RES MILITARIS Social Science Journal

A STUDY OF PATHOGEN CONTAMINATION OF A MODEL WITH TIME-LAG FORCYTOTOTIC TLYMPHOCYTES RESPONSE

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Abstract: The present paper is acquainted with an analytic study of a contaminated epidemic proto-type with effect of time-lag for CTL response. The mathematical model illustrated by every means of nonlinear differential equation and all plausible equilibrium points are determined. A Lyapunov's function is constructed to deduce the global stability of pristine equilibrium E_o, and immune depleted equilibrium E1and the endemic equilibriumE2isstudied using Routh-Hurwitz criterion.

Keywords: CTL response, Lyapunov's function, Routh-Hurwitz criterion.

Mathematical models on contagious diseases with time delay has been investigative since last decade [1, 2].The dynamical viral bale in vivo it could be studied using these models. The fundamental prototype of Pathogenic dynamics comprises 3 variables, the inhabitants of disinfected cellsx (t), contaminated cells that produce virus y(t)and uninhabited virus iotav(t) [3,4] and theses are functions of time t . A rotation of free virus is considerably swift when compared with contaminated cells, have been explored by Bart hold yet et al. [5] and Wodarz et al. [6] amidst quasi-steady state assumptions. The contagious cells y (t) could be weighing up as estimate of pathogen balev (t). The immune behaviors have been exhibit to be comprehensive and essential to eradicate or dominate the disease [7, 8] for pathogen contamination with non-cytopathic viruses. There are numerous classifications depending up on various mechanism presumptions [9, 10]. In majority of pathogen contamination, Killer T cells (CTLs) play a vital role in anti-contagious fortification by assaulting the pathogen-contaminated cells. Thus the population dynamics of pathogenic contagion with CTL behavior have been analyzed in the most recent times. Models upon time delays with immune effect and antigenic stimulation generating CTLs were determined by [11, 12]. Buric´ et. al.[11]investigated a result of the time-lag for immune response on the two-dimensional system that contains contaminated cells and CTLs, and Wang et. al. [13] studied the response of a time -lag on the three-dimensional system. Qizhi et. al. [16] studied the delay model with delay in the CTL effect in a three –dimensional system.

The mathematical equations structured for the present study are

$$\frac{dx}{dt} = A - dx(t) - \beta x(t)y(t)$$

$$\frac{dy}{dt} = \beta x(t)y(t) - ay(t) - py(t-\tau)z(t-\tau)$$

$\frac{dz}{dt} = cy(t-\tau)z(t-\tau) - bz(t-\tau)$ (1.1)

Where x(t) =amount of susceptible permissive cells,

y(t)=amount of pathogen inhabitants and

z(t)=amount of CTL's

The susceptible permissive cells are produced at a rate A, lessen at a rate of dx and turn into contingent at a βxy rate. Contingent cell lessen at ay rate and are slayed by the lytic effect or method of CTL response at a time- lag $py(t-\tau)z(t-\tau)$.The CTL behavior is operated at a rate in proportion to the amount of contingent cells at a time past$cy(t-\tau)z(t-\tau)$, furthermore degrade exponentially at rate in proportion to its present strength with a time delay $bz(t-\tau)$.

Stability Analysis

The basic reproduction number of the pathogen for (1.1) could be given as $R_0 = {A\beta}/_{ad}$ this recounts the mean number of just know contaminated cells build by a contaminate cell at the start of the process. The pristine equilibrium E_0=$\left(\frac{A}{d}, 0{,}0\right)$ is the distinctively stable inter related to the annihilation of free pathogen during $R_0 \leq 1$. Immune Exhausted equilibrium in correspond to the existence of free pathogen and annihilation of CTL is E_1=$\left(\frac{a}{\beta}, \frac{A\beta - ad}{a\beta}, 0\right)$ when $R_0 > 1 + \frac{b\beta}{cd}$. There exist yet another endemic equilibrium point E_2= $\left(\frac{cA}{cd+A\beta}, \frac{b}{c}, \frac{Ac\beta - acd - ab\beta}{cdp + bp\beta}\right)$ in relation to existence of free pathogen and CTL.

We will study the global stability of pristine equilibriumE_0, immune depleted equilibriumE_1 along with local stability of endemic equilibrium E_2.

