Host Pathogen Interactions with Recovery Rate: A Mathematical Study

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Abstract—**Research in the infection and recovery, based on mathematical understanding is aimed at developing how the immune system protects against infectious diseases, with a major focus on host-pathogen interactions. In this research article we have considered a mathematical model which represents the interplay of hosts and pathogen as in biology and manifests the time rate of change of these species. A recovery rate of the infected host to that of susceptible host is incorporated. The model is analyzed theoretically for conditions of stable solutions. Numerical solutions of the model are in conformity with those obtained theoretically. An effort is made to relate the model to prototype biological systems by exploring a probable disease free parametric region. Our analysis shows that the removal of infected host population is caused by the biological and physical realizable threshold of recovery rate.**

Keywords —Asymptotic Stability, Host Pathogen, Numerical Solutions, Time Series Solutions.

1 Introduction

The idea, that differential equations could be used potentially to understand epidemiological systems in order to contain the outbreak of epidemiological diseases, was considered by Ronald Ross way back in 1911 [1]. Sir Ross used differential equations to understand certain thresholds relating malarial outbreak within the species Homo Sapiens and this helped him immensely towards discovering malarial-vaccine. Application of mathematical concepts and techniques, to analyze epidemiological or such classes of biological systems, has been started from the time before Sir Ross when Hammer(1906) formulated and analyzed a discrete time model to understand the recurrence of measles epidemics. Even before, Daniel Bernoulli (1970) started the pioneering venture of applying mathematical concepts in case of epidemics like small pox. The fact, that mathematics can be used to enrich understanding of biological systems, is well established by now and thus the field of mathematical-Biology emerged.

*Research is supported by the Department of Mathematics Jadavpur University, PURSE DST, Government of India and its a pleasure to acknowledge All India Council for Technical Eduction for their travel support to present the research work in WCE 2010, U.K.

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Host-Pathogen models are mathematical prototypes pertaining to epidemiology and these are of immense importance in view of the emergence and re-emergence of epidemiological diseases in the present day global scenario. In this type of model the host population is divided into two classes, susceptible (S) i.e., healthy organisms and infected individuals (I). Pathogens (V) cause infection to host transforming S to I. The model actually describes the time rate of change of S, I, and V including various realistic model parameters arising out of influence from environment, immunization, inter-class contact etc. These class of models are important in their own rights and are also relevant for predator-prey or host-parasite type of models. In the predator-prey models, the effect of pathogenic diseases on the model dynamics and its constituents, is an important area from mathematical as well as ecological point of view. Researchers are paying increased attention to interlink these areas of research into a more general one [2]-[9].

To have an idea about the scope of research in the host-pathogen (or eco-epidemiological) model systems, we look into the sequence of historical events relating mathematical research in the area for last few years. Beltrami and Carroll [3] as well as Venturino [8] worked on the role of viral disease in recurrent phytoplankton considering a three species model of susceptible and infected phytoplankton as well as their predator. Chattopadhyay, Mukhopadhyay and Roy [10] took a generalized Gause model of prey-predator character including viral infection and studied the stability of the different populations. Mukherjee [11] considered a prey-predator type model with disease in the prey populations and studied the persistence of the stable solutions. Later, Chattopadhyay and Pal [12], on a modified Beltrami and Carroll model, viewed that the role of viral infection in the plankton population is entirely model dependent and hard to predict. They further emphasized the crucial role played by the virus population on the dynamics of a three species eco-epidemiological model in the marine ecosystem. With the growing research in the prey-predator and other prototypical systems, it became apparent that, the viral growth through replication influences the model dynamics. Bairagi, Roy and Chattopadhyay emphasized the same in a subsequent communication [13]. It is to be noted that Beretta and Kuang considered viral replication, but in a different context. In a recent communication, Bairagi, Roy and Chattopadhyay [14] carried a comparative study of a prey-predator model with several response functions.

