VIRUS REPLICATION FACTOR MAY BE A CONTROLLING AGENT FOR OBTAINING DISEASE-FREE SYSTEM IN A MULTI-SPECIES ECO-EPIDEMIOLOGICAL SYSTEM

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The role of viruses in marine phytoplankton-zooplankton community structure is undoubtedly very important. In this paper, we propose a simple mathematical model for phytoplankton-zooplankton (prey-predator) system with an additional factor that the viral disease is spreading only among the prey species. Considering high abundance and importance of viruses in aquatic environments we have explicitly considered here the growth equation of free viruses and have studied this four-dimensional model analytically. It is observed that the disease-free system can be obtained when the virus replication factor lies in-between certain critical values. Numerical simulations have also been performed to substantiate the analytical findings.

Keywords: Susceptible Phytoplankton; Infected Phytoplankton; Zooplankton; Virus Replication Factor; Local Stability; Global Stability.

1. Introduction

Planktons are the basis of all aquatic food chain. Phytoplanktons are very small, usually single-celled organisms, chiefly diatoms, that photosynthesize just like plants do and occupy the first trophic level in food chain. Phytoplankton provides oxygen

for human life, food for marine life and also absorb half of the carbon dioxide from the earth's atmosphere. The dynamics of rapid increase or decrease of plankton populations is an important subject for marine plankton ecology. Viruses are evidently the most abundant entities in the sea — nearshore and offshore, tropical to polar, sea surface to sea floor, and in sea ice and sediment pore water. Natural marine water contain roughly 10^9 to 10^{12} virus particles per liter. Virus infects the most important marine primary producer community, the phytoplankton and infection by viruses could be a factor regulating phytoplankton community structure and primary productivity in the oceans.[1] Viral infections also cause cell lysis in phytoplankton. Using electron microscopy, Suttle *et al.*[2] showed that the viral disease can infect bacteria and phytoplankton in coastal water. Virus-like particles have been described in many eukaryotic algae, cyanobacteria and natural phytoplankton communities.[2] Many phytoplanktonic species show spectacular bursts ("blooms") in population density and viruses have been held responsible for the collapse of *Emiliania huxleyi* blooms in mesocosms[3] and have been shown to induce lysis of *Chrysochromulinia*.[4] Quite a good number of studies[2,5] showed the presence of pathogenic viruses in phytoplankton communities. Fuhrman[6] synthesized the accumulated evidence regarding the nature of marine viruses and their ecological as well as biological effects. Nevertheless, despite the increasing number of reports, the role of virus infection in plankton population is still in a state of infancy.

Few theoretical studies have been carried out in such eco-epidemiological systems. Mukherjee[7] studied the persistence in a prey-predator system with disease in the prey. Chattopadhyay *et al.*[8] studied the effect of viral infection on the generalized Gause model of prey-predator system. Beltrami and Carroll[9] observed the role of viral disease in recurrent phytoplankton blooms by proposing a three-species model consisting of susceptible phytoplankton, infected phytoplankton and their grazer. They showed that introduction of virus-contaminated cells has significant effect on the stabilization of the system. Chattopadhyay and Pal[10] modified the model of Beltrami and Carroll[9] and the model of Venturino.[11] They concluded that the role of viral infection in plankton community is very much unpredictable and model dependent. It is to be mentioned here that though virus populations play a crucial role in the marine ecosystem, the dynamics of the free viruses were not considered explicitly in these models. Since virus is responsible for the infection and the number of new virus depends on the virus replication factor, so virus replication factor may play a crucial role in the system dynamics. Beretta and Kuang[12] studied the role of virus replication factor in a different context. They considered a simple three-dimensional mathematical model to describe the epidemics induced by bacteriophases in marine bacteria populations and showed that there exists a threshold "virus replication factor" beyond which the endemic equilibrium bifurcates from the disease-free equilibrium. Keeping this in mind, here we propose a simple mathematical model for phytoplankton-zooplankton (prey-predator) system with an additional factor that the viral disease is spreading only among

the prey species. Considering high abundance and importance of viruses in aquatic environments we have explicitly considered here the growth equation of free viruses. The main objectives of this article are:

- to study the dynamics of the system in the presence of virus population and
- to find out conditions under which the system becomes disease free.

It is observed that the co-existence of all the species is never possible but the disease-free situation can be attained only when the virus replication factor attains some critical value.

The organization of the paper is as follows: Sec. 2 deals with the basic assumption and the mathematical model. Equilibria and their existence are given in Sec. 3. Local asymptotic analysis around each equilibrium is discussed in Sec. 4. In Sec. 5, a numerical study is given and finally a summary of the results is presented in Sec. 6.

