STABILITY ANALYSIS OF EBOLA VIRUS DISEASE TRANSMISION DYNAMICS

PRESENTED

BY

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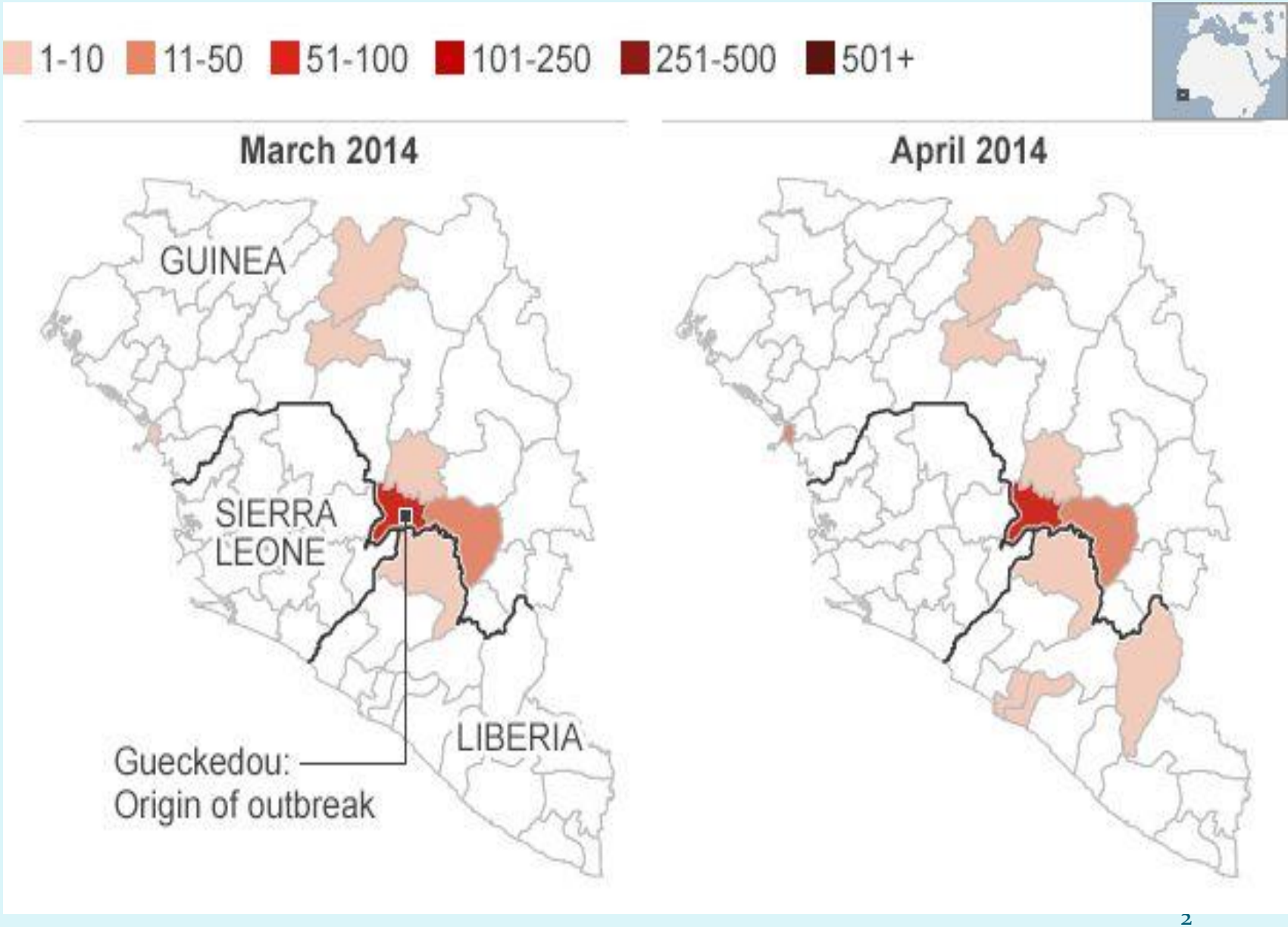
INTRODUCTION

- Definition
- Characteristics
- Symptoms
- Causes: zaire, sudan, Tai Forest, Bundibugyo, Reston, Bombali Ebola
- Transmission
- Treatment
- Statistics



Aim and Objectives

The aim of this research is to formulate and analyze a deterministic mathematical model that shows the transmission dynamics of Ebola virus disease by incorporating the isolation and proper cremation of the dead via the disease compartments as control measures while the objectives are to:

- Show that the proposed model is epidemiologically well posed and biologically meaningful.

