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Causes of backward bifurcations in some epidemiological models

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ABSTRACT

The phenomenon of backward bifurcation in disease transmission models, where a stable endemic equilibrium co-exists with a stable disease-free equilibrium when the associated reproduction number is less than unity, has been observed in a number of disease transmission models. The epidemiological consequence of backward bifurcation is that the classical requirement of the reproduction number being less than unity becomes only a necessary, but not sufficient, for disease elimination (hence, the presence of this phenomenon in the transmission dynamics of a disease makes its effective control in the community difficult). This paper addresses the problem of finding the causes of backward bifurcation in some standard deterministic models for the spread of some emerging and re-emerging diseases (it contains a brief review of some common causes, as well as some new causes, of backward bifurcation in some standard disease transmission models). It is 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.

1. Introduction

The dynamics of compartmental models for disease transmission is often characterized by the *basic reproduction number*, denoted by $\mathcal{R}_0$. The threshold quantity ($\mathcal{R}_0$) measures the average number of new cases generated by a typical infected individual introduced into a completely susceptible population [1–3]. Typically, when $\mathcal{R}_0$ is less than unity, a small influx of infected individuals will not generate large outbreaks, and the disease dies out in time (in this case, the corresponding disease-free equilibrium (DFE) is asymptotically-stable). On the other hand, the disease will persist if $\mathcal{R}_0$ exceeds unity, where a stable endemic equilibrium exists. This phenomenon, where the disease-free equilibrium loses its stability and a stable endemic equilibrium appears as $\mathcal{R}_0$ increases through one, is known as *forward bifurcation* [4–8]. Some of the main characteristics of forward bifurcation are [6]:

(i) the absence of positive (endemic) equilibria near the DFE when $\mathcal{R}_0 < 1$ (in this setting, the DFE is often the only equilibrium when $\mathcal{R}_0 < 1$);
(ii) a low level of endemicity when $\mathcal{R}_0$ is slightly above unity.

The forward bifurcation phenomenon, first noted by Kermack and McKendrick [7], has been observed in numerous disease transmission models [6,3]. For models that exhibit forward bifurcation, the requirement $\mathcal{R}_0 < 1$ is necessary and sufficient for disease elimination. A schematic diagram of forward bifurcation is given in Fig. 1.

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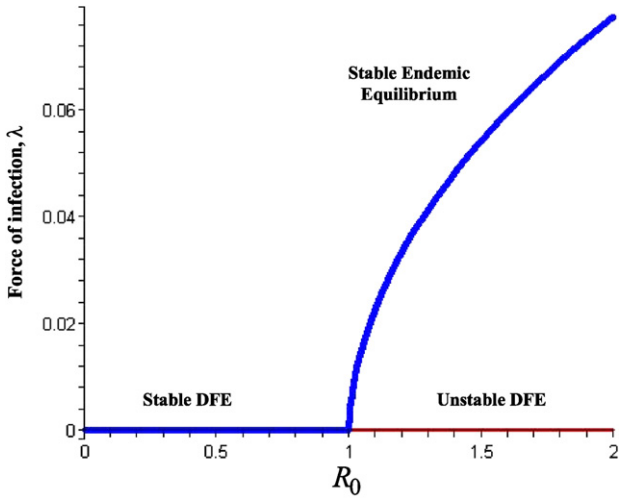

Fig. 1. Forward bifurcation.

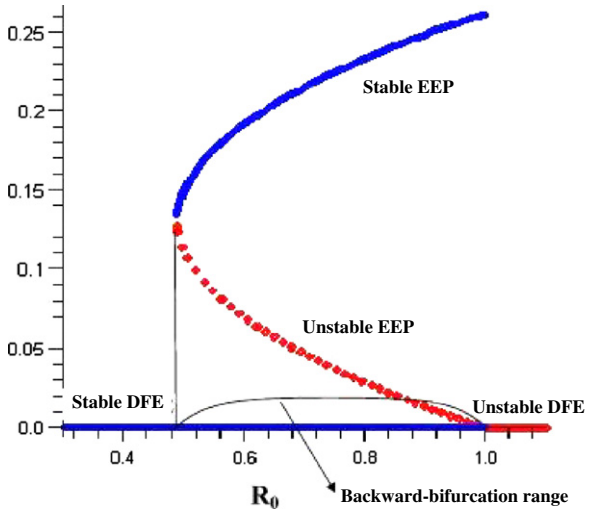

Fig. 2. Backward bifurcation.

Other models for disease transmission undergo another type of bifurcation, known as *backward bifurcation*, where a stable endemic equilibrium co-exists with a stable DFE when $\mathcal{R}_0 < 1$. The epidemiological implication of backward bifurcation is that the requirement $\mathcal{R}_0 < 1$, while necessary, is not sufficient for effective disease control. In a backward bifurcation setting, once $\mathcal{R}_0$ crosses unity, the disease can invade to a relatively high endemic level. In this case, decreasing $\mathcal{R}_0$ to its former level will not necessarily make the disease disappear [6]. A schematic diagram of backward bifurcation is depicted in Fig. 2. The common causes of backward bifurcation in disease transmission models are the use of an imperfect vaccine (see, for instance, [9–12,8]) and exogenous re-infection in the transmission dynamics of *mycobacterium tuberculosis* (TB) [13–17]. Backward bifurcation has also been observed in other models for disease dynamics, such as those for behavioral responses to perceived risks [18], multi-groups [4,5], treatment [19], resistance mechanisms and structured acquired immunity [20,21] and in-host dynamics of HTLV-I [22], public health education campaigns against the spread of HIV/AIDS [23,24].

