Backward Bifurcation in Epidemic Models of *Toxoplasma gondii*: A Qualitative Analysis

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Abstract: *Toxoplasmosis is a parasitic disease instigated by T. gondii. T. gondii can infect every warm-blooded vertebrate and the proportion of the world population that is suffering from the parasitic disease is over one-third. In this work, a nonlinear epidemic model is developed to analyze how various factors can instigate backward bifurcation phenomenon in the transmission dynamics of toxoplasmosis. The model is subjected to the usability test by employing ample mathematical techniques and is found to be usable. An analytical threshold that governed T. gondii transmissibility is derived and used to study the model qualitatively. Results from the analysis establish the existence of backward bifurcation for toxoplasmosis dynamics.*

Keywords: Toxoplasmosis, Model, Reinfection, Backward bifurcation, Threshold

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1 Introduction

Toxoplasmosis is a parasitic disorder activated by *T. gondii* [18]. The disease affects over one-third of the human population globally [15]. The main carriers of *T. gondii* are cats (Felis catus) [8], though other animals like cattle, swine, sheep, goats, dogs, birds, etc. are potential reservoirs of the disease, *T. gondii* reservoirs can be categorized into two-living and non-living reservoirs. Living reservoirs include cats (final hosts) and other animals (intermediate hosts) [21] while non-living reservoirs include contaminated water and soil [15]. It should be noted that unlike other reservoirs of *T. gondii*, cats remain asymptomatic throughout their life.

Toxoplasmosis is transmitted through ingestion of oocysts from contaminated food, water or environment. The disease can also be contracted through unhygienic contact with *T. gondii* reservoirs and their wastes [10]. Toxoplasmosis infection is severe and develops faster in immunosuppressed patients. When the infection is fully incubated, the infected individuals or animals may manifest fever, fatigue, myocarditis, lymphocytosis, abortion, meningioencephalitis, etc. [21]. Transmission and spread of toxoplasmosis can be prevented through avoidance of contact with cats, elimination of stray cats, proper cooking of vegetable and meat, drinking of portable water and adequate hygienic practices [21]. However, the disease may be treated with drugs such as sulfadiazine, clindamycin, pyrimethamine and spiramycin [21].

The qualitative behaviors of many epidemic models rely on a threshold quantity known as the basic reproductive ratio $R_\circ$ [13]. The central idea of $R_\circ$ is that a patient is unable to spread the infection and the disease disappears in time if $R_\circ < 1$. On the other hand, if $R_\circ > 1$, infection grows because the patient is able to substitute itself and the epidemic emerges. Bifurcation is a qualitative phenomenon that shows how a change in dynamical behavior and stability properties of an epidemic model instigates either disease eradication or disease persistence in epidemic modeling [1].

Backward bifurcation occurs in disease dynamics when multiple equilibria co-exist in such a way that the disease persists even when $R_\circ < 1$ [2]. Generally, a stable disease-free equilibrium (DFE) co-exists with a stable endemic equilibrium when $R_\circ < 1$ and as a result, the condition $R_\circ < 1$ is no longer sufficient for disease eradication [2, 16, 20]. The knowledge of backward bifurcation is very crucial in epidemic modeling because intervention programs will have to be designed and fortified in such a way to reduce $R_\circ$ further so as to guarantee disease elimination for epidemic models that are characterized by backward bifurcation phenomenon.

Numerous models have been designed to study the transmission dynamics of toxoplasmosis [11, 17, 19]. Some toxoplasmosis models are built around vaccinations as adequate methods of eliminating *T. gondii* [4]. However, vaccinations, in most cases, do not offer lifelong immunity as the immunity produced by the vaccines may wane with time [3]. Individuals who are protected against infections by vaccination may become susceptible again after the waning of immunity [6]. Therefore, models that are built around vaccination may exhibit backward bifurcation phenomenon. The study of backward bifurcation for the transmission dynamics of toxoplasmosis is not new. Authors in [9] and [12] proposed toxoplasmosis models and verified the existence of backward bifurcation for the models. Nevertheless, the influence of vaccination coverage as well as reinfection on the existence of backward bifurcation in the dynamics of toxoplasmosis is relatively new in the literature.