In this paper we consider a conventional host-pathogen model including a recovery of the infected individuals to the healthy organisms termed as susceptible. The essential features of a

ISBN: 978-988-17012-9-9
ISSN: 2078-0958 (Print); ISSN: 2078-0966 (Online)

conventional host pathogen system such as, logistic growth of susceptible, pathogen replication, lysis death of infected individuals and mortality of pathogens, are all incorporated in the model. We would predominantly explore the bearing of host recovery on the stability of the system and related characteristics.

The model is analyzed in two different avenues, analytical and numerical. Coupled differential equations depicting the model system are made dimensionless and the linearized fixed point solutions of these equations are obtained. Existence, uniqueness and boundedness of the non trivial fixed point solutions are checked. Stability of the system is analyzed and conditions are obtained. Model equations are solved numerically to check threshold values of different model parameters and the concurrence of these solutions with those obtained analytically are checked. Numerical findings are in agreement with the theoretical results.

2 The Basic Assumptions and the Mathematical Model

We consider a host pathogen model consisting of a host population, whose concentration is denoted by N ($[N]$ = number of host per designated area) and a pathogen population inflicting infection in the host population whose concentration is denoted by V ($[V]$ = number of pathogens per designated area). In the presence of pathogenic infection, the host population is divided into two disjoint classes, susceptible S, and infected I.

The following assumptions are made to formulate the basic model equations.

(A1): In the ideal case of no pathogen the growth of susceptible host population follows the logistic law [15] implying that this growth is entirely controlled by an intrinsic birth rate constant $r(\in R_+)$ with a carrying capacity $k(\in R_+)$. The mathematical form of such logistic growth is

$$\frac{dN}{dt} = rN(1 - \frac{N}{k}). \tag{2.1}$$

(A2): Introduction of pathogen in the system splits the host population into two disjoint classes, namely susceptible host S and infected host I, such that at any time t the total host population remains as

$$N(t) = S(t) + I(t). \tag{2.2}$$

(A3): S increases its population by reproduction as per logistic law (2.1), but I are incapable of any reproduction [15].

(A4): At any instant of time, all susceptible host population (S) are equally susceptible and all infected population are equally infectious.

(A5): It is assumed that the spread of disease takes place in two avenues namely, by pathogens as well as by contact of a susceptible host with a infected host following the law of mass action.

It should be noted here that some researchers argued in favor of proportional mixing rate of contact between S and I rather than a simple law of mass action. But Greenwood experiment [16] on prototype systems showed that quantitative results remain the same in either cases of the mentioned contact processes.

Following assumptions (A3), (A4) and (A5), equation (2.1) can be written as

$$\frac{dS}{dt} = rS(1 - \frac{S+I}{K}) - \lambda SI - \gamma SV \tag{2.3}$$

where $\lambda(\in R_+)$ is the intensity of infection by infected host and and $\gamma(\in R_+)$ is the force of infection through contact with pathogens. The equation depicting the dynamics of pathogen population thus becomes

$$\frac{dV}{dt} = -\gamma SV + \eta d_I I - \mu V \tag{2.4}$$

Where $d_I(\in R_+)$ is the death rate constant of I. Note that we consider the mortality of I to be completely due to lysis and there exists no separate base line mortality of it. Here $\eta(\in R_+)$ is the rate of cell lysis (replication of pathogens) and the natural death rate of pathogens is denoted as $\mu(\in R_+)$.

Based on the string of arguments the time rate of change of I can be written as

$$\frac{dI}{dt} = \lambda SI + \gamma SV - d_I I \tag{2.5}$$

(A6): We assume that the infected hosts do not grow or reproduce but they can recover from pathogenic infection and move to add to the susceptible host population. Such recovery would stem out from immunization or vaccination. We consider a recovery rate of I to be denoted by $\delta(\in R_+)$.