2. The Basic Assumptions and the Mathematical Model

We consider a three-species ecological system, namely phytoplankton (prey), whose concentration is denoted by N ($[N]$ = number of prey cells/liter), zooplankton, the grazer of phytoplankton, whose concentration is denoted by y ($[y]$ = number of predator animals/liter), and the virus population whose concentration is denoted by v ($[v]$ = number of viruses/liter). The phytoplankton is assumed to be susceptible to a viral disease, and in the presence of viruses the total phytoplankton population is divided into two classes, namely susceptible phytoplankton and infected phytoplankton.

The following assumptions are made for formulating the basic differential equations.

(A1): In the absence of virus disease, the phytoplankton cells grow according to a logistic fashion[13] with carrying capacity $k(\in R_+)$, and with an intrinsic birth rate constant $r(\in R_+)$ such that

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

(A2): In the presence of viruses, we assume that the total concentration of phytoplankton cell, N, is divided into two classes, namely susceptible phytoplankton, denoted by x, and infected phytoplankton, denoted by z. Therefore, at any time t the total (concentration) of phytoplankton population is

$$N(t) = x(t) + z(t). \tag{2.2}$$

(A3): We assume that the susceptible phytoplankton, x, are capable of reproducing with logistic law [Eq. (2.1)] and the infective phytoplankton, z, are removed by cell lysis before having the capability of reproducing. Though the infected cells of phytoplankton do not contribute to the growth of the overall phytoplankton cells, N, it is reasonable to assume that the infected cells, z, during

their latency period, T, still compete for resources with the susceptible cells to enable the replication of the viruses inside themselves.[14] Thus we assume that the infected prey do not grow, recover and reproduce, but contribute to the carrying capacity.

(A4): We assume that the disease spreads among the prey species only and the predator species is not affected due to predation of the infected prey. Also the infected prey is more vulnerable to predation than the susceptible prey which has been observed in the several natural systems.

(A5): A susceptible phytoplankton, x, becomes infected under the attack of many viruses, v. The contact process is admittedly debatable. Some researchers argue that a proportional mixing rate is more appropriate than that of simple mass action law. But the data of Greenwood experiment suggests that there is no change of qualitative properties upon the contact process whether it follows the law of mass action or proportional mixing rate.[15]

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

$$\frac{dx}{dt} = rx\left(1 - \frac{x+z}{k}\right) - \lambda xv \tag{2.3}$$

where λ is the force of infection.

(A6): If grazer population y predates the susceptible phytoplankton, x, at a rate $b(\in R_+)$, then Eq. (2.3) takes the form:

$$\frac{dx}{dt} = rx\left(1 - \frac{x+z}{k}\right) - \lambda xv - bxy. \tag{2.4}$$

The dynamics of the grazer population, y, may be written as

$$\frac{dy}{dt} = cxy + hyz - dy. \tag{2.5}$$

Here $d(\in R_+)$ is the death rate of grazer population. $c(\in R_+)$ and $h(\in R_+)$ are the conversion rates for susceptible and infected phytoplankton, respectively.

(A7): An infected phytoplankton z has a latent period, which is the period between the instant of infection and that of lysis, during which the virus reproduces inside the infected phytoplankton. The lysis death rate constant $\alpha(\in R_+)$ gives a measure of such latency period T being $\alpha = \frac{1}{T}$. β is the virus replication factor, i.e. lysis of infected phytoplankton, on the average, produces β virus particles ($\beta \in R_+, \gg 1$) and in future study we assume $(\beta - 1) > 0$. The dynamics of infected phytoplankton, z, and virus population v may be represented as

$$\begin{aligned} \frac{dz}{dt} &= \lambda xv - lyz - \alpha z \\ \frac{dv}{dt} &= -\lambda xv - \mu v + \alpha\beta z \end{aligned} \tag{2.6}$$

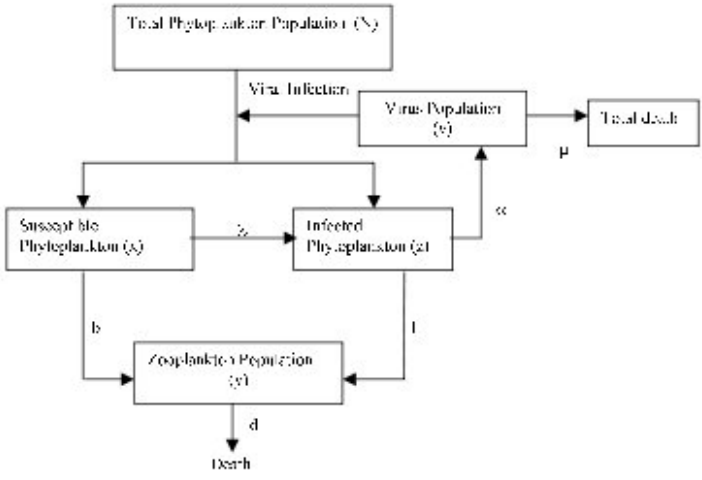

Fig. 1. Schematic diagram of the model.

