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Global Analysis of an Epidemic Mathematical Model in A Chemostat

EL Hajji M*

ENIT-LAMSIN, Tunis El Manar university, Tunisia

***Corresponding author:** EL Hajji M, ENIT-LAMSIN, Tunis-Belvédère, Tunis El Manar university, Tunisia, Tel: 0021693455629, E-mail: miled.elhajji@enit.rnu.tn

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Abstract

In this paper, a mathematical five-dimensional dynamical system involving a SVEIR model of infectious disease transmission in a chemostat is proposed. A profound qualitative analysis is given. The analysis of the local and global stability of equilibrium points is carried out. It is proved that if $\mathcal{R} > 1$, then the disease-persistence (endemic) equilibrium is globally asymptotically stable. However, if $\mathcal{R} \leq 1$, then the disease-free equilibrium is globally asymptotically stable in $\mathbb{R}^5$.

Keywords: Deterministic SVEIR Model; Equilibrium Points; Local And Global Stability; Direct Lyapunov Method, Lasalle's Invariance Principle

Mathematics Subject Classification: 34D23, 35N25, 37B25, 49K40, 60H10, 65C30, 91B70.

Introduction

Understanding how an epidemic develops once it has emerged is crucial if we want to hope to control it. To do this, various models have been developed which highlight (in particular) the crucial role played by the parameter $\mathcal{R}$, describing the average number of new infections due to a sick individual. As one can imagine, if this number is less than 1 then the epidemic will tend to go out, whereas it will be able to persist even to extend to the entire population if $\mathcal{R} > 1$. However, these classical models obviously have their limits and the parameter $\mathcal{R}$ does not really describe on its own the future of an epidemic in a real population (assuming that we know how to find it in this case). For example, the fact that a population is always finished induces random effects all the more marked that the population is small. On the other hand, most populations also have a structure in the form of groups within which individuals are closer (and therefore more easily infected) than between groups. All this requires finer models and the development of the tools necessary for their study.

In a chemostat, an epidemic model can also be understood as a competition model where various pathogen strains compete for the the same susceptible host as only resource [1,2]. Such models predict the strain with the largest basic reproduction number to be the winner. In, it is proved that this prediction amount to the same if the per capita functional responses of infective individuals to the density of susceptible are proportional to each other but that they are different if the functional responses are non-proportional [2].

The SVEIR model of Wei *et al.* incorporates the notion of delay which consists in admitting that individuals can not pass from one compartment to another directly without observing a certain time, said delay [3]. Then the dynamic behaviour of the model is studied under a so-called vaccination strategy (pulse vaccination). The strategy is to vaccinate individuals of a certain age group, not once, but several times by separating doses of a definite time.

In this work, I shall revisit the model based on a standard SEIR model proposed firstly by Hethcote, modified by Gumel *et al,* and Wei *et al,* and later studied by Nkamba *et al.* but in a continuous reactor, from an applied point of view [3-12]. The contents of this paper is arranged as following. First, we present, in Section 2, a description of the model to be investigated. Then existence, uniqueness and local stability of the equilibrium of the considered model are analysed. Global stability and asymptotic behaviour of the 5D-system are then discussed. Finally, in section 3, numerical simulations are given in order to confirm the given results.

Mathematical model and results

The considered population is subdivided into five subgroups of individuals. Each group has different epidemiological significance: the compartments of Susceptible, Vaccinated, Exposed, Infected, and finally the compartment of Recovered, which are respectively represented by the following letters S, V, E, I and R. The exposed compartment takes into account the elapsed time between the moment when the susceptible individual is infected and the moment when it becomes infected.

