Cooperative system analysis of the Ebola virus epidemic model

Karima Kablia, Soumia El Moujaddida, Khadija Niri, Abdessamad Tridane

Abstract

This paper aims to study the global stability of an Ebola virus epidemic model. Although this epidemic ended in September 2015, it devastated several West African countries and mobilized the international community. With the recent cases of Ebola in the Democratic Republic of the Congo (DRC), the threat of the reappearance of this fatal disease remains. Therefore, we are obligated to be prepared for a possible re-emerging of the disease. In this work, we investigate the global stability analysis via the theory of cooperative systems, and we determine the conditions that lead to global stability disease-free and endemic equilibrium.

1. Introduction

The Ebola Virus Disease (EVD) is a type of hemorrhagic fever caused by an infection from a virus of the Filoviridae family. Since 1976, five species of this virus have been identified; the most recent virus that caused the 2014–2015 outbreak in West Africa is one of them. This recent epidemic has been the deadliest with 28514 cases and 11313 deaths (Center for Disease Control, 2014). The case fatality rate of this outbreak has been different in different affected countries with Guinea (60%), Liberia (42%), and Sierra Leone (22%) (World Health Organization, 2017).

The natural host of the virus and how humans get infected by the virus, in the first place (World Health Organization, 2015), are among the many issues that have not yet been understood regarding this virus. The human-human infection, can happen in several ways such as via direct contact with body fluids of an infected person, contaminated needles, sexual contact (Johns Hopkins Medicine He), and direct contact with a dead person in funeral rites (Manguvo & Mafuvadze, 2015).

Mathematical modeling of the EVD has been the subject of many papers that attempted to study the epidemiological aspects of this disease or its dynamical aspects (Agusto, 2017; Althaus, 2014; Berge, Lubuma, Moremedi, Morris, & Kondera-Shava, 2017; Bodine, Cook, & Shorten, 2018; Browne, Gulbudak, & Webb, 2015; Chowell & Nishiura, 2014; Legrand, Freeman Grais, Boelle, Valleron, & Antoine, 2007; Vittoria Barbarossa et al., 2015; Webb & Browne, 2016; Weitz and Dushoff, 2015;
Wong, Bui, Chughtai, & Macintyre, 2017). From an epidemiological point of view, mathematical models were used to estimate the basic reproduction number, $R_0$ (Althaus, 2014; Bodine et al., 2018; Browne et al., 2015; Legrand et al., 2007; Wong et al., 2017), find the final epidemic size (Vittoria Barbarossa et al., 2015), estimate the effectiveness of interventions during the outbreak (Chowell & Nishiura, 2014), and finally to determine the control measure that stopped the spread from the dead bodies infected by the EVD (Weitz and Dushoff, 2015). On the other hand, the mathematical analysis the dynamic of the EVD models was investigated in (Agusto, 2017; Berge et al., 2017; Webb & Browne, 2016) by considering constant recruitment rate of the population (Agusto, 2017; Berge et al., 2017), where the standard Lyapunov approach was used to prove the global stability. The disease age density was also used to fit the data of the West African outbreak (Webb & Browne, 2016).

In this work, we propose a deterministic model to describe the spread the EVD that includes a non-constant recruitment of the population. The idea behind this assumption is the fact that the fertility rate in the African countries in general, and the countries which were infected by the recent outbreak in particular, is very high. Therefore, in order to have a better understanding of the dynamic of the disease in the coming years, we have to consider a non-constant recruitment of the population. With such an assumption, the considered model becomes a cooperative system.

The literature of cooperative dynamical systems is very rich. Muller (Müller, 1927) and Kamke (Kamke, 1932) were the first to apply monotone methods to differential equations. Later, Hirsch applied these results to dynamical systems and proved several results in this theory (Hirsch, 1982, 1983; Hirsch, 1990). The work of Smith and his collaborators (Smith & Thieme, 1990, 1991; Hirsch & Smith, 2005; Smith, 2008) improved the results of the Hirsch and used the theory of cooperative and irreducible systems in different types of ODEs with applications to biological systems. The application of the theory of cooperative systems in the epidemiological model is given in (Iggidr, Niri, & Moulay Ely, 2010), more recent works in (Niri, Kabli, & El moujaddid, 2015), and an epidemiological model with delay in (El Karkri & Niri, 2014; Niri & El Karkri, 2015).

We apply this theory to study the stability of the model of Ebola by showing that the theory of cooperative and irreducible systems could be an alternative to Lyapunov functions.

This paper is organized as follows: In the next section, section 2, we present the EVD model. The preliminary results of our analysis are in section 3, where we prove that the system is cooperative and irreducible, and we calculated the two disease thresholds, including the basic reproduction number. The local stability analysis is also given in this section. In section 4, we prove our main result: sufficient conditions of global stability for the endemic disease equilibrium. In Section 5, we present numerical simulations and support our results. Finally, the conclusion is given in Section 6, and Appendix is in Section A.

2. Introduction of the model

We adopted the model of Legrand et al. (Legrand et al., 2007) by ignoring the class of people that are dead but not yet buried. Ignoring such a class can be accepted as a modeling convention because the problem of the infection between people and the dead bodies before being buried was identified and controlled by the international community in their intervention to stop the spread of the disease via this route (Manguvo & Mafuvadze, 2015; WONG et al., 2017). Hence, our model described by the flow diagram in Fig. 1 is given by

$$
\begin{align*}
\dot{S} &= \alpha N - \mu S - \frac{\beta_I S I}{N} - \frac{\beta_H S H}{N} \\
\dot{E} &= \frac{\beta_I S I}{N} + \frac{\beta_H S H}{N} - (\mu + \sigma)E \\
\dot{I} &= \sigma E - (\mu_H + \mu_Q + \mu + \mu_R)I \\
\dot{H} &= \mu_H I - (\mu' + \mu + \mu' R)H \\
\dot{R} &= \mu_R I - \mu R + \mu' R H,
\end{align*}
$$

(1)

where $S$ is susceptible individuals, $E$ is a class of exposed people by the close contacts with infectious individuals; and people in $E$ could become infectious after an incubation period. Once people in $E$ become infectious, they are moved to $I$. A proportion
of infected people might be hospitalized and hence moved to $H$. The infected untreated people in $I$ and the infected hospitalized patients in $H$ may die or recover and hence moved to $R$. $N = S + E + I + H + R$ is the total population. Note that the population growth is proportional to the total population as expressed in $\alpha N$ in (1). Hence, we have a varying total population size. Table 1 gives the definition of all the parameters used in the model.

To proceed with our analysis, we made the following accepted assumptions:

i) The contact rate between susceptible and infected individuals is always superior to death rate due to infection $\beta_I > \mu_Q$.

ii) The contact rate between susceptible and hospitalized individuals is always superior to death rate due to infection at the hospital $\beta_H > \mu'$.