where $\mu(\in R_+)$ is the death rate of virus population and $l(\in R_+)$ is the capture rate of the infected prey by the predator. As mentioned in $(A3)$, it is assumed that $l > b$. We do not consider a separate mortality term for infected phytoplankton because we assume that the mortality of infected phytoplankton is almost completely due to lysis. Model conceptual schematic diagram is presented in Fig. 1.

Now following the above assumptions, we can now write the following differential equations describing the time evolution of the above eco-epidemiological system

$$\begin{aligned}
\frac{dx}{dt} &= rx\left(1-\frac{x+z}{k}\right)-\lambda xv-bxy\\
\frac{dy}{dt} &= cxy-dy+hyz\\
\frac{dz}{dt} &= \lambda xv-\alpha z-lyz\\
\frac{dv}{dt} &= -\lambda xv-\mu v+\alpha\beta z
\end{aligned} \tag{2.7}$$

as our model.

System (2.7) has to be analyzed with the following initial conditions:

$$x(0) > 0, \quad y(0) > 0, \quad z(0), \quad v(0) > 0. \tag{2.8}$$

We observe that the right-hand-side of Eq. (2.7) is a smooth function of the variables (x, y, z, v) and the parameters, as long as these quantities are non-negative, so local existence and uniqueness properties hold in R^4_+.

Note that $\frac{dx}{dt} = x[r(1-\frac{x+z}{k})-\lambda v-by]$. So $\frac{dx}{dt} \geq 0$ if $x = 0$ and $x \geq 0$, $y \geq 0$, $z \geq 0, v \geq 0$. Hence $x \geq 0, \forall t$. It is also true for the other variables y, z, and v.

Hence we can state the following theorem:

Theorem 2.1. $\forall j, \frac{dx_j}{dt} \geq 0$ *if* $x_j = 0$ *and* $x_i \geq 0, i \neq j$, *then* $x_j \geq 0, \forall j$.

Now we shall show that the system (2.7) *is uniformly bounded.*

Lemma 2.1. *All the solutions of* (2.7) *which initiate in* R_+^4 *are uniformly bounded if* $\frac{l}{h} > \frac{b}{c}$.

Proof. See Appendix A. □

Biological Interpretation. The expression $\frac{l}{h} > \frac{b}{c}$ states that the ratio of capture rate to conversion factor of infected phytoplankton is greater than that of susceptible phytoplankton.

3. Equilibria

System (2.7) possesses the following equilibria $E_0(0,0,0,0)$, $E_1(K,0,0,0)$, $E_2(x_2,y_2,0,0)$, $E_3(x_3,0,z_3,v_3)$ and $E^*(x^*,y^*,z^*,v^*)$, where $x_2 = \frac{d}{c}$, $y_2 = \frac{r}{b}(1 - \frac{d}{Kc})$, $x_3 = \frac{\mu}{\lambda(\beta-1)}$, $z_3 = \frac{\mu r K[1-\frac{\mu}{\lambda K(\beta-1)}]}{[1-\lambda K\alpha(\beta-1)+\mu r]}$, $v_3 = \frac{r\alpha[K\lambda(\beta-1)-m u]}{\lambda[\alpha(\beta-1)+\mu r]}$, $y^* = \frac{\lambda\alpha\beta x^*}{l(\lambda x^*+\mu)} - \frac{\alpha}{l}$, $z^* = \frac{d-cx^*}{h}$, $v^* = \frac{\alpha\beta(d-cx^*)}{h(\lambda x^*+\mu)}$ and x^* is the positive root of

$$Ax^2 - Bx - C = 0, \tag{3.1}$$

where $A = \lambda rl(h-c), B = rlh(\lambda K - \mu) + \lambda K\alpha\beta(cl - bh) + \lambda(b\alpha Kh - rld)$ and $C = rld\mu + \alpha\lambda d - \mu rlKh - \alpha Kh$. Note that Eq. (3.1) has a unique positive root, given by

$$x^* = \frac{B + \sqrt{B^2 + 4AC}}{2A}$$

if $A > 0$, $B > 0$ and $C > 0$ for which $h > c$, $\frac{rld}{\alpha K} < bh < cl$ and $\mu < \min[\lambda K, \frac{lK\lambda\alpha\beta d}{rlKh+b\alpha Kh-rld}]$. It is to be noted that E_2 exists iff $d < Kc$, E_3 exists iff $\beta > (1 + \frac{\mu}{K\lambda})$.