The aim of this study is two-fold. The first is to provide a short review of some of the common mechanisms (biological, epidemiological, social etc.) that cause the phenomenon of backward bifurcation in disease transmission models. The second is to determine some new mechanisms that cause this phenomenon. To achieve this aim, a number of standard deterministic models (which use standard incidence and variable population size) for the spread of some emerging and re-emerging diseases will be considered. The paper contains a summary of some established results (based largely on some of our previously published results on models that exhibit backward bifurcation) and some new results.

Table 1
Description of variables and parameters of the TB model (1).

Variable	Description
$S(t)$	Population of susceptible individuals
$L(t)$	Population of newly-infected individuals with latent TB
$T(t)$	Population of infected individuals with active TB
$W_T(t)$	Population of treated individuals
Parameter	**Description**
Π	Recruitment rate into the population
μ	Natural death rate
β	Effective contact rate
α	Progression rate to active TB of individuals with latent TB
ρ	Progression rate to latent TB of treated individuals
η_T	Modification parameter for reduction of infectiousness of treated individuals in comparison to untreated infectious individuals
η_r	Probability of (exogenous) re-infection of latently-infected individuals
f	Fraction of newly-infected individuals with latent TB (slow progressors)
$1-f$	Fraction of newly-infected individuals with active TB (fast progressors)
τ	Treatment rate
δ	Disease-induced death rate

2. Common sources of backward bifurcation

2.1. Exogenous re-infection in TB transmission disease

Consider the following model for the transmission dynamics of TB (see [25])

$$\begin{aligned}
\frac{dS}{dt} &= \Pi - \beta\frac{(T+\eta_T W_T)}{N}S - \mu S,\\
\frac{dL}{dt} &= f\beta\frac{(T+\eta_T W_T)}{N}S + \rho W_T - \eta_R\beta\frac{(T+\eta_T W_T)}{N}L - (\alpha+\mu)L,\\
\frac{dT}{dt} &= (1-f)\beta\frac{(T+\eta_T W_T)}{N}S + \eta_R\beta\frac{(T+\eta_T W_T)}{N}L + \alpha L - (\tau+\mu+\delta)T,\\
\frac{dW_T}{dt} &= \tau T - (\rho+\mu)W_T, \qquad N(t) = S(t)+L(t)+T(t)+W(t),
\end{aligned} \tag{1}$$

where the associated variables and parameters are described in Table 1.

The model (1) has a disease-free equilibrium (DFE) given by

$$\mathcal{E}_{0T} = (S^*, L^*, T^*, W_T^*) = (\Pi/\mu, 0, 0, 0).$$

Furthermore, the associated *reproduction number* [26,1,3,27] of the model is given by

$$\mathcal{R}_T = \frac{\beta[\alpha+\mu(1-f)](\rho+\mu+\eta_T\tau)}{\mu(\rho+\alpha+\mu)(\tau+\mu+\delta)+\alpha\rho(\mu+\delta)}. \tag{2}$$

Let β^* be the bifurcation parameter (obtained by setting $\mathcal{R}_T = 1$ and solving for β). Consider the associated invariant region for the model

$$\mathcal{D}_T = \{(S, L, T, W_T) \in \mathbb{R}^4_+ : S + L + T + W_T \leq \Pi/\mu\}.$$

The following result can be established using center manifold theory (in particular, using Theorem 4.1 in [14] given in Appendix A) [6,11,25,27].

Theorem 1. *The model (1) undergoes backward bifurcation at $\mathcal{R}_T = 1$ if*

$$\eta_R > (1-f)\left[1 + \frac{(\alpha+\mu)(\rho+\tau+\mu)}{f\beta^*(\rho+\mu+\tau\eta_T)+\tau\rho}\right].$$

It should be mentioned that the backward bifurcation of the model (1) persists even when the disease-induced mortality rate (δ) is set to zero (the consequence of setting $\delta = 0$ is that the total population becomes $N = \Pi/\mu$, a constant, as $t \to \infty$; and the resulting limiting system, with $N = \Pi/\mu$, has a mass action incidence). In other words, unlike in some other models for disease transmission (see, for instance, the models considered in [8]), substituting standard incidence with mass action incidence does not remove the backward bifurcation property of the model (1).

Table 2
Description of variables and parameters of the vaccination model (3).

Variable	Description
$S(t)$	Population of unvaccinated susceptible individuals
$V(t)$	Population of vaccinated susceptible individuals
$I(t)$	Population of unvaccinated infected individuals
$W(t)$	Population of vaccinated infected individuals (breakthrough infections)
$R(t)$	Population of recovered individuals
Parameter	**Description**
Π	Rate of recruitment into the susceptible population
β	Transmission rate
ϕ	Fraction of newly recruited susceptible individuals vaccinated (cohort vaccination)
$1-\psi$	Degree of protection ($0<\psi\leq 1$) for vaccinated susceptible individuals
ω_v	Waning rate of vaccine
ω_r	Rate of loss of infection-acquired (natural) immunity
σ_u	Recovery rate for unvaccinated infected individuals
μ	Natural death rate

2.1.1. Non-existence of backward bifurcation

It is clear from Theorem 1 that the backward bifurcation phenomenon will not occur if there is no re-infection (i.e., $\eta_R = 0$), since the right-hand side of the inequality in Theorem 1 is non-negative. To further confirm the absence of backward bifurcation in the model (1) when re-infection does not occur (i.e., $\eta_R = 0$), the following global-asymptotic stability result is given for the DFE of the model for the case when $\eta_R = 0$ (the proof, based on using a Lyapunov function, is given in Appendix B).