Following the above assumption $(A1 - A6)$, the final set of equations depicting the dynamics of susceptible host, infected host and pathogens can be written as

$$\begin{aligned} \frac{dS}{dt} &= rS(1 - \frac{S+I}{K}) - \lambda SI - \gamma SV + \delta I \\ \frac{dI}{dt} &= \lambda SI + \gamma SV - d_I I - \delta I \\ \frac{dV}{dt} &= -\gamma SV + \eta d_I I - \mu V \end{aligned} \tag{2.6}$$

$$S(0) > 0,\ I(0) > 0,\ V(0) > 0.$$

The set of equations (2.6) constitute a generalized mathematical model for host-pathogen. A schematic diagram showing the flow of different constituent masses of host and pathogens conforming to the mathematical equations (2.6) is given in Figure 1. The variables of model equations (2.6) are to be made dimensionless for the sake of simplicity. Here we rescale all the variables in terms of carrying capacity K. Thus we apply the transformation, $s = \frac{S}{K}, i = \frac{I}{K}, v = \frac{V}{K}, \tau = rt$ and get the following dimensionless form of the model equation (2.6). For notational convenience we will replace τ by t henceforth. The rescaled equations are

$$\begin{aligned} \frac{ds}{dt} &= s(1 - (s+i)) - asi - bsv + ci \\ \frac{di}{dt} &= asi + bsv - di - ci \\ \frac{dv}{dt} &= -bsv + ei - fv \end{aligned} \tag{2.7}$$

where,

$a = \frac{\lambda K}{r},\ b = \frac{\gamma K}{r},\ c = \frac{\delta}{r},\ d = \frac{d_I}{r},\ e = \frac{\eta d_I}{r},\ and\ \ f = \frac{\mu}{r}$

ISBN: 978-988-17012-9-9
ISSN: 2078-0958 (Print); ISSN: 2078-0966 (Online)

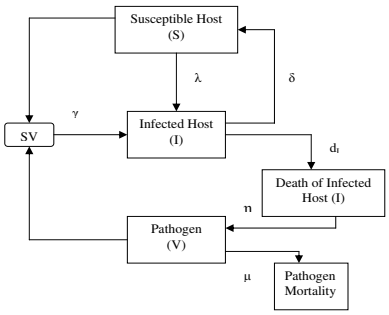

Figure 1: Schematic diagram of the model system equations(2.6) depicting the inter flow of constituent populations.

3 Existence, Uniqueness and Boundedness

We observe that right hand side of equation (2.7) are smooth functions of the variables s, i, v and parameters, as long as these quantities are non-negative, so local existence and uniqueness properties hold in the positive octant for some time interval $(0, t_f)$. In the next theorem we show that the linear combination of susceptible host, infected host and pathogens is less than a finite quantity or in other words, the solution of the system (2.7) is bounded.

Theorem 3.1 *All the solution $y(t)$ of (2.7), where $y = (s, i, v)$, is uniformly bounded for $y_0 \in R^3_{0,+}$.* **Proof:** We define a function $W(t) : R_{0,+} \to R_{0,+}$ by

$$W(t) = s + i + v \tag{3.1}$$

Observe that W is well defined and differentiable on some maximal interval $(0, t_f)$

The time derivative of (3.1) along the solutions of (2.7) is

$\frac{dW(t)}{dt} = s(1 - s - i) - di - bsv + ei - fv,$
i.e., $\frac{dW(t)}{dt} \leq (s-1)^2 - s - (d-e)i - fv + 1$

If we assume that, $0 < \rho < min.(1, d - e, f)$ then we get $\frac{dW(t)}{dt} + \rho \leq 1$ for each $t \in (0, t_f)$.

Applying the theory of differential inequality [17] we obtain, $0 < W(s, i, v) < \frac{1}{\rho}(1 - e^{-\rho t}) + W(s(0), i(0), v(0))e^{-\rho t}$, and for $t \to \infty$, we have

$$0 < W < \frac{1}{\rho}. \tag{3.2}$$

Hence all the solutions of $y(t)$ that initiate in R^3_+ are confined in the region $B = \{(s, i, v) \in R^3_+ : W = \frac{1}{\rho} + \xi, \quad for\ any\ \xi > 0\}$. Hence the proof.