2 The Model

The model presented is the extension of the mathematical model in Arenas et al. [4]. The model in [4] is extended by incorporating recovery and reinfection. Besides, the present paper considers backward bifurcation phenomenon in toxoplasmosis dynamics which was excluded by Arenas and co-researchers [4]. The

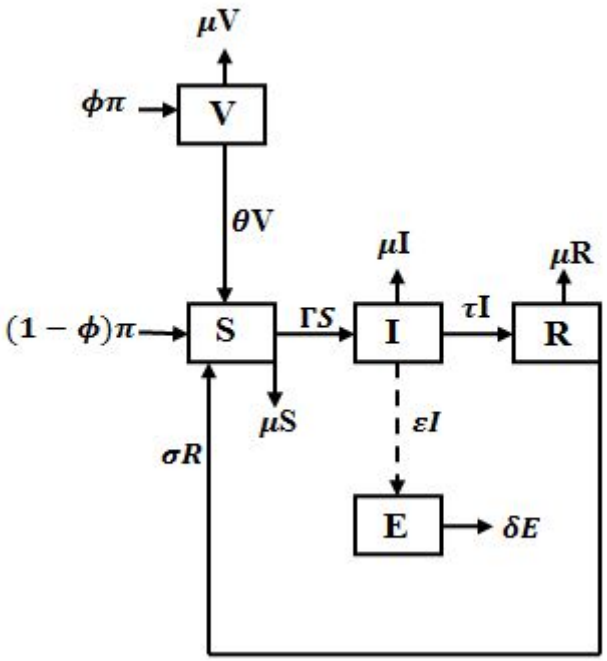

Figure 1: Flow chart of *T. gondii* model.

total population of cats and contaminated environment denoted by $N(t)$ is categorized into five subclasses: vaccinated $V(t)$, susceptible $S(t)$, infected $I(t)$, recovered $R(t)$ and contaminated environment $E(t)$. It is assumed that the cat population is recruited at rate π with some fraction of it, $(\phi\pi)$ vaccinated at birth while the remaining fraction $(1-\phi)\pi$ that do not receive vaccination at birth moves to the susceptible class. ϕ is the vaccination coverage that meets the requirement $0 \leq \phi \leq 1$. The vaccinated cats become susceptible at rate θ after the waning of immunity. Susceptible cats contract toxoplasmosis from the infected cats and also from the contaminated environment at rates α_1 and α_2 respectively. Infected cats increase oocysts in the environment at rate ε, recover at rate τ and become susceptible again at rate σ. Infection does not result in death but natural death occurs for the cat compartments at the same rate μ while oocysts are removed naturally from the environment at rate δ.

Following the aforementioned assumptions and the flow chart in Figure 1, the toxoplasmosis model is

derived as follows

$$\frac{dS}{dt} = (1-\phi)\pi + \theta V + \sigma R - \Gamma S - \mu S, \tag{1}$$
$$\frac{dV}{dt} = \phi\pi - (\theta+\mu)V, \tag{2}$$
$$\frac{dI}{dt} = \Gamma S - (\varepsilon+\tau+\mu)I, \tag{3}$$
$$\frac{dR}{dt} = \tau I - (\sigma+\mu)R, \tag{4}$$
$$\frac{dE}{dt} = \varepsilon I - \delta E. \tag{5}$$

From $S+V+I+R=1$, $R=1-S-V-I$, and so the model (1)-(5) reduce to

$$\frac{dS}{dt} = (1-\phi)\pi + \theta V + \sigma(1-S-V-I) - (\Gamma+\mu)S, \tag{6}$$
$$\frac{dV}{dt} = \phi\pi - (\theta+\mu)V, \tag{7}$$
$$\frac{dI}{dt} = \Gamma S - (\varepsilon+\tau+\mu)I, \tag{8}$$
$$\frac{dE}{dt} = \varepsilon I - \delta E, \tag{9}$$

where $\Gamma = \alpha_1 I + \alpha_2 E$.

2.1 Model validity

The system of equations (6)-(9) is valid and suitable to conduct the analysis if it satisfies the following conditions.