Remark 3.1. It is interesting to observe that E_2 arises from E_1 for the value of the parameter $K = \frac{d}{c}$, and persists for all $K > \frac{d}{c}$, and E_3 arises from E_1 for $K = \frac{\mu}{\lambda(\beta-1)}$ and persists for all $K > \frac{\mu}{\lambda(\beta-1)}$.

4. Stability Analysis

Theorem 4.1. *The system* (2.7) *is unstable around* E_0 *for all parametric values.*

Proof. The proof is obvious and hence omitted.

Theorem 4.2. *The system* (2.7) *is locally asymptotically stable around* E_1 *if* $d > cK$ *and* $\beta < \beta^*$ *where* $\beta^* = (1 + \frac{\mu}{\lambda K})$.

Proof. See Appendix B. □

Biological Interpretation. Note that, the condition $d > cK$ implies that the death rate of zooplankton is greater than its maximal growth rate. And λK determines the number of new infections per virus per unit time, while $\frac{1}{\mu+\lambda K}$ gives the average time that a virus lives if the density of the susceptible phytoplankton is K. Therefore, $\frac{\lambda K}{\mu+\lambda K}$ determines the number of new infected phytoplankton per virus, while $\beta \times \frac{\lambda K}{\mu+\lambda K}$ gives the number of new virus per virus. Thus, $\frac{\beta\lambda K}{\mu+\lambda K} < 1$ or $\beta < \frac{\mu+\lambda K}{\lambda K} = 1 + \frac{\mu}{\lambda K} = \beta^*$ implies that a virus, on the average, cannot produce at least one new virus during its life when the susceptible phytoplankton are as abundant as possible.

Remark 4.1. It is to be noted here that when E_1 is locally stable then neither E_2 nor E_3 exists.

Note. The proof of Theorems 4.3–4.6 (except 4.4) are similar to the proof of Theorem 4.2 and hence omitted.

Theorem 4.3. *The system* (2.7) *is locally asymptotically stable around* E_2 *if*

$$\text{(i) } d < Kc \quad \text{(ii) } \beta \in (\beta^*, \beta^{**}),$$

where $\beta^* = (1 + \frac{\mu}{\lambda K})$ *and* $\beta^{**} = (1 + \frac{c\mu}{\lambda d})[1 + \frac{lr}{b}(1 - \frac{d}{Kc})]$.

Biological Interpretation. The condition $d < Kc$ implies that the death rate of zooplankton is less than its maximal growth rate. And the condition $\beta \in (\beta^*, \beta^{**})$ implies that a virus, on the average, can produce at least one new virus during its life period but cannot produce more than β^{**} virus.

In the next theorem, we state sufficient conditions for which the system becomes globally asymptotically stable around E_2.

Theorem 4.4. *The system is globally asymptotically stable around* E_2 *if*

$$\text{(i) } d < \frac{Kch}{c+h} \quad \text{(ii) } \beta \in (\beta^*, \beta_c),$$

where $\beta^* = (1 + \frac{\mu}{\lambda K})$ *and* $(1 + \frac{c\mu}{\lambda d}) + \frac{\mu hr}{\alpha\lambda d}(1 - \frac{d}{Kc}) - \frac{\mu r}{\alpha\lambda K} = \beta_c < \beta^{**}$.

Proof. See Appendix C. □

Remark 4.2. Note that the values of d and β in this case are less than the corresponding values of d and β in Theorem 4.4.

Theorem 4.5. *The system* (2.7) *is unstable around* E_3 *if*

$$d < \frac{\mu}{\lambda(\beta-1)}\left[c + \frac{hr}{\alpha}\left(1 - \frac{\mu}{\lambda K(\beta-1)}\right)\right].$$

Biological interpretation. The above condition states that the system is unstable around E_3 if the death rate of the zooplankton does not exceed some critical value.

Theorem 4.6. *The positive interior equilibrium E^* is always unstable.*

5. Numerical Study

To visualize the above analytical findings we have used the following parameter values (see Table 1), which have been collected from the available literatures viz.[9,12,10,16]

For the following parameter values, the equilbrium value of E_2 is given by $(13.33, 83.33, 0, 0)$. If the solutions of the system (2.7) start with initial values (12, 80, 2, 1) (close to E_2) we observe that the infected phytoplankton and the virus population go to extinction, whereas the susceptible phytoplankton and the zooplankton co-exist in the form of a stable steady state. This ensures that the disease-free equilibrium, E_2, is locally asymptotically stable (see Fig. 2). It is to be noted that all the conditions of Theorem 4.4 are satisfied in this case.