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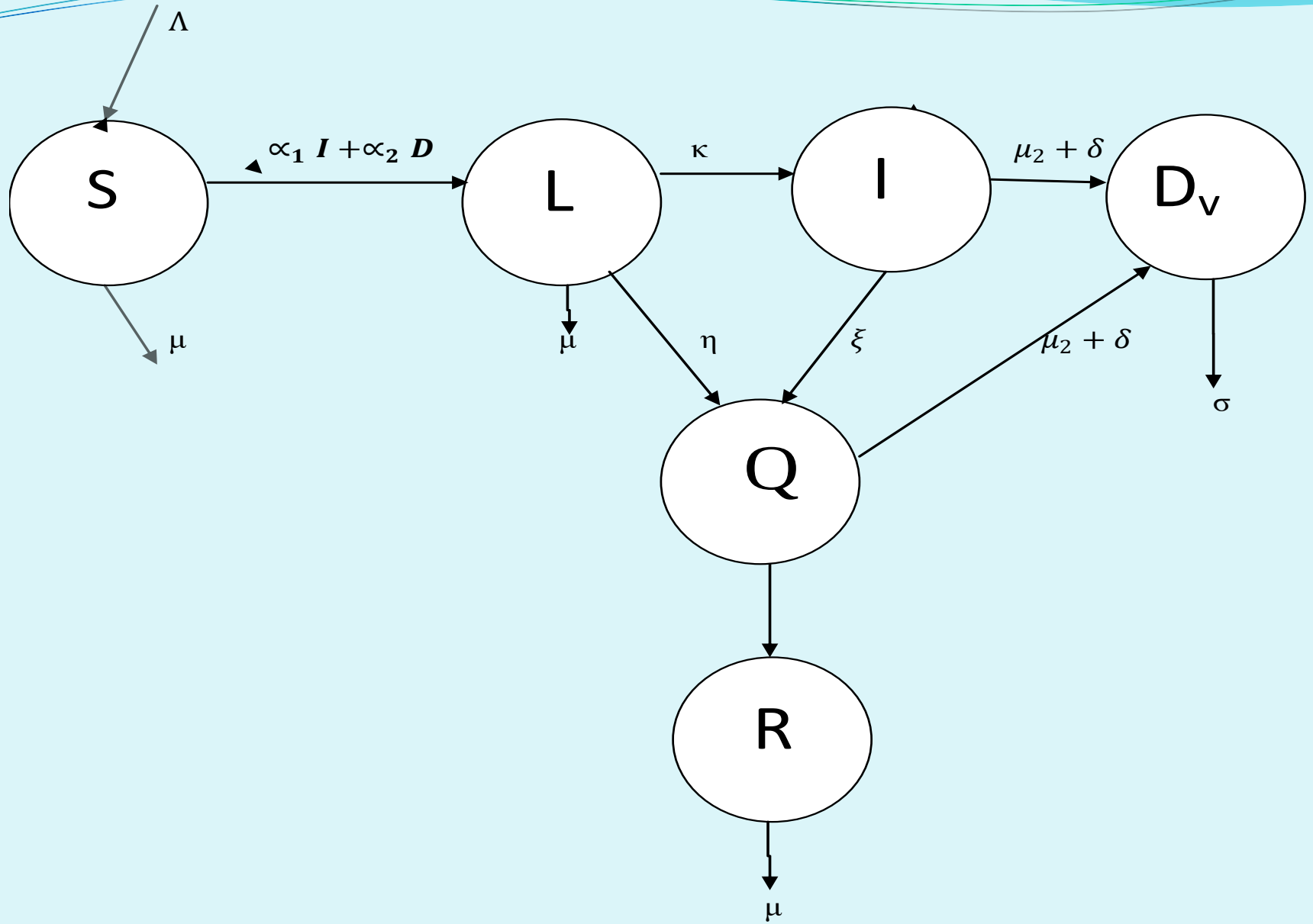
- determine the existence of the disease free equilibrium and endemic equilibrium points of the model.
- obtain the basic reproductive number
- investigate the local and global stabilities of the disease free and the endemic states of the model.
- perform the numerical simulation and deduce the effect of various parameters and intervention strategies.

LITERATURE REVIEW

S/NO	AUTHOR	TITLE	RESULT	LIMITATION
1	Tae and Young.	Modeling the spread of Ebola. (2016).	That if traditional burials of Ebola victims are allowed the disease will persist in a population.	No provision for the isolation of victims of Ebola, such that if safe burial practices are followed, more people will still get infected and more will die as a result.
2.	Afina Azizah et. al.	Spread of Ebola with susceptible exposed infected isolated recovered (SEIi_hR) model. (2017)	Based on the Ebola epidemic data in Sierra Leone, the equilibrium point of the model is unique and it is a stable disease free point.	Not considering a compartment for the carcasses of Ebola victims indicates that a whole community could be wiped off since such carcasses are very contagious.
3.	Adewale et al.	Mathematical analysis of sensitivity parameters on the dynamical transmission of Ebola Hemorrhagic fever. (2016)	Based on the sensitivity analysis, the effective contact rate and low immunity in individuals are the key parameters that influence the	There are no control measures considered, like the isolation of the infected. Also nothing is said about the infectious dead bodies.

