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INVESTIGATION OF CAUSES OF BACKWARD BIFURCATION IN SOME EPIDEMIOLOGICAL MODELS

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Abstract

This paper is intended to investigate the phenomenon of backward bifurcation in some epidemiological mathematical models. Two models were considered. Firstly, the mathematical model for the dynamics of tuberculosis under the implementation of the direct observation therapy strategy (DOTS) was investigated. The mathematical model for immune response and drug therapy in human malaria infection was considered. The analysis of the results shows that the two models exhibit the backward bifurcation phenomenon. The parameters that cause the backward bifurcation were also established.

Keywords: Backward Bifurcation, Epidemiological Model, Mathematical Model and Transmission

1. Introduction

Bifurcations are changes in the behavior or response of a dynamical system due to changes in the initial conditions or parameter values in the model. It is important to investigate the presence of these phenomena as this will go a long way to determine if the disease can be eradicated when the reproduction number is less than one (Chavez and Song, 2004). Backward bifurcation has recently received much attention due to the adaptation, continual evolution of infective agent, drug resistance infection and re-emergence of disease. It has a significant consequence on the persistence or elimination of the disease when the associated reproduction number of the model is less than unity (Gumel, 2012).

Due to the existence of backward bifurcation, reproduction number, R_0 is only necessary but not sufficient in the control of disease spread; hence backward bifurcation analysis has become an important area in epidemiology.

Backward bifurcation analysis has been done on several epidemiological models by researchers but there are still some models that backward bifurcations have not received adequate attention. For instance, Okuonghae and Omosigho (2010), Chiyaka *et al* (2008).Kribs-Zaleta and Martcheva, (2002) considered models for a disease with acute and chronic infective stages, and variable infectivity and recovery rates, within the context of a vaccination campaign. They established the presence of backward bifurcation phenomenon in the models caused by infectivity and recovery functions.

Garba *et al*., (2008), considered a deterministic model for the transmission dynamics of a strain of dengue disease which allows transmission by exposed human and mosquitoes. The model had backward bifurcation phenomenon. It was also shown that when the model was extended by incorporating an imperfect vaccine against the strain of dengue, the backward bifurcation was further sustained. They found out that the standard incidence function was the cause of the backward bifurcation both in the basic and vaccination models.

Zhang and Liu, (2008) worked on the backward bifurcation of an epidemic model with saturated treatment function. It was found out that the infected being delayed for treatment leads to the backward bifurcation.Sharomi and Gumel, (2009) designed and analyzed a two group deterministic model for Chlamydia trachomatis it was designed and analyzed to understand its transmission dynamics. The model had backward bifurcation. It was also shown that when the basic model was extended to incorporate the use of treatment for infectious individuals, backward bifurcation further was sustained.

Xue–Zhi *et al*., (2009), considered an Susceptible, Infected, Vaccinated and Recovered (SIVR) model and investigated backward bifurcation. They found out that; the rate of recruitment in the population, the contact rate, the rate of vaccination and the rate at which vaccine wanes can induce backward bifurcation in the model. Okuonghae and Omosigho, (2010) examined a backward bifurcation phenomenon in the model of case detection for tuberculosis (where four key factors were combined for an effective control of TB). They considered a situation where the susceptible class with low awareness, susceptible class with high awareness and the treatment class are considered as a single class hence reducing the original model of seven equations to a modified model of five equations. Backward bifurcation was then carried out for the modified model and it was found that the exogenous re-infection parameter (with an insignificant likelihood of susceptible individuals with high awareness level getting infected) was the cause of the backward bifurcation phenomenon in the system

Qesmi *et al*., (2010) proposed a mathematical model of ordinary differential equation describing the dynamics of hepatitis B and C virus (HBV/HCV) and its interaction with both

liver and blood cells. The model was shown to exhibit backward bifurcation which may be caused by variable efficacy of drug therapy. Wan and Zhu,(2010) considered a compartmental models for West Nile virus and investigated backward bifurcation phenomenon in the models.

Gumel and Song,(2008) addressed the problem of finding the causes of backward bifurcation in some standard deterministic models for the spread of some emerging and reemerging diseases. They investigated a brief review of some common causes, as well as some new causes, of backward bifurcation in some standard disease transmission models. It was shown that, in addition to the usual causes (such as the use of imperfect vaccine and exogenous re-infection in TB disease), a number of other biological or epidemiological mechanisms, such as vaccine-derived immunity waning at a slower rate than natural immunity, disease induced mortality in vector-borne diseases and differential susceptibility in risk-structured models, could also cause backward bifurcation in disease transmission models.

