lambda\frac{N^*C^*}{Y^*}\right)y^2 - \left(k_1 d_1\right)n^2 - k_2 C^*\left(\frac{s_0}{L} - s_2 I^*\right)c^2 \\ &- k_3\left(\theta_0 - \theta_2 N^*\right)i^2 + \left[\beta Y^* + \lambda C^* - k_1\alpha\right]yn + \lambda\left(N^* - Y^*\right)yc \\ &+ k_3\left(\theta_1 + \theta_2 I^*\right)ni + k_2 C^*\left(s_1 + s_2 C^*\right)ci\end{aligned}$$

$$= \left[\beta Y^* - k_1\alpha\right] yn - \lambda \frac{N^* C^*}{Y^*} y^2 - \left[\left(\frac{\beta}{2} Y^*\right) y^2 - \left(\lambda C^*\right) yn + \frac{k_1 d_1}{2} n^2\right]$$

$$- \left[\left(\frac{\beta}{2} Y^*\right) y^2 - \lambda\left(N^* - Y^*\right) yc + \frac{k_2}{2} C^* \left(\frac{s_0}{L} - s_2 I^*\right) c^2\right]$$

$$- \left[\frac{k_2}{2} C^* \left(\frac{s_0}{L} - s_2 I^*\right) c^2 - k_2 C^* \left(s_1 + s_2 C^*\right) ci + \frac{k_3}{2}\left(\theta_0 - \theta_2 N^*\right) i^2\right]$$

$$- \left[\frac{k_3}{2}\left(\theta_0 - \theta_2 N^*\right) i^2 - k_3\left(\theta_1 + \theta_2 I^*\right) ni + \frac{k_1 d_1}{2} n^2\right].$$

Choosing $k_1 = \frac{\beta Y^*}{\alpha}$, the conditions for $\frac{dV}{dt}$ to be negative definite can be written as follows

(C.2) $\alpha \lambda^2 C^{*2} < d_1 \beta^2 Y^{*2}$,

(C.3) $k_2 > \dfrac{\lambda^2 (N^* - Y^*)^2}{\beta Y^* C^* \left(\frac{s_0}{L} - s_2 I^*\right)}$,

(C.4) $k_2 < \dfrac{\left(\frac{s_0}{L} - s_2 I^*\right)\left(\theta_0 - \theta_2 N^*\right)}{C^*\left(s_1 + s_2 C^*\right)^2} k_3$,

(C.5) $k_3 < \dfrac{\beta Y^*}{\alpha} \dfrac{\left(\theta_0 - \theta_2 N^*\right) d_1}{\left(\theta_1 + \theta_2 I^*\right)^2}$.

Now if we choose $k_3 = \frac{1}{2} \frac{\beta Y^*}{\alpha} \frac{\left(\theta_0 - \theta_2 N^*\right) d_1}{\left(\theta_1 + \theta_2 I^*\right)^2}$, then inequality (C.5) will satisfy automatically. Now we can choose k_2 satisfying inequality (C.3) and (C.4) provided

(C.6) $$\alpha\lambda^2(N^*-Y^*)^2 < \frac{d_1\beta^2 Y^{*2}\left(\frac{s_0}{L}-s_2 I^*\right)^2\left(\theta_0-\theta_2 N^*\right)^2}{2\left(s_1+s_2 C^*\right)^2\left(\theta_1+\theta_2 I^*\right)^2}.$$

Hence $\frac{dV}{dt}$ is negative definite if (C.2) and (C.6) are satisfied. Thus, E^* is locally stable if (4.1) and (4.2) are satisfied.

Appendix D

Proof of theorem 4.2: We prove the theorem by using the following positive definite function

(D.1) $$V=\left(Y-Y^*-Y^*\ln\frac{Y}{Y^*}\right)+\frac{k_1}{2}\left(N-N^*\right)^2+k_2\left(C-C^*-C^*\ln\frac{C}{C^*}\right)+\frac{k_3}{2}\left(I-I^*\right)^2,$$

where k_1, k_2 and k_3 are positive constants to be chosen appropriately.

Differentiating (D.1) w.r.t. t and using (3.1), we get

$$\frac{dV}{dt}=\left(\frac{Y-Y^*}{Y}\right)\frac{dY}{dt}+k_1\left(N-N^*\right)\frac{dN}{dt}+k_2\left(\frac{C-C^*}{C}\right)\frac{dC}{dt}+k_3\left(I-I^*\right)\frac{dI}{dt}$$

$$=-\left[\beta+\lambda\frac{NC}{YY^*}\right](Y-Y^*)^2-k_1 d_1\left(N-N^*\right)^2-k_2\left[\frac{s_0}{L}-s_2 I^*\right]\left(C-C^*\right)^2$$