Theorem 2. *Consider the TB model (1) with $\eta_R = 0$. The DFE, $\mathcal{E}_{0T}$, is globally-asymptotically stable (GAS) in $\mathcal{D}_T$ if $\mathcal{R}_T \leq 1$.*

2.2. Models with imperfect vaccine

Consider the SVIRS vaccination model with waning vaccine-induced (ω_v) and natural (ω_r) immunity [11]:

$$\begin{aligned}
\frac{dS}{dt} &= \Pi(1-\phi) + \omega_v V + \omega_r R - \frac{\beta I}{N}S - \mu S,\\
\frac{dV}{dt} &= \Pi\phi - (1-\psi)\frac{\beta I}{N}V - (\omega_v+\mu)V,\\
\frac{dI}{dt} &= \frac{\beta I}{N}S + (1-\psi)\frac{\beta I}{N}V - (\sigma_u+\mu)I,\\
\frac{dR}{dt} &= \sigma_u I - (\omega_r+\mu)R,
\end{aligned} \tag{3}$$

where the associated variables and parameters are tabulated in Table 2.

Define:

$$\mathcal{R}_v = \mathcal{R}_0\left(1-\frac{\mu\phi\psi}{\omega_v+\mu}\right), \quad \text{with } \mathcal{R}_0 = \frac{\beta}{\sigma_u+\mu}.$$

Following [11], the vaccine failure duration (V_F) and a critical vaccine failure duration (V_F^C) are defined, respectively, by

$$V_F = \frac{1-\psi}{\mu+\omega_v}, \qquad V_F^C = \frac{\mu+\sigma_u+\omega_r}{(\mu+\omega_r)(\mu+\sigma_u)(\mathcal{R}_0-1)}.$$

The following results were established in [11].

Theorem 3. *The vaccination model (3) exhibits backward bifurcation at $\mathcal{R}_v = 1$ whenever*

$$\frac{\sigma_u\omega_r}{(\mu+\sigma_u)(\mu+\omega_r)} > \mathcal{R}_0\left\{1-\frac{\mu\phi\psi}{(\mu+\omega_v)}\left[1+\frac{\mu(1-\psi)}{(\mu+\omega_v)}\right]\right\}.$$

Theorem 4. *The vaccination model (3) does not undergo backward bifurcation at $\mathcal{R}_v = 1$ if any of the following conditions hold:*

(i) *The vaccine offers perfect protection against break-through infection (i.e., $\psi = 1$)*
(ii) *Vaccine-derived immunity wanes faster than natural immunity (i.e., $\omega_v \geq \omega_r$)*
(iii) *Vaccine failure duration does not exceed a certain critical value (i.e., $V_F \leq V_F^C$).*

Table 3
Description of variables and parameters of the dengue model (4).

Variable	Parameter
$S_H(t)$	Population of susceptible humans
$E_H(t)$	Population of exposed humans
$I_H(t)$	Population of infectious humans
$R_H(t)$	Population of recovered humans
Parameter	**Interpretation**
Π_H	Recruitment rate of humans
Π_V	Recruitment rate of mosquitoes
C_{VH}	Infection rate of humans
C_{HV}	Infection rate of mosquitoes
$\frac{1}{\mu_H}$	Average lifespan of humans
$\frac{1}{\mu_V}$	Average lifespan of mosquitoes
σ_H	Progression rate from E_H to I_H class
σ_V	Progression rate from E_V to I_V class
δ_H	Disease-induced death rate for humans
δ_V	Disease-induced death rate for mosquitoes
τ_H	Recovery rate for humans
η_H, η_V	Modification parameters

The imperfect nature of the vaccine is a well-known reason for the presence of backward bifurcation in vaccination models (Case (i) of Theorem 4 shows that if this imperfection is removed, then the phenomenon of backward bifurcation will not occur). Cases (ii) and (iii) of Theorem 4 are new additional sources of eliminating backward bifurcation in SIRS models that incorporate an imperfect vaccine. It follows from Case (iii) that the backward bifurcation will disappear if infection offers permanent immunity against e-infection ($\omega_r = 0$).

In summary, the SVIRS model (3) will not undergo backward bifurcation if any of the scenarios in Theorem 4 hold.

3. Other sources of backward bifurcation

In this section, other "un-common" sources of backward bifurcation will be discussed.

3.1. Models for vector-borne diseases

3.1.1. Dengue fever

Dengue is a mosquito-transmitted disease caused by any of four closely-related virus serotypes (DEN-1-4) of the genus *Flavivirus*. Dengue, which ranks second to malaria among deadly mosquito-borne diseases (claiming over 100 million infections and 20,000 deaths globally each year), is endemic in at least 100 countries in Africa, the Americas, the Eastern Mediterranean and subtropical regions of the world, inhibited by over 2.5 billion people [29]. Dengue is transmitted to humans through mosquito bites. Female mosquitoes (of the genus *Aedes (Stegomyia)*) acquire the infection by taking a blood meal from an infected human (in the viremic phase of illness). These infected mosquitoes pass the disease to susceptible humans.