These assumptions will help us to prove the uniqueness of the endemic equilibrium point.

3. Preliminary analysis

The dimensionless form of the model (1) is given by

$$\begin{align*}
\dot{s} &= \alpha - \beta_I s i - \beta_H s h + \mu_Q s i + \mu' h - \alpha s \\
\dot{e} &= (\beta_I + \beta_H) s - (\alpha + \sigma) e + \mu Q e + \mu' e h \\
\dot{i} &= \sigma e - (\mu_Q + \mu_R + \mu_H + \alpha) i + \mu' i h + \mu_Q i^2 \\
\dot{h} &= \mu_H i - (\mu' + \mu_R + \alpha) h + \mu_Q h i + \mu' h^2 \\
\dot{r} &= \mu_R i + \mu' h r - \sigma r + \mu R r i + \mu' rh
\end{align*}$$

(2)

with

$$s = \frac{S}{N}, \quad e = \frac{E}{N}, \quad i = \frac{I}{N}, \quad h = \frac{H}{N} \quad \text{and} \quad r = \frac{R}{N}$$

(3)

In the rest of the paper we will study the system (2) in the positively invariant convex set:

$$\Sigma = \left\{(s, e, i, h, r) \in \mathbb{R}_+^5 : s + e + i + h + r \leq 1 \right\}$$

and formulate our results accordingly. The system (2) has other properties which play a key role in our analysis. That is system (2) is cooperative; this means that an increase in any compartment causes an increase of the growth rates of all the other compartments.

**Theorem 1.** The system (2) is cooperative and irreducible on $\Sigma$.

**Proof** The system is cooperative if the sign of the off diagonal of its Jacobian matrix is positive (see (Smith, 2008), p 34).

By replacing $i$ by $1 - s - e - h - r$ and $h$ by $1 - s - e - i - r$ in the first equation, and $e$ in the second equation by $1 - s - i - h - r$, then the Jacobian matrix of the system (2) becomes

| Table 1 | Parameters used in the model. |
|---------|--------------------------------|
| Parameter | Description                  |
| $\alpha$ | Birth rate                   |
| $\mu$   | Natural death                |
| $\beta_I$ | Contact rate between susceptible and infected individuals |
| $\beta_H$ | Contact rate between susceptible and hospitalized individuals |
| $1/\sigma$ | Incubation period           |
| $1/\mu_H$ | Time until hospitalization   |
| $\mu_R$  | Recovery rate of infectious people |
| $\mu'_R$ | Recovery rate of hospitalized people |
| $\mu_Q$  | Death rate due to infection |
| $\mu'$   | Death rate due to infection in hospital |
3.2. Calculation of the basic reproduction number

Proposition 1

3.1. Positivity of solutions

The next result shows that the solutions for the system are well-defined and are non-negative.

Proposition 1. All solutions of the system (2) starting from non-negative initial conditions exist for all $t > 0$ and remain non-negative. Furthermore, if $i(0) > 0$, then $i(t) > 0 \quad \forall t > 0$.

Proof Since the system (2) is cooperative and irreducible, then it’s strongly monotone (Hirsch, 1985; Smith, 2008). Thus, we can confirm that for each initial condition $x_0 \geq 0$ corresponds a solution $y(t, x_0) \geq 0$. Suppose that if $i(0) > 0$, and there is a $t_1 > 0$ such that $i(t) > 0$ for $t \in [0, t_1)$, and $i(t_1) = 0$. Using the third equation in system (2)

$$i'(t_1) = se(t_1) \geq 0.$$ 

Then $\lim_{t \to t_1^-} \frac{i(t) - i(t_1)}{t - t_1} \geq 0$. Since $t < t_1$ we have $i(t) - i(t_1) \leq 0$. Thus $i(t) \leq i(t_1) = 0$, which is a contradiction. This implies that such a $t_1$ cannot exist, thus $i(t) > 0$ for all $t > 0$.

3.2. Calculation of the basic reproduction number $R_0$

The basic reproduction number is the expected number of secondary infected people contacted by a single infectious person. In the following, we calculate $R_0$ of (2) using the method described in (Van den DriesscheJame, 2002). Let

$$F = \begin{pmatrix} s(\beta_i + \beta_H) & 0 \\ 0 & 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} \sigma + \alpha & 0 \\ -\sigma & -\mu_H \end{pmatrix}.$$ 

Then,

$$F = \begin{pmatrix} 0 & \beta_i \\ 0 & 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} \alpha + \sigma & 0 \\ -\alpha & 0 \end{pmatrix}.$$ 

Following the same approach as (Van den DriesscheJames, 2002), we obtain,
\[
R_0 = \frac{\sigma}{(\mu_H + \mu_Q + \mu_R + \alpha)(\sigma + \alpha)}J + \frac{\sigma\mu_H}{(\mu_H + \mu_Q + \mu_R + \alpha)(\mu' + \mu'_{R} + \alpha)(\sigma + \alpha)}\beta_H.
\]

Hence,
\[
R_0 = \frac{(\mu_H + \mu_Q + \mu_R + \alpha)(\sigma + \alpha)}{(\mu_H + \mu_Q + \mu_R + \alpha)(\mu' + \mu'_{R} + \alpha)}(\beta_I + \frac{\mu_H \beta_H}{(\mu' + \mu'_{R} + \alpha)}).
\] (4)

Note that \(R_0 = R_{0i} + R_{0h}\) where \(R_{0i}\) is the reproduction number if there is no contact with hospitalized people and \(R_{0h}\) is the reproduction number if there is contact just with the hospitalized individuals.

The basic reproduction number \(R_0\) of system (1) is similarly calculated as follows:
\[
R_0^1 = \frac{(\mu_H + \mu_Q + \mu_R + \mu)(\sigma + \mu)}{(\mu_H + \mu_Q + \mu_R + \mu)(\mu' + \mu'_{R} + \mu + \sigma)}(\beta_I + \frac{\mu_H \beta_H}{(\mu' + \mu'_{R} + \mu + \sigma)}).
\] (5)

By assuming that \(\alpha > \mu\) it is easy to see that
\[
R_0^1 > R_0
\] (6)

In fact, this result is straightforward since the function \(f\) is defined by
\[
f(x) = \frac{(\mu_H + \mu_Q + \mu_R + \alpha)}{(\mu_H + \mu_Q + \mu_R + \alpha + x)}(\beta_I + \frac{\mu_H \beta_H}{(\mu' + \mu'_{R} + \alpha + x)}),
\] (7)
is a decreasing function on \(\mathbb{R}^+\) and \(R_0^1 = f(\mu)\) and \(R_0 = f(\alpha)\).

