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Dynamics of host-reservoir transmission of Ebola with spillover potential to humans

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Abstract. Ebola virus disease (EVD) is a zoonotic disease (i.e. disease that is spread from animals to people). Therefore human beings can be infected through direct contact with an infected animal (fruit-eating bat or great ape). It has been demonstrated that fruit-eating bats of pteropodidae family are potential reservoir of EVD. Moreover, it has been biologically shown that fruit-eating bats do not die due to EVD and bear the Ebola viruses lifelong. We develop in this paper, a mathematical model to assess the impact of the reservoir on the dynamics of EVD. Our model couples a bat-to-bat model with a human-to-human model and the indirect environmental contamination through a spillover process (i.e. process by which a zoonotic pathogen moves (regardless of transmission mode) from an animal host (or environmental reservoir) to a human host) from bats to humans. The sub-models and the coupled models exhibit each a threshold behavior with the corresponding basic reproduction numbers being the bifurcation parameters. Existence of equilibria, their global stability are established by combining monotone operator theory, Lyapunov–LaSalle techniques and graph theory. Control strategies are assessed by using the target reproduction numbers. The efforts required to control EVD are assessed as well through S-control. The spillover event is shown to be highly detrimental to EVD by allowing the disease to switch from bats to humans even though the disease was not initially endemic in the human population. Precisely, we show that the spillover phenomenon contributes to speed up the disease outbreak. This suggests that the manipulation and consumption of fruit-bats play an important role in sustaining EVD in a given environment.

Keywords: Ebola, spillover, reservoir, target reproduction number, S-control, global stability.

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1 Introduction

The Ebola Virus Disease (EVD) was initially identified and named so after an outbreak in Democratic Republic of Congo (DRC) in 1976 [1,8,21], which killed 280 individuals out of the 318 cases reported. In the course of the same year, another outbreak occurred in Sudan and killed 156 people [36]. Since 1976, many recommendations have been formulated by various researchers, ranging from the prevention measures to case management guidance. Other fatal outbreaks of EVD still threaten several countries: DRC (1977, 1995), Sudan (1979, 2004), Gabon (1996, 2002), Uganda (2000, 2007, 2011, 2012), Ivory Cost (1994), Congo (2002, 2003, 2005) [36].

The 2014-2015 EVD outbreak which started in Guinea in December 2013 [18] has been the largest and deadliest since its discovery, with approximately 12 000 deaths in the human population, mostly in Guinea, Liberia and Sierra Leone. This last uprising of EVD has stimulated once more the scientific community for more investigations. An illustration of such a commitment is the recent discovery of an experimental vaccine [5,10,12]. Before the development of the so called rVSV-ZEBOV vaccine, numerous supportive treatments contributed to save some patients. In spite of their mitigated outcomes, they played an important role in the control of the disease [18].

The virulence of Ebola and its rapid propagation became a big concern for researchers and triggered vibrant research topics. Besides the huge research activities in order to single out the sustainable prevention strategies, the efforts to identify the reservoir of the Ebola viruses and the means by which the virus is transmitted from the reservoir to humans occupied a prominent place. Since 2006, remarkable biological findings have demonstrated that fruit-eating bats of pteropodidae family are the reservoir of Ebola viruses [3, 8, 10]. Moreover, according to the recent findings in [14], Ebola is introduced in the human population through close contact with blood secretions, organs or other bodily fluids of infected animals such as chimpanzees, gorillas, fruit bats, monkeys, forest antelopes and porcupines found ill or dead in the rainforest. Furthermore, the index case for the 2014-2015 outbreak (and for many other previous outbreaks) caught EVD after contact with an infected bat [32].

These disease features urged the Food and Agricultural Organization (FAO) to draw the attention of the public about the fact that, almost all EVD outbreaks are initially triggered by the consumption of bats and bush meat [14,21]. Therefore, fruit-bats play an important role in the resurgence of this illness in humans. In order to deal with the above mentioned complex ecology of Ebola, more realistic mathematical models for the transmission dynamics of that disease should not underestimate or simply ignore the initial source of the virus. Thus, the incorporation of a reservoir source (bats) in the mathematical modeling of the transmission of EVD is the main motivation and novelty of the model we propose in this manuscript.

By so doing, and unlike existing models [1,4,15,20,24,27,29,31,39,40] where only human-to-human transmissions are considered, or recent works in [9,11,16,30,31,36,42], where the environmental contamination is further incorporated, our model and its analysis are different in the following two aspects: (1) It is a two-host model. (2) The spillover potential of EVD to switch from bat's population to human's population is considered.

Concisely, the purpose of our work is to assess the impact of the reservoir on the transmission dynamics of EVD by coupling a bat-to-bat model with a human-to-human model through the indirect environmental contamination and a spillover event from bats to humans. Note that we could include many other animals (great apes, monkeys, antelopes, etc...) in the EVD transmission mechanism, with some of them either as end hosts or potential reservoirs. However, given the fact that many of these animals die very quickly due to EVD, infected bats

do not suffer from EVD, and the findings in [10] demonstrating that the transmission event from bats to humans is more important than any other spillover event, we have considered only bats.

The full coupled model and the sub-models are shown to exhibit each a threshold behavior with the corresponding basic reproduction numbers being the bifurcation parameters. Existence of equilibria and global results are established by combining monotone operator techniques, Lyapunov–LaSalle techniques and graph theory. Control strategies are assessed via the concept of target reproduction number. The efforts required to control (or eliminate) EVD through the implementation of S-control (i.e. a control measure which target to protect directly the susceptible individuals, e.g. vaccination) are derived. Numerically, it is shown that the spillover event could be highly detrimental to EVD by enabling EVD to switch from bat population to human population even though the disease was not initially endemic in human population.

The paper is organized as follows: in Section 2, a simple epizootic model (describing the disease (periodic) circulation amongst animal populations) for the transmission dynamics of EVD in bat population is formulated and completely analyzed. In Section 3, human-to-human transmission model of EVD is considered. Since this latter model is similar to the one we recently proposed in [9], its main results are recalled. Section 4 presents a simple spillover event (bat-to-human) model for Ebola and its theoretical results are shown in the appendix. Section 5, deals with the control strategies for the coupled model, while Section 6 numerically assess the impact of the environment and the spillover potential in the endemicity of EVD. Finally, Section 7 concludes the paper and outline some future works.

2 A simple epizootic model for Ebola

Not much is known about bat-to-bat transmission modes of EVD. However, due to the fact that they live in colony, it is reasonable to assume that direct bat-to-bat contact is the main route of transmission in their population. Furthermore, as they can share fruit products during dry seasons (when food is rare), we assume an indirect environmental transmission [36].

2.1 Model formulation

Fruit bats are known to be an end-host of EVD and at the same time as the reservoir of Ebola viruses since they do not die due to EVD infection. Thus, there is no recovery for bats during Ebola outbreaks and the model variables can be chosen as follows.

$S_b(t)$ denotes the number of susceptible bats at time t. This class encompasses the bats who are not yet infected at time t, but able to catch the infection when they enter into contact with the bodily fluids of an infected bat.

$I_b(t)$ is the number of infected bats at time t who have contracted the disease and transmit it to susceptibles. It is assumed that infected bats remain infectious lifelong as they are the reservoir of Ebola viruses.

$P(t)$ denotes the concentration of Ebola viruses in the environment at time t. This class is replenished by Ebola viruses shed by infected bats during food sharing or delivery.

Susceptible bats are recruited at a constant rate π_b by births or immigration. They can catch infection by direct contact with an infected bat at rate β_4, or by indirect contact with the viruses shed in the environment (when they eat contaminated fruits or vegetables) at rate λ_b. Since the infected bats can die only naturally, their natural death is supposed to occur at a

Parameter	Epidemiological interpretation
η	Decay rate of viruses in the environment
σ	Deposition/shedding rate of viruses in the environment by infected bats
β_4	Effective contact rate between infected and susceptible bats
λ_b	Indirect contact rate of susceptibles bats with the environment
μ_b	Mortality rate of bats
π_b	Replenishment rate of susceptibles bats

Table 2.1: Parameters and epidemiological interpretation of model (2.1).

constant μ_b. Once infected, bats enter the infected class I_b, remain so lifelong and shed viruses into the environment at rate σ. Since there is no intrinsic growth for the free-living Ebola viruses (and for all free-living viruses in general) in the environment [30], they only deplete (naturally or through environmental decontamination techniques) at a constant rate η. Note that, we do not consider latently infected bats because their latency is still not known and controversial. Based on the above mentioned disease characteristics in the population of bats, we consider bilinear incidence rates for both direct and indirect transmissions. This resulted in the simple epizootic model below:

$$\begin{cases} \dot{S}_b(t) = \pi_b - \beta_4 S_b I_b - \lambda_b P S_b - \mu_b S_b, \\ \dot{I}_b(t) = \beta_4 S_b I_b + \lambda_b P S_b - \mu_b I_b, \\ \dot{P}(t) = \sigma I_b - \eta P. \end{cases} \tag{2.1}$$

The model parameters and their biological meanings are summarized in Table 2.1.

2.2 Theoretical analysis of model (2.1)

The well-posedness of model (2.1) can be seen as a particular case for the more general and coupled model formulated and analyzed in Section 4. The following theorem summarizes the long run dynamics of system (2.1).

Theorem 2.1. *The basic reproduction number of model (2.1) is* $\mathcal{R}_{0b} = \frac{\pi_b(\eta\beta_4+\lambda_b\sigma)}{\eta\mu_b^2}$, *and:*

(i) Whenever $\mathcal{R}_{0b} \leq 1$, *the disease free equilibrium (DFE) is globally asymptotically stable (GAS). It is unstable otherwise.*

(ii) Whenever $\mathcal{R}_{0b} > 1$, *there are exactly two equilibria: the unstable DFE and a unique globally asymptotically stable endemic equilibrium.*

Proof. Simple computations yield

$$\mathcal{R}_{0b} = \frac{\pi_b(\eta\beta_4 + \lambda_b\sigma)}{\eta\mu_b^2}.$$

It is straightforward that when $\mathcal{R}_{0b} \leq 1$ there is a unique equilibrium: the DFE $E_0 = \left(\frac{\pi_b}{\mu_b}, 0, 0\right)$. On the other hand, when $\mathcal{R}_{0b} > 1$, the DFE still exists and a unique endemic equilibrium E_1 occur, with

$$E_1 = \left(\frac{\pi_b}{\mu_b} - \frac{\eta\mu_b(\mathcal{R}_{0b}-1)}{\eta\beta_4 + \lambda_b\sigma}; \frac{\eta\mu_b(\mathcal{R}_{0b}-1)}{\eta\beta_4 + \lambda_b\sigma}; \frac{\sigma\mu_b(\mathcal{R}_{0b}-1)}{\eta\beta_4 + \lambda_b\sigma}\right).$$

Adding the first two equations of model (2.1) and letting $N_b(t)$ be the total population of bats, we obtain

$$\dot{N}_b(t) = \pi_b - \mu_b N_b. \tag{2.2}$$

Since the solutions of (2.2) converge globally to the stable equilibrium $B := \frac{\pi_b}{\mu_b}$, the asymptotic behavior of system (2.1) is the same as that of the limiting system (2.3) [17].

$$\begin{cases} \dot{I}_b(t) = \beta_4(B - I_b)I_b + \lambda_b P(B - I_b) - \mu_b I_b, \\ \dot{P}(t) = \sigma I_b - \eta P. \end{cases} \tag{2.3}$$

System (2.3) has the disease free equilibrium $E_b^0 = (0, 0)$ and whenever $\mathcal{R}_{0b} > 1$, its endemic equilibrium is

$$E_b^1 = \left(\frac{\eta\mu_b(\mathcal{R}_{0b} - 1)}{\eta\beta_4 + \lambda_b\sigma}; \frac{\sigma\mu_b(\mathcal{R}_{0b} - 1)}{\eta\beta_4 + \lambda_b\sigma} \right).$$

Suppose $\mathcal{R}_{0b} \leq 1$ and consider the following Lyapunov function candidate:

$$L_{0b} = I_b + a_3 P,$$

where a_3 is a positive real number to be determined shortly. The Lyapunov derivative of L_{ob} is

$$\begin{aligned} L'_{ob} &= I'_b + a_3 P' \\ &= \beta_4(B - I_b)I_b + \lambda_b P(B - I_b) - \mu_b I_b + a_3\sigma I_b - a_3\eta P \\ &= -\beta_4 I_b^2 - \lambda_b P I_b + I_b(\beta_4 B - \mu_b + a_3\sigma) + P(-a_3\eta + \lambda_b B). \end{aligned}$$

Choose a_3 such that $\beta_4 B - \mu_b + a_3\sigma = 0$ i.e. $a_3 = \frac{-\beta_4\pi_b + \mu_b^2}{\mu_b\sigma} = \frac{\mu_b}{\sigma}\left(1 - \mathcal{R}_{0b} + \frac{\pi_b\lambda_b\sigma}{\eta\mu_b^2}\right)$. Thus,

$$\begin{aligned} L'_{ob} &= -\beta_4 I_b^2 - \lambda_b P I_b + P\left(\frac{\beta_4\eta\pi_b - \eta\mu_b^2}{\mu_b\sigma} + \lambda_b\frac{\pi_b}{\mu_b}\right) \\ &= -\beta_4 I_b^2 - \lambda_b P I_b - P\left[\frac{\eta\mu_b^2[1 - \mathcal{R}_{0b}]}{\mu_b\sigma}\right] \leq 0, \end{aligned}$$

and L_{0b} is indeed a Lyapunov function for E_b^0. This shows that E_b^0 is stable. Moreover, the largest invariance subset contained in the set $\{X \in \mathbb{R}_+^2 / L'_{0b}(X) = 0\}$ is the DFE E_b^0. Therefore, the GAS of E_b^0 follows by LaSalle's Invariance Principle [26], and so is the GAS of E_0 of system (2.1) [17].