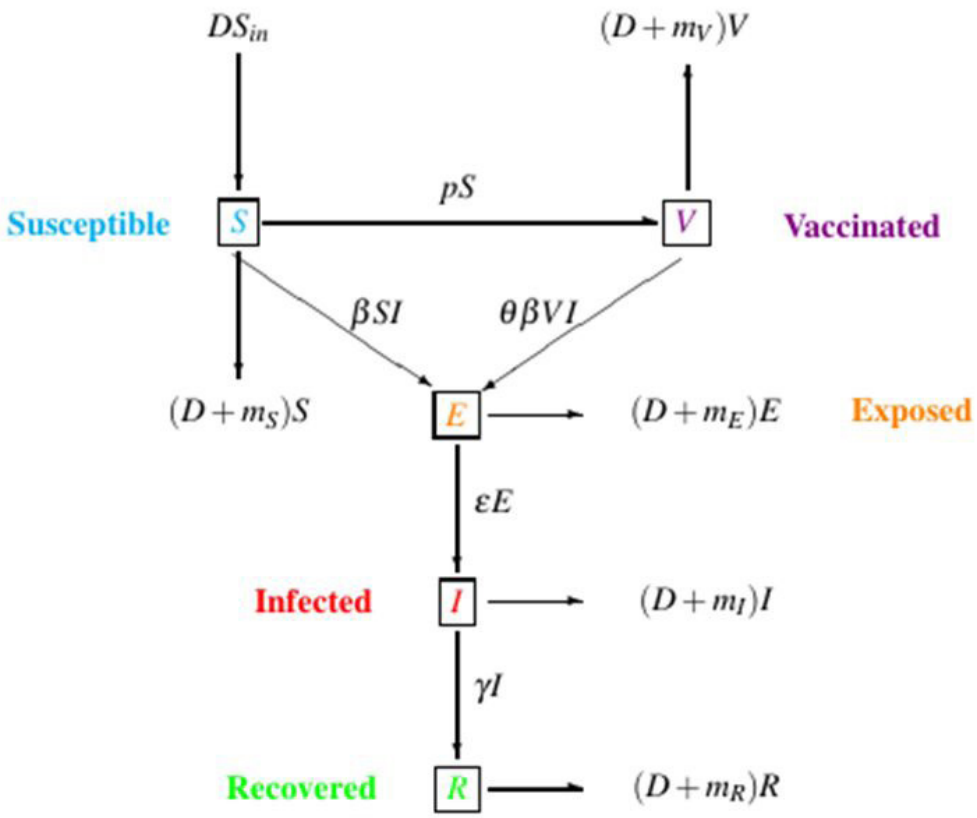

Figure1: Deterministic SVEIR Model in a chemostat

The susceptible, the vaccinated, the exposed, the infected and the recovered individuals are exposed to a natural mortality other than one caused by the disease concerned by this study, with respective positive mortality rates m_S, m_V, m_E, m_I and m_R.

As in general, the immunological status of the population of each compartment is different, mortality rates must be different. DS_{in} describes the rate of recruitment of susceptible (as input), this includes newborns who are born susceptible in the type of infection considered. The transmission coefficient, β, is the number of contacts made by an infectious individual per unit of time multiplied by the probability that contact with a susceptible person leads to an infection. ε is the rate at which individuals become infectious after spending some time in the exposed compartment. P is the vaccination rate. γ is the rate at which infectious agents recover their health. We consider here that the disease has a horizontal transmission. infection is transmitted from infected individuals to susceptible individuals on the one hand, and infected individuals are vaccinated on the other hand because the vaccination does not confer total immunity. The susceptible ones become infected by the relation βSI and the vaccinated become infected with the relation $\theta\beta VI$, where $\theta \in [0,1]$. This means that $1-\theta$ is the effectiveness of the vaccination.

The compartmental scheme of this model is illustrated by the diagram given in (Figure 1).

We take into account both, the dilution rate and all individual specific mortality (maintenance) rates. Only susceptible individuals are introduced into the reactor with a constant dilution rate D and an input concentration S_{in} (Figure 2).

The model developed here has then five components, S, V, E, I and R known as 'SVEIR' model of infectious disease transmission in a chemostat. The population are classified as Susceptible compartment (S), Vaccinated compartment (V), Exposed compartment (E), Infected compartment (I), and Recovered compartment (R) and modelled by the following five-dimensional dynamical system of ODEs:

$$\begin{cases} \dot{S} = D\left(S_{in}-S\right)-\left(m_s+p\right)S-\beta SI, \\ \dot{V} = pS-\left(D+m_V\right)V-\theta\beta VI, \\ \dot{E} = \beta I\left(S+\theta V\right)-\left(D+m_E+\varepsilon\right)E, \\ \dot{I} = \varepsilon E-\left(D+m_I+\gamma\right)I, \\ \dot{R} = \gamma I-\left(D+m_R\right)R, \end{cases} \tag{1}$$

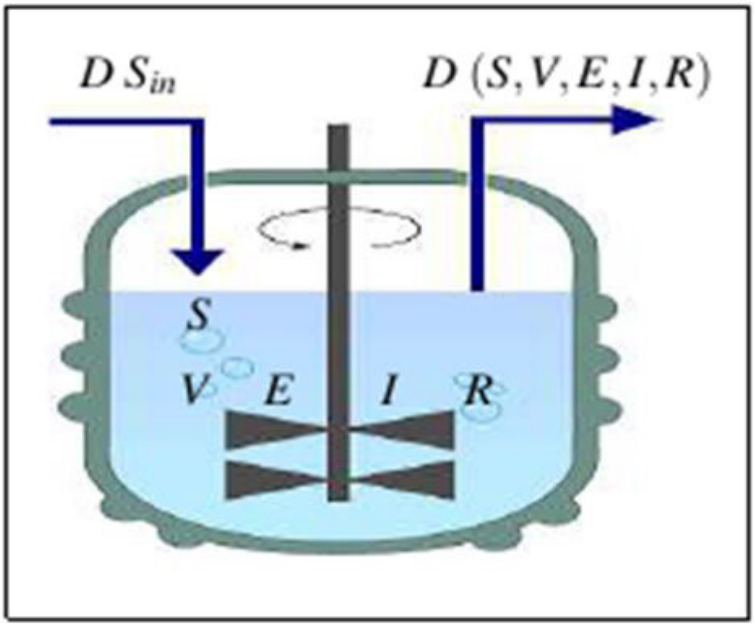

Figure 2: "SVEIR" epidemic model in a chemostat

with positive initial condition $(S(0),V(0),E(0),I(0),R(0)) \in \mathbb{R}^5_+$ where $p, \beta, \theta, \frac{1}{\varepsilon}$ and $\frac{1}{\gamma}$ are the vaccination rate, the mass action incidence rate, the vaccination factor reducing the risk of infection after vaccination, the average duration of latency in compartment *E* before progressing to compartment *I* and the average time spent in compartment *I* before recovery (*R*), respectively.

m_S, m_V, m_E, m_I and m_R are the mortality rates of , susceptible, vaccinated, exposed, infected and recovered individuals, respectively.