MODEL FORMULATION

The schematic Diagram below is used to construct the Model



SCHEMATIC DIAGRAM OF EBOLA VIRUS DYNAMICS

Table 1 : State Variables of the model

Variables	Description
S	Susceptible class
L	Latent class
I	Infected class
Q	Isolated class
R	Removed class
D_v	Infectious dead bodies

Table 2 : Parameters of the model

Parameters	Description
Λ	Recruitment rate into the susceptible class (immigration alone)
$\propto_1$	Transmission rate through the infected class
$\propto_2$	Transmission rate through dead bodies class
κ	Progression rate of disease to active Ebola disease

ϕ	Rate at which the isolated recovers
ξ	Rate at which the infectious are isolated
η	Rate at which the exposed are isolated
μ	Natural death rate
δ	Rate of death via the disease
σ	Rate of proper cremation of the death bodies
N	Total population

THE MODEL EQUATION

$$\frac{dS}{dt} = \pi - (\alpha_1 I + \alpha_2 D_v)S - \mu S \qquad S(0) = S_0$$

$$\frac{dL}{dt} = (\alpha_1 I + \alpha_2 D_v)S - (\kappa + \mu + \eta)L \qquad L(0) = L_0$$

$$\frac{dI}{dt} = \kappa L - (\mu + \delta + \xi)I \qquad I(0) = I_0$$

$$\frac{dD_v}{dt} = (\mu + \delta)(I + Q) - \sigma D_v \qquad D_v(0) = D_{v0}$$

$$\frac{dQ}{dt} = \eta L + \xi I - (\mu + \delta + \phi)Q \qquad Q(0) = Q_0$$

$$\frac{dR}{dt} = \phi Q - \mu R \qquad R(0) = R_0$$

(1)

Where $\eta=(1-\kappa)$, $\xi=(1-\alpha_1)$, $\sigma=(1-\alpha_2)$

And $N(t) = S(t) + L(t) + I(t) + Q(t) + R(t) + D(t)$

Positivity of solution

For the model system (1) to be well posed and epidemiologically meaningful, all state variables must be non-negative, $\forall\, t \geq 0$.

Theorem 1:.

Let $\Omega = \{(S, L, I, D_V, Q, R) \in \Re_+^6 : S_0 > 0,\ L_0 > 0,\ I_0 > 0,$

$Q_0 > 0,\ R_0 > 0, D_{V\,0} > 0,\}$ (2)

Then, the solution set $\{S, L, I, D_V, Q, R\}$ of the system (1) is positive for all $t \geq 0$.

The essence of this theorem is to proof that all the solutions of the equations are positive for all $t \geq 0$.

Invariant region

The invariant region in which the model solution is bounded is obtained. To do this, the theorem below is considered.

Theorem 2: The compact set Ω is positively invariant with respect to the Ebola model governed by the system of equations (1).

Applying Birkoff and Rota's theorem on differential inequality (Birkoff and Rota's, 1982), shows that the feasible solutions set of the model equation (1) enters the region

$$\left\{\Omega = (\mathrm{S},\mathrm{L},\mathrm{I},\mathrm{D_V},Q,R) \in \Re_+^6 \,|\, \mathrm{S}>0,\mathrm{L}>0,\mathrm{I}>0,\mathrm{D_V}>0,\mathrm{Q}>0,\mathrm{R}>0;\mathrm{N} \le \frac{\Lambda}{\mu}, D_v \le \frac{(\mu+\delta}{\sigma\mu}\right.$$

Thus in this region the model is well posed and biologically meaningful.

Equilibrium state of the model

At equilibrium, $\frac{dS}{dt} = \frac{dL}{dt} = \frac{dI}{dt} = \frac{dD_v}{dt} = \frac{dQ}{dt} = \frac{dR}{dt} = 0$ (3)

It can be deduced that the disease-free equilibrium state

DFE $(S, L, I, D_v, Q, R) = (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0)$

And the endemic equilibrium state is obtained as;

$$\begin{pmatrix} S^* \\ L^* \\ I^* \\ D_v^* \\ Q^* \\ R^* \end{pmatrix} = \begin{pmatrix} \frac{\sigma x_6}{\kappa x_5} \\ \frac{\Lambda x_5 - \mu\sigma x_6}{x_4 x_5} \\ \frac{\Lambda\kappa x_5 - \mu\sigma x_6}{x_5 x_4 x_2} \\ \frac{x_1(\kappa x_3 + x_7)\{\Lambda\kappa x_5 - \mu\sigma x_6\}}{\sigma\kappa x_5 x_6} \\ \frac{x_7\{\Lambda\kappa x_5 - \mu\sigma x_6\}}{\kappa x_5 x_6} \\ \frac{\phi\Lambda\kappa x_7\{x_5 - \mu\sigma x_6\}}{\mu\kappa x_5 x_6} \end{pmatrix} \quad (4).$$

Effective Basic Reproduction Number,

Applying the next generation matrix (operator) technique described by (Dikeman heesterbeek, 2000), the effective basic reproduction number, R_0 of the model equations (1) is obtained by taking the largest (dominant) eigenvalue (spectral radius) of the matrix FV^{-1}.

$$R_0 = \left[\frac{\partial \mathrm{F_i}(E_0)}{\partial x_j}\right]\left[\frac{\partial \mathrm{V_i}(E_0)}{\partial x_j}\right]^{-1} \qquad (5)$$

Where

F_i is the rate of appearance of new infection in compartment I,

$$F=\left[\frac{\partial \mathrm{F_i}(E_0)}{\partial x_j}\right]$$

V_i is the transfer of individuals out of compartment I by all other means,

$$V=\left[\frac{\partial \mathrm{V_i}(E_0)}{\partial x_j}\right]^{-1}$$

E_0 is the disease free equilibrium.