For the parameter values as in Table 1, the threshold values of β^* and β_c are respectively 7.66 and 94.5. We observe that the time series solutions of the system (2.7) converge to the disease-free equlibria E_2 when β lies between 7.66 to 94.5. In particular, we select $\beta = 15.92$ and observe that the solutions of the system (2.7) converge to the disease-free equilibrium E_2 with different initial conditions [(20, 120, 18, 11), (40, 12, 5, 2), (5, 30, 2, 27)] (other parameters are as in Table 1) (see Fig. 3). This indicates that the model system is globally asymptotically stable around the disease-free equilibrium, E_2.

The threshold value of β^{**} for the same set of parameter values is 149.32. If the virus replication factor crosses the upper threshold value β^{**}, it is observed that the disease-free equilibrium, E_2, loses its stability with growing oscillations in virus

Table 1. The parametric values used in numerical simulations.

Parameters	Symbols	Values
Intrinsic birth rate constant	r	9 day $^{-1}$
Carrying capacity	K	30 (liter day $^{-1}$)
Force of infection	λ	0.01 (liter day $^{-1}$)
Capture rate of susceptible phytoplankton	b	0.06 (liter day $^{-1}$)
Capute rate of infected phytoplankton	l	0.1 (liter day $^{-1}$)
Conversion rate of susceptible phytoplankton	c	0.03 (liter day $^{-1}$)
Conversion rate of infected phytoplankton	h	0.05 (liter day $^{-1}$)
Lysis death rate	α	1.5 day $^{-1}$
Virus death rate	μ	2 day $^{-1}$
Virus replication factor	β	15.92
Death rate of zooplankton	d	0.4 day $^{-1}$

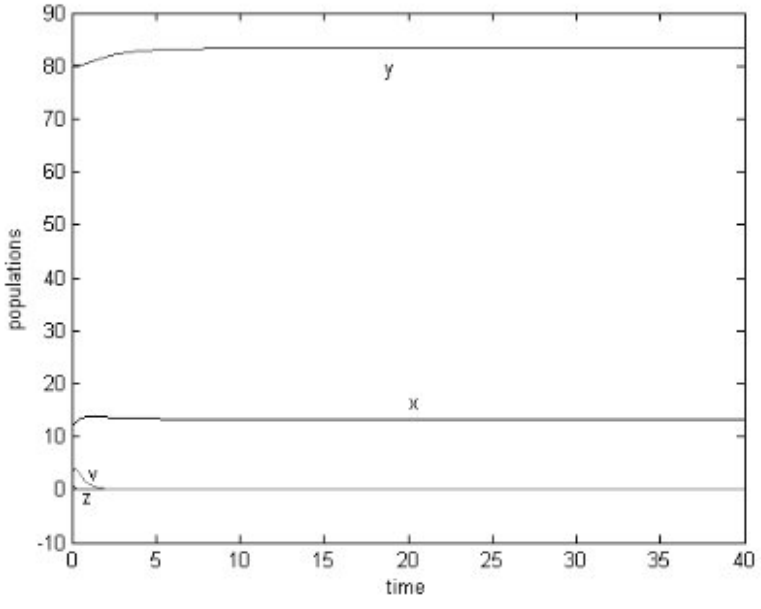

Fig. 2. Time series solutions of (2.7) with parameter values as in the Table 1 and where the conditions of Theorem 4.3 hold. The solutions starting at $(12, 80, 2, 1)$ (close to E_2) tend to E_2 $(13.33, 83.33, 0, 0)$, depicting local stability of the disease-free equilibrium, E_2.