Theorem: When $R_0 \leq 1$ the pristine equilibrium is globally asymptotically stable

Proof: Define a Lyapunov functional:

$$V = \frac{1}{2}\left(x(t) - \frac{A}{d}\right)^2 + \frac{A}{d}y(t) + \frac{\varepsilon}{c}z(t) + (\varepsilon - \delta)\int_{t-\tau}^{t} y(\theta)z(\theta)d\theta \qquad (1)$$

Where $\varepsilon > 0$ be a non-negative constant to be taken later

Proceeding with time derivative of V along the solution of the system (1) we have

$V' = \left(x(t) - \frac{A}{d}\right)\left(-d(x(t) - \frac{A}{d}\right) - \beta x(t)y(t) + \frac{A}{d}\left(\beta x(t)y(t) - ay(t) - py(t-\tau)z(t-\tau)\right) + \frac{\varepsilon}{c}\left(cy(t-\tau)z(t-\tau) - bz(t-\tau)\right) + (\varepsilon - \delta)[y(t)z(t) - y(t-\tau)z(t-\tau)]$-(2)

Let $\beta x(t)y(t) = \beta y(t)\left[x(t) - \frac{A}{d}\right] + \frac{\beta A}{d}y(t)$ and $\delta = px_1$ further retaining

$$V' = -d\left(x(t)-\frac{A}{d}\right)^2 - \beta y(t)\left(x(t)-\frac{A}{d}\right)^2 + \frac{\beta A^2}{d^2}y(t) - \frac{aA}{d}y(t) - \frac{\varepsilon b}{c}z(t) + (\varepsilon-\delta)y(t)z(t) - (3)$$

When $R_0 \leq 1, \left(\frac{aA}{d} - \frac{\beta A^2}{d^2}\right) > 0$ there exist a positive constant $\varepsilon > 0$ such that $\frac{pA}{d}$>0. Thus

$$V' = -\left(d+\beta y(t)\right)\left(x(t)-\frac{A}{d}\right)^2 - \left(\frac{aA}{d} - \frac{\beta A^2}{d^2}\right)y(t) - \frac{\varepsilon b}{c}z(t) - (x_1-\varepsilon)y(t)z(t)\text{-(4)}$$

As $x(t)$, y(t) ,z(t) are positive and $R_0 \leq 1$ that $v' \leq 0$ and $v' = 0$ subject to $(x,y,z) = \left(\frac{A}{d},0,0\right)$ so by Lyapunov-Lasalle type theorem [36] we revealed that E_0 is globally asymptotically stable.

Theorem: When 1<$R_0 \leq 1 + \frac{b\beta}{cd}$, the immune depleted equilibrium is globally asymptotically stable.

Proof: Define a Lyapunov functional:

$$V=\frac{1}{2}\left(x(t)-\frac{A}{d}\right)^2 + x_1\left(y(t)-y_1-y_1 log\frac{y(t)}{y_1}\right) + \frac{px_1}{c}z(t) + px_1\int_{t-\tau}^{t} y(\theta)z(\theta)d\theta - (5)$$

Taking the time derivative of V for the solution of the system (1) we have

$$V' = \left(x(t)-\frac{A}{d}\right)\left(A-dx(t)-\beta x(t)y(t)\right) + x_1\beta x(t)(y(t)-y_1) - ax_1(y(t)-y_1) - \frac{px_1}{y(t)}(y(t)-y_1)y(t-\tau)z(t-\tau) - \frac{px_1}{c}bz(t)+px_1y(t)z(t)\text{-(6)}$$

$$V' = -\left(x(t)-\frac{A}{d}\right)^2(d+\beta y(t)) - \frac{\beta A}{d}y(t)\left(x(t)-\frac{A}{d}\right) - x_1(y(t)-y_1)\left[a+\frac{p}{y(t)}y(t-\tau)z(t-\tau) - \beta x(t)\right] - \frac{px_1}{c}(b-cy(t)z(t)) - (7)$$

At 1<$R_0 \leq 1 + \frac{b\beta}{cd}$,(b-cy(t))>0 thus $v' \leq 0$ and $v' = 0$ if and only if $(x,y,z) = \left(\frac{a}{\beta}, \frac{\beta A - ad}{a\beta}, 0\right)$.Thus from the Lyapunov-Lasalle type theorem E_1 is globally asymptotically stable.