2.1.1 Positivity of solutions

Theorem 1. *The solutions $S(t), V(t), I(t)$ and $E(t)$ of the model are nonnegative if $S_\circ, V_\circ, I_\circ$ $E_\circ$ are positive.*

Proof. From Eq. (7),

$$\frac{d}{dt}V(t) = \phi\pi - (\theta+\mu)V(t) \tag{10}$$

Assuming $(\theta+\mu)=\vartheta$ and $\phi\pi=\beta$, then,

$$\frac{d}{dt}V(t) + \vartheta V(t) = \beta \tag{11}$$

The product of Eq. (11) and $\exp(\vartheta t)$ implies

$$\frac{d}{dt}V(t)\ exp(\vartheta t) + \vartheta V(t)\ exp(\vartheta t) = \beta\ exp(\vartheta t) \tag{12}$$

By product rule, the LHS of Eq. (12) implies

$$\frac{d}{dt}V(t)\ exp(\vartheta t) + \vartheta V(t)\ exp(\vartheta t) = \frac{d}{dt}[V(t)\ exp(\vartheta t)] \tag{13}$$

From Eq. (12) and Eq. (13), we get

$$\frac{d}{dt}[V(t)\ exp(\vartheta t)] = \beta\ exp(\vartheta t) \tag{14}$$

$$\Longrightarrow V(t) = V(0) = exp(-\vartheta t) + \frac{\beta}{\vartheta}(1-exp(-\vartheta t)) \geq 0 \ \ \forall \ \ t \geq 0 \tag{15}$$

Following the same approach, it can be shown that $S(t)$, $I(t)$ and $E(t)$ are nonnegative. Therefore, the solutions of the model are nonnegative for all $t \geq 0$. □

2.1.2 Invariant region

Theorem 2. *Given the nonnegative initial data $S_\circ, V_\circ, I_\circ$ and $E_\circ$, the solution for the model is feasible in the region*

$$\left\{S(t), V(t), I(t) \in \Re_+^3 | S(t) + V(t) + I(t) \leq \frac{\pi}{\mu}; E(t) \in \Re_+ | E(t) \leq \frac{\pi\varepsilon}{\mu}\right\} \tag{16}$$

Proof. Summing up the equations for cat population,

$$\begin{aligned}
&\frac{d}{dt}C(t) = \pi - (S+V+I)\mu + \sigma(1-S-V-I) - (\varepsilon+\mu)I,\\
\Longrightarrow &\frac{d}{dt}C(t) \leq \pi - \mu C,\\
\Longrightarrow &\frac{d}{\pi - \mu C} \leq dt,\\
\Longrightarrow &\pi - \mu C(t) \geq k_1 e^{-\mu t}.
\end{aligned}$$

As $t = 0$, $C(t) = C(0)$ gives

$$k_1 = \pi - \mu C(0)$$

. Therefore,

$$\begin{aligned}
&\pi - \mu C(t) \geq k_1(\pi - \mu C(0))e^{-\mu t},\\
\Longrightarrow &C(t) \leq \frac{\pi}{\mu} - \left(\frac{\pi - \mu C(0)}{\mu}\right)e^{-\mu t}
\end{aligned} \tag{17}$$

As $t \to \infty$, $0 \leq C(t) \leq \frac{\pi}{\mu}$, which shows that the solution for cat population is bounded within $\frac{\pi}{\mu}$.
Also, considering the population of oocysts in the environment in Eq. (9),

$$\frac{dE}{dt} = \varepsilon I - \delta E \tag{18}$$

Notice that I is a subset of $C(t)$ and $C(t) \leq \frac{\pi}{\mu}$ in Eq. (17)

$$\begin{aligned}
&\Longrightarrow \frac{dE}{dt} \leq \frac{\pi\varepsilon}{\mu} - \delta E\\
&\Longrightarrow E(t) \leq \frac{\pi\varepsilon}{\mu}(1 - k_2 e^{-\delta t}).
\end{aligned}$$

As $t \to \infty$, $E(t) \leq \frac{\pi\varepsilon}{\mu}$ which establishes that the solution for the oocysts population is bounded in the region $\frac{\pi\varepsilon}{\mu}$. □

3 Model Analysis

3.1 Disease eradication and reproduction number

When oocysts are completely eliminated from the cat population and the environment, the disease eradication point is obtained as

$$D_\circ = (S_\circ, V_\circ, I_\circ, E_\circ) = (S_\circ, V_\circ, 0, 0), \tag{19}$$

where

$$S_\circ = \frac{(1-\phi)(\theta+\mu)\pi + \theta\phi\pi + \sigma(\theta+\mu) - \sigma\phi\pi}{(\theta+\mu)(\sigma+\mu)},$$

and

$$V_\circ = \frac{\phi\pi}{\theta+\mu}$$

Infections occur when susceptible cats interact with the contaminated environment or the infected cats. The average number of new infections is quantified in terms of a nondimentional quantity known as the reproductive ratio ($R_\circ$). The quantity ($R_\circ$) is derived by the method in [7] which necessitated the derivation of the matrices M and N from the model such that

$$M = \begin{pmatrix} \alpha_1 S_\circ & \alpha_2 S_\circ \\ 0 & 0 \end{pmatrix}, \tag{20}$$

$$N = \begin{pmatrix} \varepsilon + \tau + \mu & \mu \\ -\varepsilon & \delta \end{pmatrix} \tag{21}$$