It remains to establish the GAS of E_b^1. Suppose $\mathcal{R}_{0b} > 1$ and consider the Volterra type Lyapunov function candidate

$$L_{b1} = I_b - I_b^* \ln I_b + a_1(P - P^* \ln P),$$

where $E_1^* = (I_b^*, P^*)$ is the endemic equilibrium of system (2.3) and a_1 a positive number to be determined shortly. The derivative of L_{b1} along the trajectories of system (2.3) gives

$$\begin{aligned} L'_{b1} &= I'_b\left(1 - \frac{I_b^*}{I_b}\right) + a_1 P'\left(1 - \frac{P^*}{P}\right) \\ &= [\beta_4(B - I_b)I_b + \lambda_b P(B - I_b) - \mu_b I_b]\left(1 - \frac{I_b^*}{I_b}\right) + a_1(\sigma I_b - \eta P)\left(1 - \frac{P^*}{P}\right). \end{aligned}$$

Since (I_b^*, P^*) is an equilibrium of system (2.3), we have

$$\begin{cases} \mu_b I_b^* = \beta_4(B - I_b^*)I_b^* + \lambda_b P^*(B - I_b^*), \\ \eta P^* = \sigma I_b^*. \end{cases} \tag{2.4}$$

As a consequence,

$$\begin{aligned} L'_{b1} = & \left[\beta_4(B - I_b)I_b + \lambda_b P(B - I_b) - \beta_4(B - I_b^*)I_b - \lambda_b P^*\left(\frac{B}{I_b^*} - 1\right) I_b\right]\left(1 - \frac{I_b^*}{I_b}\right) \\ & + a_1\left(\sigma I_b - \sigma\frac{I_b^*}{P^*}P\right)\left(1 - \frac{P^*}{P}\right) \\ = & -\beta_4 I_b\frac{(I_b - I_b^*)^2}{I_b} + I_b\left(-\lambda_b B\frac{P^*}{I_b^*} + \lambda_b P^* + a_1\sigma\right) + P\left(\lambda_b B + \lambda_b I_b^* - a_1\sigma\frac{I_b^*}{P^*}\right) \\ & - \lambda_b P B\frac{I_b^*}{I_b} + \lambda_b B P^* - \lambda_b I_b P - \lambda_b P^* I_b^* - a_1\sigma I_b\frac{P^*}{P} + a_1\sigma I_b^*. \end{aligned}$$

Choose a_1 such that $\lambda_b B + \lambda_b I_b^* - a_1\sigma\frac{I_b^*}{P^*} = 0$. That is $a_1 = \frac{P^*(\lambda_b B + \lambda_b I_b^*)}{\sigma I_b^*}$.

Thus,

$$\begin{aligned} L'_{b1} = & -\beta_4(I_b - I_b^*)^2 + I_b\left(-\lambda_b B\frac{P^*}{I_b^*} + \lambda_b P^* + \frac{P^*(\lambda_b B + \lambda_b I_b^*)}{I_b^*}\right) - \lambda_b P B\frac{I_b^*}{I_b} \\ & + \lambda_b B P^* - \lambda_b I_b P - \lambda_b P^* I_b^* - \frac{I_b P^{*2}(\lambda_b B + \lambda_b I_b^*)}{I_b^* P} + P^*(\lambda_b B + \lambda_b I_b^*) \\ = & -\beta_4(I_b - I_b^*)^2 + \lambda_b P^* I_b\left(2 - \frac{P}{P^*} - \frac{P^*}{P}\right) + \lambda_b B P^*\left(2 - \frac{P I_b^*}{P^* I_b} - \frac{P^* I_b}{P I_b^*}\right). \end{aligned}$$

Moreover, $L'_{b1}(I_b, P) = 0 \Leftrightarrow I_b = I_b^*$ and $P = P^*$. As a consequence, the largest invariant subset contained in $\{(I_b, P) \in \mathbb{R}_+^2 / L'_{b1} = 0\}$ is the unique point E_1^*. By LaSalle's Invariance Principle [26], E_b^1 is GAS in the feasible domain of (2.3). This implies the GAS of E_1 of system (2.1) [17]. □

The complex dynamics and the management of zoonotic disease emergence require a good understanding of the disease both in animal and in human populations [28, 32]. Therefore, after modelling the disease transmission in bats, an effort must be made to describe the transmission of Ebola in humans. This important step should be done in the next section, before the most complex and central step of coupling the two systems through a spillover process.

3 A simple epidemic model for Ebola in humans

3.1 Model formulation

We divide the human population into four exclusive compartments: $S(t)$, $I(t)$, $D(t)$ and $R(t)$, representing the number of susceptibles, infected, Ebola-deceased and recovered individuals at time t. We model the dynamics of EVD by the simple base model

$$\begin{cases} S'(t) = \pi - S(\beta_1 I + \beta_2 D + \lambda P) - \mu S \\ I'(t) = S(\beta_1 I + \beta_2 D + \lambda P) - (\mu + \delta + \gamma)I \\ R'(t) = \gamma I - \mu R \\ D'(t) = (\mu + \delta)I - dD \\ P'(t) = \xi I + \alpha D - \eta P. \end{cases} \tag{3.1}$$

Parameters	Epidemiological interpretation
π	Replacement rate of susceptible humans
η	Decay rate of viruses in the environment
ξ	Deposition/shedding rate of viruses in the environment by infected humans
α	Deposition/shedding rate of viruses in the environment by Ebola-deceased humans
δ	Mortality rate of infected humans due to the disease
β_1	Effective contact rate between infected and susceptible humans
β_2	Effective contact rate between Ebola-deceased and susceptible humans
λ	Indirect contact rate of susceptible bats with viruses in the environment
γ	Human recovery rate
μ	Natural mortality rate of humans
d	Inhumation rate of dead humans

Table 3.1: Human's model parameters and their epidemiological interpretation

The interested reader is referred to [9] for more details on the model formulation. To be self-contained, the parameters of model (3.1) are recalled in Table 3.1.

3.2 Theoretical results

The following analytical results summarize the long run behavior of system (3.1) and their proofs can be found in [9].

Theorem 3.1.

- *The model* (3.1) *has a disease free equilibrium* $E_{0h} = \left(\frac{\pi}{\mu}, 0, 0, 0, 0\right)$.
- *The basic reproduction number* $\mathcal{R}_{0H}$ *of model* (3.1) *is*

$$\mathcal{R}_{0H} = \frac{\pi\beta_1}{\mu(\mu+\delta+\gamma)} + \frac{\pi\beta_2(\mu+\delta)}{d\mu(\mu+\delta+\gamma)} + \frac{\lambda\pi(d\xi+\alpha(\mu+\delta))}{d\eta\mu(\mu+\delta+\gamma)}.$$

- *If* $\mathcal{R}_{0H} > 1$, *there exists a unique endemic equilibrium* E_h^* *whose components* $(S^*, I^*, R^*, D^*, P^*)$ *are given by:*

$$\begin{cases} I^* = \dfrac{\pi(\mathcal{R}_{0H}-1)}{\mathcal{R}_{0H}(\mu+\delta+\gamma)}, & S^* = \dfrac{\pi}{\mu\mathcal{R}_{0H}}, \\ R^* = \dfrac{\gamma\pi(\mathcal{R}_{0H}-1)}{\mu\mathcal{R}_{0H}(\mu+\delta+\gamma)}, & D^* = \dfrac{(\mu+\delta)\pi(\mathcal{R}_{0H}-1)}{b\mathcal{R}_{0H}(\mu+\delta+\gamma)}, \\ P^* = \dfrac{(b\xi+(\mu+\delta)\alpha)\pi(\mathcal{R}_{0H}-1)}{b\eta\mathcal{R}_{0H}(\mu+\delta+\gamma)}. \end{cases} \tag{3.2}$$

Theorem 3.2. *The disease free equilibrium* $E_{0h} = \left(\frac{\pi}{\mu}, 0, 0, 0, 0\right)$ *of system* (3.1) *is GAS if* $\mathcal{R}_{0H} \leqslant 1$.

Theorem 3.3. *In the absence of shedding* $(\alpha = 0)$ *or manipulation of deceased human individuals before burial* $(\xi = 0)$, *the endemic equilibrium* E_h^* *exists and is GAS whenever* $\mathcal{R}_{0H} > 1$.

The dynamics of zoonotic pathogen transmission between animal hosts and humans can be very complex and extremely variable across systems. Modeling efforts, however, are typically restricted to transmission dynamics in the human host or reservoir hosts, and rarely extend

to the coupled dynamics of pathogen transmission in the spillover process [28]. Clearly this is the most important step in zoonotic disease dynamics. It is the description of the interaction that results between humans and animals (bats) in certain environments that determines the occurrence and nature of the epidemic. The complexity of these interactions is likely the most critical barrier to understanding spillover dynamics and managing zoonotic diseases. Modeling of these complex and non-linear interactions between and within host species (disease reservoir and human host), pathogen communities, and environmental conditions, requires us to extend our approaches to engage the dynamics of these coupled systems [28]. Therefore, the coupled model below (i.e. the main purpose of our work) is a substantial extension of the model in [9] by explicitly modelling the main source of Eboba viruses in the environement through the incorporation of the dynamics of Ebola in bats.

4 A simple spillover event (bat-to-human) model for Ebola

Here, we couple the epizootic bat-to-bat model (2.1) with the epidemic human-to-human model (3.1) through the spillover potential of EVD from fruit-eating bats to human beings.

4.1 Specific/additional hypothesis

- Infected dead bats neither shed viruses into the environment nor do they infect susceptible bats [30].
- Infected dead bats can infect human beings during their manipulation for food or during bat meat selling [32].
- The latent periods of EVD in humans and bats are neglected [36].

4.2 Model derivation

Here, we borrow the model parameters in Table 2.1 and Table 3.1, with an additional parameter β_3 describing the transmission from the infected dead bats to susceptible humans. Let p be the proportion of those bats who lose their infectivity power (either by the clearance of the viruses in their corpse, or by any other means) at time t. In fact, not all infected dead bats can transmit the disease, and the parameter p can be estimated by the measure of the protection human beings (proper cooking, wearing of protective clothes) exhibit while manipulating dead bats for food or commercialization. Thus, $(1-p)$ represents the proportion of those bats who are still able to transmit the disease to humans.

Human individuals can catch the infection by direct contact with individuals in classes I and D or with the $(1-p)\mu_b I_b$ infected dead bats at transmission rates β_1, β_2 and β_3, respectively. They can also contract the disease by indirect contact with viruses shed in the environment at a contact rate λ. A constant natural mortality rate μ is assumed for the human sub-populations and infected humans die with an additional rate δ. While the transfer rate into the deceased class D is $(\delta+\mu)I$, the removal rate from that class due to burial ceremony is d.

The environment is contaminated by I_b, I and D individuals at rates σ, ξ, α, respectively. Ebola viruses in the environment decay (either by natural death or by decontamination techniques) at rate η.

Combining model (2.1) with the human-to-human model (3.1), we propose the following coupled model with spillover évent from bats to humans.

$$\begin{cases} \dot{S}(t) = \pi - (\beta_1 I + \beta_2 D + \lambda P)S - \beta_0 S I_b - \mu S, \\ \dot{I}(t) = (\beta_1 I + \beta_2 D + \lambda P)S + \beta_0 S I_b - (\mu + \delta + \gamma)I, \\ \dot{S}_b(t) = \pi_b - \beta_4 S_b I_b - \lambda_b P S_b - \mu_b S_b, \\ \dot{I}_b(t) = \beta_4 S_b I_b + \lambda_b P S_b - \mu_b I_b, \\ \dot{R}(t) = \gamma I - \mu R, \\ \dot{D}(t) = (\mu + \delta)I - dD, \\ \dot{P}(t) = \sigma I_b + \xi I + \alpha D - \eta P, \end{cases} \tag{4.1}$$

where $\beta_0 = \beta_3(1-p)\mu_b$. Actually, since not all infected dead bats can transmit the disease to humans as mentioned earlier, the effective contact rate between susceptible humans and infected bats β_0 (i.e. the spillover event) is the product of the contact rate between susceptible humans and bats (β_3) times the probability of those contacts who lead to infection ($(1-p)\mu_b$). The transmission transfer diagram is depicted in Figure (4.1).

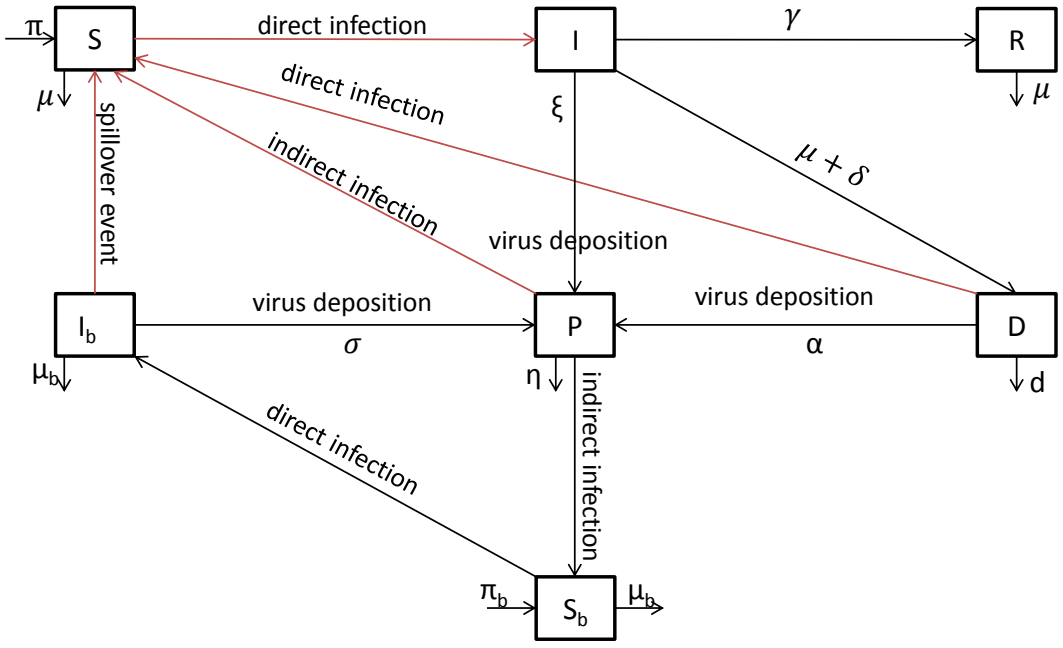

Figure 4.1: A flow diagram for the coupled bat-human spillover model.

Remark 4.1. It is worth noticing that the underlying assumptions for the coupled host-reservoir model (4.1) are two-fold: (1) the spillover event by which EVD switches from bat population to human population; (2) the two species (bats and humans) share the same living environment (hence, the consideration of only one environmental compartment). Therefore, our model is more suitable for small human populations living around or close to the forest (i.e. villages) and it is reasonable to assume bilinear incidence function rates for the coupled model and continuous dynamical system [9], even though a stochastic model could be considered.