Stability of the endemic equilibriumE_2

Let's rewrite E_2 of the system (1) to the origin

Let x(t)=u_1(t)+$\bar{x}$(t), y(t)=u_2(t)+$\bar{y}$(t), z(t)=u_3(t)+$\bar{z}$(t), whereas

$\bar{x}$(t),$\bar{y}$(t),$\bar{z}$(t),

The linearized equations are

$$\frac{dx}{dt} = \dot{u_1}(t) = -(d + \beta u_2(t))u_1(t) - \beta\bar{x}u_2(t)$$

$$\frac{dy}{dt} = \dot{u_2}(t) = \beta\bar{y}u_1(t) - p\bar{y}u_3(t-\tau)$$

$$\frac{dz}{dt} = \dot{u_3}(t) = c\bar{z}u_2(t-\tau) + c\bar{y}u_3(t-\tau) - bu_3(t-\tau)$$

The characteristic equation is given by

$$\begin{vmatrix} (-d-\beta y)-\lambda & -\beta x & 0 \\ \beta y & \beta x - a - pze^{-\lambda\tau} - \lambda & -pye^{-\lambda\tau} \\ 0 & cze^{-\lambda\tau} & (cy-b)e^{-\lambda\tau} - \lambda \end{vmatrix} = 0$$

The equation obtained is $\lambda^3 + b_1\lambda^2 + b_2\lambda + b_3$=0

Where b_1=$\beta\bar{x} - c\bar{y}$+a+d+b

b_2=ad + apc + ab+ db-d$\beta\bar{x} + d\beta\bar{z} - dc\bar{y} + p\bar{z}b\bar{y} - \beta cy^2$+b$\bar{y}\beta - b\beta\bar{x} - ac\bar{y} + p\bar{z}b$

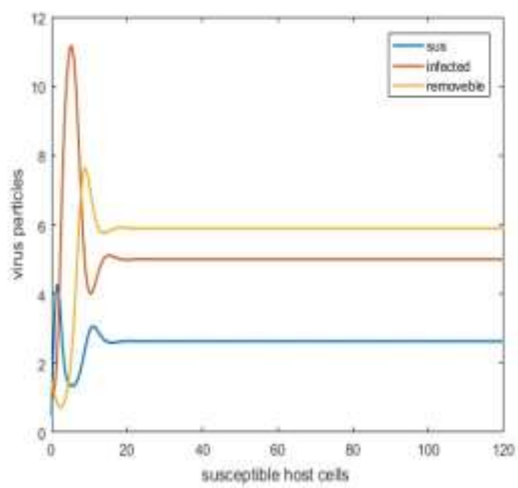
$b_3 = dpb\bar{z}$+b$\beta\bar{y}\bar{z}$

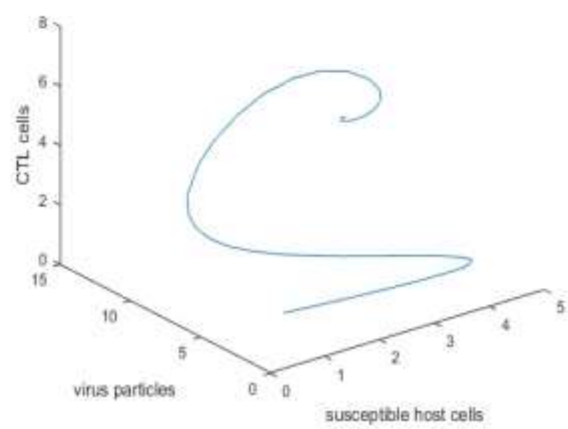
Since $(b_1b_2 - b_3) > 0$ and $b_3(b_1b_2 - b_3) > 0$

By Routh-Hurwitz criterion E_2 is asymptotically stable.