Villavicencio-Pulido *et al*.,(2013), considered the existence of backward bifurcation in some infectious disease. They investigated how the backward bifurcation can be generated and preserved or eliminated. Anguelov *et al*., (2004) presented a two stage SIS epidemiological model in animal population with bovine tuberculosis (BTB) in African buffalo as a guiding example. The analysis done in the proposed model revealed that the model exhibits the backward bifurcation phenomenon and is caused by imperfect vaccine. Nazaria and Gumel,(2015) established the presence of backward bifurcation phenomenon in the transmission dynamics of hepatitis C virus (HCV) within an IDU (Injection Drug User) population. They found out that the phenomenon exist in the presence of differential characteristics of primary infected and re-infected individual (with respect to the rates of the infectivity, recovery, disease progression and treatment, it was noted that Okuonghae and Omosigho (2010), Chiyaka *et al* (2008) did not investigate backward bifurcation in their work. This Paper is aimed at determining the causes of backward bifurcation in some epidemiological models, specifically Okuonghae and Omosigho (2010), Chiyaka *et al* (2008).

2. Procedures

It is intended to investigate the possibility of the existence of backward bifurcation where multiple equilibria exist under a condition that should ordinarily make just one of the equilibria exist alone. An endemic equilibrium point can exist with the disease free equilibrium(DFE). Generally, if $R_0 < 1$, the disease goes into extinction. However, in the case of backward bifurcation, the disease could persist at $R_0 < 1$ and reducing R_0 below unity is no longer sufficient to control the epidemic.

When R_0 is precisely unity, each infection exactly replaces itself in the linear approximation. Hence whether the disease will invade at $R_0 = 1$ will be determined by whetherthe reproduction number increase or decrease as the disease increases along the center manifold (Dushoff, 1998).

In backward bifurcation, with properties of unstable equilibrium bifurcating from the disease free equilibrium when $R_0 < 1$, giving rise to multiple stable states, one would expect the disease to be able to invade at $R_0 = 1$.

A simple criterion for a backward bifurcation is one which the disease can invade when $R_0 = 1$. This implies that the disease free equilibrium may not be globally asymptotically stable even if $R_0 < 1$. To determine the existence of backward bifurcation at $R_0 = 1$, this work use the Center Manifold Theory of Chavez and Song (2004).

2.1 Model analysis to determine backward bifurcation

2.2 Model I

Consider the model for tuberculosis with case detection (Okuonghae and Omosigho 2010).

$$\frac{dS_1}{dt} = \wedge - \alpha_1 S_1 - \frac{\beta S_1 (I + \eta J)}{N} + \theta S_2 - \mu S_1 \tag{2.1}$$

$$\frac{dS_2}{dt} = \alpha_1 S_1 - \frac{\sigma\beta S_2 (I + \eta J)}{N} - \theta S_2 - \mu S_2 \tag{2.2}$$

$$\frac{dE}{dt} = (1-p)\left[\frac{\beta S_1 (I + \eta J)}{N} + \frac{\sigma\beta S_2 (I + \eta J)}{N} + \frac{\varepsilon\beta T (I + \eta J)}{N}\right] \tag{2.3}$$

$$- \frac{\beta^* E (I + \eta J)}{N} - (k + \mu)E$$

$$\frac{dI}{dt} = p\left(\frac{\beta S_1 (I + \eta J)}{N} + \frac{\sigma\beta S_2 (I + \eta J)}{N} + \frac{\varepsilon\beta T (I + \eta J)}{N}\right) + KE + \frac{\beta^* E (I + \eta J)}{N}$$

$$- (\nu\alpha_2 + \mu + d + r_1)I \tag{2.4}$$

$$\frac{dJ}{dt} = \nu\alpha_2 I - r_2 J - \mu J \tag{2.5}$$

$$\frac{dT}{dt} = nr_2 J - \mu T - \frac{\varepsilon\beta T (I + \eta J)}{N} \tag{2.6}$$

$$\frac{dR}{dt} = r_1 I + mr_2 J - \mu R \tag{2.7}$$

Table 2.1: Description of Variables of the TB Model I

Variable	Description
S_1	Susceptible with high risk (Low level of awareness) group
S_2	Susceptible with low risk (High level of awareness) group
E	Primary latent group: those who are contracting TB for the first time and are in the latent stage and those who get infected again after effective treatment following their previous infection
I	Infections class
J	Identified infectious individuals (for treatment under DOTs-direct observation therapy strategy)
T	Effectively treated class
R	Individuals who become latent after failed treatment and those who became latent due to self-cure from the undetected infectious class.