4.3 Mathematical analysis of model (4.1)

Theorem 4.2. *The positive orthant $\mathbb{R}^7_+$ is positively invariant under the flow of (4.1). Precisely, if $S(0) > 0, I(0) \geq 0, R(0) \geq 0, D(0) \geq 0, P(0) \geq 0, S_b(0) > 0, I_b(0) \geq 0$, then for all $t \geq 0$, $S(t) > 0, I(t) \geq 0, R(t) \geq 0, D(t) \geq 0, P(t) \geq 0, S_b(t) > 0, I_b(t) \geq 0$.*

Proof. We begin by proving that, if $S(0) > 0$ then $\forall\ t \geq 0$, $S(t) > 0$. Suppose $S(0) > 0$, then from the first equation of (4.1), if $\psi(t) = ((\beta_1 I + \beta_2 D + \lambda P) + \beta_3(1-p)\mu_b I_b + \mu)$, then the integration from 0 to $t > 0$ yields

$$S(t) = S(0)\exp\left(\int_0^t -\psi(s)ds\right) + \exp\left(\int_0^t -\psi(s)ds\right) \times \int_0^t \pi \exp\left(\int_0^u \psi(w)dw\right) du.$$

Thus $S(t) > 0$, $\forall\, t \geq 0$. Similar arguments can be given to show that $S_b(t) > 0$, $\forall\, t > 0$.

To establish that $\forall\ t \geq 0$, $I(t) \geq 0$, $R(t) \geq 0$, $D(t) \geq 0$, $P(t) \geq 0$, $I_b(t) \geq 0$, whenever $I(0) \geq 0$, $R(0) \geq 0$, $D(0) \geq 0$, $P(0) \geq 0$, $I_b(0) \geq 0$, the above arguments can not be easily implemented. We then use an alternative trick.

Consider the following sub-equations related to the time evolution of variables I, I_b, R, D and P.

$$\begin{cases} \dot{I}(t) = S(\beta_1 I + \beta_2 D) + \lambda PS + \beta_0 S I_b - (\mu + \delta + \gamma)I, \\ \dot{I}_b(t) = \beta_4 S_b I_b + \lambda_b P S_b - \mu_b I_b, \\ \dot{R}(t) = \gamma I - \mu R, \\ \dot{D}(t) = (\mu + \delta)I - dD, \\ \dot{P}(t) = \sigma I_b + \xi I + \alpha D - \eta P. \end{cases} \tag{4.2}$$

System (4.2) can be written in the form:

$$\dot{Y}(t) = MY(t), \tag{4.3}$$

where

$$Y(t) = \begin{pmatrix} I(t) \\ I_b(t) \\ R(t) \\ D(t) \\ P(t) \end{pmatrix}, \qquad M = \begin{pmatrix} \beta_1 S - (\mu + \delta + \gamma) & \beta_0 S & 0 & \beta_2 S & \lambda S \\ 0 & \beta_4 S_b - \mu_b & 0 & 0 & \lambda_b S_b \\ \gamma & 0 & -\mu & 0 & 0 \\ \mu + \delta & 0 & 0 & -b & 0 \\ \xi & \sigma & 0 & \alpha & -\eta \end{pmatrix}.$$

Note that M is a Metzler matrix. Thus (4.3) is a monotone system. It follows that, $\mathbb{R}^5_+$ is invariant under the flow of (4.3). So, $I(t) \geq 0$, $I_b(t) \geq 0$, $R(t) \geq 0$, $D(t) \geq 0$ and $P(t) \geq 0$, for all $t \geq 0$. □

Theorem 4.3. *Suppose the initial conditions of system (4.1) are as in Theorem 4.2. Then the following a priori bounds hold: $H(t) \leq H_m$, $D(t) \leq D_m$, $N_b(t) \leq N_m$, $P(t) \leq P_m$, whenever $H(0) \leq H_m$, $D(0) \leq D_m$, $N_b(0) \leq N_m$ and $P(0) \leq P_m$, with $H(t) = S(t) + I(t) + R(t)$ being the total alive human population at time t,*

$$H_m = \frac{\pi}{\mu}, \quad D_m = \frac{(\mu + \delta)\pi}{d\mu}, \quad N_m = \frac{\pi_b}{\mu_b} \quad \text{and}$$
$$P_m = \frac{\sigma + \xi + \alpha}{\eta}\left(\frac{\pi_b d\mu + \mu_b d\pi + \mu_b(\mu + \delta)\pi}{d\mu\mu_b}\right).$$

Proof. The differential equation governed by $H(t)$ is:

$$\dot{H}(t) = \pi - \mu H(t) - \delta I \leq \pi - \mu H(t).$$

Since $\dot{H}(t) \leq \pi - \mu H(t)$, by Gronwall lemma, we have

$$H(t) \leq \frac{\pi}{\mu} + \left(H(0) - \frac{\pi}{\mu}\right) e^{-\mu t} \qquad \forall\, t \geq 0.$$

Hence, $H(t) \leq \frac{\pi}{\mu} = H_m$ whenever $H(0) \leq H_m$, from which we deduce that $I(t) \leq H_m$. Plugging this in the sixth equation of (4.1), we obtain $\dot{D}(t) \leq (\delta + \mu)H_m - dD(t)$. Another application of Gronwall lemma leads to $D(t) \leq \frac{(\delta+\mu)H_m}{d} \leq \frac{(\delta+\mu)\pi}{\mu d}$. Similarly, we show that $N_b(t) \leq N_m$ whenever $N_b(0) \leq N_m$.

The P-equation satisfies

$$\dot{P}(t) \leq \sigma N_m + \xi H_m + \alpha D_m - \eta P(t).$$

Thus,

$$\dot{P}(t) \leq (\sigma + \xi + \alpha)(N_m + H_m + D_m) - \eta P(t).$$

Applying Gronwall's lemma once again gives,

$$P(t) \leq \frac{\sigma + \xi + \alpha}{\eta}(N_m + H_m + D_m).$$

That is

$$P(t) \leq \frac{\sigma + \xi + \alpha}{\eta}\left(\frac{\pi_b d\mu + \mu_b d\pi + \mu_b(\mu + \delta)\pi}{d\mu\mu_b}\right).$$

□

Theorem 4.4. *System* (4.1) *is a dynamical system on*

$$\mathcal{K} = \left\{(S(t), I(t), S_b(t), I_b(t), R(t), D(t), P(t)) \in \mathbb{R}^7_+ \,/\, H(t) \leq \frac{\pi}{\mu}, N_b(t) \leq \frac{\pi_b}{\mu_b},\right.$$
$$\left. D(t) \leq \frac{(\mu + \delta)\pi}{d\mu} \text{ and } P(t) \leq \frac{\sigma + \xi + \alpha}{\eta}\left(\frac{\pi_b d\mu + \mu_b d\pi + \mu_b(\mu + \delta)\pi}{d\mu\mu_b}\right)\right\}.$$

Proof. It is a direct consequence of Theorem 4.2 and Theorem 4.3 above. □

Theorems 4.2, 4.3, 4.4 ensure the well-posedness of model (4.1).

4.4 Basic reproduction number $\mathcal{R}_0$ of model (4.1)

Consider the infected compartments I, I_b, D. The environment acts as a transition for the viruses and the shedding rate of the viruses (i.e. σI_b, ξI, αD) are placed in the transition vector $\mathcal{V}$ rather than in the transmission vector $\mathcal{F}$. Following [7, 37], one has

$$\mathcal{F} = \begin{pmatrix} (\beta_1 I + \beta_2 D + \beta_0 I_b + \lambda P)S \\ (\beta_4 I_b + \lambda_b P)S_b \\ 0 \\ 0 \end{pmatrix}, \qquad \mathcal{V} = \begin{pmatrix} (\mu + \delta + \gamma)I \\ \mu_b I_b \\ -(\mu + \delta)I + dD \\ -\sigma I_b - \xi I - \alpha D + \eta P \end{pmatrix}.$$

At DFE, $I^* = I_b^* = R^* = D^* = P^* = 0$, $S^* = \frac{\pi}{\mu}$ and $S_b^* = \frac{\pi_b}{\mu_b}$. The Jacobian matrices F and V for $\mathcal{F}$ and $\mathcal{V}$ are respectively given by

$$F = \begin{pmatrix} \frac{\beta_1\pi}{\mu} & \frac{\beta_0\pi}{\mu} & \frac{\beta_2\pi}{\mu} & \frac{\lambda\pi}{\mu} \\ 0 & \frac{\beta_4\pi_b}{\mu_b} & 0 & \frac{\lambda_b\pi_b}{\mu_b} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} (\mu+\delta+\gamma) & 0 & 0 & 0 \\ 0 & \mu_b & 0 & 0 \\ -(\mu+\delta) & 0 & d & 0 \\ -\xi & -\sigma & -\alpha & \eta \end{pmatrix}.$$

Straightforward computations yield

$$V^{-1} = \begin{pmatrix} \frac{1}{(\mu+\delta+\gamma)} & 0 & 0 & 0 \\ 0 & \frac{1}{\mu_b} & 0 & 0 \\ \frac{(\mu+\delta)}{d(\mu+\delta+\gamma)} & 0 & \frac{1}{d} & 0 \\ \frac{\xi}{\eta(\mu+\delta+\gamma)} + \frac{\alpha(\mu+\delta)}{\eta d(\mu+\delta+\gamma)} & \frac{\sigma}{\eta\mu_b} & \frac{\alpha}{\eta d} & \frac{1}{\eta} \end{pmatrix},$$

$$FV^{-1} = \begin{pmatrix} \mathcal{R}_{0H} & R_1 & \frac{\beta_2\pi}{\mu d} + \frac{\alpha\lambda\pi}{\eta d\mu} & \frac{\lambda\pi}{\eta\mu} \\ R_2 & \mathcal{R}_{0b} & \frac{\lambda_b\pi_b\alpha}{\eta d\mu_b} & \frac{\lambda_b\pi_b}{\eta\mu_b} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

where, $R_1 = \frac{\beta_0\pi}{\mu\mu_b} + \frac{\lambda\sigma\pi}{\eta\mu\mu_b}$ and $R_2 = \frac{\lambda_b\pi_b\xi}{\eta\mu_b(\mu+\delta+\gamma)} + \frac{\lambda_b\pi_b\alpha(\mu+\delta)}{\eta\mu_b d(\mu+\delta+\gamma)}$.

Thus,

$$\mathcal{R}_0 = \rho(FV^{-1}) = \rho\begin{pmatrix} \mathcal{R}_{0H} & R_1 \\ R_2 & \mathcal{R}_{0b} \end{pmatrix}.$$

Direct computation yields

$$\mathcal{R}_0 = \frac{\mathcal{R}_{0H} + \mathcal{R}_{0b} + \sqrt{(\mathcal{R}_{0H} - \mathcal{R}_{0b})^2 + 4R_1R_2}}{2}. \tag{4.4}$$

Remark 4.5. Suppose the spillover event is absent. That is no human being is infected by a bat either directly ($\beta_3 = 0$) or indirectly ($\sigma = 0$). Then $R_1 = 0$, $\widetilde{\mathcal{R}_{0b}} := \mathcal{R}_{0b}(\sigma = 0) = \frac{\pi_b\beta_4}{\mu_b^2}$ and the corresponding basic reproduction number for model (4.1) is

$$\widetilde{\mathcal{R}_0} = \max\left(\widetilde{\mathcal{R}_{0b}}, \mathcal{R}_{0H}\right) \leq \mathcal{R}_0. \tag{4.5}$$

From the inequality (4.5), it is clear that the spillover phenomenon contributes to speed up the disease outbreak.

The result below deals with the existence of equilibrium points for model (4.1) and the proof is provided in Appendix A.

Theorem 4.6. *System (4.1) exhibits no other boundary equilibrium than the disease-free equilibrium* $E_{bh} = \left(\frac{\pi}{\mu}, 0, \frac{\pi_b}{\mu_b}, 0, 0, 0, 0\right)$. *Whenever,* $\mathcal{R}_0 > 1$, *System (4.1) has a unique endemic equilibrium.*

4.5 Global stability of equilibria

Theorem 4.7. *The DFE of model (4.1) is GAS if* $\mathcal{R}_0 \leq 1$.

The proof of Theorem 4.7 is established in Appendix B.

The global asymptotic stability of the unique endemic equilibrium of model (4.1) is given in the following result, whose proof is shown in Appendix C.

Theorem 4.8. *The endemic equilibrium of (4.1) is GAS if* $\mathcal{R}_0 > 1$.

5 Control strategies

We present control efforts required to mitigate the EVD threat when controls are applied to specific subpopulations of hosts, but taking into account the fact that the infection will pass through other subpopulations (of the same species or another species, in the same or in another geographical area: bats) before causing secondary cases in the subpopulation of interest (i.e. humans). This will be done by considering the full coupled model and the simplified model without the environmental transmission. It is well known that the concept of basic reproduction number $\mathcal{R}_0$ do not always serves the purpose, and is not the right quantity to look at if one wishes to obtain insight into the control effort needed when targeting selected types of individuals in a heterogeneous population [22]. Alternatively, in the situation where we target one or more host types for control, the type-reproduction number $\mathcal{T}$ or the target reproduction number $\mathcal{T}_s$ (when a set S of the next generation matrix entries is targeted) are more closely related to the actual control effort required. In a homogeneous system, these relatively new thresholds coincide with $\mathcal{R}_0$, but in a heterogeneous system the three quantities only share their threshold behavior at $\mathcal{R}_0 = \mathcal{T} = \mathcal{T}_s = 1$ [7, 22]. Moreover, the host population becomes disease-free when a type/target reproduction number is less than 1, thus this number can be used to accurately guide disease control strategies [7, 22]

5.1 S-control on the full model (4.1)

It is not possible to reduce the transmission of the disease between bats (since nobody cares for them). However, it is possible to control the infection in humans caused either by direct human-to-human contacts or by indirect environment-to-human contacts or by direct bat-to-human contacts through application of the S-control [22]. This latter control acts primarily on reducing the availability of susceptibles humans of the target type [22]. Since an efficient vaccine against Ebola virus disease has been recently discovered, on the one hand, one could for example reduce the proportion of susceptibles by vaccination, on the other hand, by educating people through media could affect significantly humans behavior and customs and therefore contribute also to reduce the transmissibility of the disease. So, it is important to calculate the type reproduction numbers, which are useful tools to address such issues [34, 35].

5.1.1 The environment is a transition

By assuming that the environment acts as a transition, let $K_t = FV^{-1}$ be the next generation matrix. In order to implement S-control following [22], we define the target matrix K_s, which corresponds to the first row of K_t. That is

$$K_s = \begin{pmatrix} \mathcal{R}_{0H} & R_1 & \frac{\beta_2\pi}{\mu d} + \frac{\alpha\lambda\pi}{\eta d\mu} & \frac{\lambda\pi}{\eta\mu} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}.$$

Note that the spectral radius of the matrix $K_t - K_s$ is $\rho(K_t - K_s) = \mathcal{R}_{0b}$.