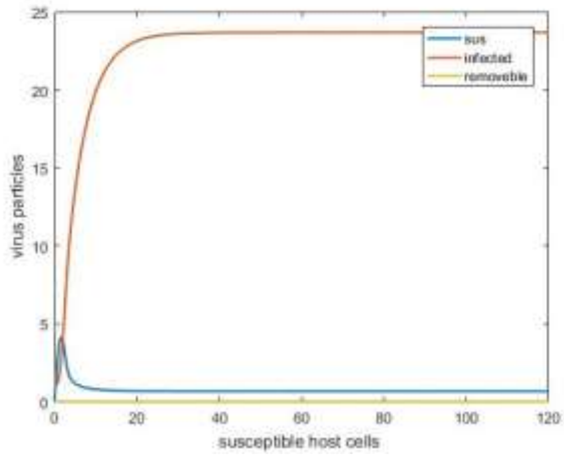
Numerical Simulation

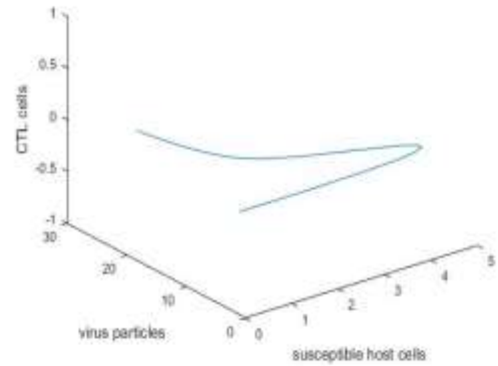
To uphold the results and CTL response on the(1.1.1) system we approximate a set of parameters as A=5,$\beta = .4, c = 0.3, a = 0.2, p = 1, d = 0.1, b = 0.5$for $R_0 > 1$ shown in fig1 .In the awol of delay for the combination of approximated parameters





The endemic equilibrium reaches stability as in fig (2)





CONCLUSION

In this paper, we have analyzed a prototype by time – lag in immune effect. Global stability of the pristine equilibrium and immune depleted equilibriums discussed using Lyapunov–La Salle type the orem and the local stability of the endemic equilibrium have been given by Routh-Hurwitz criterion.

REFERENCES

[1] MurrayJ.D.,MathematicalBiology,Springer,Berlin,Heidelberg,1993.

[2] MacDonald N., Biological Delay Systems, Cambridge UniversityPress,Cambridge,1989.

[3] Bonhoeffer S., May R.M., Shaw G.M. and Nowak M.A., Virus Dynamics and Drug Therapy, Proc. Natl. Acad.Sci.USA,94,6971–6976 (1997).

[4] Nowak M.A., Bonhoeffer S., Hill A.M., Boehme R. and Thomas H.C., Viral dynamics in hepatitis B virus infection, Proc. Natl. Acad. Sci. USA,934398–4402(1996).

[5] Bartholdy C., Christensen J.P., WodarzD. and Thomsen A.R., Persistent virus infection despitechroniccytotoxicT-lymphocyteactivationinGammainterferon-deficientmiceinfectedwithlymphocyticchoriomeningitisvirus,J. Virol. 74,10304–10311 (2000).

[6] WodarzD.,ChristensenJ.P.andThomsenA.R.,Theimportanceoflyticandnonlyticimmuneres ponsesinviral infections, Trends Immunol. 23,194–200(2002).

[7] Kagi D. and Hengartner H., Different roles for cytotoxic T-cells in the control of infections with cytopathic versusnoncy to pathic viruses, Curr. OpinImmunol.8, 472–477(1996).

[8] Schmitz J.E., Kuroda M.J., Santra S., Sasseville V.G., Simon M.A., Lifton M.A., et al, Control of viremia in simian immunodeficiency virus infection by CD8+ lymphocytes, Science 283, 857–860(1999).

[9] De Boer R.J. and Perelson A.S., Towards a general function describing T cell proliferation, J. The oret. Biol. 175,567–576(1995).

[10] De Boer R.J. and Perelson A.S., Target cell limited and immune control models of HIV infection: a comparison, J.Theoret.Biol.,190,201–214(1998).
[11] Buric´ N., Mudrinic M. and Vasovic´ N., Time delay in a basic model of the immune response, ChaosSolitonsFract.12,483–489(2001).
[12] Kajiwara T. and Iuchi T., Stability of delay differential equation models of infectious diseases in vivo, personal communication.
[13] Wang K., Wang W., Pang H. and Liu X., Complex dynamic behavior in a viral model with delayed immune response, Physica D,226,197–208 (2007).
[14] Kuang Y., Delay Differential Equations with Applications in Population Dynamics, Academic Press,SanDiego, 1993.
[15] Wang K., Wang W. and Liu X., Global stability in a viral infection model with lytic and nolyticimmuneresponse,Comput.Math.Appl.51,1593–1610(2006).
[16] QizhiXie, Dongwei Huang, Shuangde Zhang and Jin Cao, Analysis of a viral infection model with delayed immune response, Applied mathematicalmodeling,34, 2388-2395 (2010).
[17] Stability Analysis Of A Viral Infection Model With delay for ctl response InternationalJournalofScientificandInnovativeMathematicalResearch(IJSIMR).Volume 3, Special Issue 1, July 2015, PP 264-267, ISSN 2347-307X