4 Equilibria Conditions

System (2.7) possesses the following equilibria: $E_0(0, 0, 0)$, $E_1(1, 0, 0)$, and $E^*(s^*, i^*, v^*)$. Where $i^* = \frac{s^*(1-s^*)}{s^*+d}$, and $v^* = \frac{es^*(1-s^*)}{(s^*+d)(bs^*+f)}$ and s^* is the positive root of

$$\chi_1(s^*)^2 - \chi_2 s^* - \chi_3 = 0 \tag{4.1}$$

where $\chi_1 = ab$, $\chi_2 = bd + bc - af - be$ and $\chi_3 = (d + c)f$. Note that equation (4.1) has a unique positive root, given by $s^* = \frac{\chi_2 + \sqrt{\chi_2^2 + 4\chi_1\ \chi_3}}{2\chi_1}$
if $\chi_1 > 0$, $\chi_2 > 0$ and $\chi_3 > 0$ for which $b(d+c) > af + be$.

It is to be noted that

$$s^* + i^* \leq 1 \tag{4.2}$$

This condition is due to the fact that $s(t) + i(t) \leq 1, \forall\ t > 0$.

5 Stability Analysis

Constructing the variational matrix about any arbitrary equilibrium $E(s, i, v)$, we state and prove the following theorems

Theorem 5.1 The system (2.7) is unstable around E_0 for all parametric values. (The proof is obvious).

Theorem 5.2 The system (2.7) is asymptotically stable around E_1 if $a + \frac{be}{b+f} < c + d$.

Proof: The variational matrix corresponding to E_1 is

$$\begin{pmatrix} -1 & -1 - a + c & -b \\ 0 & a - d - c & -b \\ 0 & e & -(b + f) \end{pmatrix} \tag{5.2.1}$$

Proof: The eigenvalue of the variational matrix corresponding to equilibrium E_1 is

$$\zeta = -1 \quad and \quad \zeta^2 - \nu_1\zeta - \nu_2 = 0 \tag{5.2.2}$$

where,

$$\nu_1 = a - d - c - b - f \quad and \quad \nu_2 = (a - d - c)(b + f) + be$$

The last equation of (5.2.2) containing two eigenvalues implies that it has two roots and it is obvious that the system (2.7) is asymptotically stable around E_1 if $a + \frac{be}{b+f} < c + d$.

Theorem 5.3 The system (2.7) is always stable around E^* for all parametric values if
(i) $max.(ae, be, \frac{bf}{b-a}) < c < min.(as^*, \frac{(a+1)bes^*}{a(bs^*+f)}, \frac{(a+1)f}{b})$
(ii) $a < b < a + 1$
(iii) $f > max.(be, b^2v^*)$
(iv) $i^* > \frac{e}{a(a+1)}$
Proof: Observe that from first two equations of the system (2.7), we always have

$$\frac{d(s+i)}{dt} = s(1 - (s + i)) - 2bsv - di < (s + i)(1 - (s + i))$$

Hence [18] we have $\lim_{t\to\infty} \{s(t) + i(t)\} < 1$. Thus we have $s^* + i^* < 1$ and the last condition (4.2) is always satisfied.

The characteristic equation of the linearized system of (2.7), corresponding to E_*, is given by

$$\zeta^3 + \alpha_2\zeta^2 + \alpha_1\zeta + \alpha_0 = 0 \tag{5.3.1}$$

ISBN: 978-988-17012-9-9
ISSN: 2078-0958 (Print); ISSN: 2078-0966 (Online)

where,

$$\begin{aligned}
\alpha_2 &= \tfrac{ci^*}{s^*} + s^* + \tfrac{bs^*v^*}{i^*} + bs^* + f \\
\alpha_1 &= cbv^* + cbi^* + \tfrac{cfi^*}{s^*} + \tfrac{b(s^*)^2v^*}{i^*} + b(s^*)^2 + fs^* \\
&\quad + \tfrac{b^2(s^*)^2v^*}{i^*} + \tfrac{bfs^*v^*}{i^*} - ebs^* - aci^* - bcv^* \\
&\quad + a(a+1)i^*s^* + b(a+1)v^*s^* - b^2v^*s^* \\
\alpha_0 &= cb^2v^*s^* - cebi^* + \tfrac{b^2v^*(s^*)3}{i^*} + \tfrac{bfv^*(s^*)^2}{i^*} - eb(s^*)^2 \\
&\quad - abci^*s^* - acfi^* + a(a+1)bi^*(s^*)^2 + a(a+1)fi^*s^* \\
&\quad + a(a+1)bfv^*s^* + abei^*s^* + b^2ev^*s^* - \tfrac{b^3(v^*)^2(s^*)^2}{i^*}
\end{aligned} \tag{5.3.2}$$