Consider the following model for the transmission dynamics of dengue fever [29] (the associated variables and parameters are described in Table 3)

$$\begin{aligned}
\frac{dS_H}{dt} &= \Pi_H - \frac{C_{HV}}{N_H}(\eta_V E_V + I_V)S_H - \mu_H S_H,\\
\frac{dE_H}{dt} &= \frac{C_{HV}}{N_H}(\eta_V E_V + I_V)S_H - (\sigma_H + \mu_H)E_H,\\
\frac{dI_H}{dt} &= \sigma_H E_H - (\tau_H + \mu_H + \delta_H)I_H,\\
\frac{dR_H}{dt} &= \tau_H I_H - \mu_H R_H,\\
\frac{dS_V}{dt} &= \Pi_V - \frac{C_{HV}}{N_H}(\eta_H E_H + I_H)S_V - \mu_V S_V,\\
\frac{dE_V}{dt} &= \frac{C_{HV}}{N_H}(\eta_H E_H + I_H)S_V - (\sigma_V + \mu_V)E_V,\\
\frac{dI_V}{dt} &= \sigma_V E_V - (\mu_V + \delta_V)I_V.
\end{aligned} \tag{4}$$

It should be mentioned that, in the formulation of the model (4), the conservation law of bites (i.e., the total number of bites made by mosquitoes equals the total number of bites received by the human hosts) has been applied. The consequence of the application of such law is that the infection rate for both humans and mosquitoes is normalized by the total human population, $N_H(t)$ (see [29] for more details). The following result holds for the model (4).

Lemma 1. *The closed set*

$$\Gamma = \left\{(S_H, E_H, I_H, R_H, S_V, E_V, I_V) \in \mathbb{R}^7_+ : S_H + E_H + I_H + R_H \leq \frac{\Pi_H}{\mu_H}; S_V + E_V + I_V \leq \frac{\Pi_V}{\mu_V}\right\}$$

is invariant for the dengue model (4).

It is convenient to define:

$$\mathcal{R}_d = \sqrt{\frac{C_{HV}^2 \Pi_V \mu_H (\eta_H Q_2 + \sigma_H)(\eta_V Q_4 + \sigma_V)}{\Pi_H \mu_V Q_1 Q_2 Q_3 Q_4}},$$

where $Q_1 = \sigma_H + \mu_H$, $Q_2 = \tau_H + \mu_H + \delta_H$, $Q_3 = \sigma_V + \mu_V$ and $Q_4 = \mu_V + \delta_V$.

Garba et al. [29] proved the following result (the result in [29] was probably the first time backward bifurcation has been established in the transmission dynamics of a vector-borne disease).

Theorem 5. *The dengue model (4) undergoes backward bifurcation at $\mathcal{R}_d = 1$ under certain conditions.*

Consider next the model (4) in the absence of dengue-induced mortality in humans (i.e., $\delta_H = 0$). With $\delta_H = 0$, the total human population becomes asymptotically constant (i.e., $N_H(t) \to \Pi_H/\mu_H$ as $t \to \infty$) and the standard incidence model (4) reduces to a mass action model. Furthermore, consider the following invariant region for the dengue model (4):

$$\Gamma_m = \{(S_H, E_H, I_H, R_H, S_V, E_V, I_V) \in \Gamma : S_H \leq S_H^*, S_V \leq S_V^*\}.$$

Define (where, now, $Q_2 = \tau_H + \mu_H$):

$$\mathcal{R}_{dm} = \mathcal{R}_d|_{\delta_H = 0} = \sqrt{\frac{C_{HV}^2 \Pi_H \Pi_V (\eta_H Q_2 + \sigma_H)(\eta_V Q_4 + \sigma_V)}{\mu_H \mu_V Q_1 Q_2 Q_3 Q_4}}.$$

The following result was proven in [29] (see also Appendix C for details):

Theorem 6. *The DFE of the dengue model (4) with $\delta_H = 0$ is GAS in Γ_m if $\mathcal{R}_{dm} \leq 1$.*

Thus, the analyses in this section show that the backward bifurcation property of the dengue transmission model (4) is caused by the dengue-induced mortality in humans ($\delta_H > 0$). The backward bifurcation is removed if the dengue-induced mortality is set to zero.

Niger and Gumel [30] also established the presence of backward bifurcation in the transmission dynamics of malaria (using a repeated exposure model), another vector-borne disease, and showed that the phenomenon can be removed if the disease-induced mortality in humans is zero.

3.1.2. West Nile virus

West Nile virus (WNV) is an arbovirus and a single-stranded RNA virus of the genus *Flavivirus* and the family *Flaviviridae* first isolated in the West Nile district of Uganda in 1937. WNV is spread among humans and domestic animals (mainly horses) by female mosquitoes that have fed from the blood of infected birds (in particular, by the principal vector *Culex* [31]) with birds (primarily, crows and songbirds) as intermediate hosts. The virus has spread in Africa, Europe, the Middle East, west and central Asia, Oceania and North America [31]. WNV is different from other mosquito-borne diseases, since it involves a cross-infection between birds and mosquitoes (i.e., it involves the mosquito–bird–mosquito transmission cycle).

Consider the following model [31] for the transmission dynamics of WNV within the mosquito, bird and human populations (the variables and parameters of the model are described in Table 4)

$$\begin{aligned}
\frac{dM_s}{dt} &= \lambda_M - \frac{b_1 \beta_1 M_s B_i}{N_B} - \mu_M M_s,\\
\frac{dM_i}{dt} &= \frac{b_1 \beta_1 M_s B_i}{N_B} - \mu_M M_i,\\
\frac{dB_s}{dt} &= \lambda_B - \frac{b_1 \beta_2 M_i B_s}{N_B} - \delta_B B_s - \mu_B B_s,\\
\frac{dB_i}{dt} &= \frac{b_1 \beta_2 M_i B_s}{N_B} - d_B B_i - \delta_B B_i - \mu_B B_i,
\end{aligned}$$

Table 4
Description of variables and parameters of the WNV model (5).