Table 2.2: Description of Parameters of the TB Model I

Parameter	Description	Parameter	Description
α_1	Awareness rate	r_1	Self-cure rate
α_2	Cough identification rate	N	Treatment success
θ	Immunity measure	r_2	Recovery rate
μ	Natural death rate	D	TB-induced
σ	Effect of program	v	Cost factor
β	Transmission rate	η	Modification parameter
β^*	Transmission rate	ε	Reduce infection
^	Recruitment rate	d	Disease Induced death
P	Fraction of fast program		
K	Programme rate		

2.2.2 Disease Free Equilibrium (DFE) of Model I

The DFE of model I is given as

$$S_1^0 = \frac{\Lambda}{\mu}\left(\frac{\mu+\theta}{\mu+\theta+\alpha_1}\right)$$

$$S_2^0 = \frac{\Lambda}{\mu}\left(\frac{\alpha_1}{\mu+\theta+\alpha_1}\right) \quad (2.9)$$

$E^0 = I^0 = J^0 = T^0 = R^0 = 0$; written as

$$\varepsilon_0 = \left(S_1^0, S_2^0, E^0, I^0, J^0, T^0, R^0\right) = \left(\frac{\wedge}{\mu}\left(\frac{\mu+\theta}{\mu+\theta+\alpha_1}\right), \frac{\wedge}{\mu}\left(\frac{\alpha_1}{\mu+\theta+\alpha_1}\right), 0,0,0,0,0\right) \quad (2.10)$$

The associated reproduction number of model I was given by

$$R\tau = \frac{\beta}{d+\mu+r_1+\upsilon\alpha_2}\,\frac{(k+p\mu)}{k+\mu}\,\frac{(\mu+r_2+\eta\upsilon\alpha_2)}{\mu+r_2}$$ (Okuonghae and Omosigho, 2010)

2.2.3 Determination of backward bifurcation

Let $x_1 = S_1, \quad x_2 = S_2, \quad x_3 = E, \quad x_4 = I, \quad x_5 = J, \quad x_6 = T, \quad x_7 = R$

$$N = x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7 \quad (2.11)$$

Then the model (2.1) – (2.7) becomes

$$\dot{x}_1 = \Lambda - (\mu+\alpha_1)x_1 - \frac{\beta x_4 + \eta x_5 x_1}{N} + \theta x_2 \quad (2.12)$$

$$\dot{x}_2 = \alpha_1 x_1 - (\mu+\theta)x_2 - \frac{\sigma\beta(x_4+\eta x_5)x_2}{N} \quad (2.13)$$

$$\dot{x}_3 = (1-p)\frac{\beta(x_4+\eta x_5)x_1}{N} + (1-p)\frac{\sigma\beta(x_4+\eta x_5)x_2}{N} + (1-p)\frac{\varepsilon\beta(x_4+\eta x_5)x_6}{N} - \frac{\beta^*(x_4+\eta x_5)x_3}{N} - (k+\mu)x_3 \quad (2.14)$$

$$\dot{x}_4 = \frac{p\beta(x_4+\eta x_5)x_1}{N} + \frac{p\sigma\beta(x_4+\eta x_5)x_2}{N} + \frac{p\varepsilon\beta(x_4+\eta x_5)x_6}{N} + kx_3 + - \frac{\beta^*(x_4+\eta x_5)x_3}{N} - (\upsilon\alpha_2+\mu+d+r_1)x_4 \quad (2.15)$$

$$\dot{x}_5 = \upsilon\alpha_2 x_4 - (r_2+\mu)x_5 \quad (2.16)$$

$$\dot{x}_6 = nr_2x_5 - \mu x_6 - \frac{\varepsilon\beta(x_4+\eta x_5)x_6}{N} \quad (2.17)$$

$$\dot{x}_7 = r_1x_4 + mr_2x_5 - \mu x_7 \quad (2.18)$$

The associated Jacobian J_{ε^0} of the system (2.12)-(2.18) at DFE is given as

$$J\varepsilon^0 = \begin{pmatrix} -g_1 & \theta & 0 & \frac{-\beta x_1^0}{N^*} & \frac{-\eta\beta x_1^0}{N^*} & 0 & 0 \\ \alpha_1 & -g_2 & 0 & \frac{-\sigma\beta x_2^0}{N^*} & -\sigma\eta\beta x_2^0 & 0 & 0 \\ 0 & 0 & -g_3 & \frac{(1-p)\beta}{N^*}g_4 & \frac{(1-p)\eta\beta}{N^*}g_4 & 0 & 0 \\ 0 & 0 & K & \frac{p\beta}{N^*}g_4 - g_5 & \frac{p\eta\beta}{N^*}g_4 & 0 & 0 \\ 0 & 0 & 0 & \upsilon\alpha_2 & -g_6 & 0 & 0 \\ 0 & 0 & 0 & 0 & nr_2 & -\mu & 0 \\ 0 & 0 & 0 & r_1 & mr_2 & 0 & -\mu \end{pmatrix}$$