From Routh-Hurwitz criterion, E^* is locally asymptotically stable if and only if $\alpha_2 > 0, \alpha_0 > 0$ and $\alpha_2\alpha_1 - \alpha_0 > 0$.

From the signs of those defined in (5.3.2), it is clear that $\alpha_2 > 0$. It is easy to verify that $\alpha_0 > 0$ for all parametric values, provided

$$\begin{aligned}
&(i)\ \ c < min.(as^*, \tfrac{(a+1)bes^*}{a(bs^*+f)}, \tfrac{(a+1)f}{b}), \quad (ii)\ \ f > b^2v^*, \\
&(iii)\ \ i^* > \tfrac{e}{a(a+1)},
\end{aligned} \tag{5.3.3}$$

It is also easy to verify that, $\alpha_2\alpha_1 - \alpha_0 > 0$ for all parametric values provided,

$$\begin{aligned}
&(i)'\ \ c > max.(ae, be, \tfrac{bf}{b-a}), \quad (ii)'\ \ f > be, \\
&iii)'\ \ a < b < a+1,
\end{aligned} \tag{5.3.4}$$

From (5.3.3) and (5.3.4) it is obvious that system (2.7) is always for all parametric values and hence completes the theorem.

6 Numerical solutions of the model Equations

Theoretical analysis of the model is done to explore stability, equilibria and uniqueness of the solutions and their boundedness. But, for physical realization of the time evolution of different host and pathogen populations with varying model parameters, we consider numerical solutions of the set of equations (2.6). This enables us to visualize the dynamical behaviors of variables S, I, and V. Values of different constant model parameters, as given in Table.1, were chosen from the amassed literature in the field. Note that we want to emphasize the role of the recovery rate within the model.

Table.1. Values of parameters used for models dynamics calculations.

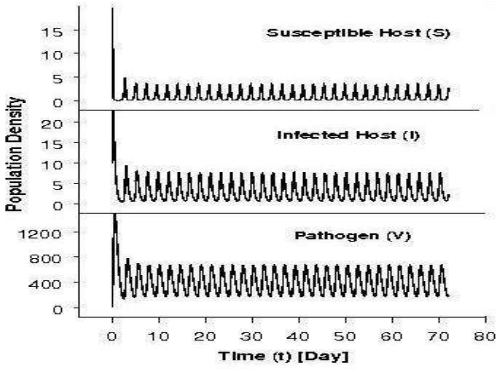

Figure 2: Population densities of Susceptible host (S), Infected host (I) and Pathogen (V) are plotted as a function of time for the Recovery rate $\delta = 0.2$. Other parameters are as in Table.1.

Parameter	Definition	Default Value (day $^{-1}$)
r	Maximal growth rate of susceptible host	11
K	Carrying capacity	35 unit designated area
λ	Force of infection through contact with infected host	0.2 unit designated area
γ	Force of infection through contact with pathogens	0.03 unit designated area
d_I	Lysis death rate of infected host	2.5 liter
η	Pathogens replication factor	115
μ	Mortality rate of pathogen	2.2

With the positive octant restriction on S, I, V at $t = 0$ (i.e., $S > 0$, $I > 0$, $V > 0$) we have chosen $S(0) = 20$, $I(0) = 10$, $V(0) = 10$. We have considered variation in the recovery rate (δ) in a wide range from $\delta = 0$ to about $\delta = 110$. It is to be mentioned here that δ is taken in arbitrary units. To begin with, we check the time evolution of S, I, and V with increasing δ.