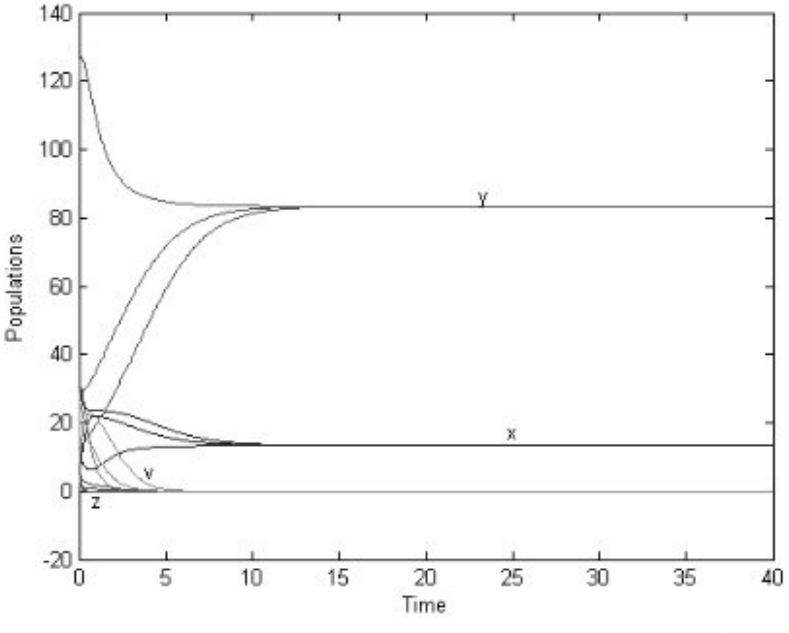

Fig. 3. Time series solutions of (2.7) with different initial conditions (20, 120, 18, 11), (40, 12, 5, 2), (5, 30, 2, 27) converge to the disease-free equilibrium E_2 (13.33, 83.33, 0, 0), depicting global asymptotic stability of the disease-free equilibrium, E_2 Parameter values are given in Table 1.

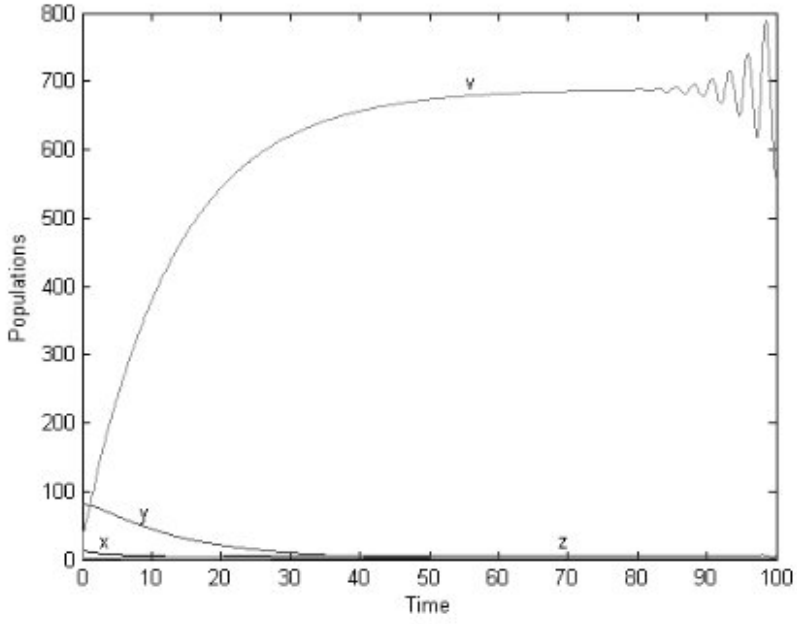

Fig. 4. Time series solutions of (2.7) with initial values (12, 80, 2, 1) for the parameter values as in Table 1 except $\beta = 160$. Clearly the solution bifurcates from a stable to an unstable one when virus replication factor crosses the value $\beta^{**} = 148$.

population. We choose $\beta^{**} = 160$, keeping all other parameters unchanged, and observe that the solution bifurcates from a stable to an unstable one (see Fig. 4). Note that the virus population increases significantly when β, the virus replication factor, increases.

6. Summary

The effect of diseases on the ecological system is an important issue from the mathematical and ecological point of view. Reports of high abundance of viruses in aquatic environments are known for quite some time and their role in regulating the phytoplankton community structure and primary productivity in the ocean have been implicated.[2,5] In this paper we propose and analyze, both analytically and numerically, a simple phytoplankton-zooplankton (prey-predator) system in which phytoplankton are infected by a transmissible disease and thus form a new group, namely the infected phytoplankton which becomes more vulnerable to predation due to the disease. Furthermore, we have introduced the growth equation of free viruses in the system equations and studied the dynamics. Our model consists of four nonlinear differential equations, namely a susceptible phytoplankton, infected phytoplankton, their predator zooplankton and the virus population. In the absence of the free viruses, the system is more or less similar to the model