If $\mathcal{R}_{0b} < 1$, the target reproduction number is

$$\mathcal{T}_s = \rho(K_s(I - K_t + K_s)^{-1}).$$

It is straightforward that,

$$K_s(I-K_t+K_s)^{-1}=\begin{pmatrix}\mathcal{R}_{0H}+\frac{R_1R_2}{1-\mathcal{R}_{0b}} & \star & \star & \star\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\end{pmatrix},$$

where, each "$\star$" is a wild-card for the entry we did not determine as we do not need to know it for the following considerations. Thus,

$$\mathcal{T}_s=\rho(K_s(I-K_t+K_s)^{-1})=\mathcal{R}_{0H}+\frac{R_1R_2}{1-\mathcal{R}_{0b}}. \tag{5.1}$$

Remark 5.1. Following [22,34] it is well know that, if $\mathcal{R}_{0b}<1$, the disease can be eradicated by targeting only the susceptible humans S. More precisely, the effort devoted by S-control alone is sufficient to prevent EVD in the whole population if a proportion v of susceptible humans greater than $1-\frac{1}{\mathcal{T}_s}$ is controlled.

Note that, contrary to Theorem 4.3 in [34] where the corresponding next generation matrix was irreducible, the matrix K_t here is reducible. However a similar result can be shown in the proposition below to relate the basic reproduction number $\mathcal{R}_0$ and the target reproduction number $\mathcal{T}_s$.

Proposition 5.2. *Assume $\mathcal{R}_{0b}<1$. Then exactly one of the following statements hold:*

(1) $1<\mathcal{R}_0<\mathcal{T}_s$,

(2) $\mathcal{T}_s=\mathcal{R}_0=1$,

(3) $\mathcal{T}_s<\mathcal{R}_0<1$.

Proof. It is enough to observe that

$$R_1R_2=(\mathcal{R}_0-\mathcal{R}_{0b})(\mathcal{R}_0-\mathcal{R}_{0H})=(1-\mathcal{R}_{0b})(\mathcal{T}_s-\mathcal{R}_{0H}), \tag{5.2}$$

and use (4.4) and (5.1) to conclude. □

5.1.2 The environment is a reservoir

When the environment is a reservoir of viruses [7], the entries of the next generation matrix K_r below are easy to interpret. In this case, secondary viruses are added into the environment through virus shedding by infectious hosts (humans and bats). Moreover the shedding rates $\sigma I_b, \xi I, \alpha D$ are placed in the transmission vector $\widetilde{\mathcal{F}}$. Furthermore, we consider also that the transfer term $(\mu+\delta)I$ stands for new infections into class D. Therefore, according to [7,37], one has

$$\widetilde{\mathcal{F}}=\begin{pmatrix}(\beta_1 I+\beta_2 D+\beta_0 I_b+\lambda P)S\\ (\beta_4 I_b+\lambda_b P)S_b\\ (\mu+\delta)I\\ \sigma I_b+\xi I+\alpha D\end{pmatrix},\qquad \widetilde{\mathcal{V}}=\begin{pmatrix}(\mu+\delta+\gamma)I\\ \mu_b I_b\\ dD\\ \eta P\end{pmatrix}.$$

The Jacobian matrices $\widetilde{F}$ and $\widetilde{V}$ of $\widetilde{\mathcal{F}}$ and $\widetilde{\mathcal{V}}$ evaluated at DFE are given respectively by:

$$\widetilde{F} = \begin{pmatrix} \frac{\beta_1\pi}{\mu} & \frac{\beta_0\pi}{\mu} & \frac{\beta_2\pi}{\mu} & \frac{\lambda\pi}{\mu} \\ 0 & \frac{\beta_4\pi_b}{\mu_b} & 0 & \frac{\lambda_b\pi_b}{\mu_b} \\ \mu+\delta & 0 & 0 & 0 \\ \xi & \sigma & \alpha & 0 \end{pmatrix} \quad \text{and} \quad \widetilde{V} = \begin{pmatrix} (\mu+\delta+\gamma) & 0 & 0 & 0 \\ 0 & \mu_b & 0 & 0 \\ 0 & 0 & d & 0 \\ 0 & 0 & 0 & \eta \end{pmatrix}.$$

Let

$$K_r := \widetilde{F}\widetilde{V}^{-1} = \begin{pmatrix} \frac{\beta_1\pi}{\mu(\mu+\delta+\gamma)} & \frac{\beta_0\pi}{\mu\mu_b} & \frac{\beta_2\pi}{\mu d} & \frac{\lambda\pi}{\eta\mu} \\ 0 & \frac{\beta_4\pi_b}{\mu_b^2} & 0 & \frac{\lambda_b\pi_b}{\eta\mu_b} \\ \frac{\mu+\delta}{\mu+\delta+\gamma} & 0 & 0 & 0 \\ \frac{\xi}{\mu+\delta+\gamma} & \frac{\sigma}{\mu_b} & \frac{\alpha}{d} & 0 \end{pmatrix}$$

be the next generation matrix. K_r is nonnegative and irreducible. To implement the S-control strategy, we define the target matrix corresponding to the first row of K_r by :

$$K_s' = \begin{pmatrix} \frac{\beta_1\pi}{\mu(\mu+\delta+\gamma)} & \frac{\beta_0\pi}{\mu\mu_b} & \frac{\beta_2\pi}{\mu d} & \frac{\lambda\pi}{\eta\mu} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}.$$

Note that

$$\rho(K_r - K_s') = \frac{\frac{\beta_4\pi_b}{\mu_b^2} + \sqrt{\left(\frac{\beta_4\pi_b}{\mu_b^2}\right)^2 + \frac{4\lambda_b\pi_b\sigma}{\eta\mu_b^2}}}{2}. \tag{5.3}$$

When $\rho(K_r - K_s') < 1$, the target reproduction number is $\mathcal{T}_s' = \rho(K_s(I - K_r + K_s')^{-1})$, which is computed as follows:

Let

$$a = \eta(\mu_b^2 - \beta_4\pi_b), \quad c = a - \sigma\lambda_b\pi_b = \eta\mu_b^2(1 - \mathcal{R}_{0b}), \quad f = \alpha(\mu+\delta) + \xi d, \quad g = (\mu+\delta+\gamma).$$

Simple calculations lead to

$$K_S(I - K_r + K_s')^{-1} = \begin{pmatrix} \frac{\beta_1\pi}{\mu g} + \frac{\beta_0\pi\pi_b\lambda_b f}{\mu gcd} + \frac{\beta_2\pi(\mu+\delta)}{\mu dg} + \frac{\lambda\pi fa}{\mu\eta dgc} & \star & \star & \star \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

where, each "$\star$" stands for unnecessary term for the computation of the target reproduction number below. Therefore,

$$\mathcal{T}_s' = \rho(K_S(I - K_r + K_s')^{-1}) = \frac{\beta_1\pi}{\mu g} + \frac{\beta_0\pi\pi_b\lambda_b f}{\mu gcd} + \frac{\beta_2\pi(\mu+\delta)}{\mu dg} + \frac{\lambda\pi fa}{\mu\eta dgc}.$$

A similar conclusion as in Remark 5.1 above also applies here. Moreover, the following result shows that the S-control do not depend on the interpretation of the environment either as a transition or as a reservoir.

Proposition 5.3. *If $\rho(K_r - K_s')$ given in (5.3) is less than one, so that the target reproduction numbers $\mathcal{T}_s'$ and $\mathcal{T}_s$ are well defined, then they are equal.*

Proof. It is straightforward that $\rho(K_r - K_s') < 1$ implies $\mathcal{R}_{0b} < 1$, so that $\mathcal{T}_s'$ and $\mathcal{T}_s$ are well defined since the matrices $(I - K_r + K_s')$ and $(I - K_t + K_s)$ are invertible.

$$\begin{aligned}\mathcal{T}_s' &= \frac{\beta_1\pi}{\mu(\mu+\delta+\gamma)} + \frac{\beta_0\pi\pi_b\lambda_b(\alpha(\mu+\delta)+\xi d)}{\mu(\mu+\delta+\gamma)d[\eta(\mu_b^2-\beta_4\pi_b)-\sigma\lambda_b\pi_b]} + \frac{\beta_2\pi(\mu+\delta)}{\mu d(\mu+\delta+\gamma)} \\ &\quad + \frac{\lambda\pi\eta(\mu_b^2-\beta_4\pi_b)(\alpha(\mu+\delta)+\xi d)}{\mu\eta d(\mu+\delta+\gamma)[\eta(\mu_b^2-\beta_4\pi_b)-\sigma\lambda_b\pi_b]} \\ &= \frac{\beta_1\pi}{\mu(\mu+\delta+\gamma)} + \frac{\beta_0\pi R_2}{\mu\mu_b(1-\mathcal{R}_{0b})} + \frac{\beta_2\pi(\mu+\delta)}{\mu d(\mu+\delta+\gamma)} + \frac{\lambda\pi R_2(\mu_b^2-\beta_4\pi_b)}{\lambda_b\pi_b\mu\mu_b(1-\mathcal{R}_{0b})}.\end{aligned}$$

Since

$$\frac{\beta_0\pi}{\mu\mu_b} = R_1 - \frac{\lambda\sigma\pi}{\eta\mu\mu_b},$$

we have

$$\mathcal{T}_s' = \frac{\beta_1\pi}{\mu(\mu+\delta+\gamma)} + \frac{R_1R_2}{1-\mathcal{R}_{0b}} - \frac{\lambda\pi\sigma R_2}{\eta\mu\mu_b(1-\mathcal{R}_{0b})} + \frac{\beta_2\pi(\mu+\delta)}{\mu d(\mu+\delta+\gamma)} + \frac{\lambda\pi R_2(\mu_b^2-\beta_4\pi_b)}{\lambda_b\pi_b\mu\mu_b(1-\mathcal{R}_{0b})}.$$

Simple computations show that

$$-\frac{\lambda\pi\sigma R_2}{\eta\mu\mu_b(1-\mathcal{R}_{0b})} + \frac{\lambda\pi R_2(\mu_b^2-\beta_4\pi_b)}{\lambda_b\pi_b\mu\mu_b(1-\mathcal{R}_{0b})} = \frac{\pi\lambda\mu_b R_2}{\mu\lambda_b\pi_b},$$

$$\mathcal{T}_s' = \frac{\beta_1\pi}{\mu(\mu+\delta+\gamma)} + \frac{R_1R_2}{1-\mathcal{R}_{0b}} + \frac{\beta_2\pi(\mu+\delta)}{\mu d(\mu+\delta+\gamma)} + \frac{\pi\lambda\mu_b R_2}{\mu\lambda_b\pi_b}.$$

Using the expression of R_2, we have

$$\begin{aligned}\mathcal{T}_s' &= \frac{\beta_1\pi}{\mu(\mu+\delta+\gamma)} + \frac{\beta_2\pi(\mu+\delta)}{\mu d(\mu+\delta+\gamma)} + \frac{\pi\lambda\xi}{\mu\eta(\mu+\delta+\gamma)} + \frac{\lambda\pi\alpha(\mu+\delta)}{\eta\mu d(\mu+\delta+\gamma)} + \frac{R_1R_2}{1-\mathcal{R}_{0b}}. \\ &= \mathcal{R}_{0H} + \frac{R_1R_2}{1-\mathcal{R}_{0b}} \\ &= \mathcal{T}_s.\end{aligned}$$

□

Even though the indirect transmission route of EVD has been demonstrated [9], it is however well known that this latter mode is less important than the direct transmission route. Furthermore, we shall prove in the next subsection that, the S-control strategy seems to be more demanding for the full model than for the simplified model without the environment (i.e., $\mathcal{T}_s > \mathcal{T}_s^{''}$). Therefore, if human individuals are well educated and provided with safe sanitary facilities, then the environmental transmission can be neglected.

5.2 The simplified model (4.1) without environment

Let $\mathcal{R}_{0b}'$, $\mathcal{R}_{0H}'$ and $\mathcal{R}_0'$ be the corresponding basic reproduction numbers of the simplified models for bats, for humans and for the coupled bat-human model, obtained from (2.1), (3.1) and (4.1), respectively. One has:

$$\mathcal{R}_{0b}' = \frac{\beta_4\pi_b}{\mu_b^2}, \quad \mathcal{R}_{0H}' = \frac{\beta_1\pi}{\mu(\mu+\delta+\gamma)} + \frac{\beta_2\pi(\mu+\delta)}{\mu d(\mu+\delta+\gamma)}, \quad \mathcal{R}_0' = \max\left(\mathcal{R}_{0b}', \mathcal{R}_{0H}'\right).$$

Let K' be the corresponding next generation matrix obtained from K_r above (where $(\mu+\delta)I$ stands for new infections). Then

$$K' = \begin{pmatrix} \frac{\beta_1\pi}{\mu(\mu+\delta+\gamma)} & \frac{\beta_0\pi}{\mu\mu_b} & \frac{\beta_2\pi}{\mu d} \\ 0 & \frac{\beta_4\pi_b}{\mu_b^2} & 0 \\ \frac{\mu+\delta}{\mu+\delta+\gamma} & 0 & 0 \end{pmatrix}.$$

5.2.1 S-control of the simplified model (4.1)

Let the target matrix

$$K_s'' = \begin{pmatrix} \frac{\beta_1\pi}{\mu(\mu+\delta+\gamma)} & \frac{\beta_0\pi}{\mu\mu_b} & \frac{\beta_2\pi}{\mu d} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}.$$

Then, whenever $\rho(K' - K_s'') = \mathcal{R}'_{0b} < 1$, one has

$$K_s''(I - K' + K_s'')^{-1} = \begin{pmatrix} \frac{\beta_1\pi}{\mu(\mu+\delta+\gamma)} + \frac{\beta_2\pi(\mu+\delta)}{\mu d(\mu+\delta+\gamma)} & \star & \star \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix},$$

where each "$\star$" stands for an unnecessary term in the computation of the target reproduction number below. The target reproduction number is then given by

$$\mathcal{T}_s'' = \frac{\beta_1\pi}{\mu(\mu+\delta+\gamma)} + \frac{\beta_2\pi(\mu+\delta)}{\mu d(\mu+\delta+\gamma)} := \mathcal{R}'_{0H}.$$

Note that, as expected, since $\mathcal{R}_{0H} > \mathcal{R}'_{0H}$, the type reproduction number $\mathcal{T}_s$ for the full model (4.1) is greater than the type reproduction number $\mathcal{T}_s''$ for the simplified model. This overestimates the effort required to control EVD when the environment is taken into account. Note that a remark similar to (5.1) applies here as well.