$$-k_3\left(\theta_0-\theta_2 N^*\right)\left(I-I^*\right)^2+\left[\beta-k_1\alpha+\lambda\frac{C}{Y^*}\right]\left(Y-Y^*\right)\left(N-N^*\right)$$

$$+\lambda\left[\frac{N^*}{Y^*}-1\right]\left(Y-Y^*\right)\left(C-C^*\right)+k_2\left[s_1+s_2 C\right]\left(C-C^*\right)\left(I-I^*\right)$$

$$+k_3\left[\theta_1+\theta_2 I\right]\left(I-I^*\right)\left(N-N^*\right).$$

Taking $k_1=\frac{\beta}{\alpha}$, we get

$$\frac{dV}{dt}=-\lambda\frac{NC}{YY^*}\left(Y-Y^*\right)^2-\frac{\beta}{2}\left(Y-Y^*\right)^2+\lambda\frac{C}{Y^*}\left(Y-Y^*\right)\left(N-N^*\right)-\frac{k_1d_1}{2}\left(N-N^*\right)^2$$
$$-\frac{\beta}{2}\left(Y-Y^*\right)^2+\lambda\left(\frac{N^*}{Y^*}-1\right)\left(Y-Y^*\right)\left(C-C^*\right)-\frac{k_2}{2}\left(\frac{s_0}{L}-s_2I^*\right)\left(C-C^*\right)^2$$
$$-\frac{k_2}{2}\left(\frac{s_0}{L}-s_2I^*\right)\left(C-C^*\right)^2+k_2\left(s_1+s_2C\right)\left(C-C^*\right)\left(I-I^*\right)$$
$$-\frac{k_3}{2}\left(\theta_0-\theta_2N^*\right)\left(I-I^*\right)^2-\frac{k_1d_1}{2}\left(N-N^*\right)^2+k_3\left(\theta_1+\theta_2I\right)\left(I-I^*\right)\left(N-N^*\right)$$
$$-\frac{k_3}{2}\left(\theta_0-\theta_2N^*\right)\left(I-I^*\right)^2$$

Now $\frac{dV}{dt}$ will be negative definite if following conditions holds

$$\alpha\lambda^2C^2<d_1\beta^2Y^{*2},\ k_2>\frac{\lambda^2\left(\frac{N^*}{Y^*}-1\right)^2}{\beta\left(\frac{s_0}{L}-s_2I^*\right)},\ k_2<\frac{\left(\frac{s_0}{L}-s_2I^*\right)(\theta_0-\theta_2N^*)}{(s_1+s_2C)^2}k_3\ ,$$

$$k_3<\frac{(\beta/\alpha)d_1(\theta_0-\theta_2N^*)}{(\theta_1+\theta_2I)^2}\ .$$

Now on maximizing the left hand sides and minimizing right hand side of above inequalities, we get

(D.2) $$\alpha\lambda^2{C_m}^2<d_1\beta^2Y^{*2},$$

(D.3) $$k_2>\frac{\lambda^2\left(N^*-Y^*\right)^2}{\beta\, Y^{*2}\left(\frac{s_0}{L}-s_2I^*\right)},$$

(D.4) $$k_2<\frac{\left(\frac{s_0}{L}-s_2I^*\right)(\theta_0-\theta_2N^*)}{(s_1+s_2C_m)^2}k_3,$$

(D.5) $$k_3 < \frac{(\beta/\alpha)d_1(\theta_0 - \theta_2 N^*)}{(\theta_1 + \theta_2 I_m)^2}.$$

If we choose $k_3 = \frac{1}{2}\frac{(\beta/\alpha)d_1(\theta_0 - \theta_2 N^*)}{(\theta_1 + \theta_2 I_m)^2}$, the inequality (D.5) will satisfy automatically and we can choose k_2 satisfying inequality (D.3) and (D.4) provided

(D.6) $$\frac{\lambda^2\left(\frac{N^*}{Y^*} - 1\right)^2}{\beta\left(\frac{s_0}{L} - s_2 I^*\right)} < k_2 < \frac{\left(\frac{s_0}{L} - s_2 I^*\right)(\theta_0 - \theta_2 N^*)}{(s_1 + s_2 C_m)^2}\frac{1}{2}\frac{(\beta/\alpha)d_1(\theta_0 - \theta_2 N^*)}{(\theta_1 + \theta_2 I_m)^2},$$

i.e. $$\alpha\lambda^2(N^* - Y^*)^2 < \frac{d_1\beta^2 Y^{*2}\left(\frac{s_0}{L} - s_2 I^*\right)^2\left(\theta_0 - \theta_2 N^*\right)^2}{2\left(s_1 + s_2 C_m\right)^2\left(\theta_1 + \theta_2 I_m\right)^2}.$$

Hence $\frac{dV}{dt}$ is negative definite if (D.2) and (D.6) are satisfied. Thus E^* is nonlinearly asymptotically stable if (4.3) and (4.4) are satisfied, as stated in theorem 4.2.