3.3. Local stability of disease free equilibrium point

The aim of this section is to investigate the local stability of free equilibrium of the system (2). Clearly the system (2) has the disease free equilibrium given by \(E_f = (1; 0; 0; 0)\).

**Theorem 2.** (i) If \(R_0 < 1\), then the disease-free equilibrium \(E_f\) is locally asymptotically stable. (ii) If \(R_0 > 1\), then \(E_f\) is unstable.

**Proof** Since the variable \(r\) does not intervene in the first 4 equations, then we reduce the system (2) to a system of four equations, and we can get \(r\) by \(r = 1 - s - e - i - h\). Therefore, the system (2) is equivalent to:
\[
\begin{align*}
\dot{s} &= \alpha - (\beta_I - \mu_Q)s + (\mu' - \beta_H)sh - \alpha s \\
\dot{e} &= (\beta_I + \beta_H)e - (\alpha + \sigma)e + \mu_Qie + \mu'eh \\
\dot{i} &= \sigma e - (\mu_Q + \mu_R + \mu_H + \alpha)i + \mu'ih + \mu_i^2 \\
\dot{h} &= \mu_i^2 - (\mu' + \mu'_{R} + \alpha)h + \mu_Qhi + \mu'_{h}h^2.
\end{align*}
\] (8)

(i) The Jacobian matrix of system (2) at \(E_f\) is given by
\[
J_{E_f} = \begin{pmatrix}
-\alpha & 0 & -\beta_I + \mu_Q & (\mu' - \beta_H) \\
0 & -(\sigma + \alpha) & -\beta_I & 0 \\
0 & \sigma & -\alpha & 0 \\
0 & 0 & \mu_H & -b
\end{pmatrix}
\]

The characteristic equation is given by
\[
(\lambda + \alpha)(\lambda^3 + p_1\lambda^2 + p_2\lambda + p_3) = 0.
\] (9)

It is clear that \(\lambda = -\alpha < 0\) is a root of (9), and we can solve
\[
P(\lambda) = \lambda^3 + p_1\lambda^2 + p_2\lambda + p_3 = 0,
\] (10)
where
\[ p_1 = a + b + \sigma + \alpha \]
\[ p_2 = ab + (a + b)(\sigma + \alpha) - \sigma \beta_l \]
\[ p_3 = ab(\sigma + \alpha) - \sigma(\beta_l b + \beta_H \mu_H) \]

In terms of Routh-Hurwitz criterion (Gradshteyn & Ryzhik, 2000), it is sufficient to show that
\[ p_1 > 0, \ p_2 > 0, \ p_3 > 0 \] and \[ p_1 p_2 - p_3 > 0. \]

We have
\[
\mathcal{R}_0 = \frac{b \sigma}{ab(\sigma + \alpha)} \beta_l + \frac{\mu_H}{ab(\sigma + \alpha)} \beta_H \\
\quad = \frac{\sigma(b \beta_l + \mu_H \beta_H)}{ab(\sigma + \alpha)}.
\]

(11)

Then
\[
ab(\sigma + \alpha)(1 - \mathcal{R}_0) = ab(\sigma + \alpha) - \sigma(\beta_l b + \beta_H \mu_H).
\]

Thus
\[
p_1 = a + b + \sigma + \alpha \\
p_2 = ab + b(\sigma + \alpha) + a(\sigma + \alpha) - \sigma \beta_l \\
p_3 = ab(\sigma + \alpha)(1 - \mathcal{R}_0). 
\]

From (11) if \( \mathcal{R}_0 < 1 \), we have
\[
ab(\alpha + \sigma) > \sigma b \beta_l + \sigma \mu_H \beta_H = b(\alpha(\alpha + \sigma) - \sigma \beta_l) > \sigma \mu_H \beta_H \\
\Rightarrow ab(\sigma + \alpha) > \sigma \beta_l.
\]

Since \( b > 0, \sigma \mu_H \beta_H > 0 \) and if \( \mathcal{R}_0 < 1 \) then \( p_1, p_2 \) and \( p_3 \) are positive. Moreover, we can easily see that
\[ p_1 p_2 - p_3 > 0. \]

Therefore, by the Routh-Hurwitz criterion, all roots of (10) have negative real parts, concluding that if \( \mathcal{R}_0 < 1 \), then \( E_f \) is locally asymptotically stable.

(ii) If \( \mathcal{R}_0 > 1 \), then \( P(0) = p_3 < 0 \), and we have \( P(\lambda) \rightarrow \infty \) as \( \lambda \rightarrow \infty \). Therefore, there exists at least one positive root of the polynomial \( P(\lambda) \). Moreover, the equilibrium \( E_f \) is unstable if \( \mathcal{R}_0 > 1 \).

3.4. Existence and uniqueness of the endemic equilibrium point

Proposition 2. The system (1) has an infinity equilibrium points \( (S^*; E^*; I^*; H^*; R^*) \) with positive components.

\[
\begin{align*}
S^* &= \left( \frac{\alpha}{\mu} \left( \frac{\mu Q}{\mu - \alpha} + \frac{\mu' \mu_H}{(\alpha - \mu)(\mu' + \mu + \mu' R)} \right) \right) I^* , \\
E^* &= \left( \frac{\mu_H + \mu Q + \mu R + \mu'}{\sigma} \right) I^* , \\
H^* &= \left( \frac{\mu_H}{\mu + \mu + \mu R} \right) I^* , \\
R^* &= \left( \frac{\mu R + \mu' \mu_H}{\mu + (\mu' + \mu + \mu' R)} \right) I^* , \\
N^* &= \left( \frac{\mu Q}{\alpha - \mu} + \frac{\mu' \mu_H}{(\alpha - \mu)(\mu' + \mu + \mu' R)} \right) I^* .
\end{align*}
\]

(12)
Proof To find the endemic disease equilibrium of system (2), we solve the system:

\[
\begin{align*}
\alpha N - \mu S - \beta IS / N - \beta HI / N &= 0, \\
\beta IS / N + \beta HI / N - \mu E - \sigma E &= 0, \\
\sigma E - \mu H - \mu_0 I - \mu_{HI} - \mu_{SH} &= 0, \\
\mu H - \mu' H - \mu_0 H - \mu_0' H &= 0, \\
\mu_0 I - \mu R + \mu_0' H &= 0, \\
\alpha N - \mu N - \mu_0 I - \mu' H &= 0.
\end{align*}
\]

Which gives

\[
\begin{align*}
S^* &= \frac{\alpha \mu^* - \mu + \sigma}{\mu} E^*, \\
E^* &= \frac{\mu_H + \mu_0 + \mu_R + \mu'}{\sigma} I^*, \\
H^* &= \frac{\mu_H}{\mu' + \mu + \mu'} I^*, \\
R^* &= \left( \frac{\mu_R}{\mu} - \frac{\mu' \mu_H}{\mu' + \mu + \mu'} \right) I^*, \\
N^* &= \left( \frac{\mu_0}{\alpha - \mu} + \frac{\mu_0' \mu_H}{(\alpha - \mu)(\mu' + \mu + \mu_0')} \right) I^*.
\end{align*}
\]

Let’s have

\[
(s^*; e^*; i^*; h^*; r^*) = \left( \frac{S^*}{N^*}, \frac{E^*}{N^*}, \frac{I^*}{N^*}, \frac{H^*}{N^*}, \frac{R^*}{N^*} \right),
\]

with

\[
N^* = S^* + E^* + I^* + H^* + R^*.
\]

then we have the following result.