Variable	Description
M_s	Population of susceptible mosquitoes
M_i	Population of infected mosquitoes
B_s	Population of susceptible birds
B_i	Population of infected birds
S	Population of susceptible humans
E	Population of exposed humans
I	Population of infectious humans
H	Population of hospitalized humans
R	Population of recovered humans
Parameter	**Description**
λ_B	Recruitment rate of susceptible birds
λ_H	Recruitment rate of susceptible humans
λ_M	Recruitment rate of uninfected mosquitoes
$1/\mu_B$	Average lifespan of birds
$1/\mu_H$	Average lifespan of humans
$1/\mu_M$	Average lifespan of mosquitoes
b	Average biting rate of mosquitoes
$b_1\beta_1$	Transmission rate from birds to mosquitoes
$b_1\beta_2$	Transmission rate from mosquitoes to birds
$b_2\beta_3$	Transmission rate from mosquitoes to humans
d_B	WNV-induced death rate of birds
d_H	WNV-induced death rate for humans
δ_B	Migration rate of birds
$1/\alpha$	Incubation period in humans
δ	Hospitalization rate of humans
r	Recovery rate of infectious humans
τ	Recovery rate of hospitalized humans

$$\begin{aligned}
\frac{dS}{dt} &= \lambda_H - \frac{b_2\beta_3 M_i S}{N_H} - \mu_H S, \\
\frac{dE}{dt} &= \frac{b_2\beta_3 M_i S}{N_H} - \alpha E - \mu_H E, \\
\frac{dI}{dt} &= \alpha E - \delta I - d_I I - rI - \mu_H I, \\
\frac{dH}{dt} &= \delta I - d_H H - \tau H - \mu_H H, \\
\frac{dR}{dt} &= \tau H + rI - \mu_H R.
\end{aligned} \tag{5}$$

The total mosquito (N_M), bird (N_B) and human (N_H) populations are given, respectively, by $N_M(t) = M_s(t) + M_i(t)$, $N_B(t) = B_s(t) + B_i(t)$ and $N_H(t) = S(t) + E(t) + I(t) + H(t) + R(t)$. The biting rates ($b_1$ and b_2) are defined as (density-dependent rates)

$$b_1 = \frac{bN_B}{N_B + N_H} \quad \text{and} \quad b_2 = \frac{bN_H}{N_B + N_H}.$$

The DFE of the model (5) is given by:

$$\mathcal{E}_0 = (M_s^*, M_i^*, B_s^*, B_i^*, S^*, E^*, I^*, H^*, R^*) = (\lambda_M/\mu_M, 0, \lambda_B/(\mu_B + \delta_B), 0, \lambda_H/\mu_H, 0, 0, 0, 0).$$

Define:

$$\mathcal{R}_w = \frac{b\sqrt{\mu_M k_2 \beta_1 \beta_2 M_s^* B_S^*}}{\mu_M k_2 (B_S^* + S^*)}, \tag{6}$$

where, $k_1 = \mu_B + \delta_B$, $k_2 = \mu_B + \delta_B + d_B$, $k_3 = \mu_H + \alpha$, $k_4 = \delta + d_I + r + \mu_H$, $k_5 = \tau + \mu_H + d_H$. Blayneh et al. [31] proved the following result.

Theorem 7. *The WNV model (5) undergoes backward bifurcation at $\mathcal{R}_w = 1$ under certain conditions.*

Furthermore, it can be shown that the backward bifurcation property of the model disappears if the host mortality rates are set to zero (i.e., $\delta_B = \delta_H = 0$). Jiang et al. [32] also established the presence of backward bifurcation in models for WNV that consider the mosquito–bird–mosquito transmission cycle only.

Table 5
Description of variables and parameters of the risk-structured model (7).

Variable	Description
$S_l(t)$	Population of low-risk susceptible individuals
$S_h(t)$	Population of high-risk susceptible individuals
$E(t)$	Population of exposed (latent) individuals
$I(t)$	Population of infectious individuals
Parameter	**Description**
Π	Recruitment rate into the population (assumed susceptible)
f	Fraction of recruited susceptible individuals who are high-risk
μ	Natural death rate
β	Effective contact rate
ψ_h	Transition rate from high-risk to low-risk susceptible class
ψ_l	Transition rate from low-risk to high-risk susceptible class
θ_h	Modification parameter for assumed increased susceptibility of high-risk individuals
γ	Recovery rate
δ	Disease-induced death rate

In summary, the analyses in this section show that backward bifurcation arises in the transmission dynamics of vector-borne diseases (notably dengue fever, malaria and WNV), and that such dynamic phenomenon can be removed if the host(s) mortality rate(s) is set to zero.

3.2. Backward bifurcation in a risk-structured model

Consider the following risk-structured disease transmission model (where the susceptible individuals are stratified according to their risk of acquiring infection):

$$\begin{aligned}
\frac{dS_l}{dt} &= (1-f)\Pi + \psi_h S_h - \beta\frac{I}{N}S_l - \psi_l S_l - \mu S_l,\\
\frac{dS_h}{dt} &= f\Pi + \psi_l S_l - \theta_h\beta\frac{I}{N}S_h - \psi_h S_h - \mu S_h,\\
\frac{dE}{dt} &= \beta\left[S_l + \theta_h S_h\right]\frac{I}{N} - (\sigma+\mu)E,\\
\frac{dI}{dt} &= \sigma E - (\gamma+\mu+\delta)I,
\end{aligned} \tag{7}$$

where the variables and parameters are described in Table 5.