In Figure 2 we have shown these hosts and pathogen populations as a function of time for $\delta = 0.2$. Note that, we have gone upto a time $t = 70$ days. This is because, a thorough check on the system reveals stabilization of all these populations well before $t = 70$ and within this the characteristic features of the system are manifested. In Figure 2 we find oscillatory solutions for all three populations bounded by stable upper and lower limits. As we increase δ, the upper and lower limits of solutions come closer (see Figure3). Beyond some δ the two limits of solutions merge into one and thereafter, unique stable solutions for all three populations exist (see Figure4).

ISBN: 978-988-17012-9-9
ISSN: 2078-0958 (Print); ISSN: 2078-0966 (Online)

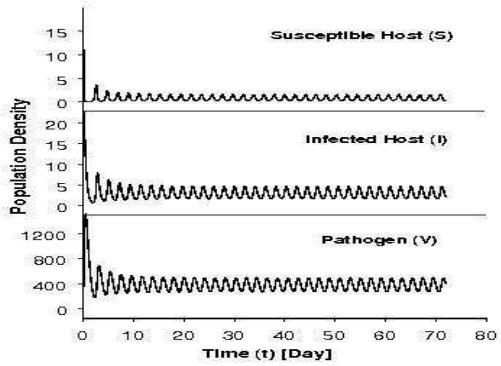

Figure 3: Populations S, I and V are plotted as a function of time for $\delta = 0.4$.

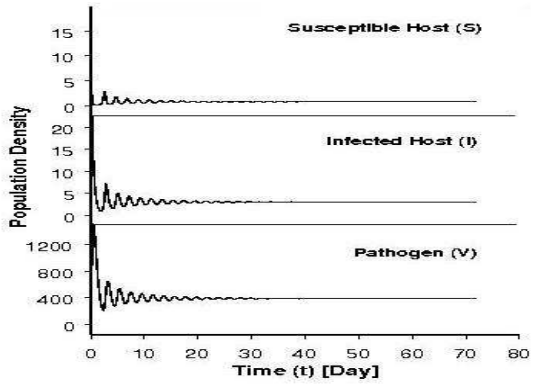

Figure 4: Densities of S, I and V populations are plotted as a function time for $\delta = 0.6$

In Figure 5(a) we have plotted stable solutions for S and I populations for small values of δ and the same for V is in Figure 5(b). Here we find that with $\delta \leq 0.6$ stable solutions are oscillatory for all three populations where bifurcating line towards lower δ denote the stable upper and lower boundary of such oscillatory solutions.

Figures 6(a) & 6(b) contains stable and unique solutions for different populations for larger ($\delta \geq 0.6$). We find that stable (solution) value of susceptible host increases monotonically, but the same for infected host rises faster in Figure 6(a) and similar rise in pathogen stable solution is the steepest. But beyond certain δ, rise in I and V stable values are arrested and they turn downwards. Stable value of V turns downward at a $\delta \sim 31$ which is smaller than that for stable I turnaround at $\delta \sim 35.5$. At a very large $\delta \sim 100$ extinction of I as well as V take place. The I stable value goes to Zero at $\delta = 99$ which is slightly lower than that for stable V. At $\delta \geq 99$, where extinction of I takes place, stable solution S becomes completely flat and attains the numerical value of the carrying capacity $K = 35$. This is characteristic of the model equations (2.6). Here, extinction of I and V means $I = V = 0$ and single valued stable solutions implies $\frac{dS}{dt} = \frac{dI}{dt} = \frac{dV}{dt} = 0$. Thus, from equations (2.6), we get $1 - \frac{S}{K} = 0$ *i.e.*, $S = K$