6 Impact of environment and spillover potential

Here, we provide few simulations using MatLab, to investigate the effects of the contaminated environment and the spillover potential on the endemicity level of EVD within human population. In order to achieve that goal, we concentrate on the coupled model and choose different values for the effective environmental contact λ and bat-to-human contact β_3. In Figure 6.1, the infected human subpopulation is represented over time for one month (30 days). One can observe three phases of the disease. An initial phase whereby, high environmental transmission ($\lambda = 0.05$) and high spillover event ($\beta_3 = 0.1$) increase the number of infected individuals (for approximately 2 days). The second phase during which high environmental transmission and high spillover event reverse the situation (from the 3th to the 8th day). The last phase which is similar to the first one. Moreover, it shows that the number of infected stabilizes and that for high environmental contact ($\lambda = 0.05$) and high spillover ($\beta_3 = 0.1$) (red curve), the corresponding endemic infected is greater than the same individuals when low environmental contact ($\lambda = 0.0000001$) and low spillover ($\beta_3 = 0.00001$) are considered. Furthermore, this latter setting where λ and β_3 are very low, the disease can disappear (blue curve). Similar patterns are observed in Figure 6.2 when only the spillover potential (β_3) decreases, driven the disease to extinction. This Figure 6.2 suggests that the spillover event can

Parameters	Estimates	Sources	Parameters	Estimates	Sources
π	10	Assumed	π_b	8	Assumed
η	0.6	Assumed	ξ	$(0,\infty)$	Assumed
α	0.0006	Assumed	δ	0.5	Assumed
β_1	0.003	[15,27]	β_2	0.0012	Assumed
β_3	0.1	Assumed	β_4	0.0016	Assumed
λ	0.05	Assumed	λ_b	0.0001	Assumed
μ	0.03	[29]	μ_b	0.09	Assumed
d	0.8	[20]	σ	$(0,1)$	Assumed
p	0.5	Assumed	γ	0.06	[15,27]

Table 6.1: Hypothetical/estimated parameters values to simulate system (4.1)

be very detrimental to EVD by allowing switching of the disease from bats to humans even though the disease was not initially endemic in human ($\mathcal{R}_{0H} < 1$).

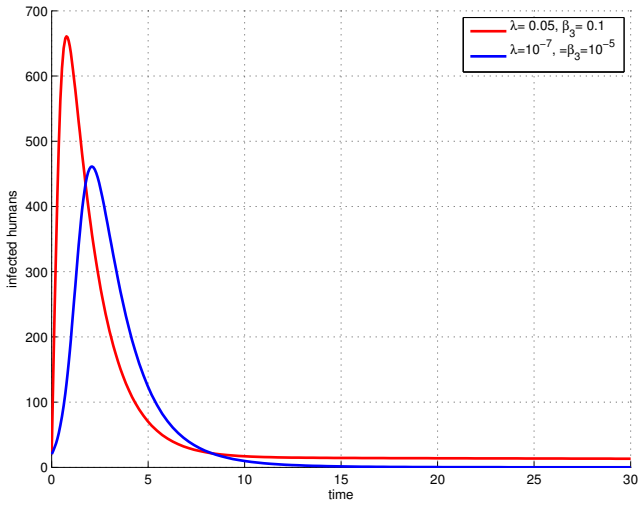

Figure 6.1: Impact of manipulation and consumption of bats on the evolution of infected humans. High environmental transmission ($\lambda = 0.05$) and high spillover event ($\beta_3 = 0.1$): red curve. Low environmental transmission ($\lambda = 0.0000001$) and low spillover event ($\beta_3 = 0.00001$): blue curve. The other parameters are as in Table 6.1.

7 Conclusion and perspectives

The aim of this study was to assess the impact of the spillover event on the dynamics of EVD. To achieve that goal, a two-host model for Ebola with indirect transmission, which extends numerous existing EVD transmission models in the literature was developed, theoretically and numerically analyzed. Many disease cycles were taken into consideration:

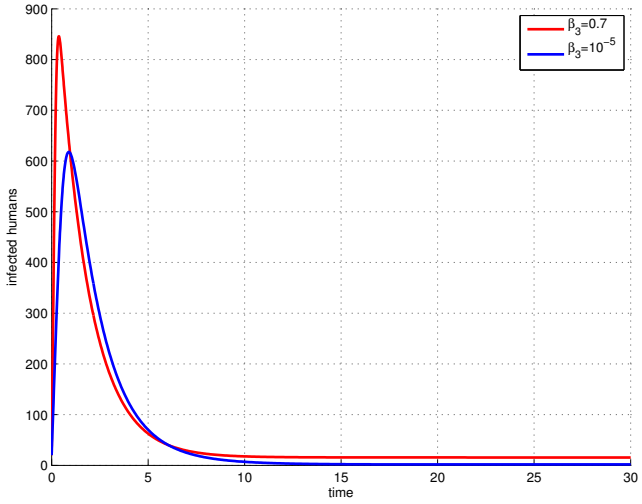

Figure 6.2: (Spillover event: invasion of a disease-free human population by an endemic bat population (i.e. $\mathcal{R}_{0b} > 1$ and $\mathcal{R}_{0H} < 1$ but $\mathcal{R}_0 > 1$). High spillover event ($\beta_3 = 0.7$): red curve. Low spillover event ($\beta_3 = 0.00001$): blue curve. The other parameters are as in Table 6.1.

(i) bat-to-bat transmission.

(ii) bat-to-human transmission (i.e. the spillover event).

(iii) human-to-human transmission.

(iv) environment-to-bat transmission.

(v) environment-to-human transmission.

The main results, including the efforts needed to control (or eliminate) EVD and the assessment of the spillover event, are summarized as follows.

1. The sub-model for bat population exhibits a sharp threshold behavior with the corresponding basic reproduction number $\mathcal{R}_{0b}$ being the bifurcation parameter. Namely, the DFE is globally asymptotically stable whenever $\mathcal{R}_{0b} \leq 1$ and a globally asymptotically stable endemic equilibrium occurs when $\mathcal{R}_{0b} > 1$.

2. For the human sub-model a similar result is given with the corresponding basic reproduction number $\mathcal{R}_{0H}$ standing for the bifurcation parameter. Here, the obtained result substantially improved (by extending) a similar result in [9].

3. As far as the coupled model is concerned, a fixed point theorem is used to establish the existence and uniqueness of the endemic equilibrium and the graph theory approach is called on to prove its global stability. As a whole, this coupled model exhibits a sharp threshold behavior as well.

4. We have numerically shown that the spillover event can be very detrimental to EVD by allowing the switching of the disease from bats to humans and by contributing to speed

up the disease outbreak. This suggests the fact that the consumption and manipulation of bats can play an important role in the sustainability of Ebola virus disease.

Different extensions of the model on which we are still working include:

(a) the incorporation of the control strategies such as contact tracing, ring vaccination, isolation, quarantine, media coverage;

(b) a multi-patch modeling approach to consider the circulation of EVD between villages and countries.

Appendices

Appendix A: Proof of Theorem 4.6

We first prove that model (4.1) has a unique boundary equilibrium. In fact

(i) If $I = 0$, from the fifth and sixth equations of system (4.1), $D = R = 0$. Moreover, the second equation yields $\lambda PS + \beta_0 S I_b = 0$ i.e $I_b = P = 0$. Thus, the boundary equilibrium is the DFE.

(ii) If $D = 0$, then $I = 0$ and you are back to the case (i).

(iii) If $I_b = 0$, from the fourth equation of (4.1), $\lambda_b P S_b = 0\, i.e\, P = 0$. The seventh equation gives $I = D = 0$. Thus, the only boundary equilibrium is again the DFE.

Therefore, the only boundary equilibrium of system (4.1) is the DFE.

Suppose $\mathcal{R}_0 > 1$, the following theorem is instrumental.

Theorem 7.1 (Hethcote and Thieme [23]). *Let F(x) be a continuous, monotone, nondecreasing, strictly sub-linear bounded function which maps the nonnegative orthant $\mathbb{R}^n_+$ into itself. Let F(0)=0 and F'(0) exist and be irreducible. Then F(x) does not have a nontrivial fixed point on the boundary of $\mathbb{R}^n_+$. Moreover, F(x) has a positive fixed point iff $\rho(F'(0)) > 1$. If there is a positive fixed point then it is unique.*

Consider system (2.2). Since $B = \frac{\pi_b}{\mu_b}$ is GAS for (2.2), the existence of endemic equilibria of system (4.1) is equivalent to the existence of positive equilibria of

$$\begin{cases} \dot{S} = \pi - S(\beta_1 I + \beta_2 D) - \lambda PS - \beta_0 S I_b - \mu S, \\ \dot{I} = S(\beta_1 I + \beta_2 D) + \lambda PS + \beta_0 S I_b - (\mu + \delta + \gamma) I, \\ \dot{I}_b = \beta_4 (B - I_b) I_b + \lambda_b P (B - I_b) - \mu_b I_b, \\ \dot{R} = \gamma I - \mu R, \\ \dot{D} = (\mu + \delta) I - dD, \\ \dot{P} = \sigma I_b + \xi I + \alpha D - \eta P. \end{cases} \tag{7.1}$$

Thus, we deal with model (7.1). Let $E^* = (S^*, I^*, I_b^*, R^*, D^*, P^*)$ be an equilibrium point of

system (7.1). Its components satisfy the following equations

$$\begin{cases} 0 = \pi - S^*(\beta_1 I^* + \beta_2 D^*) - \lambda P^* S^* - \beta_0 S^* I_b^* - \mu S^*, \\ 0 = S^*(\beta_1 I^* + \beta_2 D^*) + \lambda P^* S^* + \beta_0 S^* I_b^* - (\mu + \delta + \gamma) I^*, \\ 0 = \beta_4 (B - I_b^*) I_b^* + \lambda_b P^* (B - I_b^*) - \mu_b I_b^*, \\ 0 = \gamma I^* - \mu R^*, \\ 0 = (\mu + \delta) I^* - d D^*, \\ 0 = \sigma I_b^* + \xi I^* + \alpha D^* - \eta P^*. \end{cases} \tag{7.2}$$

Thus, solving (7.2), one can write

$$\begin{aligned} S^* &= \frac{\pi - (\mu + \delta + \gamma) I^*}{\mu}, & R^* &= \frac{\gamma}{\mu} I^*, \\ D^* &= \frac{\mu + \delta}{d} I^*, & P^* &= \frac{1}{\eta} \left(\sigma I_b^* + \xi I^* + \alpha \frac{\mu + \delta}{d} I^* \right), \end{aligned} \tag{7.3}$$

and

$$\begin{cases} I^* = \dfrac{1}{\mu + \delta + \gamma} [S^*(\beta_1 I^* + \beta_2 D^*) + \lambda P^* S^* + \beta_0 S^* I_b^*], \\ I_b^* = \dfrac{1}{\mu_b} [\beta_4 (B - I_b^*) I_b^* + \lambda_b P (B - I_b^*)]. \end{cases} \tag{7.4}$$

Substituting (7.3) into (7.4) yields

$$\begin{cases} I^* = \dfrac{\pi - (\mu + \delta + \gamma) I^*}{\mu(\mu + \delta + \gamma)} \left[\beta_1 I^* + \beta_2 \dfrac{\mu + \delta}{d} I^* + \lambda \dfrac{d\sigma I_b^* + d\xi I^* + \alpha(\mu + \delta) I^*}{\eta d} + \beta_0 I_b^* \right], \\ I_b^* = \dfrac{1}{\mu_b} \left[\beta_4 (\dfrac{\pi_b}{\mu_b} - I_b^*) I_b^* + \dfrac{\lambda_b}{\eta d} (d\sigma I_b^* + d\xi I^* + \alpha(\mu + \delta) I^*)(B - I_b^*) \right], \end{cases} \tag{7.5}$$

i.e.

$$\begin{cases} I^* + \dfrac{1}{\mu} I^* \left[\beta_1 I^* + \beta_2 \dfrac{\mu + \delta}{d} I^* + \lambda \dfrac{d\sigma I_b^* + d\xi I^* + \alpha(\mu + \delta) I^*}{\eta d} + \beta_0 I_b^* \right] \\ \qquad = \dfrac{\pi}{\mu(\mu + \delta + \gamma)} \left[\beta_1 I^* + \beta_2 \dfrac{\mu + \delta}{d} I^* + \lambda \dfrac{d\sigma I_b^* + d\xi I^* + \alpha(\mu + \delta) I^*}{\eta d} + \beta_0 I_b^* \right], \\ I_b^* + \dfrac{\beta_4}{\mu_b} I_b^{*2} + \dfrac{\lambda_b}{\eta d \mu_b} (d\sigma I_b^* + d\xi I^* + \alpha(\mu + \delta) I^*) I_b^* \\ \qquad = \left[\beta_4 \dfrac{\pi_b}{\mu_b^2} I_b^* + \dfrac{\lambda_b B}{\eta d \mu_b} (d\sigma I_b^* + d\xi I^* + \alpha(\mu + \delta) I^*) \right], \end{cases} \tag{7.6}$$

which can be rewritten in the following from:

$$\begin{cases} I^* = g_1(I^*, I_b^*), \\ I_b^* = g_2(I^*, I_b^*), \end{cases} \tag{7.7}$$

where

$$g_1(I^*, I_b^*) = \frac{\eta d\mu}{\mu\eta d + I^*(\eta d\beta_1 + \eta\beta_2(\mu+\delta) + \lambda d\xi + \lambda\alpha(\mu+\delta)) + I_b^*(\lambda d\sigma + \eta d\beta_0)} \times \frac{\pi}{\mu(\mu+\delta+\gamma)}\left[\beta_1 I^* + \beta_2\frac{\mu+\delta}{d}I^* + \lambda\frac{d\sigma I_b^* + d\xi I^* + \alpha(\mu+\delta)I^*}{\eta d} + \beta_0 I_b^*\right],$$

$$g_2(I^*, I_b^*) = \frac{\eta d\mu_b}{\eta d\mu_b + I_b^*(\eta d\beta_4 + \lambda_b d\sigma) + I^*(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))} \times \left[\frac{\beta_4\pi_b}{\mu_b^2}I_b^* + \frac{\lambda_b B}{\eta d\mu_b}(d\sigma I_b^* + d\xi I^* + \alpha(\mu+\delta)I^*)\right].$$

g_1 and g_2 are differentiable functions with,

$$\frac{\partial g_1}{\partial I^*}(0,0) = \frac{\pi}{\mu(\mu+\delta+\gamma)}\left(\beta_1 + \frac{\beta_2(\mu+\delta)}{d} + \frac{\lambda\xi}{\eta} + \frac{\lambda\alpha(\mu+\delta)}{\eta d}\right),$$

$$\frac{\partial g_1}{\partial I_b^*}(0,0) = \frac{\pi}{\mu(\mu+\delta+\gamma)}\left(\frac{\lambda\sigma}{\eta} + \beta_0\right),$$

$$\frac{\partial g_2}{\partial I^*}(0,0) = \frac{\lambda_b\pi_b}{\eta d\mu_b^2}(d\xi + \alpha(\mu+\delta)),$$

$$\frac{\partial g_2}{\partial I_b}(0,0) = \frac{1}{\mu_b}\left(\frac{\beta_4\pi_b}{\mu_b} + \frac{\lambda_b\sigma\pi_b}{\eta\mu_b}\right).$$

Set $X = (I, I_b)$ and $G = (g_1, g_2)$.