Thus,

$$R_\circ = \frac{(\alpha_1 \delta + \alpha_2 \varepsilon)}{\delta(\varepsilon + \tau + \mu)} S_\circ \tag{22}$$

3.2 Stability of disease eradication

The stability of the point where oocysts are eradicated from the contaminated environment and the population is analyzed.

Theorem 3. *The disease eradication point $D_\circ$ is stable locally if $R_\circ < 1$ and unstable if otherwise, i.e., if $R_\circ > 1$.*

Proof. The variational matrix of the system (6)-(9) evaluated at $D_\circ$ is obtained as

$$\mathbf{J}(\mathbf{D}_\circ) = \begin{pmatrix} -(\sigma+\mu) & \theta - \sigma & -\sigma - \alpha_1 S_\circ & -\alpha_2 S_\circ \\ 0 & -(\theta+\mu) & 0 & 0 \\ 0 & 0 & \alpha_1 S_\circ - (\varepsilon + \tau + \mu) & \alpha_2 S_\circ \\ 0 & 0 & \varepsilon & -\delta \end{pmatrix} \tag{23}$$

The first two eigenvalues of $\mathbf{J}(\mathbf{D}_\circ)$ are negative and are $\lambda_1 = -(\sigma + \mu)$ and $\lambda_2 = -(\theta + \mu)$.
The remaining eigenvalues can be determined from submatrix $\mathbf{B}$ given as

$$\mathbf{B} = \begin{pmatrix} \alpha_1 S_\circ - (\varepsilon + \tau + \mu) & \alpha_2 S_\circ \\ \varepsilon & -\delta \end{pmatrix} \tag{24}$$

The characteristic equation of submatrix $\mathbf{B}$ is evaluated as

$$\lambda^2 + (\delta + \varepsilon + \tau + \mu - \alpha_1 S_\circ)\lambda - \alpha_1 \delta S_\circ - \alpha_2 \varepsilon S_\circ + \delta(\varepsilon + \tau + \mu) = 0 \tag{25}$$

The two roots in the Eq. (25) are negative if

$$(\delta + \varepsilon + \tau + \mu) > \alpha_1 S_\circ, \tag{26}$$

and

$$-\alpha_1 \delta S_\circ - \alpha_2 \varepsilon S_\circ + \delta(\varepsilon + \tau + \mu) > 0 \tag{27}$$

From Eq. (27),

$$(\alpha_1 \delta + \alpha_2 \varepsilon) S_\circ < \delta(\varepsilon + \tau + \mu).$$

Therefore,

$$\frac{(\alpha_1 \delta + \alpha_2 \varepsilon)}{\delta(\varepsilon + \tau + \mu)} S_\circ < 1.$$

By Eq. (22),

$$R_\circ < 1.$$

Since it is proved that $R_\circ < 1$, then $(\delta + \varepsilon + \tau + \mu) > \alpha_1 S_\circ$ in Eq. (26) and the two roots in Eq. (25) are negative. The result of the proof indicates that the disease eradication equilibrium $D_\circ$ is locally asymptotically stable. □

3.3 Existence of backward bifurcation

The stability of the disease eradication implies that toxoplasmosis can be eradicated from the cat population within the framework of the model when $R_\circ < 1$. However, a change in the value of a parameter or changes in the values of some parameters of a model may alter the qualitative structure of the model. The alterations in the qualitative structure of a model are referred to as bifurcations in Mathematical Epidemiology and the parameter whose values alteration results in bifurcation is referred to as a bifurcation parameter [14]. Backward bifurcation is characterized by the simultaneous existence of stable disease eradication and stable disease persistence when the associated reproductive ratio is less than unity. Backward bifurcation has a serious implication in disease management because of disease persistence irrespective of stable disease eradication when $R_\circ < 1$.