**Theorem 3.** 1. If \( \mathcal{R}_0^* > 1 \), then \( (s^*; e^*; i^*; h^*; r^*) \) is an endemic equilibrium point of the system (2), it belongs to \( \Sigma \), with

\[
\begin{align*}
S^* &= \frac{1}{\mathcal{R}_0^*}, \\
e^* &= \frac{\mu}{\mu + \sigma} \mathcal{R}_0^*, \\
i^* &= \frac{1}{K} \mathcal{R}_0^*, \\
h^* &= \frac{\mu_H}{Kd} \mathcal{R}_0^*,
\end{align*}
\]

with

\[
\mathcal{R}_0^* = \frac{\alpha}{\mu} - \frac{1}{\mathcal{R}_0^*}.
\]

\[
c = \mu_H + \mu_0 + \mu_R + \mu,
\]

\[
d = \mu' + \mu_R' + \mu,
\]

\[
K = \frac{c(\mu + \sigma)}{\mu \sigma}.
\]

2. If \( \mathcal{R}_0^* < 1 \), then the system (2) has only a disease-free equilibrium.

**Proof 1.** Let \( \mathcal{R}_0^* > 1 \)

i) Let’s take \( X = (S, E, I, H, R) \) and \( x = (s, e, i, h, r) \), with \( x = \frac{X}{N} \). From the system (2), the vector field \( f = (f_1; f_2; f_3; f_4; f_5) \) can be writing on the form:

\[
\begin{align*}
f_1 &= \alpha - \mu S - \beta IS - \beta HI, \\
f_2 &= \beta IS N - \mu E - \sigma E, \\
f_3 &= \sigma E - \mu H - \mu_0 I - \mu_{HI} - \mu_{SH}, \\
f_4 &= \mu H - \mu' H - \mu_0 H - \mu_0' H, \\
f_5 &= \alpha N - \mu N - \mu_0 I - \mu' H.
\end{align*}
\]
\[ f(x) = \left( \begin{array}{c} \alpha - (\beta_1 - \mu_Q) s i + (\mu - \beta_H) s h - \alpha s \\
(\beta_1 i + \beta_2 h) s - (\sigma + \sigma e + \mu_Q i e + \mu e h) \\
\sigma e - (\mu_Q + \mu_R + \mu_H + \alpha i + \mu ih + \mu Q i) \\
(\mu_H i - (\mu + \mu_R + \alpha) h + \mu_Q hi + \mu h^2) \\
\mu_R i + \mu Q ri + \mu rh \end{array} \right) \]

If \((S^*; E^*; I^*; H^*; R^*)\) is an equilibrium point of the system \((1)\). Then we have:

\[
\begin{align*}
\alpha N^* - \mu S^* - \beta_1 S^* I^*/N^* - \beta_2 H^* S^*/N^* &= 0, \\
\beta_1 S^* I^*/N^* + \beta_2 H^* S^*/N^* - \mu E^* - \sigma E^* &= 0, \\
\sigma E^* - \mu_H I^* - \mu Q I^* - \mu_R I^* - \mu_I^* &= 0, \\
\mu_H I^* - \mu I^* H^* - \mu Q I^* - \mu_R I^* - \mu_R^* H^* &= 0, \\
\mu_R I^* - \mu R^* + \mu_F^* H^* &= 0, \\
\alpha N^* - \mu N^* - \mu Q I^* - \mu Q I^* - \mu H^* &= 0.
\end{align*}
\]

\[ \text{(16)} \]

Our goal is to prove that \(x^* = (s^*; e^*; i^*; h^*; r^*)\) is an equilibrium point of system \((2)\), which means
\[ f(x^*) = 0. \]

We have:
\[ f_1(s^*; e^*; i^*; h^*; r^*) = f_1 \left( \frac{S^*}{N^*}, \frac{E^*}{N^*}, \frac{I^*}{N^*}, \frac{H^*}{N^*}, \frac{R^*}{N^*} \right) = \frac{1}{N^*} \left( \alpha N^* - \mu S^* - \beta_1 S^* \frac{I^*}{N^*} - \beta_2 H^* \frac{S^*}{N^*} \right) - \frac{S^*}{N^*} (\alpha - \mu) N^* - \mu Q I^* - \mu H^*. \]

Using the first and the last equations of \((16)\), we have
\[ \alpha N^* - \mu S^* - \beta_1 S^* \frac{I^*}{N^*} - \beta_2 H^* \frac{S^*}{N^*} = 0 \]
and
\[ (\alpha - \mu) N^* - \mu Q I^* - \mu H^* = 0. \]

Which concludes that
\[ f_1(s^*; e^*; i^*; h^*; r^*) = 0. \]

Similarly, we obtained,
\[ f_i(s^*; e^*; i^*; h^*; r^*) = 0 \quad \text{for} \quad i = 2, \cdots, 5, \]
and conclude that
\[ f(s^*; e^*; i^*; h^*; r^*) = 0. \]

Thus \((s^*; e^*; i^*; h^*; r^*) = \left( \frac{S^*}{N^*}, \frac{E^*}{N^*}, \frac{I^*}{N^*}, \frac{H^*}{N^*}, \frac{R^*}{N^*} \right)\) is an equilibrium of system \((2)\). In addition, it is clear that \((s^*; e^*; i^*; h^*; r^*) \in \Sigma. \)

ii) To find the endemic equilibrium point of system \((2)\), we solve the following equations...
\[ aN^* - \mu S^* - \frac{\beta_i S^* I^*}{N} - \frac{\beta_H S^* H^*}{N} = 0, \]
\[ \frac{\beta_i S^* I^*}{N} + \frac{\beta_H S^* H^*}{N} - (\mu + \sigma) E^* = 0, \]
\[ \sigma E^* - (\mu_H + \mu_Q + \mu + \mu_R) I^* = 0, \]
\[ \mu_H I^* - (\mu' + \mu_R) H^* = 0, \]
\[ \mu_R I^* - \mu R^* + \mu' R^* = 0. \]