The existence of equilibria for (7.2) is then equivalent to the determination of the positive solutions for the equation

$$X = G(X).$$

Note that $G(X)$ is differentiable at $0 = (0,0)$ and the corresponding Jacobian is

$$G'(0) = \begin{pmatrix} \frac{\pi}{d\eta\mu(\mu+\delta+\gamma)}(\eta d\beta_1 + \eta\beta_2(\mu+\delta) + d\lambda\xi + \lambda\alpha(\mu+\delta)) & \frac{\pi}{\mu(\mu+\delta+\gamma)}(\frac{\lambda\sigma}{\eta} + \beta_0) \\ \frac{\lambda_b\pi_b(d\xi+\alpha(\mu+\delta))}{\eta d\mu_b^2} & \frac{\beta_4\pi_b}{\mu_b^2} + \frac{\lambda_b\sigma\pi_b}{\eta\mu_b^2} \end{pmatrix}.$$

Let

$$A = \begin{pmatrix} \frac{\pi}{d\eta\mu(\mu+\delta+\gamma)}(\eta d\beta_1 + \eta\beta_2(\mu+\delta) + d\lambda\xi + \lambda\alpha(\mu+\delta)) & \frac{\beta_0\pi}{\mu\mu_b} + \frac{\lambda\sigma\pi}{\eta\mu\mu_b} \\ \frac{\lambda_b\pi_b\xi}{\eta\mu_b(\mu+\delta+\gamma)} + \frac{\lambda_b\pi_b\alpha(\mu+\delta)}{\eta\mu_b d(\mu+\delta+\gamma)} & \frac{\beta_4\pi_b}{\mu_b^2} + \frac{\lambda_b\sigma\pi_b}{\eta\mu_b^2} \end{pmatrix},$$

$$E = \begin{pmatrix} \frac{\beta_2\pi}{\mu d} + \frac{\alpha\lambda\pi}{\eta d\mu} & \frac{\lambda\pi}{\eta\mu} \\ \frac{\lambda_b\pi_b\alpha}{\eta d\mu_b} & \frac{\lambda_b\pi_b}{\eta\mu_b} \end{pmatrix} \quad \text{and} \quad T = \begin{pmatrix} 0 & 0 \\ 0 & 0 \end{pmatrix}.$$

Then

$$FV^{-1} = \begin{pmatrix} A & E \\ T & T \end{pmatrix}, \quad \text{and} \quad \rho(FV^{-1}) = \rho(A).$$

On the other hand, if

$$Q = \begin{pmatrix} \mu+\delta+\gamma & 0 \\ 0 & \mu_b, \end{pmatrix},$$

then it is straightforward that $G'(0) = Q^{-1}AQ$. Therefore, $G'(0)$ and A are similar matrices. Hence,

$$\rho(FV^{-1}) = \rho(A) = \rho(G'(0)).$$

We have,

$$G'(X) = \begin{pmatrix} \frac{\partial g_1}{\partial I^*}(X) & \frac{\partial g_1}{\partial I_b^*}(X) \\ \\ \frac{\partial g_2}{\partial I^*}(X) & \frac{\partial g_2}{\partial I_b^*}(X) \end{pmatrix} = \begin{pmatrix} G_{11}(X) & G_{12}(X) \\ \\ G_{21}(X) & G_{22}(X) \end{pmatrix},$$

where,

$$\begin{aligned}
G_{11}(X) &= \frac{\partial g_1}{\partial I^*} \\
&= \frac{-\eta d\pi(\eta d\beta_1 + \eta\beta_2(\mu+\delta) + \lambda d\xi + \lambda\alpha(\mu+\delta))}{(\mu+\delta+\gamma)[\mu\eta d + I^*(\eta d\beta_1 + \eta\beta_2(\mu+\delta) + \lambda d\xi + \lambda\alpha(\mu+\delta)) + I_b^*(\lambda d\sigma + \eta d\beta_0)]^2} \\
&\quad \times \left[\beta_1 I^* + \beta_2\frac{(\mu+\delta)}{d}I^* + \lambda\frac{(d\sigma I_b^* + d\xi I^* + \alpha(\mu+\delta)I^*)}{\eta d} + \beta_0 I_b^*\right] \\
&\quad + \frac{\eta d\pi\left[\beta_1 + \beta_2\frac{\mu+\delta}{d} + \lambda\frac{(d\xi+\alpha(\mu+\delta))}{\eta d}\right]}{(\mu+\delta+\gamma)[\mu\eta d + I^*(\eta d\beta_1 + \eta\beta_2(\mu+\delta) + \lambda d\xi + \lambda\alpha(\mu+\delta)) + I_b^*(\lambda d\sigma + \eta d\beta_0)]^2} \\
&\quad \times [\mu\eta d + I^*(\eta d\beta_1 + \eta\beta_2(\mu+\delta) + \lambda d\xi + \lambda\alpha(\mu+\delta)) + I_b^*(\lambda d\sigma + \eta d\beta_0)].
\end{aligned}$$

$$\begin{aligned}
G_{12}(X) &= \frac{\partial g_1}{\partial I_b^*} \\
&= \frac{-\eta d\pi(\lambda d\sigma + \eta d\beta_0)}{(\mu+\delta+\gamma)[\mu\eta d + I^*(\eta d\beta_1 + \eta\beta_2(\mu+\delta) + \lambda d\xi + \lambda\alpha(\mu+\delta)) + I_b^*(\lambda d\sigma + \eta d\beta_0)]^2} \\
&\quad \times \left[\beta_1 I^* + \beta_2\frac{(\mu+\delta)}{d}I^* + \lambda\frac{(d\sigma I_b^* + d\xi I^* + \alpha(\mu+\delta)I^*)}{\eta d} + \beta_0 I_b^*\right] \\
&\quad + \frac{\eta d\pi}{(\mu+\delta+\gamma)[\mu\eta d + I^*(\eta d\beta_1 + \eta\beta_2(\mu+\delta) + \lambda d\xi + \lambda\alpha(\mu+\delta)) + I_b^*(\lambda d\sigma + \eta d\beta_0)]^2} \\
&\quad \times \left(\frac{\lambda\sigma}{\eta} + \beta_0\right)[\mu\eta d + I^*(\eta d\beta_1 + \eta\beta_2(\mu+\delta) + \lambda d\xi + \lambda\alpha(\mu+\delta)) + I_b^*(\lambda d\sigma + \eta d\beta_0)],
\end{aligned}$$

$$\begin{aligned}
G_{21}(X) &= \frac{\partial g_2}{\partial I^*} \\
&= \frac{-\eta d(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))}{[\eta d\mu_b + I_b^*(\eta d\beta_4 + \lambda_b d\sigma) + I^*(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))]^2} \\
&\quad \times \left[\frac{\beta_4\pi_b}{\mu_b}I_b + \frac{\lambda_b\pi_b}{\mu_b\eta d}(d\sigma I_b^* + d\xi I^* + \alpha(\mu+\delta)I^*)\right], \\
&\quad + \frac{\eta d\left[\frac{\lambda_b\pi_b}{\mu_b\eta d}(d\xi + \alpha(\mu+\delta))\right]}{[\eta d\mu_b + I_b^*(\eta d\beta_4 + \lambda_b d\sigma) + I^*(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))]^2} \\
&\quad \times [\eta d\mu_b + I_b^*(\eta d\beta_4 + \lambda_b d\sigma) + I^*(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))],
\end{aligned}$$

$$\begin{aligned}
G_{22}(X) &= \frac{\partial g_2}{\partial I_b^*} \\
&= \frac{-\eta d(\eta d\beta_4 + \lambda_b d\sigma))}{[\eta d\mu_b + I_b^*(\eta d\beta_4 + \lambda_b d\sigma) + I^*(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))]^2},
\end{aligned}$$

$$\times \left[\frac{\beta_4\pi_b}{\mu_b}I_b^* + \frac{\lambda_b\pi_b}{\mu_b\eta d}(d\sigma I_b^* + d\xi I^* + \alpha(\mu+\delta)I^*)\right]$$
$$+ \frac{\eta d[\frac{\beta_4\pi_b}{\mu_b} + \frac{\lambda_b\pi_b\sigma}{\mu_b\eta}]}{[\eta d\mu_b + I_b^*(\eta d\beta_4 + \lambda_b d\sigma) + I^*(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))]^2}$$
$$\times [\eta d\mu_b + I_b^*(\eta d\beta_4 + \lambda_b d\sigma) + I^*(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))].$$

To prove that $G(X)$ is monotone increasing, it is sufficient to show that $G_{21}(X)$ and $G_{12}(X)$ are non-negative for all X. Simple calculations lead us to:

$$G_{21} = \eta d\left[\frac{-(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))\left(\frac{\beta_4\pi_b}{\mu_b}I_b^* + \frac{\lambda_b\pi_b}{\mu_b\eta d}(d\sigma I_b^* + d\xi I^* + \alpha(\mu+\delta)I^*)\right)}{[\eta d\mu_b + I_b^*(\eta d\beta_4 + \lambda_b d\sigma) + I^*(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))]^2}\right]$$
$$+ \frac{\lambda_b\pi_b}{\mu_b}\left[\frac{(d\xi + \alpha(\mu+\delta))(\eta d\mu_b + I_b^*(\eta d\beta_4 + \lambda_b d\sigma) + I^*(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))}{[\eta d\mu_b + I_b^*(\eta d\beta_4 + \lambda_b d\sigma) + I^*(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))]^2}\right],$$
$$G_{21} = -\eta d\left[\frac{(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))\left(\frac{\beta_4\pi_b}{\mu_b}I_b^* + \frac{\lambda_b\pi_b}{\mu_b\eta d}(d\sigma I_b^* + d\xi I^* + \alpha(\mu+\delta)I^*)\right)}{[\eta d\mu_b + I_b^*(\eta d\beta_4 + \lambda_b d\sigma) + I^*(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))]^2}\right]$$
$$+ \eta d\left[\frac{(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))\left(\pi_b + \frac{\beta_4\pi_b}{\mu_b}I_b^* + \frac{\lambda_b\pi_b}{\mu_b\eta d}(d\sigma I_b^* + d\xi I^* + \alpha(\mu+\delta)I^*)\right)}{[\eta d\mu_b + I_b^*(\eta d\beta_4 + \lambda_b d\sigma) + I^*(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))]^2}\right] \geq 0.$$

Similarly,

$$G_{12} = \frac{-\eta b\pi(\lambda b\sigma + \eta b\beta_4)\left[\beta_1 I^* + \beta_2\frac{\mu+\delta}{d}I^* + \lambda\frac{(d\sigma I_b^* + d\xi I^* + \alpha(\mu+\delta)I^*)}{\eta d} + \beta_4 I_b^*\right]}{(\mu+\delta+\gamma)[\mu\eta d + I^*(\eta d\beta_1 + \eta\beta_2(\mu+\delta) + \lambda d\xi + \lambda\alpha(\mu+\delta)) + I_b^*(\lambda d\sigma + \eta d\beta_0)]^2}$$
$$+ \frac{\eta d\pi(\lambda b\sigma + \eta b\beta_4)\left[\mu + \beta_1 I^* + \beta_2\frac{\mu+\delta}{d}I^* + \lambda\frac{(d\sigma I_b^* + d\xi I^* + \alpha(\mu+\delta)I^*)}{\eta d} + \beta_4 I_b^*\right]}{(\mu+\delta+\gamma)[\mu\eta d + I^*(\eta d\beta_1 + \eta\beta_2(\mu+\delta) + \lambda d\xi + \lambda\alpha(\mu+\delta)) + I_b^*(\lambda d\sigma + \eta d\beta_0)]^2}$$
$$\geq 0$$

Therefore, $G(X)$ is monotone increasing. Moreover, $G(X)$ is a continuous and bounded function which satisfies $G(0) = 0$. Since $G'(0)$ is positive, it is an irreducible matrix.

Since $\rho(G'(0)) = \mathcal{R}_0$, it remains to prove that $G(X)$ is strictly sub-linear. Let $r \in]0,1[$ be a positive real number, simple computations show that,

$$\frac{rg_1(X)}{g_1(rX)} = \frac{\mu\eta d + rI^*(\eta d\beta_1 + \eta\beta_2(\mu+\delta) + \lambda d\xi + \lambda\alpha(\mu+\delta)) + rI_b^*(\lambda d\sigma + \eta d\beta_0)}{\mu\eta d + I^*(\eta d\beta_1 + \eta\beta_2(\mu+\delta) + \lambda d\xi + \lambda\alpha(\mu+\delta)) + I_b^*(\lambda d\sigma + \eta d\beta_0)} < 1,$$
$$\frac{rg_2(X)}{g_2(rX)} = \frac{\eta d\mu_b + rI_b^*(\eta d\beta_4 + \lambda_b d\sigma) + rI^*(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))}{\eta d\mu_b + I_b^*(\eta d\beta_4 + \lambda_b d\sigma) + I^*(\lambda_b d\xi + \lambda_b\alpha(\mu+\delta))} < 1.$$

Thus, $G(X)$ is strictly sub-linear. Now the application of Theorem 7.1 yields a unique positive fixed point of $G(X)$ iff $\mathcal{R}_0 > 1$. This completes the proof.

Appendix B: Proof of Theorem 4.7

Consider the linear Lyapunov function candidate:

$$L_{bh} = a_1 I + a_2 D + a_3 I_b + a_4 P$$

where a_1, a_2, a_3 and a_4 are positive constants to be determined shortly.

The derivative of $L_{bh:}$ in the direction of the vector field gives:

$$\begin{aligned} L'_{bh} = I[a_1\beta_1 S_0 - (\mu+\delta+\gamma)a_1 + a_2(\mu+\delta) + a_4\xi] + D[a_1\beta_2 S_0 - a_2 d + a_4\alpha] \\ + I_b[a_1\beta_0 S_0 + \beta_4 a_3 S_{0b} - a_3\mu_b + a_4\sigma] + P[a_1\lambda S_0 + \lambda_b a_3 S_{0b} - a_4\eta], \end{aligned}$$

with $S_0 = \frac{\pi}{\mu}$ and $S_{0b} = \frac{\pi_b}{\mu_b}$.