The associated Jacobean matrices of F and V at disease free equilibrium are obtained as thus:

$$FV^{-1} = \begin{bmatrix} \frac{\alpha_1 \Lambda \kappa}{\mu x_2 x_4} & \frac{\alpha_2 \Lambda x_1 (\eta x_2 + \kappa \xi - \kappa x_3)}{\mu x_2 x_3 x_4 \sigma} & \frac{\alpha_1 \Lambda}{\mu x_2} & \frac{\alpha_2 \Lambda x_1 (\xi - x_3)}{\mu x_2 x_3 \sigma} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \quad (6)$$

It can be shown that the largest (dominant) Eigen-value of FV^{-1} is R_0, and that is the basic reproduction number

$$R_0 = [\frac{\Lambda(\kappa x_1 x_3 \alpha_2 - \kappa\xi x_1 \sigma^2 + \kappa\sigma x_3 \alpha_1 - \eta\alpha_2 x_2 x_1}{\mu x_2 x_3 x_4 \sigma}] \quad (7)$$

Local Stability of Disease Free Equilibrium

Using the Jacobean stability approach to prove the stability of the disease free equilibrium state of the model equation (1), the following theorem is considered:

THEOREM 3: The disease free equilibrium point is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

The disease free equilibrium is locally asymptotically stable. The implication of this is that a small influx of infected individuals into a completely susceptible population does not have any significant effect on the population

Global Stability of Disease Free Equilibrium

Global stability of equilibrium removes the restrictions on the initial conditions of the model variables. In global asymptotic stability, solutions approach the equilibrium for all initial conditions.

Theorem 4: The disease-free equilibrium, E_0 of (1) is globally asymptotically stable in Ω if $R_0 < 1$ and unstable if $R_0 > 1$ where R_0 is the basic reproduction number and the two conditions H1 and H2 stated in Castillo-Chavez et al. (2000) are satisfied.

The disease free equilibrium (E_0) is globally asymptotically stable. This implies that irrespective of the initial condition i.e. the number of influx of infected individuals into a population, the disease does not persist.

LOCAL STABILITY OF ENDEMIC EQUILIBRUM STATE

To explore the possibility of backward or forward bifurcation of the normalized model system of equation (1), the centre manifold theory is used (Gumel *et al*, 2008). This is done by renaming the variables as thus;

Let $p_1=S$, $p_2=L$, $p_3=I$, $p_4=Q$, $p_5=R$, $p_6=D_V$,

It can be written in vector notation $p=(p_1+p_2+p_3+p_4+p_5+p_6)^T$ and the model can be re-written in the form of $\frac{dp}{dt} = F(p)$, with $F=(f_1,f_2,f_3,f_4,f_5,f_6)^T$ as follows;

$$\frac{dp_1}{dt} = f_1(p_1,p_2,p_3,p_4,p_5,p_6) = \Lambda - (\alpha_1 p_3 + \alpha_2 p_6)p_1 - \mu p_1 \qquad s(0) = s_0$$

$$\frac{dp_2}{dt} = f_2(p_1,p_2,p_3,p_4,p_5,p_6) = (\alpha_1 p_3 + \alpha_2 p_6)p_1 - (\kappa + \mu + \eta)p_2 \qquad l(0) = l_0$$

$$\frac{dp_3}{dt} = f_3(p_1,p_2,p_3,p_4,p_5,p_6) = \kappa p_2 - (\mu + \delta + \xi)p_3 \qquad i(0) = i$$

$$\frac{dp_4}{dt} = f_4(p_1,p_2,p_3,p_4,p_5,p_6) = \eta p_2 + \xi p_3 - (\mu + \delta + \phi)p_4 \qquad q(0) = q_0$$

$$\frac{dp_5}{dt} = f_5(p_1,p_2,p_3,p_4,p_5,p_6) = \phi p_4 - \mu p_5 \qquad r(0) = r_0$$

$$\frac{dp_6}{dt} = f_6(p_1,p_2,p_3,p_4,p_5,p_6) = (\mu + \delta)(p_3 + p_4) - \sigma p_6 \qquad d_v(0) = d_{v0}$$

(8)

The nature of the bifurcation is investigated as follows:

First, the Jacobean matrix of the system of equations (8) at the point $(E_{0,}\alpha^{*})$ given as

$$J(E_0,\alpha^{*})=\begin{bmatrix} -\mu & 0 & -\frac{\alpha_1\Lambda}{\mu} & 0 & 0 & -\frac{\alpha_2\Lambda}{\mu} \\ 0 & -x_4 & -\frac{\alpha_1\Lambda}{\mu} & 0 & 0 & \frac{\alpha_1\Lambda}{\mu} \\ 0 & \kappa & -x_2 & 0 & 0 & 0 \\ 0 & \eta & \xi & -x_3 & 0 & 0 \\ 0 & 0 & 0 & \phi & -\mu & 0 \\ 0 & 0 & -x_1 & x_1 & 0 & -\sigma \end{bmatrix} \quad (9)$$

The characteristic equation of (9) is,

$$\left| J(E_o, \alpha^*) - \lambda I \right| = 0$$

$$\begin{bmatrix} -\mu-\lambda & 0 & -\frac{\alpha_1\Lambda}{\mu} & 0 & 0 & -\frac{\alpha_2\Lambda}{\mu} \\ 0 & -x_4-\lambda & \frac{\alpha_1\Lambda}{\mu} & 0 & 0 & \frac{\alpha_2\Lambda}{\mu} \\ 0 & \kappa & -x_2-\lambda & 0 & 0 & 0 \\ 0 & \eta & \xi & -x_3-\lambda & 0 & 0 \\ 0 & 0 & 0 & \phi & -\mu-\lambda & 0 \\ 0 & 0 & x_1 & x_1 & 0 & -\sigma-\lambda \end{bmatrix} = 0 \qquad (10)$$

The direction of the bifurcation at $R_0 = 1$ is determined by the signs of the bifurcation coefficients a and b given below. If a is negative and b is positive, the system undergoes a forward bifurcation, while if both a and b are positive it will undergo a backward bifurcation.