Generalities

The basic reproduction number is denoted by *R*. This concept is now unanimously recognized as a key concept in epidemiology[13,14]. It is defined "heuristically" as the average number of new cases of infection, caused by an average infected individual (in the course of its infectious period) in a population that is fully susceptible. For the last thirty years, has been part of the majority of research using mathematical modeling.

Generally, if *R<1*, then an individual infects on average less than one, which means that the disease will disappear from the population eventually. In contrast, if *R>1*, then the disease can spread in the population. Determining according to the parameters of the model thus makes it possible to calculate the conditions under which the disease is spreading.

Define the following parameters: $\overline{S} = \frac{DS_{in}}{D+m_S+p}, \overline{V} = \frac{pDS_{in}}{(D+m_V)(D+m_S+p)}, \overline{E} = 0, \overline{I} = 0$ and $\overline{R} = 0$.

The basic reproduction number *R*, in this case, is given by:

$$\mathcal{R} = \frac{\varepsilon\beta\left(\overline{S} + \theta\overline{V}\right)}{(D+m_E+\varepsilon)(D+m_I+\gamma)}. \tag{2}$$

By replacing $\overline{S}$ and $\overline{V}$ by their expressions in (2), one obtains:

$$\mathcal{R}_0 = \mathcal{R}|_{p=0} = \frac{DS_{in}\varepsilon\beta}{(D+m_E+\varepsilon)(D+m_I+\gamma)(D+m_S)}. \tag{3}$$

When there is no vaccination (p=0), system (1) without the fifth equation (*V*) becomes the standard SEIR model with

$$\mathcal{R}_0 = \mathcal{R}|_{p=0} = \frac{DS_{in}\varepsilon\beta}{(D+m_E+\varepsilon)(D+m_I+\gamma)(D+m_S)}. \tag{4}$$

$\mathbb{R}^5_+$, the closed non-negative cone in $\mathbb{R}^5$, is positively invariant[4,5,6,7,8,9,11,18] by the system (1). More precisely, let $m = \min(m_S, m_V, m_E, m_I, m_R)$, then I get

Proposition 1:

1. For all initial condition in $\mathbb{R}_+^5$, the solution of system (1) is bounded and has positive components and thus is defined for all $t>0$.

2. System (1) admits a positive invariant attractor set of all solution given by

$$\Omega_1 = \left\{ \left(S,V,E,I,R\right) \in \mathbb{R}_+^5 \ / \ S+V+E+I+R \le \frac{D}{D+m} S_{in} \right\}.$$

Proof.

1. The positivity of the solution is proved by the fact that :

If $S = 0$ then $S = DS_{in}>0$ and if $V= 0$ then $V= pS >0$. If $E = 0$ then $\dot{E} = \beta I\left(S+\theta V\right) > 0$ and if $I = 0$ then $\dot{I} = \varepsilon E > 0$. Finally, if $R = 0$ then $\dot{R} = \gamma I > 0$.

Next I have to prove the boundedness of solutions of (1). By adding all equations of system (1), one obtains, for $T = S+V+E+I+R-\frac{D}{D+m}S_{in}$, a single equation :

$$\begin{aligned}
\dot{T} &= \dot{S}+\dot{V}+\dot{E}+\dot{I}+\dot{R} \\
&= D\left(S_{in}-S-V-E-I-R\right)-m_S S-m_V V-m_E E-m_I I-m_R R \\
&\le D\left(S_{in}-S-V-E-I-R\right)-mS-mV-mE-mI-mR \\
&\le \left(D+m\right)\left(\frac{D}{D+m}S_{in}-S-V-E-I-R\right) \\
&\le -\left(D+m\right)T
\end{aligned}$$

then $S+V+E+I+R \le \frac{D}{D+m}S_{in}+\left(S\left(0\right)+V\left(0\right)+E\left(0\right)+I\left(0\right)+R\left(0\right)-\frac{D}{D+m}S_{in}\right)e^{-(D+m)t}$. (5)

Since all terms of the sum are positive, then the solution of system (1) is bounded.

2. The second point is simply a direct consequence of equality (5)

Proposition 2: *System (1) admits a unique disease-free equilibrium* $\overline{E} = \left(\overline{S},\overline{V},\overline{E},\overline{I},\overline{R}\right)$ and a unique disease-persistence (endemic) equilibrium $E^* = \left(S^*,V^*,E^*,I^*,R^*\right)$ as possible equilibrium points with $S^*,V^*,E^*,I^*,R^* > 0$.