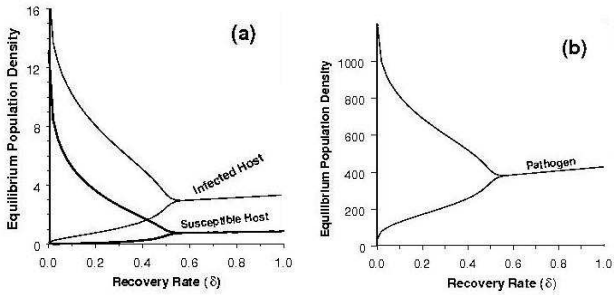

Figure 5: Equilibrium solutions of S, I and V are plotted as a function of recovery rate $\delta \leq 1.0$

7 Discussion and Conclusions

We have considered a mathematical model of a host-pathogen system including a recovery of the infected host to the susceptible. The set of differential equations of the model are solved both analytically and numerically. Here, we put emphasis on the recovery of the infected host to their healthy class. We have analyzed the model in-depth, particularly to see the effects of host recovery on the model dynamics and its solutions.

Our theoretical analysis of the existence, uniqueness and boundedness of the asymptotic solutions show that perimetrically conditioned solutions for the model equations do exist and they are unique and bounded in well defined regions of the parameter space. The analysis further show that the system possesses several equilibria, some of which are denoted by $E_o(0,0,0), E_1(1,0,0)$, and $E^*(s^*, i^*, v^*)$. However, by stability analysis of equilibria, we find that the system is unstable around E_0 for all parametric values and E_1 is locally asymptotically stable. Also the system is locally asymptotically stable around E^*. In fact E^* is globally asymptotically stable.

Complete numerical solutions of the model equations for the parameters as in (Table.1), yield results which are consistent with the parametric conditions obtained analytically. In this case too we put emphasis on how the model dynamics evolve with the recovery rate (δ). We find that, for very small to moderate values of δ (≤ 0.6), stable solutions for all three populations are oscillatory. But, for $\delta > 0.6$, the solutions are single valued and stable. When recovery rate attains a threshold $\delta \sim 100$ (in units of per designated area), only the susceptible host population (S) survives asymptotically while infected host (I) and pathogen (V) populations are pushed to extinction. This feature of recovery and sustenance of the host population subsiding any pathogenic attack, in biological terms, means that the system enters a disease-free zone. Our numerical calculations show that the removal of infected host population, coupled

ISBN: 978-988-17012-9-9
ISSN: 2078-0958 (Print); ISSN: 2078-0966 (Online)

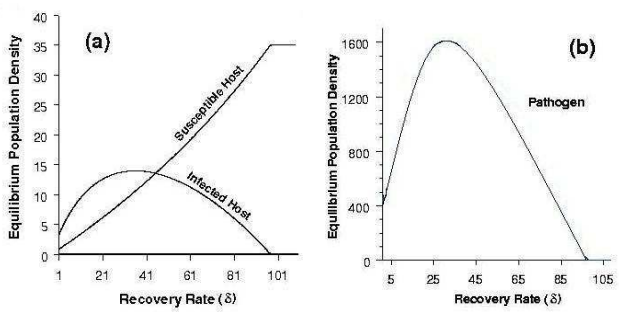

Figure 6: Equilibrium solutions for S, I and V are plotted as a function of $\delta \geq 1.0$ to emphasize the unique solutions and associated characteristics of different variables for higher δ

with a finite rate of death of pathogen, actually forces the pathogen population towards extinction path. Notice that the threshold value of the recovery rate in the present case is higher than its biologically realizable value. This threshold δ can be scaled down to sensible limits provided we can set the death rate of infected host (d_I) to a value higher than that considered here, and also the rate of contacts (λ & γ) of S with I and V respectively to their further lower values. Actually, in a biological prototype of host-pathogen model, numerical values of the parameters d_I, λ, γ are externally controllable. Hence the prediction that, a disease free situation for the host population can be effected at biologically and physically realizable threshold of recovery rate, only setting the externally controllable parameters to their respective suitable values.

Acknowledgements: Its a pleasure to thank Dr. Nandadulal Bairagi, Department of Mathematics, Jadavpur University for useful discussions and Jhumpa Bhadra Junoir Research Fellow, Department of Mathematics, Jadavpur University for her technical support.

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