where $g_1 = \mu+\alpha_1$, $g_2 = \mu+\theta$, $g_3 = k+\mu$, $g_5(\upsilon\alpha_2+\mu+d+r_1)$, $g_6 = r_2+\mu$

$$g_4 = x_1^0 + \sigma x_2^0 = \frac{\Lambda}{\mu}\left(\frac{\mu+\theta+\sigma\alpha_1}{\mu+\theta+\alpha_1}\right) \quad (2.19)$$

$$N^* = x_1^0 + x_2^0 = \frac{\Lambda}{\mu}$$

Suppose $\beta = \beta^b$ is chosen as the bifurcation parameter. At $R_\tau = 1$

$$\beta^b = \frac{(d+\mu+r_1+\upsilon\alpha_2)(k+u)(\mu+r_2)}{(k+p\mu)(\mu+r_2+\eta\upsilon\alpha_2)} \tag{2.20}$$

The Jacobian J_{β^b} of (2.1) – (2.7) evaluated at the DFE when $\beta = \beta^b$ has a right eigenvector (corresponding to the zero eigenvalue) which is given as

$$w = [w_1, w_2, w_3, w_4, w_5, w_6, w_7]^T$$

In the same way, the left eigenvector is given as

$$v = [v_1, v_2, v_3, v_4, v_5, v_6, v_7,]$$

the components of w and v are obtained as follows;

$$w_1 = \frac{1}{g_1}\left(\theta w_2 - \frac{\beta^b x_1^*}{N*}(w_4+\eta w_5)\right), w_2 = \frac{1}{g_2}\left(\alpha_1 w_1 - \frac{\sigma\beta^b x_2^0}{N*}(w_4+\eta w_5)\right)$$

$$w_3 = \frac{1}{g_3}\frac{(1-p)\beta^b g_4}{N*}(w_4+\eta w_5), w_4 = w_4 > 0, \; w_5 = \frac{\upsilon\alpha_2}{g_6} w_4 \tag{2.21}$$

$$w_6 = \frac{nr_2}{\mu} w_5, \; w_7 = \frac{1}{\mu}(r_1 w_4 + m r_2 w_5)$$

and

$$v_1 = \frac{\alpha_1}{g_1 g_2} = \frac{\alpha_1}{(\mu+\alpha_1)(\mu+\theta)}, v_2 = \frac{g_1}{\theta\alpha_1} = \frac{\mu+\alpha_1}{\theta\alpha_1} \; v_3 = \frac{k}{g_3} v_4 = \left(\frac{k}{k+\mu}\right) v_4,$$

$$v_4 = v_4 > 0, v_5 = \frac{1}{r_2+\mu}\left(\frac{-\eta\beta^b x_1^0}{N*} v_1 \frac{-\sigma\eta\beta^b x_2^0}{N*} v_2 + \frac{(1-p)\beta^b \eta g_4}{N*} v_3 + \frac{p\beta^b \eta g_4}{N*} v_4\right)$$

$$v_6 = 0, v_7 = 0 \tag{2.22}$$

2.2.4 Determination of a and b for Model I

The associated non-zero second order partial derivatives of(2.12)-(2.18) at DFE were obtain and resulted to

$$a = \sum_{kij=1}^{7} v_k w_i w_j \frac{\partial^2 f_k(0,0)}{\partial x_i \partial x_j}$$

$$\begin{aligned} a = {} & v_1\left[A_1(w_1+w_2+\cdots+w_7)w_4 + \eta A_1(w_1+w_2+\cdots+w_7)w_5\right] + \\ & v_2\left[\sigma A_2(w_1+w_2+\cdots+w_7)w_4 + \sigma\eta A_2(w_1+w_2+\cdots+w_7)w_5\right] + \\ & v_3\left[A_8(w_1+\sigma w_2+\varepsilon w_6)w_4 + A_8\eta(w_1+\sigma w_2+\varepsilon w_6)w_5\right] + \\ & v_4\left[A_9(w_1+\sigma w_2+\varepsilon w_6)w_4 + A_9\eta(w_1+\sigma w_2+\varepsilon w_6) + A_{10}(w_3 w_4 + \eta w_3 w_5)\right] \\ & - v_1\left[A_7(w_1 w_4 + \eta w_1 w_5) - v_2\left[\sigma A_7(w_2 w_4 + \eta w_2 w_5)\right.\right. \end{aligned}$$

$$-v_3\left[A_3(w_1+w_2+\cdots+w_7)w_4+\eta A_3(w_1+w_2+\cdots+w_7)w_5+\sigma A_4(w_1+w_2+\cdots+w_7)w_4\right.$$
$$\left.+\eta\sigma A_4(w_1+w_2+\cdots+w_7)w_5+A_{10}(w_3w_4+\eta w_3w_5)\right]$$