of Chattopadhyay and Pal.[10] We first showed that all the solutions which initiate in R_4^+ are uniformly bounded. The system admits four boundary equilibria and one interior equilibrium under suitable parametric conditions. We observed that the trivial equilibrium, E_0, and the interior equilibrium, E^*, are always unstable with respect to all perturbations, whereas the equilibrium E_3 is unstable when $d < \frac{\mu}{\lambda(\beta-1)}[c + \frac{hr}{\alpha}(1 - \frac{\mu}{\lambda K(\beta-1)})]$. The axial equilibrium, E_1, is stable if $cK < d$ and the virus replication factor, β, is less than β^*, where $\beta^* = 1 + \frac{\mu}{\lambda K}$. In other words, the axial equilibrium, E_1, is stable if the death rate of zooplankton is greater than its maximal growth rate and if a virus, on the average, be unable to produce at least one new virus during its life when the susceptible phytoplankton are as abundant as possible. On the other hand, the necessary condition for E_2 to be locally stable is that a virus, on the average, have to produce at least one new virus during its life cycle and the death rate of zooplankton is less than its maximal growth rate. One of the basic motivations of an eco-epidemiological problem is to find out the conditions for which the system eventually becomes disease free. From the previous study it is clear that the considered system will be disease free (i.e. E_2 will be stable) if $d < cK$ and the virus replication factor, $\beta \in (\beta^*, \beta^{**})$. Another interesting question is under what condition the system will be disease free regardless of initial conditions. Our global stability of the disease free equilibrium, E_2, ensures this.

In conclusion, we like to mention that our model can be made more meaningful and realistic if one consider the latency period of infected phytoplankton explicitly in the model equations and/or new variable resources to this system (stoichiometry). And we leave these for future study.

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Appendix A

We define a function

$$w = x + \frac{b}{c}y + z + \frac{1}{\beta}v. \tag{A.1}$$

The time derivative of (A.1) along the solutions of (2.7) is

$$\frac{dw}{dt} = rx\left(1 - \frac{x+z}{k}\right) - yz\left(\frac{lc - bh}{c}\right) - \frac{bd}{c}y - \frac{\lambda}{\beta}xv - \frac{\mu}{\beta}v.$$

If we take $lc \geq bh$ i.e. $\frac{l}{h} > \frac{b}{c}$, then for each $\delta(> 0)$ the following inequality holds:

$$\frac{dw}{dt} + \delta w \leq \left(rx + \delta x - \frac{rx^2}{k}\right) + \frac{b}{c}(\delta - d)y + \delta z + \frac{1}{\beta}(\delta - \mu)v,$$

i.e.

$$\frac{dw}{dt} + \delta w < \frac{k}{4r}(r + \delta)^2 + fbc(\delta - d)y + \delta z + \frac{1}{\beta}(\delta - \mu)v \tag{A.2}$$

Note that the right-hand-side of (A.2) is bounded for $\delta \geq \max(d, \mu)$. Then we can find a constant L say, such that

$$\frac{dw}{dt} + \delta w < L.$$

Applying the theory of differential inequality,[17] we obtain

$$0 < w(x, y, z, v) < \frac{L}{\mu}(1 - e^{-\delta t}) + w(x(0), y(0), z(0), v(0))e^{-\delta t}$$

and for $t \to \infty$, we have

$$0 < w < \frac{L}{\delta}. \tag{A.3}$$

Hence, all the solutions of (2.7) that initiate in R^4_+ are confined in the region

$$B = \{(x, y, z, v) \in R^4_+ : w = \frac{L}{\delta} + \epsilon \text{ for any, , } \in > 0\}.$$

Hence, we state the following lemma:

Lemma 2.1. *All the solutions of* (2.7) *which initiate in* R^4_+ *are uniformly bounded if* $\frac{l}{h} > \frac{b}{c}$.

Appendix B

We shall first state a theorem relating to the characteristic polynomial of a matrix[18] and then study the stability properties of our system.

Theorem B.1. *Let* A *be* $n \times n$ *matrix which is symmetrically partitioned into upper-or lower-triangular-block matrices labeled*

$$A = \begin{bmatrix} A_1 & A_2 \\ 0 & A_3 \end{bmatrix}$$

or

$$A = \begin{bmatrix} A_1 & 0 \\ A_2 & A_3 \end{bmatrix}.$$

Then the characteristic polynomial of the matrix A *is equal to the product of the characteristic polynomials of* A_1 *and* A_3. *Now we prove the Theorem* 4.2.