At the bifurcation point when $R_\circ = 1$, one can investigate whether the bifurcation parameter activates backward bifurcation or not. The existence of backward bifurcation shall be verified for the present toxoplasmosis model following the Center Manifold Theory formulated by [5] to be sure if the existence of the stable disease eradication in the analysis is sufficient to eliminate toxoplasmosis.

To apply the theorem, the variables of the model are transformed in such a way that $x_1 = S, x_2 = V, x_3 = I$ and $x_4 = E$. If $\mathbf{X} = (x_1, x_2, x_3, x_4)^T$, the system of Eqs. (6)-(9) becomes $\dfrac{d\mathbf{X}}{dt} = \mathbf{F}(\mathbf{X})$ where $\mathbf{F} = (f_1, f_2, f_3, f_4)$. Thus, the model Eqs. (6)-(9) are transformed to

$$\frac{dx_1}{dt} = (1-\phi)\pi + \theta x_2 + \sigma(1 - x_1 - x_2 - x_3) - (\alpha_1 x_3 + \alpha_2 x_4)x_1 - \mu x_1, \tag{28}$$

$$\frac{dx_2}{dt} = \phi\pi - (\theta + \mu)x_2, \tag{29}$$

$$\frac{dx_3}{dt} = (\alpha_1 x_3 + \alpha_2 x_4)x_1 - (\varepsilon + \tau + \mu)x_3, \tag{30}$$

$$\frac{dx_4}{dt} = \varepsilon x_3 - \delta x_4. \tag{31}$$

If α_1 is chosen as the bifurcation parameter at $R_\circ = 1$ and if it is expressed in terms of other parameter at the point, then

$$\alpha_1 = \frac{\varepsilon + \tau + \mu}{S_\circ} - \frac{\alpha_2 \varepsilon}{\delta} \tag{32}$$

With $\alpha_1 = \alpha_1^*$, the transformed model Eqs. (28)-(31) consist of a simple eigenvalue that has zero real part. Hence, with the variational matrix, the behavior of the system (28)-(31) around $\alpha_1 = \alpha_1^*$ can be investigated via the Center Manifold Theory.

The variational matrix of the system (28)-(31) when α_1 changes to α_1^* is obtained as

$$\mathbf{J}(\mathbf{D}_\circ)|_{\alpha_1=\alpha_1^*} = \begin{pmatrix} -(\sigma+\mu) & \theta - \sigma & -\sigma - \alpha_1^* S_\circ & -\alpha_2 S_\circ \\ 0 & -(\theta+\mu) & 0 & 0 \\ 0 & 0 & \alpha_1^* S_\circ - (\varepsilon + \tau + \mu) & \alpha_2 S_\circ \\ 0 & 0 & \varepsilon & -\delta \end{pmatrix} \tag{33}$$

The associated right eigenvectors of $\mathbf{J}(\mathbf{D}_\circ)|_{\alpha_1=\alpha_1^*}$ that are represented by $\mathbf{w} = (w_1, w_2, w_3, w_4)^T$ can be obtained and,

$$w_1 = \frac{\alpha_1^* \delta S_\circ + \alpha_2 \varepsilon S_\circ + \sigma\delta}{\delta(\sigma+\mu)} w_3 > 0, \tag{34}$$

$$w_2 = \frac{\alpha_1^* \delta S_\circ + \alpha_2 \varepsilon S_\circ + \sigma\delta + \delta(\sigma + \alpha_1^* S_\circ) + \alpha_2 \varepsilon \delta S_\circ}{\delta(\theta - \sigma)} w_3 > 0, \tag{35}$$

$$w_3 = w_3 > 0, \tag{36}$$

$$w_4 = \frac{\varepsilon}{\delta} w_3 > 0. \tag{37}$$

Inequality (36) is true if $\theta > \sigma$ or if $\sigma = 0$.
Likewise, the left eigenvectors of the transformed model represented by $v = (v_1, v_2, v_3, v_4)^T$ can be derived

and, $v_1 = v_2 = v_3 = 0$ but $v_3 = v_3 > 0$. Now, the task is to derive the bifurcation coefficients a and b, the procedure of which is described in Theorem 4.1 in [5]. As specified in Theorem 4.1 in [5], the model undergoes backward bifurcation if a and b are both positive. The existence of a backward bifurcation necessitates a simultaneous coexistence of a stable and an unstable non-trivial equilibrium with stable disease eradication equilibrium.