Computation of a.

The coefficient of a is defined as:

$$a = \sum_{i=j=k=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial p_i \partial p_j}(E_0, \alpha^*),$$

Where k is the *kth* component of f and its values are $k = 2, 3, 4$ and 6 since $v_1 = v_5 = 0$.

For system (8), the associated non-zero partial derivative at disease free equilibrium is given by;

$$\therefore a = v_2 \sum_{i=j=2}^{6} w_i w_j \frac{\partial^2 f_2}{\partial p_i \partial p_j}(E_0, \alpha^*)$$

$$a = 2\mathrm{v}_2 w_1 (w_3 \alpha^* + w_6 \alpha_2)$$

But,

$$w_1 = -\frac{\Lambda(\alpha^* w_3 - \alpha_2 w_6)}{\mu^2}$$

Substituting w_1 into a, we have that

$$a = \frac{-2\Lambda(\alpha^* w_3 + \alpha_2 w_6)^2 v_2}{\mu^2} \qquad (11)$$

Equation (11) shows that a$<$ 0 (negative)

Computation of b:

$$b = \sum_{i=k=1}^{6} \mathrm{v}_k w_i \frac{\partial^2 f_k}{\partial p_i \partial \alpha^*}(E_0, \alpha^*)$$

$$b = v_2 w_1 \frac{\partial^2 f_2}{\partial p_1 \partial \alpha^*} + v_2 w_2 \frac{\partial^2 f_2}{\partial p_2 \partial \alpha^*} + v_2 w_3 \frac{\partial^2 f_2}{\partial p_3 \partial \alpha^*} + v_2 w_4 \frac{\partial^2 f_2}{\partial p_4 \partial \alpha^*} + v_2 w_5 \frac{\partial^2 f_2}{\partial p_5 \partial \alpha^*} + v_2 w_6$$