Proof. Equilibrium points of system (1) satisfy

$$\begin{cases}
0 = D\left(S_{in}-S\right)-\left(m_s+p\right)S-\beta SI, \\
0 = pS-\left(D+m_V\right)V-\theta\beta VI, \\
0 = \beta I\left(S+\theta V\right)-\left(D+m_E+\varepsilon\right)E, \\
0 = \varepsilon E-\left(D+m_I+\gamma\right)I, \\
0 = \gamma I-\left(D+m_R\right)R,
\end{cases} \quad (6)$$

which means

$$
\begin{aligned}
S &= \frac{DS_{in}}{\left(D+m_s+p+\beta I\right)},\\
V &= \frac{pS}{\left(D+m_V+\theta\beta I\right)} = \frac{pDS_{in}}{\left(D+m_V+\theta\beta I\right)\left(D+m_s+p+\beta I\right)},\\
E &= \frac{\beta I}{\left(D+m_E+\varepsilon\right)}\left(S+\theta V\right) = \frac{\beta DS_{in}\left(D+m_V+\theta p+\theta\beta I\right)}{\left(D+m_E+\varepsilon\right)\left(D+m_s+p+\beta I\right)\left(D+m_V+\theta\beta I\right)} I,\\
I &= \frac{\varepsilon}{\left(D+m_I+\gamma\right)} E = \frac{\varepsilon\beta DS_{in}\left(D+m_V+\theta p+\theta\beta I\right)}{\left(D+m_I+\gamma\right)\left(D+m_E+\varepsilon\right)\left(D+m_s+p+\beta I\right)\left(D+m_V+\theta\beta I\right)} I,\\
R &= \frac{\gamma}{\left(D+m_R\right)} I = \frac{\gamma\varepsilon\beta DS_{in}\left(D+m_V+\theta p+\theta\beta I\right)}{\left(D+m_R\right)\left(D+m_I+\gamma\right)\left(D+m_E+\varepsilon\right)\left(D+m_s+p+\beta I\right)\left(D+m_V+\theta\beta I\right)} I
\end{aligned}
\tag{7}
$$

Using only the fourth equation, I obtain:

$$
I = \frac{\varepsilon\beta DS_{in}\left(D+m_V+\theta p+\theta\beta I\right)}{\left(D+m_I+\gamma\right)\left(D+m_E+\varepsilon\right)\left(D+m_s+p+\beta I\right)\left(D+m_V+\theta\beta I\right)} I.
$$

As all parameters are assumed to be non-negative then either $I = 0$ or

$$
\varepsilon\beta DS_{in}\left(D+m_V+\theta p+\theta\beta I\right) = \left(D+m_I+\gamma\right)\left(D+m_E+\varepsilon\right)\left(D+m_s+p+\beta I\right)\left(D+m_V+\theta\beta I\right).
$$

• If $I = 0$ then from system (7), one obtains $R = 0, E = 0, S = \frac{DS_{in}}{D+m_S+p}$ and $V = \frac{pS}{\left(D+m_V\right)} = \frac{pDS_{in}}{\left(D+m_V\right)\left(D+m_S+p\right)}$

This equilibrium is the so called disease-free equilibrium denoted by $\overline{E} = \left(\overline{S}, \overline{V}, \overline{E}, \overline{I}, \overline{R}\right)$ where $\overline{S} = \frac{DS_{in}}{D+m_S+p}$, $\overline{V} = \frac{pDS_{in}}{\left(D+m_V\right)\left(D+m_S+p\right)}, \overline{E} = 0, \overline{I} = 0$ and $\overline{R} = 0$.

• If then one must have $\varepsilon\beta DS_{in}\left(D+m_V+\theta p+\theta\beta I\right) = \left(D+m_I+\gamma\right)\left(D+m_E+\varepsilon\right)\left(D+m_s+p+\beta I\right)\left(D+m_V+\theta\beta I\right)$.

This can be reduced to

$$
\begin{aligned}
&\theta\beta^2\left(D+m_I+\gamma\right)\left(D+m_E+\varepsilon\right)I^2 + \left(\beta\left(D+m_I+\gamma\right)\left(D+m_E+\varepsilon\right)\left(\theta D+\theta m_s+\theta p+D+m_V\right)\right.\\
&\left.-\varepsilon\theta\beta^2 DS_{in}\right)I + \left(D+m_I+\gamma\right)\left(D+m_E+\varepsilon\right)\left(D+m_s+p\right)\left(D+m_V\right) - \varepsilon\beta DS_{in}\left(D+m_V+\theta p\right) = 0
\end{aligned}
$$

having the form

$$
aI^2 + bI + c = 0, \tag{8}
$$

where

$$
a = \theta\beta^2\left(D+m_I+\gamma\right)\left(D+m_E+\varepsilon\right) > 0,
$$

$$
b = \beta\left(D+m_I+\gamma\right)\left(D+m_E+\varepsilon\right)\left(\theta D+\theta m_s+\theta p+D+m_V\right) - \varepsilon\theta\beta^2 DS_{in}
$$

and

$$
c = \left(D+m_I+\gamma\right)\left(D+m_E+\varepsilon\right)\left(D+m_s+p\right)\left(D+m_V\right) - \varepsilon\beta DS_{in}\left(D+m_V+\theta p\right).
$$