From the third and fourth equations of the system (17), we have
\[ E^* = \frac{\mu_H + \mu_Q + \mu + \mu_R I^*}{\sigma}, \]
\[ H^* = \frac{\mu_H}{\mu' + \mu + \mu_R} I^*. \]

Next, we replace \( E^* \) and \( H^* \) in the second equation of the system (17) and we get
\[ S^* = \frac{(\mu + \sigma)(\mu_H + \mu_Q + \mu + \mu_R)}{\sigma(\beta_i + \beta_H \mu_R)} = \frac{1}{\mathcal{R}_0}. \]

Now, we sum up the first and second equations of the system (17) and we divide on \( N^* \) to get
\[ \frac{E^*}{N^*} = \frac{a}{\mu + \sigma} - \frac{\mu}{\mu + \sigma} \frac{S^*}{N^*}. \]

Using equation (18) and the following notations
\[ \mathcal{R}^* = \frac{a}{\mu} - \frac{1}{\mathcal{R}_0}, \]
\[ c = \mu_H + \mu_Q + \mu_R + \mu, \]
\[ d = \mu' + \mu_R + \mu, \]
\[ K = \frac{c(\mu + \sigma)}{\mu \sigma}, \]

we obtain
\[
\begin{align*}
\frac{S^*}{N^*} &= \frac{1}{\mathcal{R}_0} \\
\frac{E^*}{N^*} &= \frac{\mu}{\mu + \sigma} \left( \frac{a}{\mu} - \frac{1}{\mathcal{R}_0} \right) = \frac{\mu}{\mu + \sigma} \mathcal{R}^* \\
\frac{I^*}{N^*} &= \frac{1}{K} \left( \frac{a}{\mu} - \frac{1}{\mathcal{R}_0} \right) = \frac{1}{K} \mathcal{R}^* \\
\frac{H^*}{N^*} &= K(\mu' + \mu + \mu_R) \left( \frac{a}{\mu} - \frac{1}{\mathcal{R}_0} \right) = \frac{\mu_H}{Kd} \mathcal{R}^* 
\end{align*}
\]

Which concludes (15).

2. Since \( \frac{S^*}{N^*} = \frac{1}{\mathcal{R}_0} \), then \( \mathcal{R}_0^1 < 1 \) implies that the system (2) has only a disease-free equilibrium.

Before proving the uniqueness of an endemic equilibrium point, we need to give the following results (Smith, 2008): For an autonomous system of ordinary differential equations
\[
\dot{x} = f(x) \tag{20}
\]

**Definition 1.** For each \(i, f_i(a) \leq f_i(b)\) for any two points \(a\) and \(b\) in \(D\) satisfying \(a \leq b\) and \(a_i = b_i\). Hence, if \(x_0, y_0 \in D\) such that \(x_0 < y_0; t \geq 0\) then \(x(t, x_0) \leq y(t, y_0)\) for \(t \geq 0\). Moreover, if \(D\) is a \(p\)-convex and \(\frac{d}{dt}\) \(x) \geq 0; i \neq j, x \in D\), then \(f\) is of type \(K\) in \(D\).

**Proposition 3.** The endemic equilibrium point \((s^*, e^*, i^*, h^*, r^*)\) of the system (2) is unique.

Proof: By contradiction, let assume that \(z^* = (s^*, e^*, i^*, h^*, r^*)\) and \(z_1 = (s_1, e_1, i_1, h_1, r_1)\) be the two endemic equilibrium points such that \(z^* \neq z_1\) and in particular, \(i^* > i_1\). Let \(P_1 = (s^*, e^*, i_1, h^*, r^*)\), then \(z^* > P_1\). Since the system in (2) is cooperative, \(f\) is type \(K\), where \(f = (f_1, \ldots, f_5)\) and \(f_i\) represents the right-hand side of the system in (2) such that \(s = f_1, \ldots, r = f_5\). Hence

\[
f_1(z^*) \geq f_1(P_1). \tag{21}
\]

On the other hand, by substituting \(z^*\) and \(P_1\) in \(f_1\) of (2), we find that

\[
i^*(\mu_Q - \beta_i) \leq i_1(\mu_Q - \beta_i).
\]

Since \(\beta_i > \mu_Q\) then \(i^* \leq i_1\), which contradicts to \(i^* > i_1\). By the same token, when we suppose that \(i^* < i_1\) we will find that \(i^* \geq i_1\), which contradicts \(i^* < i_1\). Thus, \(i^* = i_1\).

Suppose \(h^* > h_1\) and let \(P_2 = (s^*, e^*, i^*, h_1, r^*)\), then \(z^* > P_2\). Using the fact that \(f_1(z^* \geq f_1(P_2)\) for \(i = 1, 2\), we have

\[
h^*(\mu' - \beta_H) \geq h_1(\mu' - \beta_H).
\]

Since \(\beta_H > \mu'\), we have \(\mu' - \beta_H < 0\). Thus \(h^* \leq h_1\) which contradicts \(h^* > h_1\). If we assume \(h^* < h_1\) using the same terminology, we can find, \(h^* \geq h_1\), again we deduce that \(h^* = h_1\).

Since,

\[
f_3(z^*) = f_3(z_1) = 0
\]

and we have \(i^* = i_1\) and \(h^* = h_1\), it is easy to see that \(e^* = e_1\).

Back to the first equation of (2),

\[
f_1(z^*) = f_1(z_1) = 0,
\]

We have \(s^* = s_1\).

Using the fact that, \(s^* + e^* + i^* + h^* + r^* = 1 = s_1 + e_1 + i_1 + h_1 + r_1\), we conclude \(r^* = r_1\), and therefore \(z^* = z_1\).

**4. Global stability of equilibrium**

In order to prove the global stability results, we first prove the following theorems.

**Lemma 1.** Let \(\Sigma\) be a convex subset of \(\mathbb{R}^n\). Assume that system (20) is cooperative and irreducible in \(\Sigma\), and all solutions of (20) are bounded in \(\Sigma\).

(a) If there is one equilibrium, it attracts all solutions. So this unique equilibrium is globally asymptotically stable.

(b) Assume that there are two equilibria \(p\) and \(q\) not ordered and simple. Then if \(p\) is unstable, \(q\) attracts all solutions. So, \((\forall x \in \Sigma) y(t, x) \rightarrow q\)

The proof of this result is in the Appendix.

Using the fact that the system (2) is cooperative and irreducible on the set \(\Sigma\) which is convex and positively invariant set, we first prove the global stability of \(E_f\) as follows.

In the next result, we give sufficient conditions that allow all solutions to converge to the disease free equilibrium or the disease endemic equilibrium. For this purpose, we use the following definition:

**Definition 2.** An equilibrium \(X^*\) is called simple if \(0 \notin \text{Spec}(J(X^*))\) with \(J\) is the Jacobian matrix.