Therefore,

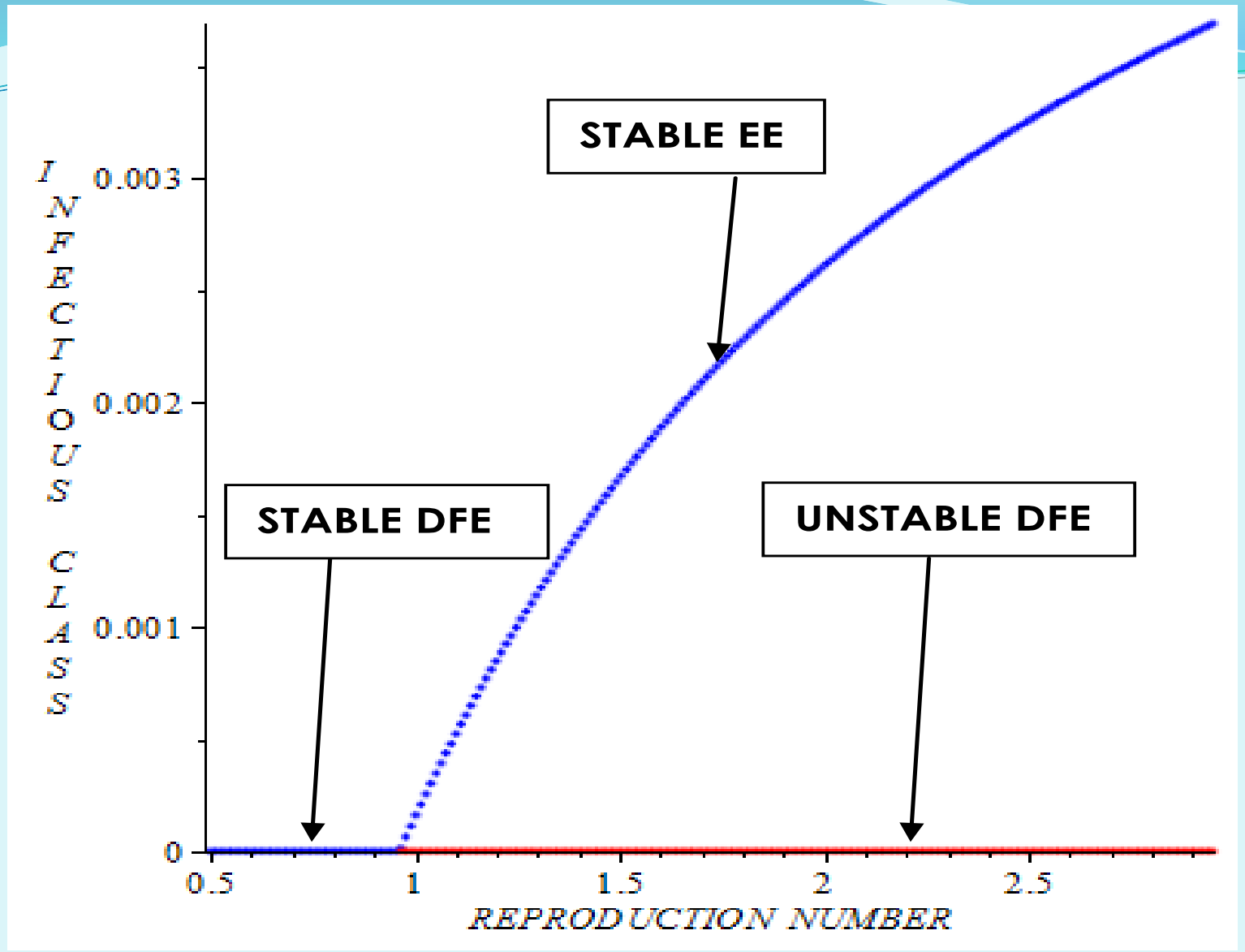
$$b = \mathrm{v}_2 w_3 p_1$$

$b = \mathrm{v}_2 w_3 \frac{\Lambda}{\mu} > 0$. This is positive

This means that the endemic equilibrium is asymptotically stable.

Therefore, it suffice to say that since a< 0 and $b > 0$, for $R_0 > 1$ the model exhibits a forward bifurcation as R_0 crosses the threshold, $R_0 = 1$.

This means that the endemic equilibrium is asymptotically stable.



The forward bifurcation graph for Ebola virus disease

The bifurcation graph for the model (1) shows that the disease-free and endemic equilibriums exchange stability when $R_0 = 1$ for arbitrary set of parameter values. The blue continuous curves depict stable equilibria and dashed red curves depicts unstable equilibria.

By implication, the above result shows that a small inflow of infectious individuals into a completely susceptible population will lead to the persistence of the disease in a population whenever $R_0 > 1$.

Global Stability of Endemic Equilibrium State

If all solutions that start out near an equilibrium point stay near the equilibrium point over indefinite time, then the system is said to be globally asymptotically stable.

Theorem 5: The endemic equilibrium E^* of the equation (1) is globally asymptotically stable whenever $R_0>1$.

By implication, this means that the disease will remain in the population whenever $R_0 > 1$ irrespective of the initial size of the infectious individuals in the population,

SIMULATION RESULTS

- For the purpose of model validation and to show that the model is in agreement with reality maple 16 software was used to approximate the solutions to the system of equations (1) with varying values of the control parameters, ξ and δ