The DFE of the risk-structured model (7) is given by

$$\mathcal{E}_{0r}:\ (S_l^*, S_h^*, E^*, I^*) = \left(\frac{(1-f)\Pi + \psi_h S_h^*}{\mu+\psi_l},\ \frac{\Pi\left[f(\psi_l+\mu)+\psi_l(1-f)\right]}{\mu(\mu+\psi_l+\psi_h)}, 0, 0\right),$$

and the associated reproduction number is given by (where $N^* = \Pi/\mu$)

$$\mathcal{R}_r = \frac{\beta\sigma(S_l^* + \theta_h S_h^*)}{N^*(\sigma+\mu)(\mu+\gamma+\delta)}.$$

It is convenient to define the following inequality (obtained from the application of center manifold theorem on the system (7)):

$$\left[(w_1+w_3+w_4)S_h^* - w_2 S_l^*\right]\theta_h < w_1 S_h^* - (w_2+w_3+w_4)S_l^*, \tag{8}$$

where,

$$w_1 = \frac{w_2\psi_h(S_l^*+S_h^*) - \beta w_4 S_l^*}{(\psi_l+\mu)(S_l^*+S_h^*)}, \qquad w_2 = \frac{w_1\psi_l(S_l^*+S_h^*) - \beta\theta_h w_4 S_h^*}{(\psi_h+\mu)(S_l^*+S_h^*)},$$
$$w_3 = w_3 > 0, \qquad w_4 = \frac{\sigma w_3}{\gamma+\mu+\delta}.$$

Theorem 8. *The risk-structured model (7) undergoes backward bifurcation at $\mathcal{R}_r = 1$ whenever inequality (8) holds.*

It is worth noting that the inequality (8) will never hold if the high-risk susceptible individuals are equally likely to acquire infection than low-risk susceptible individuals (i.e., $\theta_h = 1$). Thus, the backward bifurcation property of the model (7) is caused by the variability (heterogeneity) in susceptibility between the two susceptible risk groups. To further confirm the above, global asymptotic stability of the DFE of the model (7) is given below for the special case with $\theta_h = 1$ (the proof is given in Appendix D).

Theorem 9. *The DFE of the risk-structured model (7) with $\theta_h = 1$ is GAS whenever $\mathcal{R}_r \leq 1$.*

In summary, the analyses in this section show that stratifying the susceptible population based on the risk (low or high) of acquiring infection could induce the phenomenon of backward bifurcation (see also [28] for similar result associated with the transmission dynamics of chlamydia *trachomatis*).

4. Conclusions

This paper identifies some epidemiological mechanisms that can induce the phenomenon of backward bifurcation in standard Kermack–McKendrick type disease transmission models (that use standard incidence rate for the infection rate). It is shown that backward bifurcation, which has significant consequences on the persistence or elimination of the disease when the associated reproduction number of the model is less than unity, could arise due to mechanisms such as:

(1) Exogenous re-infection (of latently-infected individuals) in models for the spread of mycobacterium tuberculosis. Re-infection, in general, causes backward bifurcation (see, for instance, [33,28] for the role of re-infection in the backward bifurcation phenomenon observed in Chlamydia transmission dynamics);
(2) Vaccination. The main sources of backward bifurcation in vaccination models are (see also [11]):
  (i) Imperfect vaccine efficacy against infection (i.e., vaccine does not offer 100% protection against infection in vaccinated individuals);
  (ii) Vaccine-derived immunity wanes at a slower rate than natural immunity;
  (iii) Vaccine failure duration exceeds a certain critical value;
(3) Host(s) disease-induced mortality in models for the spread of vector-borne diseases (such as those associated with the transmission dynamics of dengue fever, malaria and West Nile virus);
(4) Differential susceptibility in risk-structured disease transmission models.

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Appendix A. Backward bifurcation

Theorem 10 (*Castillo-Chavez and Song [14]*)**.** *Consider the following general system of ordinary differential equations with a parameter ϕ*

$$\frac{dx}{dt} = f(x, \phi), \qquad f : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R} \quad \text{and} \quad f \in \mathbb{C}^2(\mathbb{R}^n \times \mathbb{R}), \tag{9}$$

where 0 is an equilibrium point of the system (that is, $f(0, \phi) \equiv 0$ for all ϕ) and assume

A1: $A = D_x f(0, 0) = \left(\frac{\partial f_i}{\partial x_j}(0, 0)\right)$ *is the linearization matrix of the system (9) around the equilibrium 0 with ϕ evaluated at 0. Zero is a simple eigenvalue of A and other eigenvalues of A have negative real parts;*
A2: *Matrix A has a right eigenvector w and a left eigenvector v (each corresponding to the zero eigenvalue).*

Let f_k be the kth component of f and

$$a = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0, 0),$$

$$b = \sum_{k,i=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \phi}(0, 0).$$

The local dynamics of the system around 0 is totally determined by the signs of a and b.