**Proposition 4.** i) If \(\frac{\xi}{\mu_1} < \frac{\pi_1}{\pi_1 + \pi_2}\), then \(E_{DEE}\) is a simple equilibrium. ii) The disease free equilibrium \(E_f\) is a simple equilibrium.

Proof: i) In order to show that \(E_{DEE}\) is a simple equilibrium, we need to show \(0 \notin \text{Spec}(J(E_{DEE}))\), which is equivalent to showing that \(\text{det}(J(E_{DEE})) \neq 0\). The Jacobian matrix of the system (2) at \(E_{DEE}\) is given by:
It's obvious that g is an increasing function on I and

Using the elementary row operation, we get

\[
\mathcal{J} = \begin{pmatrix}
\alpha R_0^1 - \mu & -(\sigma + \mu) & \frac{\beta I}{R_0^1} + \frac{\mu Q}{\mu + \sigma} R^* & \frac{\beta H}{R_0^1} + \frac{\mu'}{\mu + \sigma} R^*\\
0 & \sigma & -c + \frac{\mu Q}{K} R^* & \frac{\mu'}{K} R^* \\
0 & 0 & \mu_H + \frac{\mu Q \mu_H}{K d} R^* & -d + \frac{\mu' \mu_H}{K d} R^* \\
0 & 0 & 0 & 0 & E
\end{pmatrix}
\]

With

\[
E = \left(\mu_H + \frac{\mu Q \mu_H}{K d} R^*\right) D + C \left(d - \frac{\mu' \mu_H}{K d} R^*\right).
\]

and

\[
C = \sigma A + \alpha (\sigma + \mu) R_0^1 \left(-c + \frac{\mu Q}{K} R^*\right) \quad \text{and} \quad D = \sigma B + \alpha (\sigma + \mu) R_0^1 \left(\frac{\mu'}{K} R^*\right) > 0,
\]

and

\[
A = \mu Q R^* + \frac{\alpha Q}{\sigma + \mu} R_0^1 R^* > 0 \quad \text{and} \quad B = \mu' R^* + \frac{\alpha Q}{\sigma + \mu} R_0^1 R^* > 0.
\]

Using the fact that \(i^* = \frac{1}{F} R^* < 1\) and \(Q < c\), we can easily show that \(\frac{\mu Q}{K} R^* < c\). Similarly, since \(h^* = \frac{\mu H}{K d} R^* < 1\) and \(\mu' < d\), we have \(-d + \frac{\mu' \mu_H}{K d} R^* < 0\). On the other hand

\[
\det(\mathcal{J}) = \sigma (\alpha R_0^1 - \mu) \left(\mu_H + \frac{\mu Q \mu_H}{K d} R^*\right) E.
\]

Hence, to show that \(\det(\mathcal{J}) > 0\) is equivalent to showing that \(E > 0\). By the form of \(E\) it suffices to show that \(C > 0\). We have

\[
C = \sigma A + \alpha (\sigma + \mu) R_0^1 \left(-c + \frac{\mu Q}{K} R^*\right)
\]

\[
= \sigma \mu Q R^* + \frac{\alpha Q}{\sigma + \mu} R_0^1 R^* + \frac{\alpha R_0^1}{c(\sigma + \mu)} \mathcal{g}(R^*).
\]

With \(g\) is a function defined on \(l = \left[\frac{n}{m} - 1; \frac{n}{m}\right]\) by

\[
g(x) = \sigma \mu Q (c + \sigma + \mu)x - c^2 (\sigma + \mu)^2.
\]

It's obvious that \(g\) is an increasing function on \(l\) and
By using Theorem 4, we deduce that the outbreak of Liberia and Sierra Leone as follows.

\[ g\left( \frac{\alpha}{\mu} - 1 \right) = c\sigma \mu Q (\alpha - \mu) + (\sigma + \mu) \left( \alpha \sigma \mu Q - \sigma \mu Q - c^2 (\sigma + \mu) \right). \]

Since \( \alpha - \mu > 0 \) and \( \frac{c^2}{\mu} \overset{\mu}{\sigma (\alpha - \mu)} \left( \frac{\mu Q}{\mu H + \mu Q + \mu R} \right) \left( \frac{\mu Q}{\mu H + \mu Q + \mu R} \right) > 1. \)

Clearly, this can not be true except if the birth rate \( \alpha \) is significantly large.

**Theorem 4.** a) If \( R_0^1 < 1 \), the disease free equilibrium \( E_f \) is globally asymptotically stable in \( \Sigma \). b) If \( R_0^1 > 1 \) and \( \frac{c^2}{\mu} \overset{\mu}{\sigma (\alpha - \mu)} \), there are two cases:

i) \( R_0 < 1 < R_0^1 \), then the disease free equilibrium \( E_f \) is globally asymptotically stable, and the disease endemic equilibrium \( E_{DEE} \) is unstable.

Proof a) If \( R_0^1 < 1 \), then \( R_0 < 1 \). Hence, the set of equilibrium consists of one point \( E_f \) which is locally asymptotically stable. Moreover, from Lemma 1 (a), all solutions with initial value in \( \Sigma \) converge to \( E_f \). Therefore \( E_f \) is globally asymptotically stable in \( \Sigma \).

b) To prove b), we will use Definition 2 and Proposition 4, recall that \( R_0 < R_0^1 \). Suppose \( R_0^1 > 1 \), there are two cases:

i) If \( R_0 < 1 < R_0^1 \), the two equilibrium points \( E_f \) and \( E_{DEE} \) exists. We have \( R_0 < 1 \) then the disease free equilibrium \( E_f \) is globally asymptotically stable. Since system (2) is cooperative and irreducible and equilibriums are simple then the disease endemic equilibrium \( E_{DEE} \) is unstable.

ii) If \( 1 < R_0 < R_0^1 \), then from Theorem 2 the disease free equilibrium \( E_f \) is unstable, and then from Proposition 4, \( E_{DEE} \) is stable.

5. Numerical simulation

In this section, we present the numerical simulations of our findings using parameters which are taken from the 2014 West Africa Ebola Outbreak (Rivers, Lofgren, Marathe, Stephen, & Lewis, 2014) (see Table 2). The parameters were fit to the data of the outbreak of Liberia and Sierra Leone as follows.

With \( \alpha = 0.01 \), the basic infection reproduction number in Liberia is \( R_0 = 0.5236159 \) and in Sierra Leone \( R_0 = 0.5256533 \). By using Theorem 4, we deduce that \( E_f \) is globally asymptotically stable. Numerical simulation illustrates our results see Fig. 2.

By choosing the following set of parameters, \( \alpha = 0.25, \beta_H = 0.46, \beta_I = 0.75, \sigma = 0.85, \mu_Q = 0.15, \mu'_Q = 0.25, \mu_H = 0.01, \mu_R = 0.006, \mu'_R = 0.005 \), and \( \mu = 0.007 \). We have \( R_0 = 1.4 \) and \( \frac{c^2}{\mu} \overset{\mu}{\sigma (\alpha - \mu)} \), we get the time series presented in Fig. 3.