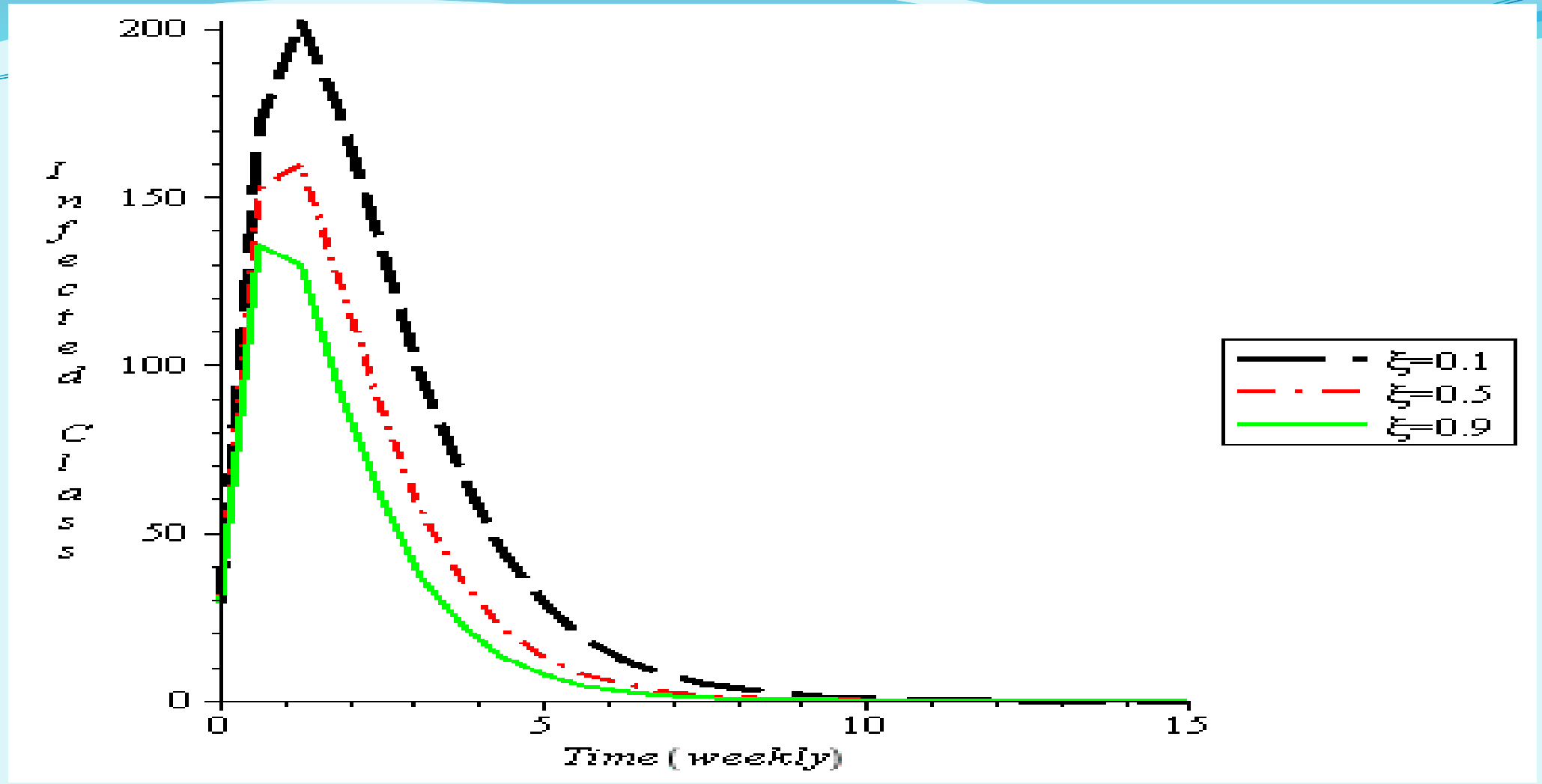


Figure 1.:The simulation showing the effect of changes in the isolation rate of infected on the infected group.

$$\Lambda = 0.06333, \mu = 0.011, \delta = 0.8, \kappa = 0.5189, \xi = 0.5,$$
$$\eta = 0.3333, \phi = 0.17, \sigma = 0.5, \alpha_1 = 0.2605, \alpha_2 = 0.12.$$

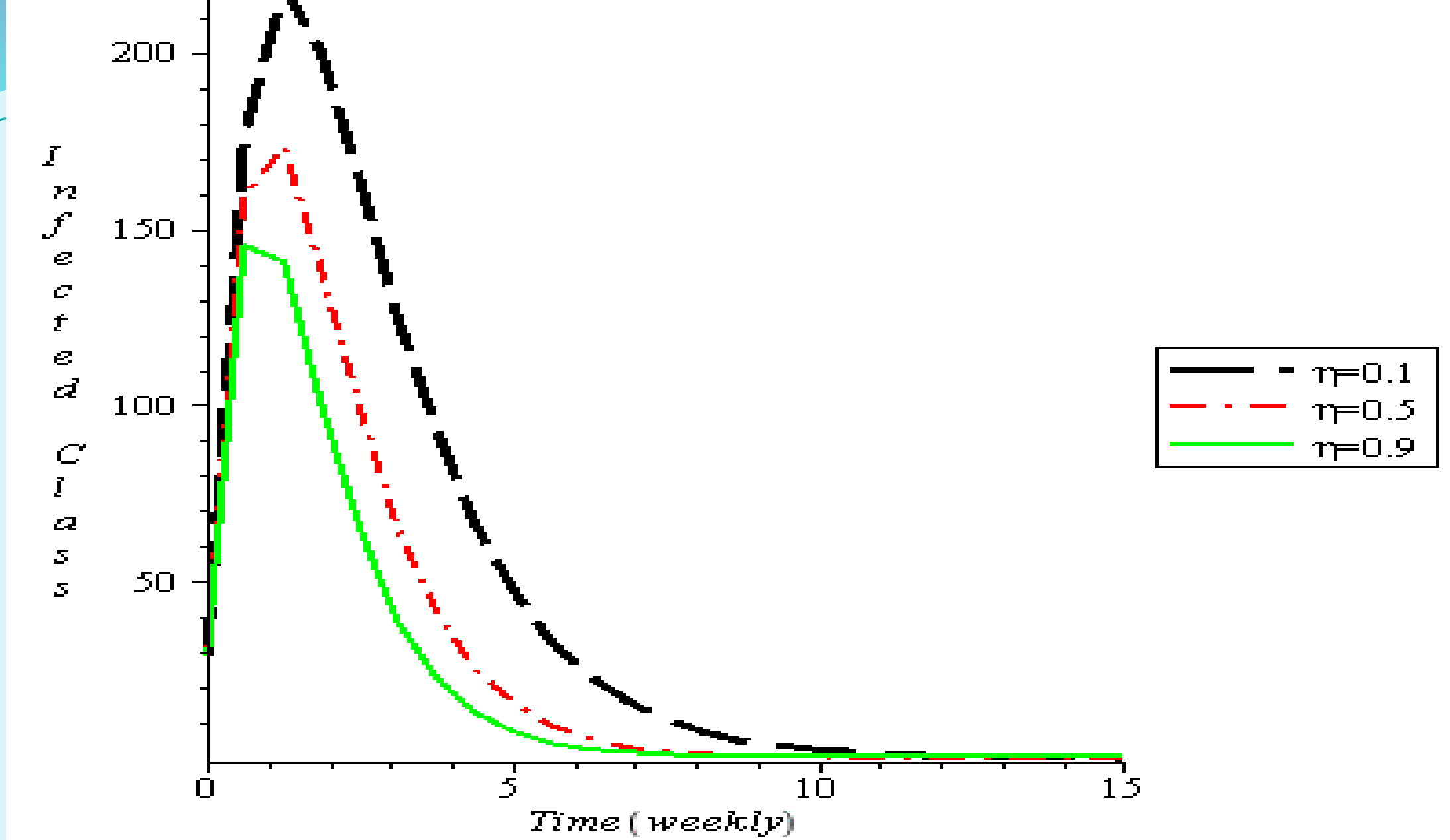


Figure 2: The simulation showing the effect of varying the rate at which the latent are isolated on the infected group.