Computation of a: Following the procedure in Theorem 4.1 in [5],

$$\frac{2v_3w_1w_3\partial^2 f_3}{\partial x_1\partial x_3}(0,0) = 2v_3w_1w_3\alpha_1^*,$$
$$\frac{2v_3w_1w_3\partial^2 f_3}{\partial x_1\partial x_4}(0,0) = 2v_3w_1w_4\alpha_2.$$

Hence,

$$\begin{aligned} a &= \sum_{k,i,j=1}^{4} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0) \\ &= 2v_3w_3^3\left[\frac{(\alpha_1^*\delta + \alpha_2\varepsilon)S_\circ + \sigma\delta}{\delta(\sigma+\mu)}\right]\left\{\alpha_1^* + \frac{\varepsilon\alpha_2}{\delta}\right\}. \end{aligned} \tag{38}$$

Computation of b: Following the same theorem as in computing a,

$$\begin{aligned} b &= \sum_{k,i=1}^{3} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \alpha_1^*}(0,0) \\ &= v_3w_3S_\circ > 0 \end{aligned} \tag{39}$$

Since the two bifurcation coefficients a and b are positive, the toxoplasmosis model exhibits a backward bifurcation according to Theorem 4.1 in [5].

The existence of backward bifurcation phenomenon for the toxoplasmosis model implies that a stable toxoplasmosis-free and a stable toxoplasmosis-endemic equilibrium co-exist when the toxoplasmosis reproductive ratio is below unity. The epidemiological implication therefore is that the established condition of having the toxoplasmosis reproductive ratio below unity to eradicate toxoplasmosis is no longer enough. The existence of stable toxoplasmosis disease eradication when $R_\circ < 1$ in the analysis is not sufficient to eliminate toxoplasmosis from the cat population.

4 Conclusions

In this study, a nonlinear epidemic model is developed to assess the possibility of the existence of a backward bifurcation in mathematical models of *T. gondii*. The model is shown to possess the basic properties of a robust epidemiological model. Equilibrium analysis is conducted and the disease eradication equilibrium is derived. The reproductive ratio of the model is also derived and the stability analysis of the disease eradication equilibrium is performed. The model is transformed by changing the value of a parameter to assess the effect on the qualitative structure of the model and the possibility of the existence of a backward bifurcation phenomenon. The transformed model is analyzed and the analysis establishes the existence of a backward bifurcation for the toxoplasmosis model which allow a stable toxoplasmosis endemic equilibrium to co-exist with a stable toxoplasmosis-free equilibrium when the toxoplasmosis reproductive ratio is less than unity. The existence of a backward bifurcation for toxoplasmosis dynamics implies that toxoplasmosis may remain in the cat population regardless of the implementation of necessary measures against the spread of *T. gondii*.

The present analysis has offered a theoretical background for controlling toxoplasmosis. Since toxoplasmosis does not confer permanent immunity upon recovery which means that $\sigma > 0$ for all $t \geq 0$ and given the existence of a backward bifurcation for toxoplasmosis dynamics, attempts should be made toward supervising recovered cats from interacting with the infected cats or contaminated environment. Every policy that is capable of eliminating *T. gondii* from the environment and cat population must be formulated and

implemented with all seriousness if toxoplasmosis is to be eradicated from the cat population. Furthermore, another critical factor to toxoplasmosis eradication in cat populations given the existence of a backward bifurcation is vaccination coverage ϕ. Since toxoplasmosis susceptibility in cat populations can be prevented by adequate vaccinations as indicated in the transmission diagram in Figure 1, every measure must be put in place to ensure that vaccination coverage attains the highest possible level in such a way that $\phi \to 1$. It is clearly indicated in Figure 1 that backward bifurcation in toxoplasmosis dynamics is a function of reinfection and vaccination coverage.

It should be noted that cats can spread toxoplasmosis into human and livestock populations. It is therefore necessary that efforts are intensified to eradicate toxoplasmosis from cat populations because *T. gondii* infection may be inimical to human well-being and livestock production. The infection may result in fever, fatigue, myocarditis, lymphocytosis, abortion, meningioencephalitis, etc. in man and animals [21]. Due to data unavailability, it is impossible to conduct numerical simulations. However, it is hoped that the analysis has revealed vital information that the traditional requirement of reducing $R_\circ$ below unity to eradicate infectious diseases in Mathematical Epidemiology is not sufficient to eradicate toxoplasmosis.

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