With this set of data and by taking the initial condition \( (s(0), e(0), i(0), h(0), r(0)) = (0.2, 0.2, 0.2, 0.2, 0.2) \), it is clearly shown that the disease persists. In fact, the hospitalized and recovered people are below 1% (hospitalized 0.7% and recovered 0.96%).

| Parameter | Liberia Fitted Values | Sierra Leone Fitted Values |
|-----------|-----------------------|---------------------------|
| \( \beta_I \) | 0.160 | 0.128 |
| \( \beta_H \) | 0.062 | 0.080 |
| 1/\( \sigma \) | 12 days | 10 days |
| 1/\( \mu_H \) | 3.24 days | 4.12 days |
| \( \mu_R \) | 1/15 | 1/20 |
| \( \mu'_R \) | 1/15.88 | 1/15.88 |
| \( \mu_Q \) | 1/13 | 1/10.38 |
| \( \mu' \) | 1/10.07 | 1/6.26 |
6. Conclusion and discussion

The exposed people reach 13.68%, the susceptible population does not exceed 46.25%, while the infected people reach almost one third of the population 31.73%. We should also notice that the disease equilibrium is reached faster compared to the disease free equilibrium.

The Ebola Virus Disease (EVD) is one of the most devastating viruses to have infected the African continent in recent years. As the threat of this disease reminds, it is important to have a clear understanding of the dynamics of the disease.

In this work, we presented a mathematical model of the spread of Ebola epidemic. The model is adapted from Legrand et al. (Legrand et al., 2007), where the parameters of the model were estimated from the recent Ebola outbreak (2014–2015). Using the monotone system theory in this work, is an alternative to the standard approach of analyzing the mathematical models of epidemiological systems.

First, we proved that the proportion population model (2) is cooperative and irreducible on a positively invariant convex set. Using the next generation population approach, we found the basic reproduction number $R_0$ of the population proportions model. We notice that the basic reproduction number of the original model, $R_1$ was bigger than $R_0$. To show the local
stability of the disease-free equilibrium (DFE), we used the Routh-Hurwitz criterion, and for the DEE, we proved the uniqueness via type K propriety and the fact that the system (2) is cooperative.

To prove the global stability of the DFE, we showed, in Lemma 1 (a), that if the system is cooperative, irreducible and all its solutions are bounded, then the unique equilibrium is globally asymptotically stable. For the global stability of the disease-endemic equilibrium (DEE), we found the condition \( \frac{c^2}{\mu b} < \frac{\sigma (\alpha - \mu)}{\sigma + \mu} \) that made this equilibrium simple, and with the threshold condition, \( R_0 > 1 \), we ensured the global stability of DEE.

Our simulation was performed, using the most recent outbreak data, showed the global stability of the DFE. To illustrate the global stability of DEE, we choose a set of parameters that verified the simple equilibrium condition and the threshold condition.

As we mentioned in Remark 2, the condition \( \frac{c^2}{\mu b} < \frac{\sigma (\alpha - \mu)}{\sigma + \mu} \) holds if the birth rate \( \alpha \) is significantly large. In fact, the countries that were affected by the Ebola outbreak are among the highest birth rate in the African continent, 4.52 births per woman in Sierra Leone and 4.65 in Liberia (world bank data). This shows that although the basic reproduction number of the Ebola virus that were affected by the Ebola outbreak are among the highest birth rate in the African continent, 4.52 births per woman in Sierra Leone and 4.65 in Liberia (world bank data). This shows that although the basic reproduction number of the Ebola virus was above one (Althaus, 2014) in the recent outbreak (for example Sierra Leone 2.53 and Liberia 1.59), the fact that these countries have high birth rate has contributed to the outbreak. Moreover, the Ebola will continue to be a treat to these countries if the virus gains ground in the future.

Acknowledgement

The authors would like to thank the referees for valuable comments and suggestions that help to improve the quality of this work.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.idm.2018.09.004.

Appendix

To prove the Theorem 4 and 5, we need the following the results:

**Theorem 5.** (Hirsch & Smith, 2005) If \( I \subset X \) is a totally ordered arc, \( I \setminus Q \) is at most countable

**Theorem 6.** Sequential Limit Set Trichotomy (Smith, 2008) Let \( x \in D \) have the property that it can be approximated from below in \( D \) by a sequence \( \xi_n \). Then there exists a sequence \( x_n \) of \( \xi_n \) such that \( x_n < x_{n+1} < x, n \geq 1 \), with \( x_n \to x \) satisfying one of the following.

(a) There exists \( u \in E \) such that

\[ \omega(x_n) < \omega(x_{n+1}) < u = \omega(x), \; n \geq 1 \]

and

\[ \lim_{n \to \infty} \text{dist}(\omega(x_n), u) = 0. \]

(b) There exists \( u \in E \) such that

\[ \omega(x_n) = u < \omega(x), \; n \geq 1 \]

If \( v \in E \) and \( v < \omega(x) \) then \( v < u \).

**Lemma 2.** (Hirsch, 1985) Let \( p \) be an \( \omega \)-colimit point \( x, y \). Then \( p \in E \). If \( x(t), y(t) \) converge to \( p \) as \( t \to \infty \), then \( p \) is a trap.

**Proof of Lemma 1.** (a): Let \( p \) be the unique equilibrium. If \( x \in D \), there exists a totally order line segment \( I \subset D \) and convergent points \( u, v \in I \) with \( u < x < v \), by Theorem 5.

(c) \( \omega(x_n) = \omega(x) \leq E \) for \( n \geq 1 \)

Therefore \( y(t, u) \to p \) and \( y(t, v) \to p \), since the system is cooperative and irreducible then strongly monotone, so \( y(t, x) \to p \).

If \( x \in \partial D \), there exists \( x_n \in D \) such that \( \lim_{n \to \infty} x_n = x \).

\[ x_n \in D \Rightarrow \lim_{n \to \infty} y(t, x_n) = p. \; \forall n, \text{by the first part of the Proof}. \;
\]

Moreover \( \lim_{n \to \infty} \left( \lim_{t \to \infty} y(t, x_n) \right) = p \).

By continuity,
\[ \lim_{n \to \infty} \left( \lim_{t \to \infty} y(t, x_n) \right) = \lim_{t \to \infty} \left( \lim_{n \to \infty} y(t, x_n) \right) = \lim_{t \to \infty} y(t, \lim_{n \to \infty} x_n) = \lim_{t \to \infty} y(t, x) \]

We deduce that \( \lim_{t \to \infty} y(t, x) = p \) for all \( x \in \mathbb{R} \).