i. *$a > 0$, $b > 0$. When $\phi < 0$ with $|\phi| \ll 1$, 0 is locally asymptotically stable and there exists a positive unstable equilibrium; when $0 < \phi \ll 1$, 0 is unstable and there exists a negative, locally asymptotically stable equilibrium;*
ii. *$a < 0$, $b < 0$. When $\phi < 0$ with $|\phi| \ll 1$, 0 is unstable; when $0 < \phi \ll 1$, 0 is locally asymptotically stable equilibrium, and there exists a positive unstable equilibrium;*
iii. *$a > 0$, $b < 0$. When $\phi < 0$ with $|\phi| \ll 1$, 0 is unstable, and there exists a locally asymptotically stable negative equilibrium; when $0 < \phi \ll 1$, 0 is stable, and a positive unstable equilibrium appears;*
iv. *$a < 0$, $b > 0$. When ϕ changes from negative to positive, 0 changes its stability from stable to unstable. Correspondingly a negative unstable equilibrium becomes positive and locally asymptotically stable.*

Particularly, if $a > 0$ and $b > 0$, then a backward bifurcation occurs at $\phi = 0$.

Appendix B. Proof of Theorem 2

Proof. Consider the model (1) with $\eta_R = 0$. It is convenient to define $k_1 = \alpha + \mu$, $k_2 = \tau + \mu + \delta$ and $k_3 = \rho + \mu$, so that $\mathcal{R}_T = \frac{\beta(k_3+\eta_T T)[k_1(1-f)+f\alpha]}{k_1k_2k_3-\alpha\rho\tau}$. It is worth mentioning that $k_1k_2k_3 - \alpha\rho\tau = \mu(\rho+\alpha+\mu)(\tau+\mu+\delta) + \alpha\rho(\mu+\delta) > 0$.

Consider the Lyapunov function

$$\mathcal{V} = \alpha(k_3+\eta_T\tau)L + k_1(k_3+\eta_T\tau)T + (\rho\alpha+\eta_T k_1k_2)W_T,$$

with Lyapunov derivative (where a dot represents differentiation with respect to t):

$$\begin{aligned}
\dot{\mathcal{V}} &= \alpha(k_3+\eta_T\tau)\dot{L} + k_1(k_3+\eta_T\tau)\dot{T} + (\rho\alpha+\eta_T k_1k_2)\dot{W}_T,\\
&= \alpha(k_3+\eta_T\tau)\left[\frac{f\beta(T+\eta_T W_T)S}{N} + \rho W_T - k_1L\right]\\
&\quad + k_1(k_3+\eta_T\tau)\left[\frac{\beta(1-f)(T+\eta_T W_T)S}{N} + \alpha L - k_2T\right] + (\rho\alpha+\eta_T k_1k_2)(\tau T - k_3W_T),\\
&\le \alpha(k_3+\eta_T\tau)\left[f\beta(T+\eta_T W_T) + \rho W_T - k_1L\right] + k_1(k_3+\eta_T\tau)\left[\beta(1-f)(T+\eta_T W_T) + \alpha L - k_2T\right]\\
&\quad + (\rho\alpha+\eta_T k_1k_2)(\tau T - k_3W_T) \quad \text{since } S \le N \text{ in } \mathcal{D}_T,\\
&= (k_1k_2k_3 - \alpha\rho\tau)(\eta_T W_T + T)(\mathcal{R}_T - 1).
\end{aligned}$$

Thus, $\dot{\mathcal{V}} \le 0$ if $\mathcal{R}_T \le 1$ with $\dot{\mathcal{V}} = 0$ if and only if $T = W_T 0$. Substituting $T = W_T = 0$ in (1) shows that $L(t) \to 0$ as $t \to \infty$ and $S(t) \to \Pi/\mu$ as $t \to \infty$. Further, the largest compact invariant set in $\{(S, L, T, W_T) \in \mathcal{D}_T : \dot{\mathcal{V}} = 0\}$ is the singleton $\mathcal{E}_{0T}$. It follows from the LaSalle's Invariance Principle that every solution to the equations in (1) with $\eta_R = 0$ and initial conditions in $\mathcal{D}_T$ converge to the DFE $\mathcal{E}_{0T}$ as $t \to \infty$ whenever $\mathcal{R}_T \le 1$. That is, $(S(t), L(t), T(t), W_T(t)) \to (\Pi/\mu, 0, 0, 0)$ as $t \to \infty$. □

Appendix C. Proof of Theorem 6

Proof. The proof, given in [29], is based on using the Lyapunov function:

$$\mathcal{F} = g_1E_H + g_2I_H + g_3E_V + g_4I_V,$$

where,

$$\begin{aligned}
g_1 &= \Pi_V\mu_H Q_4C_{HV}(\eta_V Q_4+\sigma_V)(\eta_H Q_2+\sigma_H),\\
g_2 &= \Pi_V\mu_H Q_1Q_4C_{HV}(\eta_V Q_4+\sigma_V),\\
g_3 &= \mu_V\mu_H Q_1Q_2Q_4\mathcal{R}_{dm}(\eta_V Q_4+\sigma_V),\\
g_4 &= \mu_V\mu_H Q_1Q_2Q_3Q_4\mathcal{R}_{dm}.
\end{aligned}$$