$$-v_4\left[A_5(w_1+w_2+\cdots+w_7)w_4+\eta A_5(w_1+w_2+\cdots+w_7)w_5+\sigma A_6(w_1+w_2+\cdots+w_7)w_4\right.$$
$$\left.+\eta\sigma A_6(w_1+w_2+\cdots+w_7)w_5\right]$$

where $A_1=\frac{\beta^b x_1^0}{N^{*2}}$, $A_2=\frac{\beta^b x_2^0}{N^{*2}}$, $A_3=\frac{(1-p)\beta^b x_1^0}{N^{*2}}$, $A_4=\frac{(1-p)\beta^b x_2^0}{N^{*2}}$

$A_5=\frac{p\beta^b x_1^0}{N^{*2}}, A_6=\frac{p\beta^b x_1^0}{N^{*2}}$, $A_7=\frac{\beta^b}{N^*}$, $A_8=\frac{(1-p)\beta^b}{N^*}$, $A_9=\frac{p\beta^b}{N^*}$, $A_{10}=\frac{\beta^*}{N^*}$

Let

$$w_1+w_2+w_3+w_4+w_5+w_6+w_7=Q^* \text{ and } (w_1+\sigma w_2+\varepsilon w_6)=T^*$$

Hence

$$a=Q^*(w_4+\eta w_5)[v_1A_1+v_2A_2\sigma]+T^*(w_4+\eta w_5)[v_3A_8+v_4A_9]+(w_4+\eta w_5)w_3v_4A_{10}$$
$$-(w_4+\eta w_5)[v_1A_7w_1-v_2A_7\sigma w_2]-Q^*(w_4+\eta w_5)v_3[A_3+A_4\sigma]-v_3(w_4+\eta w_5)w_3A_{10}$$

$$-Q^*(w_4+\eta w_5)v_4(A_5+\sigma A_6)$$

Substituting for the A_i, $1\le i\le 10$

Thus,

$$a=2\frac{\mu}{\wedge}(w_4+\eta w_5)\left[\beta^b\left(Q^*\left[\frac{v_1(\mu+\theta)}{\mu+\theta+\alpha_1}+\frac{v_2(\alpha_1+\sigma)}{\mu+\theta+\alpha_1}\right]+T^*(v_3(1-p)+pv_4)\right)+\beta^* w_3v_4\right]$$
$$-2\frac{\mu}{\wedge}(w_4+\eta w_5)\left[\beta^b(Q^*[(1-p)v_3+pv_4])\left(\frac{\mu+\theta+\alpha_1\sigma}{\mu+\theta+\alpha_1}\right)+(v_1w_1+\sigma v_2w_2)+\beta^* w_3v_3\right]$$
$$=-2\frac{\mu}{\wedge}(w_4+\eta w_5)\left[\beta^b\left(((1-p)v_3+pv_4)\left(Q^*\left(\frac{\mu+\theta+\alpha_1\sigma}{\mu+\theta+\alpha_1}\right)-T^*\right)\right)+\right.$$
$$\left.+(v_1w_1+\sigma v_2w_2)-\frac{Q^*(v_1(\mu+\theta)+v_2(\alpha_1\sigma))}{\mu+\theta+\alpha_1}\right]+\beta^*(v_3-v_4)w_3$$

With $v_3-v_4=\frac{-\mu}{k+\mu}v_4<0$

Let

$$\psi=\left[\beta^b\left(((1-p)v_3+pv_4)\left(Q^*\left(\frac{\mu+\theta+\alpha_1\sigma}{\mu+\theta+\alpha_1}\right)-T^*\right)\right)+(v_1w_1+\sigma v_2w_2)-\frac{Q^*(v_1(\mu+\theta)+v_2(\alpha_1\sigma))}{\mu+\theta+\alpha_1}\right]$$

$$\therefore a = -2\frac{\mu}{\wedge}(w_4 + \eta w_5)\left[\beta^b \psi + \beta^*(v_3 - v_4)w_4\right]$$

Hence $a > 0$ if and only if $\beta^* > \dfrac{\beta^b \psi}{(v_4 - v_3)w_3}$

Now, the non-zero partial derivatives is also obtainedand gives

$$b = v_k \sum_{i=1}^{7} \frac{w_i \partial^2 f_k}{\partial x_i \partial \beta} = (w_4 + \eta w_5)\left[((1-p)v_3 + pv_4)\phi + \left(\frac{-(v_1(\mu+\theta)+\alpha_1\sigma v_2)}{(\mu+\theta+\alpha_1)}\right)\right]$$

$$= w_4 + \eta w_5\left[((1-p)v_3 + pv_4)\phi - \left(\frac{(v_1(\theta+\mu)+\alpha_1\sigma v_2)}{(\mu+\theta+\alpha_1)}\right)\right] > 0. \text{ Where } \phi = \left(\frac{\mu+\theta+\alpha_1\sigma}{\mu+\theta+\alpha_1}\right)$$