I write b and c in the following forms

$$b=\beta\left(D+m_I+\gamma\right)\left(D+m_E+\varepsilon\right)\left(D+m_s+p\right)\left(D+m_V\right)\left(\frac{\theta\left(D+m_s+p\right)+D+m_V}{\left(D+m_s+p\right)\left(D+m_V\right)}-\frac{\theta\mathcal{R}}{\left(D+m_V+\theta p\right)}\right)$$

$$=\theta\beta\frac{\left(D+m_I+\gamma\right)\left(D+m_E+\varepsilon\right)\left(D+m_s+p\right)\left(D+m_V\right)}{\left(D+m_V+\theta p\right)}\left(\frac{\theta\left(D+m_s+p\right)+D+m_V}{\theta\left(D+m_s+p\right)\left(D+m_V\right)}\left(D+m_V+\theta p\right)-\mathcal{R}\right)$$

$$=\varepsilon\theta\beta^2\frac{DS_{in}}{\mathcal{R}}\left(\frac{\theta\left(D+m_s+p\right)+D+m_V}{\theta\left(D+m_s+p\right)\left(D+m_V\right)}\left(D+m_V+\theta p\right)-\mathcal{R}\right)$$

$$=\varepsilon\theta\beta^2\frac{DS_{in}}{\mathcal{R}}\left(D+m_V+\frac{\theta p}{D+m_V}+\frac{\left(D+m_V\right)\left(D+m_V+\theta p\right)}{\theta\left(D+m_s+p\right)\left(D+m_V\right)}+\left(1-\mathcal{R}\right)\right)$$

and

$$c=\left(D+m_I+\gamma\right)\left(D+m_E+\varepsilon\right)\left(D+m_s+p\right)\left(D+m_V\right)\left(1-\mathcal{R}\right).$$

If $R>1$ then $c<0$ and since $a>0$, Equation (7) admits at most two solutions where only one of them is non-negative (I^*) and that can be considered here due to proposition 1.

Now If $R<1$ then $c>0$ and since $a>0$, Equation (7) admits at most two solutions having the same sign. But if $R<1$ then $b>0$ then both solutions of (7) are negative and then it can't be considered here due to proposition 1.

Then there exists at most one disease-persistence (endemic) equilibrium $E^*=(S^*,V^*,E^*,I^*,R^*)$ with $E^*=(S^*,V^*,E^*,I^*,R^*)$. Note that S^*,V^*,E^* and R^* can be expressed on I^* from system (7). This completes the proof.

Corollary 1: $\Omega_2=\left\{\left(S,V,E,I,R\right)\in\mathbb{R}_+^5\ /\ S+V+E+I+R\le\frac{D}{D+m}S_{in};S\le\overline{S},V\le\overline{V}\right\}$ *is a positive invariant attractor set of all solutions of system (1).*

Proof. I proved in Proposition 1 that Ω_1 is a positive invariant attractor set of all solution of system (1). Now, since $\dot{S}(t)<0$ for $S(t)>\overline{S}$ then $\liminf S\left(t\right)\le\overline{S}$.

For a positive constant $\xi>0$, and for a given initial condition, there exists $T\ge0$ such that $S\left(t\right)\le\overline{S}+\xi$ for all $t\ge T$.

Then $\dot{V}\left(t\right)<p\left(\overline{S}+\xi\right)-\left(D+m_V\right)V=-\left(D+m_V\right)\left(V-\frac{p\left(\overline{S}+\xi\right)}{\left(D+m_V\right)}\right)$ for all $t\ge T$.

Then by applying the theory of differential inequalities [2], I obtain

$$V\left(t\right)\le\frac{p\left(\overline{S}+\xi\right)}{\left(D+m_V\right)}+\left(V\left(0\right)-\frac{p\left(\overline{S}+\xi\right)}{\left(D+m_V\right)}\right)e^{-\left(D+m_V\right)t}. \tag{9}$$

One obtains therefore $\liminf V\left(t\right)\le\frac{p\left(\overline{S}+\xi\right)}{\left(D+m_V\right)}$. This holds for all $\xi>0$ and so $\liminf V\left(t\right)\le\frac{p\overline{S}}{\left(D+m_V\right)}=\overline{V}$.

This completes the proof.

The solutions of system (1) are exponentially convergent towards the set Ω_2 and we are interested in the asymptotic behavior of these solutions. It is enough to restrict the study of the asymptotic behaviour of system (1) to Ω_2. In fact the asymptotic behaviour of the solutions of the restriction of (1) on Ω_2 will be informative for the complete system.

From Equation (3), I obtain the following result.

Proposition 3: $\mathcal{R}\le\mathcal{R}_0$ *if and only if* $\theta\left(D+m_S\right)\le\left(D+m_V\right)$.

Proof.

$$\begin{aligned}\mathcal{R} &= \frac{DS_{in}\varepsilon\beta\left(D+m_V+\theta p\right)}{\left(D+m_E+\varepsilon\right)\left(D+m_I+\gamma\right)\left(D+m_S+p\right)\left(D+m_V\right)}\\ &= \frac{\left(D+m_V+\theta p\right)}{\left(D+m_S+p\right)}\frac{DS_{in}\varepsilon\beta}{\left(D+m_E+\varepsilon\right)\left(D+m_I+\gamma\right)\left(D+m_V\right)}\\ &= \frac{\left(D+m_V+\theta p\right)}{\left(D+m_S+p\right)}\frac{\left(D+m_S\right)}{\left(D+m_V\right)}\mathcal{R}_0\\ &\le \mathcal{R}_0\end{aligned}$$

if and only if $\left(D+m_V+\theta p\right)\left(D+m_S\right)\le\left(D+m_V\right)\left(D+m_S+p\right)$ which equivalent to $\theta p\left(D+m_S\right)\le\left(D+m_V\right)p$. This completes the proof.

The value of *R* determines whether there exists an endemic equilibrium or not (as in [1], Theorem 2.3).