The a_i, $i = 1, \ldots, 4$ can be chosen such that :

$$\begin{cases} a_1\beta_2 S_0 - a_2 d + a_4\alpha = 0, \\ a_1\lambda S_0 + a_3\lambda_b S_{0b} - a_4\eta = 0, \\ a_1\beta_0 S_0 + a_3\beta_4 S_{0b} - a_3\mu_b + a_4\sigma = 0, \end{cases} \tag{7.8}$$

If we choose $a_1 = 1$, then $a_2 = \frac{\beta_2 S_0 + a_4\alpha}{d}$ and $a_4 = \frac{\lambda S_0 + a_3\lambda_b S_{0b}}{\eta}$.
From the third equation of (7.8) we have:

$$\begin{aligned} & \beta_0 S_0 + a_3\beta_4 S_{0b} - a_3\mu_b + \left(\tfrac{\lambda S_0 + a_3\lambda_b S_{0b}}{\eta}\right)\sigma = 0 \\ \iff \quad & \eta\beta_0 S_0 + \sigma\lambda S_0 + (\beta_4\eta S_{0b} - \mu_b\eta + \lambda_b\sigma S_{0b})a_3 = 0 \\ \iff \quad & \eta\beta_0 S_0 + \sigma\lambda S_0 + a_3\mu_b\eta\left(\tfrac{\pi_b(\eta\beta_4 + \lambda_b\sigma)}{\eta\mu_b^2} - 1\right) = 0 \\ \iff \quad & \eta\beta_0 S_0 + \sigma\lambda S_0 + a_3\mu_b\eta(\mathcal{R}_{0b} - 1) = 0. \end{aligned}$$

Since $\mathcal{R}_0 < 1$ implies $\mathcal{R}_{0b} < 1$, we have $a_3 = \frac{\eta\beta_0 S_0 + \sigma\lambda S_0}{\mu_b\eta(1-\mathcal{R}_{0b})} > 0$,

$$a_4 = S_0\left(\frac{\lambda\mu_b\eta(1-\mathcal{R}_{0b}) + (\eta\beta_0 + \sigma\lambda)\lambda_b S_{0b}}{\mu_b\eta^2(1-\mathcal{R}_{0b})}\right) > 0$$

and

$$a_2 = \frac{\mu_b\eta^2\beta_2 S_0(1-\mathcal{R}_{0b}) + \alpha S_0[\lambda\mu_b\eta(1-\mathcal{R}_{0b}) + (\eta\beta_0 + \sigma\lambda)\lambda_b S_{0b}]}{\mu_b d\eta^2(1-\mathcal{R}_{0b})} > 0.$$

Consequently,

$$\begin{aligned} L'_{bh} &= I\left[\beta_1 S_0 - (\mu+\delta+\gamma)\right] \\ &\quad + \left[\frac{\mu_b\eta^2\beta_2 S_0(1-\mathcal{R}_{0b}) + \alpha S_0[\lambda\mu_b\eta(1-\mathcal{R}_{0b}) + (\eta\beta_0 + \sigma\lambda)\lambda_b S_{0b}]}{\mu_b d\eta^2(1-\mathcal{R}_{0b})}\right](\mu+\delta)I \\ &\quad + S_0\xi\left(\frac{\lambda\mu_b\eta(1-\mathcal{R}_{0b}) + (\eta\beta_0 + \sigma\lambda)\lambda_b S_{0b}}{\mu_b\eta^2(1-\mathcal{R}_{0b})}\right)I \\ &= I\Bigg[\beta_1 S_0 - (\mu+\delta+\gamma) + \frac{\beta_2(\mu+\delta)S_0}{d} + \frac{\alpha S_0(\mu+\delta)\lambda}{d\eta} + \frac{S_0\xi\lambda}{\eta} \\ &\quad + \frac{(\mu+\delta)\alpha S_0(\eta\beta_0 + \sigma\lambda)\lambda_b S_{0b} + (\eta\beta_0 + \sigma\lambda)\lambda_b S_{0b} S_0\xi d}{\mu_b d\eta^2(1-\mathcal{R}_{0b})}\Bigg] \\ &= I\left[(\mu+\delta+\gamma)(\mathcal{R}_{0H} - 1) + \frac{(\eta\beta_0 + \sigma\lambda)\lambda_b S_{0b} S_0(\alpha(\mu+\delta) + \xi d)}{\mu_b d\eta^2(1-\mathcal{R}_{0b})}\right] \\ &= I\left[(\mu+\delta+\gamma)(\mathcal{R}_{0H} - 1) + \frac{R_1 R_2(\mu+\delta+\gamma)}{(1-\mathcal{R}_{0b})}\right] \\ &= I\frac{(\mu+\delta+\gamma)}{(1-\mathcal{R}_{0b})}\left[\mathcal{R}_{0H} + \mathcal{R}_{0b} + R_1 R_2 - \mathcal{R}_{0b}\mathcal{R}_{0H} - 1\right]. \end{aligned}$$

From the expression of $\mathcal{R}_0$, one has

$$R_1R_2 = \frac{[2\mathcal{R}_0 - (\mathcal{R}_{0H} + \mathcal{R}_{0b})]^2 - (\mathcal{R}_{0H} - \mathcal{R}_{0b})^2}{4}.$$

Therefore, Since $1 > \mathcal{R}_0 \geq \max(\mathcal{R}_{0b}; \mathcal{R}_{0H})$,

$$\begin{aligned}
L'_{bh} &= I\frac{(\mu+\delta+\gamma)}{(1-\mathcal{R}_{0b})}\left[\mathcal{R}_{0H} + \mathcal{R}_{0b} + \frac{[2\mathcal{R}_0 - (\mathcal{R}_{0H} + \mathcal{R}_{0b})]^2 - (\mathcal{R}_{0H} - \mathcal{R}_{0b})^2}{4} - \mathcal{R}_{0H}\mathcal{R}_{0b} - 1\right] \\
&= I\frac{(\mu+\delta+\gamma)}{(1-\mathcal{R}_{0b})}\left[\mathcal{R}_{0H} + \mathcal{R}_{0b} + \frac{(2\mathcal{R}_0 - 2\mathcal{R}_{0H})(2\mathcal{R}_0 - 2\mathcal{R}_{0b})}{4} - \mathcal{R}_{0H}\mathcal{R}_{0b} - 1\right] \\
&= I\frac{(\mu+\delta+\gamma)}{(1-\mathcal{R}_{0b})}\left[\mathcal{R}_{0H} + \mathcal{R}_{0b} + \mathcal{R}_0^2 - \mathcal{R}_0\mathcal{R}_{0H} - \mathcal{R}_0\mathcal{R}_{0b} - 1\right] \\
&= I\frac{(\mu+\delta+\gamma)}{(1-\mathcal{R}_{0b})}\left[\mathcal{R}_{0H}(1-\mathcal{R}_0) + \mathcal{R}_{0b}(1-\mathcal{R}_0) + \mathcal{R}_0^2 - 1\right] \\
&= I\frac{(\mu+\delta+\gamma)(1-\mathcal{R}_0)}{(1-\mathcal{R}_{0b})}\left[(\mathcal{R}_{0H} - \mathcal{R}_0) + (\mathcal{R}_{0b} - 1)\right] \leq 0.
\end{aligned}$$

Moreover, the largest invariance subset contained in the set $\{X \in \mathbb{R}_+^7 / L'_{bh}(X) = 0\}$ when $\mathcal{R}_0 < 1$ is $\{E_{bh}\}$. The conclusion follows by LaSalle's Invariance Principle [26].

Appendix C: Proof of Theorem 4.8

Set

$$\begin{aligned}
D_1 &= S - S^* - S^* \ln\frac{S}{S^*} + I - I^* - I^* \ln\frac{I}{I^*}, \\
D_2 &= 2\left(S_b - S_b^* - S_b^* \ln\frac{S_b}{S_b^*}\right) + 2\left((I_b - I_b^* - I_b^* \ln\frac{I_b}{I_b^*}\right), \\
D_3 &= 2\left(D - D^* - D^* \ln\frac{D}{D^*}\right), \\
D_4 &= P - P^* - P^* \ln\frac{P}{P^*}.
\end{aligned}$$

Then,

$$\begin{aligned}
D'_1 = {} & \frac{S-S^*}{S}\left(\mu S^* + \beta_1 S^* I^* + \beta_2 S^* D^* + \lambda P^* S^* + \beta_0 S^* I_b^* - \mu S - \beta_1 SI - \beta_2 SD - \lambda PS - \beta_0 SI_b\right) \\
& + \frac{I-I^*}{I}\left((\beta_1 SI + \beta_2 SD + \lambda PS + \beta_0 SI_b - \beta_1 S^* I - \beta_2 \frac{S^* D^* I}{I^*} - \lambda \frac{S^* P^* I}{I^*} - \beta_0 \frac{S^* I_b^* I}{I^*}\right) \\
D'_1 = {} & -\mu\frac{(S-S^*)^2}{S} + \beta_1 S^* I^*\left(2 - \frac{S^*}{S} + \frac{I}{I^*} - \frac{SII^*}{S^* I^* I} - \frac{I}{I^*}\right) \\
& + \beta_2 S^* D^*\left(2 - \frac{S^*}{S} + \frac{D}{D^*} - \frac{SDI^*}{S^* D^* I} - \frac{I}{I^*}\right) + \lambda P^* S^*\left(2 - \frac{S^*}{S} + \frac{P}{P^*} - \frac{SPI^*}{S^* P^* I} - \frac{I}{I^*}\right) \\
& + \beta_0 I_b^* S^*\left(2 - \frac{S^*}{S} + \frac{I_b}{I_b^*} - \frac{SI_b I^*}{S^* I_b^* I} - \frac{I}{I^*}\right).
\end{aligned}$$

Here, it is instrumental to show that

$$2 - \frac{S^*}{S} + \frac{D}{D^*} - \frac{SDI^*}{S^* D^* I} - \frac{I}{I^*} \leq \frac{D}{D^*} - \frac{I}{I^*} - \ln\frac{D}{D^*} + \ln\frac{I}{I^*},$$

which is equivalent to

$$2-\frac{S^*}{S}-\frac{SDI^*}{S^*D^*I}\leq \ln\frac{ID^*}{I^*D}.$$

Since $1-x+\ln x\leq 0$ for $x>0$, one has for $x=\dfrac{SDI^*}{S^*D^*I}$,

$$1-\frac{SDI^*}{S^*D^*I}\leq -\ln\frac{SDI^*}{S^*D^*I}\Longleftrightarrow 1-\frac{SDI^*}{S^*D^*I}+\ln\frac{S}{S^*}\leq \ln\frac{ID^*}{I^*D}.$$

Similarly,

$$1-\frac{S^*}{S}\leq \ln\frac{S}{S^*}.$$

Combining the last two equations we obtain the desired result. Thus,

$$\begin{aligned}
D_1' &\leq \beta_1 S^*I^*\left(\frac{I}{I^*}-\frac{I}{I^*}-\ln\frac{I}{I^*}+\ln\frac{I}{I^*}\right)+\beta_2 S^*D^*\left(\frac{D}{D^*}-\frac{I}{I^*}-\ln\frac{D}{D^*}+\ln\frac{I}{I^*}\right)\\
&\quad+\beta_0 S^*I_b^*\left(\frac{I_b}{I_b^*}-\frac{I}{I^*}-\ln\frac{I_b}{I_b^*}+\ln\frac{I}{I^*}\right)+\lambda P^*S^*\left(\frac{P}{P^*}-\frac{I}{I^*}-\ln\frac{P}{P^*}+\ln\frac{I}{I^*}\right)\\
&:= a_{13}G_{13}+a_{12}G_{12}+a_{14}G_{14},
\end{aligned}$$

where

$$\begin{aligned}
a_{13}&=\beta_2 S^*D^*, \qquad G_{13}=\left(\frac{D}{D^*}-\frac{I}{I^*}-\ln\frac{D}{D^*}+\ln\frac{I}{I^*}\right),\\
a_{12}&=\beta_0 S^*I_b^*, \qquad G_{12}=\left(\frac{I_b}{I_b^*}-\frac{I}{I^*}-\ln\frac{I_b}{I_b^*}+\ln\frac{I}{I^*}\right),\\
a_{14}&=\lambda P^*S^*, \qquad G_{14}=\left(\frac{P}{P^*}-\frac{I}{I^*}-\ln\frac{P}{P^*}+\ln\frac{I}{I^*}\right),
\end{aligned}$$

$$\begin{aligned}
D_2' &= \frac{2\left(S_b-S_b^*\right)}{S_b}\left(\mu_b S_b^*+\beta_4 S_b^*I_b^*+\lambda_b P^*S_b^*-\mu_b S_b-\beta_4 S_bI_b-\lambda_b PS_b\right)\\
&\quad+\frac{2(I_b-I_b^*)}{I_b}\left(\beta_4 S_bI_b+\lambda_b S_bP-\beta_4 S_b^*I_b-\lambda_b\frac{S_b^*P^*I_b}{I_b^*}\right)\\
&= -2\mu_b\frac{(S_b-S_b^*)^2}{S_b}+2\beta_4 S_b^*I_b^*\left(2-\frac{S_b^*}{S_b}+\frac{I_b}{I_b^*}-\frac{S_bI_bI_b^*}{S_b^*I_b^*I_b}-\frac{I_b}{I_b^*}\right)\\
&\quad+2\lambda_b S_b^*P^*\left(2-\frac{S_b^*}{S_b}+\frac{P}{P^*}-\frac{S_bPI_b^*}{S_b^*P^*I_b}-\frac{I_b}{I_b^*}\right)\\
&\leq 2\beta_4 S_b^*I_b^*\left(\frac{I_b}{I_b^*}-\frac{I_b}{I_b^*}-\ln\frac{I_b}{I_b^*}+\ln\frac{I_b}{I_b^*}\right)+2\lambda_b P^*S_b^*\left(\frac{P}{P^*}-\frac{I_b}{I_b^*}-\ln\frac{P}{P^*}+\ln\frac{I_b}{I_b^*}\right)\\
&:= a_{24}G_{24},
\end{aligned}$$

where

$$a_{24}=\lambda_b P^*S_b^*,\ G_{24}=2\left(\frac{P}{P^*}-\frac{I_b}{I_b^*}-\ln\frac{P}{P^*}+\ln\frac{I_b}{I_b^*}\right).$$