$\therefore b > 0$

Hence we establish that

$$\beta^* > \frac{\beta^b \psi}{(v_4 - v_3)w_3}$$

with $(v_4\text{-}v_3)>0$

Then the model 1 undergoes a backward bifurcation at $R_\tau=1$. This is caused by the exogenous re-infection, β^*

2.3Model II

Consider the model of immune response and drug therapy in human malaria infection (Chiyaka *et al*, 2008) given by

$$\frac{dX(t)}{dt} = \lambda_X + \sigma Y(t) - \frac{\beta X(t)M(t)}{1+c_0 A(t)} - \mu_X X(t) - \omega X(t)M(t)B(t) \quad (2.23)$$

$$\frac{dY(t)}{dt} = \frac{\beta X(t)M(t)}{1+c_0 A(t)} - \mu_Y Y(t) - K_Y B(t)Y(t) \quad (2.24)$$

$$\frac{dM(t)}{dt} = \frac{r\mu_Y Y(t)}{1+c_1 B(t)} - \mu_m M(t) - k_M B(t)M(t) - \frac{BX(t)M(t)}{1+c_0 A(t)} \quad (2.25)$$

$$\frac{dB(t)}{dt} = \lambda_B + B(t)\left(\rho_Y \frac{Y(t)}{k_0 M(t)} + \rho_M \frac{M(t)}{k_1 + M(t)}\right) - \mu_B B(t) \quad (2.26)$$

$$\frac{dA(t)}{dt} = \eta B(t) - \frac{M(t)}{k_1 + M(t)} - \mu_A A(t) \quad (2.27)$$

Table 2.3 Description of the variables and parameter used in the model (2.23)-(2.27)

Variables	Description
X(t)	The concentrations of uninfected RBCs
Y(t)	The concentration of infected RBCs (IRBCs)
M(t)	The merozoites (parasites) that infects RBSc
B(t)	The immune cells
A(t)	The antibodies
Parameter	**Description**
λ_x	Source of the red blood cells from the bone.
λ_B	Source of immune cells
β	Rate of infection of RBC
μ_x	Death rate of RBCs
μ_A	Rate at which the antibodies decay
μ_r	Death rate of IRBCs
μ_B	Natural death rate of the immune cells
R	Average number of merozoites produced each bursting IRBC
μ_m	Death rate of merozoites
σ	Rate of concentration of IRBCs
c_0	Efficiency of antibodies in reducing erythrocyte invasion
k_y	Represent immunosensitivity of IRBC
c_1	Efficiency of immune cells in suppressing parasite production
k_m	Represent immunosensitivity of the merozoites
ρ_y	Immunogenicity of IRBC
ρ_m	Immunogenicity of merozoites
k_0	Density of IRBCs (at which immune cells grow at rate $\rho_y/_2$)
k_1	Density of merozoites (at which immune cells grow at rate $\rho_y/_2$ in the absence of IRBCs
η	Maximum rate of increase of antibodies

2.3.1 The Disease free Equilibrium (DFE) of Model II

The model (2.23)-(2.27) has a DFE obtained by setting the right hand sides of the equations to zero.

Therefore $$\varepsilon_0 = \left(\hat{X}, \hat{Y}, \hat{M}, \hat{B}, \hat{A}\right) = \left(\frac{\lambda_X}{\mu_X}, 0, 0, \frac{\lambda_B}{\mu_B}, 0\right) \tag{2.28}$$

The associated reproduction number

$$R_0 = \frac{r\mu_y \beta \lambda_x \mu_B^3}{\left(\mu_B + c_1\lambda_B\right)\left(\mu_B\mu_y + k_y\lambda_B\right)\left(\mu_B\mu_m\mu_X + \mu_X k_m \lambda_B + \mu_B\beta\lambda_x\right)} \tag{2.29}$$