Theorem 1: *The disease-free equilibrium* $\overline{E}$ *exists always and it is unique. If* $R < 1$*, then the disease-free equilibrium point* $\overline{E}$ *is locally asymptotically stable and it is unstable if* $R > 1$*.*

Proof. The Jacobian matrix at a point $\left(S,V,E,I,R\right)$ is given by:

$$J=\begin{pmatrix}-\left(D+m_S+p\right)-\beta I & 0 & 0 & -\beta S & 0\\ p & -\left(D+m_V\right)-\theta\beta I & 0 & -\theta\beta V & 0\\ \beta I & \theta\beta I & -\left(D+m_E+\varepsilon\right) & \beta\left(S+\theta V\right) & 0\\ 0 & 0 & \varepsilon & -\left(D+m_I+\gamma\right) & 0\\ 0 & 0 & 0 & \gamma & -\left(D+m_R\right)\end{pmatrix}.$$

The Jacobian matrix evaluated at $\overline{E}$ is then given by:

$$\overline{J}=\begin{pmatrix}-\left(D+m_S+p\right) & 0 & 0 & -\beta\overline{S} & 0\\ p & -\left(D+m_V\right) & 0 & -\theta\beta\overline{V} & 0\\ 0 & 0 & -\left(D+m_E+\varepsilon\right) & \beta\left(\overline{S}+\theta\overline{V}\right) & 0\\ 0 & 0 & \varepsilon & -\left(D+m_I+\gamma\right) & 0\\ 0 & 0 & 0 & \gamma & -\left(D+m_R\right)\end{pmatrix}.$$

$\overline{J}$ admits five eigenvalues. The first three eigenvalues are given by $\lambda_1=-\left(D+m_S+p\right)<0,\lambda_2=-\left(D+m_V\right)<0,\lambda_3=-\left(D+m_R\right)<0$. the other two eigenvalues are those of the following sub-matrix

$$\begin{pmatrix}-\left(D+m_E+\varepsilon\right) & \beta\left(\overline{S}+\theta\overline{V}\right)\\ \varepsilon & -\left(D+m_I+\gamma\right)\end{pmatrix}$$

where the characteristic polynomial is given by

$$P\left(\lambda\right)=\lambda^2+\left(2D+m_E+m_I+\varepsilon+\gamma\right)\lambda+\left(1-\mathcal{R}\right)\left(D+m_E+\varepsilon\right)\left(D+m_I+\gamma\right).$$

It clear that the roots of $P(\lambda)$ have negative real parts if and only if $R < 1$. It follows that the disease-free equilibrium $\overline{E}$ is locally asymptotically stable whenever $R < 1$ and unstable when $R > 1$. This completes the proof.

The global stability of the disease-free equilibrium $\overline{E}$ is given in the following theorem (cf. ([5]).

Theorem 2: *If* $\mathcal{R}\le 1$*, then the disease-free equilibrium* $\overline{E}$ *is globally asymptotically stable. If* $R > 1$*, then the disease-free equilibrium* $\overline{E}$ *is unstable.*

Proof. Consider the following Lyapunov function:

$$F = \varepsilon E + \left(D + m_E + \varepsilon\right) I$$

with Lyapunov derivative,

$$\begin{aligned}
\dot{F} &= \varepsilon \dot{E} + \left(D + m_E + \varepsilon\right) \dot{I} \\
&= \varepsilon\left(\beta\left(S + \theta V\right) I - \left(D + m_E + \varepsilon\right) E\right) + \left(D + m_E + \varepsilon\right)\left(\varepsilon E - \left(D + m_I + \gamma\right) I\right) \\
&= \varepsilon\beta\left(S + \theta V\right) I - \left(D + m_E + \varepsilon\right)\left(D + m_I + \gamma\right) I \\
&= \left(\varepsilon\beta\left(S + \theta V\right) - \left(D + m_E + \varepsilon\right)\left(D + m_I + \gamma\right)\right) I \\
&= \left(D + m_E + \varepsilon\right)\left(D + m_I + \gamma\right)\left(\frac{\varepsilon\beta\left(S + \theta V\right)}{\left(D + m_E + \varepsilon\right)\left(D + m_I + \gamma\right)} - 1\right) I \\
&\le \left(D + m_E + \varepsilon\right)\left(D + m_I + \gamma\right)\left(\frac{\varepsilon\beta\left(\overline{S} + \theta\overline{V}\right)}{\left(D + m_E + \varepsilon\right)\left(D + m_I + \gamma\right)} - 1\right) I \quad \text{since} \quad S \le \overline{S}, V \le \overline{V} \\
&= \left(D + m_E + \varepsilon\right)\left(D + m_I + \gamma\right)\left(\mathcal{R} - 1\right) I, \ \forall \left(S, V, E, I, R\right) \in \Omega_2.
\end{aligned}$$

Since all parameters of the model are non-negative, it follows that $\dot{F} \le 0$ for $\mathcal{R} \le 1$ with F = 0 only if $I = 0$. Hence, F is a Lyapunov function on Ω_2. Further, by Corollary 1, Ω_2 is a compact, absorbing subset of $\mathbb{R}^5_+$, and the largest compact invariant set in $\left\{\left(S, V, E, I, R\right) \in \Omega_2 : \dot{F} = 0\right\}$ is the singleton $\left\{\overline{E}\right\}$. Therefore, by the Lasalle's invariance principle (see, for instance, Theorem 3.1] and for other application), every solution of system (1) with initial conditions in $\mathbb{R}^5_+$ converges to $\overline{E}$ as $t \mapsto +\infty$ [11,15].