The Lyapunov derivative is given by

$$\begin{aligned}
\dot{\mathcal{F}} &= g_1\dot{E}_H + g_2\dot{I}_H + g_3\dot{E}_V + g_4\dot{I}_V,\\
&= \Pi_V\mu_H Q_4C_{HV}(\eta_H Q_2+\sigma_H)(\eta_V Q_4+\sigma_V)[C_{HV}(\eta_V E_V + I_V)S_H - Q_1E_H]\\
&\quad + \Pi_V\mu_H Q_1Q_4C_{HV}(\eta_V Q_4+\sigma_V)(\sigma_H E_H - Q_2I_H)\\
&\quad + \mu_V\mu_H Q_1Q_2Q_4\mathcal{R}_{dm}(\eta_V Q_4+\sigma_V)[C_{HV}(\eta_H E_H + I_H)S_V - Q_3E_V]\\
&\quad + \mu_V\mu_H Q_1Q_2Q_3Q_4\mathcal{R}_{dm}(\sigma_V E_V - Q_4I_V),\\
&= \mu_H Q_1Q_4C_{HV}(\eta_V Q_4+\sigma_V)[-\Pi_V(\eta_H Q_2+\sigma_H) + \Pi_V\sigma_H + \mu_V Q_2\eta_H\mathcal{R}_{dm}S_V]E_H\\
&\quad - \mu_H Q_1Q_2Q_4C_{HV}(\eta_V Q_4+\sigma_V)[\Pi_V - \mu_V\mathcal{R}_{dm}S_V]I_H\\
&\quad + \mu_H\left\{\Pi_V C_{HV}^2\eta_V Q_4(\eta_H Q_2+\sigma_H)(\eta_V Q_4+\sigma_V)S_H + \mu_V Q_1Q_2Q_3Q_4\mathcal{R}_{dm}[\sigma_V - (\eta_V Q_4+\sigma_V)]\right\}E_V\\
&\quad + \mu_H Q_4[\Pi_V C_{HV}^2(\eta_H Q_2+\sigma_H)(\eta_V Q_4+\sigma_V)S_H - \mu_V Q_1Q_2Q_3Q_4\mathcal{R}_{dm}]I_V,\\
&\le \Pi_V\mu_H\eta_H Q_1Q_2Q_4C_{HV}(\eta_V Q_4+\sigma_V)(\mathcal{R}_{dm}-1)E_H + \mu_H\Pi_V Q_1Q_2Q_4C_{HV}(\eta_V Q_4+\sigma_V)(\mathcal{R}_{dm}-1)I_H\\
&\quad + \mu_H\left[\mu_V Q_1Q_2Q_3\eta_V Q_4^2(\mathcal{R}_{dm})^2 - \mu_V Q_1Q_2Q_3\eta_V Q_4^2\mathcal{R}_{dm}\right]E_V\\
&\quad + \mu_H Q_4[\mu_V Q_1Q_2Q_3Q_4(\mathcal{R}_{dm})^2 - \mu_V Q_1Q_2Q_3Q_4\mathcal{R}_{dm}]I_V, \quad \text{since } S_H \le S_H^* \text{ and } S_V \le S_V^*,\\
&= \eta_H\Pi_V\mu_H C_{HV}Q_1Q_2Q_4(\eta_V Q_4+\sigma_V)(\mathcal{R}_{dm}-1)E_H + \Pi_V\mu_H C_{HV}Q_1Q_2Q_4(\eta_V Q_4+\sigma_V)(\mathcal{R}_{dm}-1)I_H\\
&\quad + \eta_V\mu_V\mu_H Q_1Q_2Q_3Q_4^2\mathcal{R}_{dm}(\mathcal{R}_{dm}-1)E_V + \mu_V\mu_H Q_1Q_2Q_3Q_4^2\mathcal{R}_{dm}(\mathcal{R}_{dm}-1)I_V,\\
&= \mu_H Q_1Q_2Q_4\left[\Pi_V C_{HV}(\eta_V Q_4+\sigma_V)(\eta_H E_H + I_H) + \mu_V Q_3Q_4\mathcal{R}_{dm}(\eta_V E_V + I_V)\right](\mathcal{R}_{dm}-1).
\end{aligned}$$

Thus, $\dot{\mathcal{F}} \leq 0$ if $\mathcal{R}_{dm} \leq 1$ with $\dot{\mathcal{F}} = 0$ if and only if $E_H = I_H = E_V = I_V = 0$. Further, the largest compact invariant set in

$$\{(S_V, E_H, I_H, R_H, S_V, E_V, I_V) \in \Gamma_m : \dot{\mathcal{F}} = 0\}$$

is the disease-free equilibrium for the model (4). The proof is completed as in the proof in Appendix B. □

Appendix D. Proof of Theorem 9

Proof. Consider the model (7) with $\theta_h = 1$. It follows that $S_l^* + S_h^* = N^* = \Pi/\mu$. Further, consider the Lyapunov function

$$\mathcal{F} = \frac{\sigma}{\sigma + \mu} E + I,$$

with Lyapunov derivative:

$$\begin{aligned}
\dot{\mathcal{F}} &= \frac{\sigma}{\sigma + \mu}\left[\beta(S_l + S_h)\frac{I}{N} - (\sigma + \mu)E\right] + \sigma E - (\gamma + \mu + \delta)I, \\
&\leq \frac{\beta\sigma}{\sigma + \mu} I - \sigma E + \sigma E - (\gamma + \mu + \delta)I, \quad \text{since } S_l + S_h \leq N \\
&= \left[\frac{\beta\sigma}{(\sigma + \mu)(\gamma + \mu + \delta)} - 1\right] I, \\
&= (\mathcal{R}_r - 1)I \leq 0 \quad \text{for } \mathcal{R}_r \leq 1.
\end{aligned}$$

The proof is completed as in the proof in Appendix B. □

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