2.3.2 Determination of the backward bifurcation

Let

$$x_1 = X,\ x_2 = Y,\ x_3 = M, x_4 = B,\ x_5 = A$$

Then the model (2.23)-(2.27) gives:

$$\dot{x}_1 = f_1 = \lambda_x + \sigma x_2 - \frac{\beta x_1 x_3}{1 + c_0 x_5} - \mu_x x_1 - w x_1 x_3 x_4$$

$$\begin{aligned}
\dot{x}_2 &= f_2 = \frac{\beta x_1 x_3}{1+c_0 x_5} - \mu_y x_2 - k_y x_4 x_5 \\
\dot{x}_3 &= f_3 = \frac{r\mu_y x_2}{1+c_1 x_4} - \mu_m x_3 - k_m x_4 x_3 - \frac{\beta x_1 x_3}{1+c_0 x_5} \\
\dot{x}_4 &= f_4 = \lambda_B + x_4\left(\rho_y \frac{x_2}{k_0 + x_2} + \rho_m \frac{x_3}{k_1 + x_3}\right) - \mu_3 x_4 \\
\dot{x}_5 &= f_5 = \eta\, x_4 \frac{x_3}{k_1 + x_3} \mu_A x_5
\end{aligned} \tag{2.30}$$

The associated Jacobian J_{ε_0} of the system (2.30) at DFE is given by

$$J_{\varepsilon_0} = \begin{pmatrix}
-\mu_x & \sigma & -\frac{\beta\lambda_x}{\mu_x} - \omega\frac{\lambda_x}{\mu_x}\frac{\lambda_B}{\mu_B} & 0 & 0 \\
0 & -(k_y\frac{\lambda_B}{\mu_B} + \mu_y) & -\beta\frac{\lambda_x}{\mu_x} & 0 & 0 \\
0 & \frac{r\mu_y\mu_B}{\mu_B + c_1\lambda_B} & -\left(\mu_m + \beta\frac{\lambda_x}{\mu_x} + k_m\frac{\lambda_B}{\mu_B}\right) & 0 & 0 \\
0 & \frac{\rho_y}{k_0}\frac{\lambda_B}{\mu_B} & \frac{\rho_m}{k_1}\frac{\lambda_B}{\mu_B} & -\mu_B & 0 \\
0 & 0 & \frac{\eta}{k_1}\frac{\lambda_B}{\mu_B} & 0 & -\mu_A
\end{pmatrix}$$

Suppose $\beta = \beta^*$ is chosen as the bifurcation parameter at $R_0 = 1$,

$$\beta^* = \frac{(\mu_\beta + c_1\lambda_B)(\mu_B\mu_y + k_y\lambda_B)(\mu_B\mu_m\mu_x + \mu_x k_n\lambda_B)}{r\mu_y\lambda_x\mu_B^3 - \mu_B\lambda_x(\mu_\beta + c_1\lambda_B)(\mu_B\mu_y + k_y\lambda_B)} \tag{2.31}$$

2.3.3 Determination of Eigen-vectors of Model II

The right eigenvector (associated with the zero eigenvalue) is obtained and denoted as $w = [w_1, w_2, w_3, w_4, w_5]^T$ where,

$$\begin{aligned}
w_1 &= \frac{1}{\mu_x}\left[\sigma w_2 - (\frac{\beta\lambda_x}{\mu_x} + \omega\frac{\lambda_x}{\mu_x}\frac{\lambda_B}{\mu_B})w_3\right],\ w_2 = w_2 > 0 \\
w_3 &= \frac{r\mu_y\mu_x\mu_B^2}{(\mu_B + c_1\lambda_B)(\mu_B\mu_m\mu_X + \mu_X k_m\lambda_B + \mu_B\lambda_x\beta)},\ w_4 = \frac{\lambda_\beta}{\mu_B^2}\left[\frac{\rho_y}{k_0}w_2 + \frac{\rho_m}{k_1}w_3\right] \\
w_5 &= \frac{1}{\mu_A}\left(\frac{\eta}{k_1}\frac{\lambda_\beta}{\mu_B}w_3\right)
\end{aligned} \tag{2.32}$$

Give the left eigenvector

$$v_1 = 0, v_2 = v_2 > 0, v_3 = -\frac{\beta\lambda_x\mu_B}{(\mu_B\mu_m\mu_X + \mu_X k_m\lambda_B + \mu_B\lambda_x\beta)}, v_4 = 0, v_5 = 0 \tag{2.33}$$