$\Lambda = 0.06333, \mu = 0.011, \delta = 0.8, \kappa = 0.5189, \xi = 0.197, \eta$

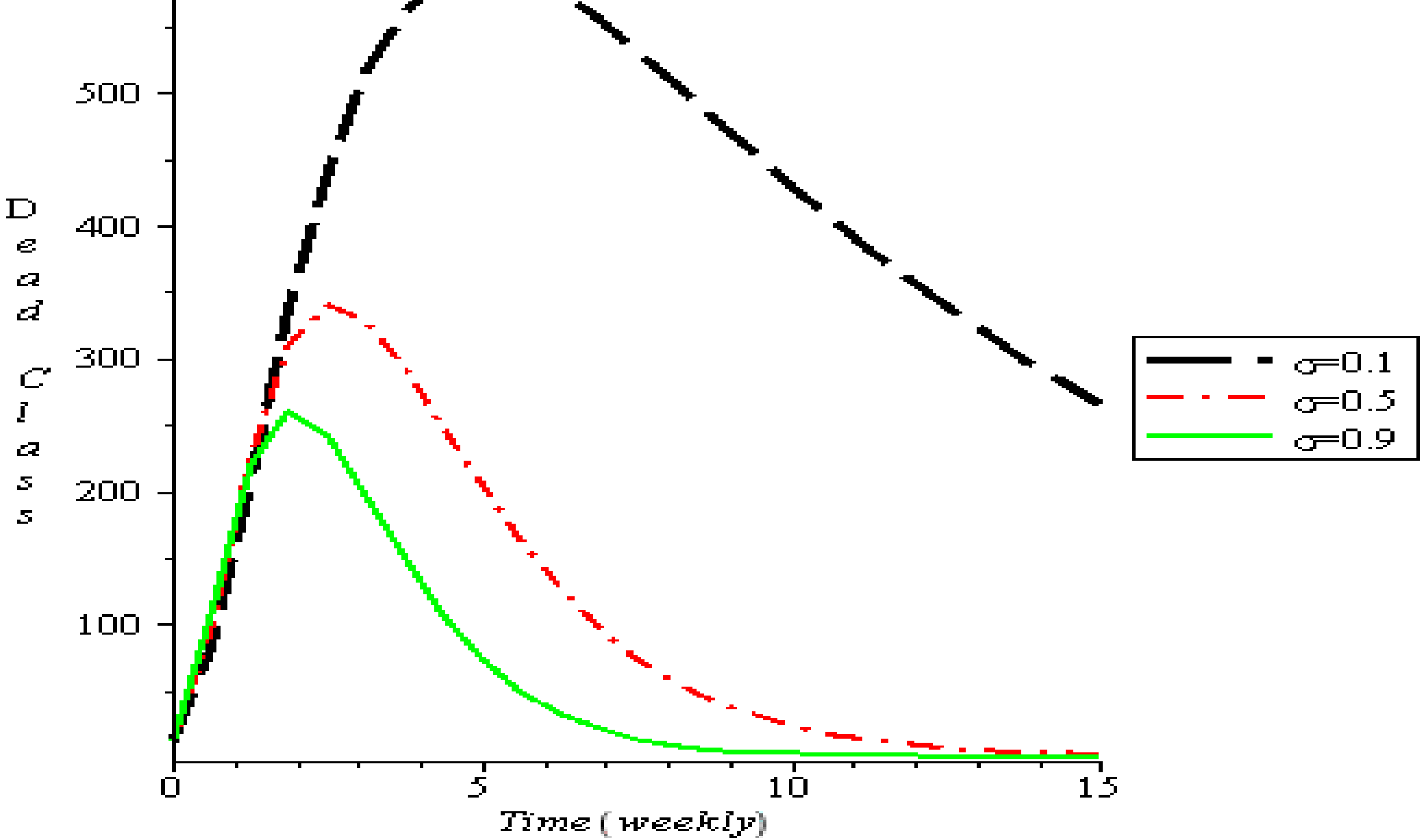


Figure 4: The simulation showing the effect of varying values of proper cremation of the infectious dead bodies on the dead class.

$\Lambda = 0.06333, \mu = 0.011, \delta = 0.8, \kappa = 0.5189, \xi = 0.197,$

CONCLUSIONS

The research shows that the proposed model for the stability of EVD is epidemiologically well posed and biologically meaningful and that the disease can be controlled when the basic reproduction number $R_0 < 1$.

CONTRIBUTION TO KNOWLEDGE

The following are the contributions these research work has added to scientific Knowledge:

- The presented mathematical model can be used to better understand the dynamics of Ebola virus disease and to develop strategies on how to combat an outbreak.
- The incorporation of isolation and the dead via the disease compartments were seen as control parameters that can help achieve a disease free state whenever an outbreak occurs.

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