The global stability of the disease-persistence (endemic) equilibrium E^* is given in the following theorem.

Theorem 3: If $R > 1$, then the disease-persistence equilibrium $E^* = \left(S^*, V^*, E^*, I^*, R^*\right)$ is globally asymptotically stable. If $\mathcal{R} \le 1$, then the disease-persistence equilibrium E^* is unstable.

Proof. Consider the following Lyapunov function:

$$\mathcal{V} = \left(S - S^* \ln\left(\frac{S}{S^*}\right)\right) + \left(V - V^* \ln\left(\frac{V}{V^*}\right)\right) + \left(E - E^* \ln\left(\frac{E}{E^*}\right)\right) + \frac{D + m_E + \varepsilon}{\varepsilon}\left(I - I^* \ln\left(\frac{I}{I^*}\right)\right)$$

The equilibrium E^* is the only internal stationary point of system (1). The function $V(t)$ admits its minimum value $\mathcal{V}_{\min} = S^* + V^* + E^* + \frac{D + m_E + \varepsilon}{\varepsilon} I^*$ when $S = S^*, V = V^*, E = E^*, I = I^*$, and $\mathcal{V}(t) \mapsto +\infty$ at the boundary of the positive quadrant. Consequently, E^* is the global minimum point, and the function is bounded from below.

The derivative, of V(t), along solutions of system (1) is given by

$$\begin{aligned}
\dot{\mathcal{V}} &= \left(1 - \frac{S^*}{S}\right)\dot{S} + \left(1 - \frac{V^*}{V}\right)\dot{V} + \left(1 - \frac{E^*}{E}\right)\dot{E} + \frac{D + m_E + \varepsilon}{\varepsilon}\left(1 - \frac{I^*}{I}\right)\dot{I} \\
&= \left(1 - \frac{S^*}{S}\right)\left(D\left(S_{in} - S\right) - \left(m_s + p\right) S - \beta I S\right) + \left(1 - \frac{V^*}{V}\right)\left(pS - \left(D + m_V\right) V - \theta\beta I V\right) \\
&+ \left(1 - \frac{E^*}{E}\right)\left(\beta I\left(S + \theta V\right) - \left(D + m_E + \varepsilon\right) E\right) + \frac{D + m_E + \varepsilon}{\varepsilon}\left(1 - \frac{I^*}{I}\right)\left(\varepsilon E - \left(D + m_I + \gamma\right) I\right) \\
&= DS_{in} - \left(D + m_s\right) S - DS_{in}\frac{S^*}{S} + \left(D + m_s\right) S^* + pS^* + \beta I S^* \\
&_ \left(D + m_V\right) V - pS\frac{V^*}{V} + \left(D + m_V\right) V^* + \theta\beta I V^* - \beta I\left(S + \theta V\right)\frac{E^*}{E} + \left(D + m_E + \varepsilon\right) E^* \\
&- \left(\frac{D + m_E + \varepsilon}{\varepsilon}\right)\left(D + m_I + \gamma\right) I - \left(D + m_E + \varepsilon\right) E\frac{I^*}{I} + \left(\frac{D + m_E + \varepsilon}{\varepsilon}\right)\left(D + m_I + \gamma\right) I^*.
\end{aligned}$$

Using the fact that $\left(S^*, V^*, E^*, I^*, R^*\right)$ is solution of system 7) then the expression of V reduces to

$$\dot{\mathcal{V}} = \left(D + m_S\right)S^* - \left(D + m_S\right)S - \left(D + m_S\right)\frac{S^{*2}}{S} + \left(D + m_S\right)S^*$$
$$+\left(D + m_V\right)V^* - \left(D + m_V\right)\frac{S^*}{S}V^* + \left(D + m_V\right)V^*$$
$$-\left(D + m_V\right)V + \left(D + m_V\right)V^* + \left(D + m_V\right)V^* - \left(D + m_V\right)\frac{V^{*2}}{V}\frac{S}{S^*} + \beta I^*\left(S^* + \theta V^*\right)$$
$$-\beta I^*\frac{S^{*2}}{S} - \theta\beta I^*V^*\frac{S^*}{S} + \theta\beta I^*V^* + \beta I^*S^* - \theta\beta I^*\frac{V^{*2}}{V}\frac{S}{S^*}$$
$$+\theta\beta IV^* - \beta I\left(S + \theta V\right)\frac{E^*}{E} + \beta I\left(S^* + \theta V^*\right)$$
$$-\left(\frac{D + m_E + \varepsilon}{\varepsilon}\right)\left(D + m_I + \gamma\right)I - \left(D + m_E + \varepsilon\right)E\frac{I^*}{I} + \left(\frac{D + m_E + \varepsilon}{\varepsilon}\right)\left(D + m_I + \gamma\right)I^*.$$