2.3.4 Determination of *a* and *b* for Model II

The associated non-zero second order partial derivatives of (2.30) at DFE were computed and gives

$$a = \sum v_k w_i w_j \frac{\partial^2 f_k(0,0)}{\partial x_i \partial x_j}$$

$$= \beta^* \left[\left(v_2 w_2^{\,2} + \frac{w_3 w_5 \beta^* \lambda_x \mu_B}{(\mu_B \mu_m \mu_X + \mu_X k_m \lambda_B + \mu_B \lambda_x \beta^*)} \right) \frac{\sigma}{\mu_x} + \frac{w_4 r \mu_y \mu_x \mu_B^{\,3} k_m \lambda_x}{(\mu_B + c_1 \lambda_B)(\mu_B \mu_m \mu_X + \mu_X k_m \lambda_B + \mu_B \lambda_x \beta^*)^2} \right]$$

$$- \beta^* \left[v_2 w_2 w_3 \frac{\beta^* \lambda_x}{\mu_x^{\,2}} + v_2 w_2 \frac{\omega \lambda_x \lambda_B}{\mu_x^{\,2} \mu_B} + \frac{w_2 w_4 r c_1 \mu_y \mu_B^{\,3} \lambda_x}{(\mu_B + c_1 \lambda_B)^2 (\mu_B \mu_m \mu_x + \mu_x k_m \lambda_B + \mu_B \lambda_x \beta^*)} \right.$$

$$+ \frac{w_3 \beta^* \mu_B c_0 \lambda_x^{\,2}}{\mu_x (\mu_B \mu_m \mu_X + \mu_X k_m \lambda_B + \mu_B \lambda_x \beta^*)} + \frac{v_2 w_3 w_5 c_0 \lambda_x}{\mu_x} + \frac{w_3^{\,2} \beta^{*2} \lambda_x^{\,2} \mu_B}{\mu_X^{\,2} (\mu_B \mu_m \mu_X + \mu_X k_m \lambda_B + \mu_B \lambda_x \beta^*)}$$

$$\left. + \frac{w_3^{\,2} \beta^* \lambda_B \lambda_x^{\,2}}{\mu_x (\mu_B \mu_m \mu_X + \mu_X k_m \lambda_B + \mu_B \lambda_x \beta^*)} \right] - v_2 w_2 w_4 k_y$$

Let

$$\eta_b = \left[\left(v_2 w_2^{\,2} + \frac{w_3 w_5 \beta^* \lambda_x \mu_B}{(\mu_B \mu_m \mu_X + \mu_X k_m \lambda_B + \mu_B \lambda_x \beta^*)} \right) \frac{\sigma}{\mu_x} + \frac{w_4 r \mu_y \mu_x \mu_B^{\,3} k_m \lambda_x}{(\mu_B + c_1 \lambda_B)(\mu_B \mu_m \mu_X + \mu_X k_m \lambda_B + \mu_B \lambda_x \beta^*)^2} \right] \tag{2.34}$$

and

$$\phi = v_2 w_2 w_3 \frac{\beta^* \lambda_x}{\mu_x^{\,2}} + v_2 w_2 \frac{\omega \lambda_x \lambda_B}{\mu_x^{\,2} \mu_B} + \frac{w_2 w_4 r c_1 \mu_y \mu_B^{\,3} \lambda_x}{(\mu_B + c_1 \lambda_B)^2 (\mu_B \mu_m \mu_x + \mu_x k_m \lambda_B + \mu_B \lambda_x \beta^*)}$$

$$+ \frac{w_3 \beta^* \mu_B c_0 \lambda_x^{\,2}}{\mu_x (\mu_B \mu_m \mu_X + \mu_X k_m \lambda_B + \mu_B \lambda_x \beta^*)} + \frac{v_2 w_3 w_5 c_0 \lambda_x}{\mu_x} + \frac{w_3^{\,2} \beta^{*2} \lambda_x^{\,2} \mu_B}{\mu_X^{\,2} (\mu_B \mu_m \mu_X + \mu_X k_m \lambda_B + \mu_B \lambda_x \beta^*)} \tag{2.35}$$

Then, $a > 0$ if and only if $\eta_b > \phi$

The non-zero partial derivatives of the system were obtained and the bifurcation parameter *b*is given by

$$b = \sum_{ki=1}^{5} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \beta} = v_2 \frac{\lambda_x}{\mu_x} - \frac{\lambda_x}{\mu_x} v_3 = \frac{\lambda_x}{\mu_x} (v_2 - v_3) \tag{2.36}$$

b > 0, with $v_2 > v_3$

Hence model II is established and it undergoes a phenomenon of backward bifurcation at $R_0 = 1$. This is caused by the production of merozoites and the concentration of the infected red blood cells.

3. Conclusion

Both models exhibit backward bifurcation when$a > 0$ while $b > 0$ in each system.Thus, it is established that model I and II undergoes a backward bifurcation at $R_0 = 1$. In model I, the exogenous re-infection of latently infected individuals was the cause of the backward bifurcation. In Model II, the backward bifurcation wascaused by the production of merozoites and the concentration of the infected red blood cells.

Model I and II were investigated using Centre manifold theory to depict the causes of backward bifurcation. However, in this work some epidemiological parameters that can induce the backward bifurcation phenomenon that were not treated in Okuonghae and Omosigho (2010) and Chiyaka *et al* (2008) were identified.

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