We obtain the following Jacobian matrix, say J_1^1, for the system (2.7) at E_1:

$$J_1^1 = \begin{bmatrix} J_2^1 & J_3^1 \\ 0 & J_4^1 \end{bmatrix}$$

where

$$J_2^1 = \begin{bmatrix} -r & -bK \\ 0 & cK - d \end{bmatrix},$$

$$J_3^1 = \begin{bmatrix} 0 & -\lambda K \\ 0 & 0 \end{bmatrix},$$

$$J_4^1 = \begin{bmatrix} -\alpha & -\lambda K \\ \alpha\beta & -\lambda K\mu \end{bmatrix}.$$

The eigenvalues of the matrix J_2^1 will all be negative if $cK < d$, whereas all the eigenvalues of the matrix J_4^1, obtained from the characteristic equation

$$\xi^2 + \xi(\lambda K + \mu + \alpha) + \alpha(\lambda K + \mu) - \alpha\lambda\beta k = 0,$$

will have negative real parts if and only if $\beta < \beta^*$ where $\beta^* = (1 + \frac{\mu}{\lambda K})$. By applying Theorem B.1 we can show that all the eigenvalues of J_1^1 are negative if $cK < d$ and $\beta < \beta^*$. Thus we can state the Theorem 4.2 as follows:

Theorem 4.2. *The system* (2.7) *is locally asymptotically stable around* E_1 *if* $d > cK$ *and* $\beta < \beta^*$ *where* $\beta^* = (1 + \frac{\mu}{\lambda K})$.

Appendix C

We restrict ourselves to the admissible subset with a biologically meaning, B, of the plane

$$B = \{(x, y, z, v), x > 0, y > 0, z > 0, v > 0\}.$$

We will now show the global stability of the equilibrium point E_2.
We define the following Lyapunov function

$$G = \left(x - x_2 - x_2 \ln \frac{x}{x_2}\right) + k_1 \left(y - y_2 - y_2 \ln \frac{y}{y_2}\right) + k_2 z + k_3 v,$$

where $k_i > 0$, $(i = 1, 2, 3)$ is to be determined. Now taking the time derivative of G along the solution of (2.7), we have

$$\begin{aligned} \dot{G} = (x - x_2)\left[r\left(1 - \frac{x+z}{K}\right) - \lambda v - by\right] + k_1(y - y_2)(cx - d + hz) \\ + k_2\lambda xv - k_2\alpha z - k_2 lyz - k_3\lambda xv - k_3\mu v + k_3\alpha\beta z, \end{aligned}$$

which can be written as

$$\dot{G} = -\frac{r}{K}(x-x_2)^2 - \lambda x v(1+k_3-k_2) - v(k_3\mu - \lambda x_2) - (x-x_2)(y-y_2)(b-k_1c)$$
$$- yz(lk_2 - hk_1) - z\left(hk_1y_2 + \alpha k_2 - \alpha k_3\beta - \frac{rx_2}{K}\right) - \frac{rzx}{K}.$$

If we select $K_1 = \frac{b}{c}$ and $K_3 = \frac{\lambda d}{c\mu}$, then the above equation becomes

$$\dot{G} = -\frac{r}{K}(x-x_2)^2 - \lambda x v(1+k_3-k_2) - z\left(\alpha k_2 - \alpha k_3\beta + hk_1y_2 - \frac{rx_2}{K}\right)$$
$$- yz(k_2l - hk_1) - \frac{rzx}{K}.$$

Now choose K_2 in such a way that

$$\max\left[\frac{hb}{cl}\left\{\frac{\beta\lambda d}{\mu c} + \frac{rd}{Kc\alpha} - \frac{hr}{c\alpha}\left(1-\frac{d}{kc}\right)\right\}\right] < K_2 < 1 + \frac{\lambda d}{c\mu},$$

where $\beta < (1+\frac{c\mu}{\lambda d}) + \frac{\mu hr}{\alpha\lambda d}(1-\frac{d}{Kc}) - \frac{\mu r}{\alpha\lambda K} = \beta_c$ (say). Note that $\beta_c < \beta^{**}$ and $\beta_c > \beta^*$ when $d < \frac{Kch}{c+h}$. Then $\dot{G} < 0$, for all $(x,y,z,v) \in B$. Consider the following subset X of B

$$X \equiv \{(x,y,z,v) \in \bar{B} : \dot{G} = 0\},$$

then the largest invariant set Y in X is

$$\{(x,y,z,v) \in \bar{B}, x = x_2, y = y_2, z = 0, v = 0\},$$

and we obtain $Y = \{x_2, y_2, 0, 0\}$. Thus the proof follows directly from Lasalle's invariance principle[19] and we have the following theorem:

Theorem 4.4. *The system is globally asymptotically stable around E_2 if*

$$\text{(i) } d < \frac{Kch}{c+h} \quad \text{(ii) } \beta \in (\beta^*, \beta_c),$$

where $\beta^* = (1+\frac{\mu}{\lambda K})$ and $(1+\frac{c\mu}{\lambda d}) + \frac{\mu hr}{\alpha\lambda d}(1-\frac{d}{Kc}) - \frac{\mu r}{\alpha\lambda K} = \beta_c < \beta^{**}$.