$$\begin{aligned} D_3 =& \frac{2(D-D^*)}{D}\left((\mu+\delta)I-(\mu+\delta)\frac{I^*D}{D^*}\right) \\ &= 2(\mu+\delta)I^*\left(\frac{I}{I^*}-\frac{D^*I}{DI^*}-\frac{D}{D^*}+1\right) \\ &\leq 2(\mu+\delta)I^*\left(\frac{I}{I^*}-\ln\frac{I}{I^*}-\frac{D}{D^*}+\ln\frac{D}{D^*}\right) \\ &:= a_{31}G_{31}, \end{aligned}$$

where

$$a_{31}=(\mu+\delta)I^*, \qquad G_{31}=2\left(\frac{I}{I^*}-\ln\frac{I}{I^*}-\frac{D}{D^*}+\ln\frac{D}{D^*}\right).$$

$$\begin{aligned} D_4' &= \frac{P-P^*}{P}\left(\sigma I_b+\alpha D+\xi I-\sigma\frac{I_b^*P}{P^*}-\xi\frac{I^*P}{P^*}-\alpha\frac{D^*P}{P^*}\right) \\ &= \sigma I_b^*\left(\frac{I_b}{I_b^*}-\frac{I_bP^*}{I_b^*P}-\frac{P}{P^*}+1\right) \\ &\quad +\xi I^*\left(\frac{I}{I^*}-\frac{IP^*}{I^*P}-\frac{P}{P^*}+1\right)+\alpha D^*\left(\frac{D}{D^*}-\frac{DP^*}{D^*P}-\frac{P}{P^*}+1\right). \end{aligned}$$

$$\begin{aligned} D_4' \leq{}& \sigma I_b^*\left(\frac{I_b}{I_b^*}-\ln\frac{I_b}{I_b^*}-\frac{P}{P^*}+\ln\frac{P}{P^*}\right)+\xi I^*\left(\frac{I}{I^*}-\ln\frac{I}{I^*}-\frac{P}{P^*}+\ln\frac{P}{P^*}\right) \\ &+\alpha D^*\left(\frac{D}{D^*}-\ln\frac{D}{D^*}-\frac{P}{P^*}+\ln\frac{P}{P^*}\right) \\ :={}& a_{42}G_{42}+a_{41}G_{41}+a_{43}G_{43}, \end{aligned}$$

where

$$\begin{aligned} a_{42}&=\sigma I_b^*, & G_{42}&=\left(\frac{I_b}{I_b^*}-\ln\frac{I_b}{I_b^*}-\frac{P}{P^*}+\ln\frac{P}{P^*}\right), \\ a_{41}&=\xi I^*, & G_{41}&=\left(\frac{I}{I^*}-\ln\frac{I}{I^*}-\frac{P}{P^*}+\ln\frac{P}{P^*}\right), \\ a_{43}&=\alpha D^*, & G_{43}&=\left(\frac{D}{D^*}-\ln\frac{D}{D^*}-\frac{P}{P^*}+\ln\frac{P}{P^*}\right). \end{aligned}$$

Simple calculations yield

$$G_{41}+G_{24}+G_{12}+G_{43}+G_{14}+G_{13}+G_{31}+G_{42}=0.$$

Thus, following [33], there exist $(c_i)_{1\leq i\leq 4}$ such that $D=\sum_{i=1}^{4}c_iD_i$ is a Lyapunov function.

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References

[1] F. B. Agusto, M. I. Teboh-Ewungkem, A. B. Gumel, Mathematical assessment of the effect of traditionnal beliefs and customs on the transmission dynamics of the 2014 Ebola outbreaks, *BMC* **13**(2015), No. 96, 1–18. https://doi.org/10.1186/s12916-015-0318-3.

[2] F. B. Agusto, Mathematical model of Ebola transmission dynamics with relapse and re-infection, *Math. Biosci.* **283**(2017), 48–59. https://doi.org/10.1016/j.mbs.2016.11.002; MR3584919

[3] S. Aina, J. Leendertz, J. F. Gogarten, A. Düx, S. Calvignac-Spencer, F. H. Lendertz, Assessing the evidence supporting fruit bats as the primary reservoirs of Ebola viruses, *EcoHealth* **13**(2016), 18–25. https://doi.org/10.1007/s10393-015-1053-0

[4] C. L. Althaus, N. Low, E. O. Musa, F. Schuaib, S. Gsteiger, Ebola virus disease outbreak in Nigeria: transmission dynamics and rapid control, *Epidemics* **11**(2015), 80–84. https://doi.org/10.1016/j.epidem.2015.03.001

[5] I. Area, F. Ndaïrou, J. J. Nieto, C. J. Silva, D. F. M. Torres, Ebola model and optimal controls with vaccination constraints, *J. Ind. Manag. Optim.* **278**(2017), 1–21. https://doi.org/10.3934/jimo.2017054

[6] P. Auger, E. Kouokam, G. Sallet, M. Tchuente, B. Tsanou, The Ross–Macdonald model in a patchy environment, *Math. Biosci.* **216**(2008), 123–131. https://doi.org/10.1016/j.mbs.2008.08.010; MR2476998

[7] M. Bani-Yaghoub, R. Gautam, Z. Shuai, P. van den Driessche, R. Ivanek, Reproduction number for infections with free-living pathogens growing in the environment, *J. Biol. Dyn.* **6**(2012), 923–940. https://doi.org/10.1080/17513758.2012.693206

[8] M. V. Barbarossa, A. Dénes, G. Kiss, Y. Nakata, G. Röst, Z. Vizi, Transmission dynamics and final epidemic size of Ebola Virus Disease outbreaks with varying interventions, *Plos One* **10**(2015), No. 7, e0131398. https://doi.org/10.1371/journal.pone.0131398

[9] T. Berge, J. M.-S. Lubuma, G. M. Moremedi, N. Morris, R. Kondera-Shava, A simple mathematical model for Ebola in Africa, *J. Biol. Dyn.* **11**(2017), No. 1, 42–74. https://doi.org/10.1080/17513758.2016.1229817; MR3733426

[10] T. Berge, S. Bowong, J. M.-S. Lubuma, M. L. M. Manyombe, Modelling Ebola virus disease transmissions with reservoir in a complex virus life ecology, *Math. Biosci. Eng.* **15**(2018), 21–56. https://doi.org/10.3934/mbe.2018002.; MR3707035

[11] K. Bibby, R. J. Fisher, L. W. Casson, E. Stachler, C. N. Haas, Ebola virus persistence in the environment: state of the knowledge and research needs, *Environ. Sci. Technol. Lett.* **2**(2015), No. 9, 245–249. https://doi.org/10.1021/ez5003715

[12] E. N. Bodine, C. Cook, M. Shorten, The potential impact of a prophylactic vaccine for Ebola virus disease in Sierra Leone, *Math. Biosci. Eng.* **15**(2018), 337–359. https://doi.org/10.3934/mbe.2018015; MR3707048

[13] C. Castillo-Chavez, B. Song, Dynamical models of tuberculosis and their applications, *Math. Biosci. Eng.* **1**(2004), No. 2, 261–404. https://doi.org/10.3934/mbe.2004.1.361; MR2130673

[14] CDC, Ebolavirus Ecology, https://www.cdc.gov/vhf/ebola/pdf/ebola_ecology_800px.pdf

[15] G. Chowell, N. W. Hengartner, C. Castillo-Chavez, P. W. Fenimore, J. M. Hyman, The basic reproductive number of Ebola and the effects of public health measures: the cases of Congo and Uganda, *J. Theor. Biol.* **229**(2004), 119–126. https://doi.org/10.1016/j.jtbi.2004.03.006; MR2082775

[16] G. Chowell, H. Nishiura, Transmission dynamics and control of Ebola Virus Disease (EVD), *BMC* **12**(2014), No. 196, 2–16. https://doi.org/10.1186/s12916-014-0196-0

[17] M. Diaby, A. Iggidr, M. Sy, A. Sène, Global analysis of a schistosomiasis infection model with biological control, *J. Appl. Math. Comput.* **246**(2014), 731–742. https://doi.org/10.1016/j.amc.2014.08.061; MR3265908

[18] J. M. Drake, R. B. Kaul, L. W. Alexander, S. M. O. Regan, A. M. Kramer, J. T. Pulliam, M. J. Ferrari, A. W. Park, Ebola cases and health system demand in Liberia, *PLOS Biol.* **13**(2015), No. 1, 1–20. https://doi.org/10.1371/journal.pbio.1002056

[19] M. O. Durojaye, I. J. Ajie, Mathematical model of the spread and control of Ebola Virus Disease, *Appl. Math.* **7**(2017), 23–31. https://doi.org/10.5923/j.am.20170702.02

[20] F. O. Fasina, A. Shittu, D. Lazarus, O. Tomori, L. Simonsen, C. Viboud, G. Chowell, Transmission dynamics and control of Ebola Virus Disease outbreak in Nigeria, *Euro. Surveil.* **19**(2014), No. 40, 1–8. https://doi.org/10.1016/j.epidem.2015.03.001

[21] H. Gumsova, A. Shittu, M. Sanbul, H. Leblebicioglu, Ebola Virus Disease and the veterinary perspective, *BMC* **14**(2015), No. 30, 1–5. https://doi.org/10.1186/s12941-015-0089-x

[22] J. A. P. Heesterbeek, M. G. Roberts, The type-reproduction number T in models for infectious disease control, *Math. Biosci.* **206**(2007), 3–10. https://doi.org/10.1016/j.mbs.2004.10.013; MR2311668

[23] H. W. Hethcote, H. R. Thieme, Stability of the endemic equilibrium in epidemic models with subpopulations, *Math. Biosci.* **75**(1985), 205–227. https://doi.org/10.1016/0025-5564(85)90038-0; MR0810991

[24] B. Ivorra, D. Ngom, A. M. Ramos, A mathematical model to predict the risk of human disease spread between countries-validation and application to 2014–2015 Ebola Virus Disease epidemic, *Bull. Math. Biol.* **77**(2015), 1668–1704. https://doi.org/10.1007/s11538-015-0100-x; MR3423058

[25] D. Knipl, A new approach for designing disease intervention strategies in metapopulation models, *J. Biol. Dyn.* **10**(2016), 71–94. https://doi.org/10.1080/17513758.2015.1107140; MR3546133

[26] J. P. LaSalle, The stability of dynamical systems, *SIAM*, (1976), 51–55. MR0481301

[27] J. Legrand, R. F. Grais, P. Y. Boelle, A. J. Valleron, A. Flahault, Understanding the dynamics of Ebola epidemics, *Epidemiol. Infect.* **135**(2007), 610–621. https://doi.org/10.1017/s0950268806007217

[28] J. O. Lloyd-Smith, P. C. Cross, C. J. Briggs, M. Daugherty, W. M. Getz, J. Latto, M. S. Sanchez, A. B. Smith, A. Swei, Should we expect population thresholds for wildlife disease? *Trends Ecol. Evolution* **20**(2005), 511–519. https://doi.org/10.1016/j.tree.2005.07.004

[29] D. Ndanguza, J. M. Tchuenche, H. Haario, Statistical data analysis of the 1995 Ebola outbreak in the Democratic Republic of Congo, *Afr. Mat.* **24**(2013), 55–68. https://doi.org/10.1007/s13370-011-0039-5; MR3019805

[30] T. J. Piercy, S. J. Smither, J. A. Steward, L. Eastaugh, M. S. Lever, The survival of filoviruses in liquids, on solid substrates and in a dynamics aerosol, *J. Appl. Microbiol.* **109**(2010), 1531–1539. https://doi.org/10.1111/j.1365-2672;2010.04778.x

[31] A. Rachah, D. F. M. Torres, Optimal control strategies for the spread of Ebola in West Africa, *J. Math. Anal.* **7**(2016), 102–114. https://doi.org/10.1155/2015/842792; MR3476198

[32] M. Roberts, First Ebola boy likely infected by playing in bat tree, *BBC*, 30 December 2014, www.bbc.com/news/health-30632453.

[33] Z. Shuai, P. van den Driessche, Global stability of infections disease models using Lyapunov functions, *SIAM J. Appl. Math.* **73**(2013), No. 4, 1513–1532. https://doi.org/10.1137/120876642

[34] Z. Shuai, J. A. P. Heesterbeek, P. van Den Driessche, Extending the type reproduction number to infectious disease control targeting contact between types, *J. Math. Biol.* **67**(2013), 255–257. https://doi.org/10.1007/s00285-012-0579-9; MR3111982

[35] Z. Shuai, J. A. P. Heesterbeek, P. van den Driessche, Erratum to: Extending the type reproduction number to infectious disease control targeting contact between types, *J. Math. Biol.* **71**(2015), 1067–1082. https://doi.org/10.1007/s00285-012-0579-9; MR3345968

[36] B. Tsanou, S. Bowong, J. Mbang, J. Lubuma, Assessing the impact of the environmental contamination on the transmission of Ebola Virus Disease (EVD), *J. Appl. Math. Comput.* **55**(2017), 205-243. https://doi.org/10.1007/s12190-016-1033-8; MR3694945

[37] P. van den Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, *Math. Biosci.* **180**(2002), 29–48. https://doi.org/10.1016/S0025-5564(02)00108-6; MR1950747

[38] M. Vidyasagar, Decomposition techniques for large-scale systems with nonadditive interactions: stability and stabilizability, *IEEE Trans. Autom. Control* **25**(1980), 773–779. https://doi.org/10.1109/TAC.1980.1102422; MR0583455

[39] X.-S. Wang, L. Zhong, Ebola outbreak in West Afica: real-time estimation and multiple-wave prediction, *Math. Biosci. Eng.* **12**(2015), No. 5, 1055–1063. https://doi.org/103934/mbe.2015.12.1055; MR3356525

[40] G. F. Webb, C. J. Browne, A model of the Ebola epidemics in West Africa incorporating age of infection, *J. Biol. Dyn.* **10**(2015), No. 1, 18–30. https://doi.org/10.1080/17513758.2015.1090632; MR3546130

[41] S. Wiafe, E. Veilleux-Gravel, R. Smith, Using sensitivity analysis to examine the effects of an Ebola vaccine, in: *SummerSim'17, Proceedings of the Summer Simulation Multi-Conference*, Art. No. 12, pp. 61–72.

[42] D. Youkee, C. S. Brown, P. Lilburn, N. Shetty, T. Brooks, A. Simpson, N. Bentley, M. Lado, T. B. Kamara, N. F. Walker, O. Johnson, Assessment of environmental contamination and environmental decontamination practices within an Ebola unit, Freetown, Sierra Leone, *PLOS One* **10**(2015), No. 12, 1–10. https://doi.org/10.1371/journal.pone.0145167