We conclude that for each \( x \in \Sigma \), \( y(t, x) \) converges to \( p \).

**Remark 2.** It is well known that a sink is asymptotically stable and a simple trap is a sink.

**Proof of Lemma 1 (b):** Let \( x \in \Sigma \). By Theorem 6 (c), there exists a sequence \( (x_n) \) such that: \( x_n < x_{n+1} < x \) (\( \forall n \geq 1 \)) and \( x_n \to x \).

Since \( p \) and \( q \) are not ordered, we have necessarily:

\[ \omega(x_n) = \omega(x_{n+1}) = \omega(x) \subset E, (\forall n \geq 1) . \]

So, \( \omega(x) = p \) or \( \omega(x) = q \).

Suppose that \( \omega(x) = p \). We will prove that \( \alpha = q \). In fact:

\[ x_n < x \Rightarrow y(t_k, x_n) < y(t_k, x) \]

by strongly monotone property and \( \omega(x) = \alpha \Rightarrow \exists t_k \to \infty \) such that \( y(t_k, x) \to \alpha \) and \( y(t_k, x_n) \to \alpha \). By lemma (2) \( x \) is a simple trap. By Remark 2, \( x \) is asymptotically stable. Consequently \( \alpha = q \).

**References**

Agusto, F. B. (2017). Mathematical model of ebola transmission dynamics with relapse and reinfection. *Mathematical Biosciences*, 283(Supplement C), 48–59.

Althaus, C. L. (2014). Estimating the reproduction number of ebola virus (ebov) during the 2014 outbreak in west africa. *PLOS Currents Outbreaks*, 2(6).

Berger, T., Lubuma, J. M.-S., Moremedi, G. M., Morris, N., & Kondera-Shava, R. (2017). A simple mathematical model for ebola in africa. *Journal of Biological Dynamics*, 11(1), 42–74.

Bodin, E. N., Cook, C., & Shorten, M. (2018). The potential impact of a prophylactic vaccine for ebola in Sierra Leone. *Mathematical Biosciences and Engineering*, 15(2), 337–359.

Browne, C., Gulbudak, H., & Webb, G. (2015). Modeling contact tracing in outbreaks with application to ebola. *Journal of Theoretical Biology*, 384(Supplement C), 33–49.

Center for Disease Control and Prevention. (2014). *Ebola outbreak in west africa - case counts*.

Chowell, G., & Nishiura, H. (2014). Transmission dynamics and control of ebola virus disease (evd): A review. *BMC Medicine*, 12(1), 196.

Smith, H. L., & Thieme, H. R. (1991). Convergence for strongly order-preserving semiflows. *SIAM Journal on Mathematical Analysis*, 22(4), 1081–1101.

El Karkri, J., & Niri, K. (2014). Global stability of an epidemiological model with relapse and delay. *Applied Mathematical Sciences*, 8(73), 3619–3631.

Gradsteyn, I. S., & Ryzhik, I. M. (2000). *Routh-hurwitz Theorem, Tables of integrals, series, and products*.

Hirsch, M. W. (1982). Systems of differential equations which are competitive or cooperative: I. Limit sets. *SIAM Journal on Mathematical Analysis*, 13(2), 667–179.

Hirsch, M. W. (1983). Differential equations and convergence almost everywhere in strongly monotone semiflows. *Contemporary Mathematics*, 17, 267–285.

Hirsch, M. W. (1985). Systems of differential equations that are competitive or cooperative ii: convergence almost everywhere. *SIAM Journal on Mathematical Analysis*, 16(3), 423–439.

Hirsch, M. W. (1990). Systems of differential equations that are competitive or cooperative. iv: Structural stability in three dimensional systems. *SIAM Journal on Mathematical Analysis*, 21(5), 1225–1234.

Hirsch, M., & Smith, H. L. (2005). Monotone dynamical systems. In *Handbook of differential equations* (Vol. 2) Elsevier.

Ilgdrir, A., Niri, K., & Moulay Ely, E. O. (2010). Fluidations in a sis epidemic model with variable size population. *Applied Mathematics and Computation*, 217(11), 55–64.

Johns Hopkins Medicine Health Library, Ebola. Kamke, E. (1932). Zur theorie der systeme gewöhnlicher differentialgleichungen, ii. *Acta Mathematica*, 58(1), 57–85.

Legrand, J., Freeman Grais, R., Boelle, P.-Y., Valleron, A.-J., & Antoine, F. (2007). Understanding the dynamics of ebola epidemics. *Epidemiology and Infection*, 135(4), 610–621.

Manguevo, A., & Mafuvadze, B. (2015). The impact of traditional and religious practices on the spread of ebola in West africa: Time for a strategic shift. *The Pan African Medical Journal*, 22(9).

Muller, M. (1927). Uber das fundamenthal Theorem in der theorie der gewohnlichen differential gleichungen.

Niri, K., Kabli, K., & El moujaddid, S. (2015). Global asymptotic stability of siri diseases models using monotone dynamical systems theory. *Journal of Biological Dynamics*, 9(98), 4881–4896.

Rivers, C. M., Lofgren, E. T., Marathe, M., Stephen, E., & Lewis, B. L. (2014). Modeling the impact of interventions on an epidemic of ebola in Sierra Leone and Liberia. *PLoS Currents*, 6.

Smith, H. L. (2008). *Monotone dynamical systems: An introduction to the theory of competitive and cooperative systems*. no. 41. American Mathematical Soc.

Smith, H. L., & Thieme, H. R. (1990). Quasi convergence and stability for strongly order-preserving semiflows. *SIAM Journal on Mathematical Analysis*, 21(3), 573–602.

Van den Driessche, P., & James, W. (2002). Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical Biosciences*, 180(1), 29–48.

Vittoria Barbarossa, M., Deines, A., Kiss, G., Nakata, Y., Röst, G., & Vizi, Z. (2015). Transmission dynamics and final epidemic size of ebola virus disease outbreaks with varying interventions. *PLoS One*, 10(7), 1–21.

Weibel, C. F., & Browne, C. J. (2016). A model of the ebola epidemics in west africa incorporating age of infection. *Journal of Biological Dynamics*, 10(1), 18–30.

Weitz, J. S., & Dushoff, J. (2015). Modeling post-death transmission of ebola: Challenges for inference and opportunities for control. *Scientific Reports*, 5, 8751.

Wong, Z. S. Y., Bui, C. M., Chughtai, A. A., & Macintyre, C. R. (2017). A systematic review of early modelling studies of ebola virus disease in west africa. *Epidemiology and Infection*, 145(6), 1069–1094.

World Health Organization. (2015 January). Origins of the 2014 ebola epidemic.

World Health Organization. (June 2017). *Ebola virus disease, fact sheet*. 