More simply,

$$\dot{\mathcal{V}} = \left(D + m_S\right)S^*\left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) + \left(D + m_V\right)V^*\left(3 - \frac{S^*}{S} - \frac{V}{V^*} - \frac{V^*}{V}\frac{S}{S^*}\right)$$
$$+3\beta I^*S^* - \beta I^*\frac{S^{*2}}{S} - \beta I^*S^*\frac{E}{E^*}\frac{I^*}{I} - \beta IS\frac{E^*}{E}$$
$$-3\theta\beta I^*V^* + \theta\beta I^*V^* - \theta\beta I^*\frac{V^{*2}}{V}\frac{S}{S^*} - \theta\beta IV\frac{E^*}{E} - \theta\beta I^*V^*\frac{E}{E^*}\frac{I^*}{I}$$
$$-\theta\beta I^*V^*\frac{S^*}{S} - \left(\frac{D + m_E + \varepsilon}{\varepsilon}\right)\left(D + m_I + \gamma\right)I + \beta I\left(S^* + \theta V^*\right).$$

I obtain finally

$$\dot{\mathcal{V}} = \left(D + m_S\right)S^*\left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) + \left(D + m_V\right)V^*\left(3 - \frac{S^*}{S} - \frac{V}{V^*} - \frac{V^*}{V}\frac{S}{S^*}\right)$$
$$+\beta S^*I^*\left(3 - \frac{S^*}{S} - \frac{I}{I^*}\frac{S}{S^*}\frac{E^*}{E} - \frac{E}{E^*}\frac{I^*}{I}\right) + \theta\beta V^*I^*\left(4 - \frac{V^*}{V}\frac{S}{S^*} - \frac{I}{I^*}\frac{V}{V^*}\frac{E^*}{E} - \frac{E}{E^*}\frac{I^*}{I} - \frac{S^*}{S}\right)$$

Note that

$$\frac{S}{S^*}\frac{S^*}{S} = 1, \frac{S^*}{S}\frac{V}{V^*}\frac{V^*}{V}\frac{S}{S^*} = 1, \frac{S^*}{S}\frac{I}{I^*}\frac{S}{S^*}\frac{E^*}{E}\frac{E}{E^*}\frac{I^*}{I} = 1$$

and

$$\frac{V^*}{V}\frac{S}{S^*}\frac{I}{I^*}\frac{V}{V^*}\frac{E^*}{E}\frac{E}{E^*}\frac{I^*}{I}\frac{S^*}{S} = 1.$$

I recall also the following inequality :

$$x_1 + x_2 + x_3 + \cdots + x_n \geq n\sqrt[n]{x_1.x_2.x_3\cdots x_n}, \quad x_1, x_2, x_3, \cdots, x_n \geq 0 \tag{10}$$

Since arithmetical mean of nonnegative real numbers is greater than the geometrical one, we have the following inequalities

$$\left(2-\frac{S}{S^*}-\frac{S^*}{S}\right)\le 0,$$
$$\left(3-\frac{S^*}{S}-\frac{V}{V^*}-\frac{V^*}{V}\frac{S}{S^*}\right)\le 0,$$
$$\left(3-\frac{S^*}{S}-\frac{I}{I^*}\frac{S}{S^*}\frac{E^*}{E}-\frac{E}{E^*}\frac{I^*}{I}\right)\le 0,$$
$$\left(4-\frac{V^*}{V}\frac{S}{S^*}-\frac{I}{I^*}\frac{V}{V^*}\frac{E^*}{E}-\frac{E}{E^*}\frac{I^*}{I}-\frac{S^*}{S}\right)\le 0.$$

Therefore $\dot{\mathcal{V}}\le 0$. Thank's to the stability Lyapunov theorem, one deduces that $E^*=\left(S^*,V^*,E^*,I^*,R^*\right)$ is stable. It remains to show that $E^*=\left(S^*,V^*,E^*,I^*,R^*\right)$ is asymptotically stable using the Lasalle invariance principle (see, for instance, [Theorem 3.1] and for other application).

Define [11,15]

$$A=\left(2-\frac{S}{S^*}-\frac{S^*}{S}\right),$$
$$B=\left(3-\frac{S^*}{S}-\frac{V}{V^*}-\frac{V^*}{V}\frac{S}{S^*}\right),$$
$$C=\left(3-\frac{S^*}{S}-\frac{I}{I^*}\frac{S}{S^*}\frac{E^*}{E}-\frac{E}{E^*}\frac{I^*}{I}\right),$$
$$D=\left(4-\frac{V^*}{V}\frac{S}{S^*}-\frac{I}{I^*}\frac{V}{V^*}\frac{E^*}{E}-\frac{E}{E^*}\frac{I^*}{I}-\frac{S^*}{S}\right).$$

Then one has

$$\dot{\mathcal{V}}\left(S,V,E,I,R\right)=0\Leftrightarrow A=B=C=D=0.$$

Using to the above relations, one obtains the following implications.

$$A=0\Rightarrow S=S^*,$$
$$\left(S=S^*,B=0\right)\Rightarrow V=V^*,$$
$$\left(S=S^*,C=0\right)\Rightarrow\left(\frac{E}{E^*}=\frac{I}{I^*}\right).$$

Finally, I obtain

$$\dot{\mathcal{V}}\left(S,V,E,I,R\right)=0\Leftrightarrow S=S^*,V=V^*,\frac{E}{E^*}=\frac{I}{I^*}$$

Since in the endemic equilibrium, I have

$$A=0\Rightarrow S=S\ ,$$
$$\left(S=S^*,B=0\right)\Rightarrow V=V^*,$$
$$\left(S=S\ ,C=0\right)\Rightarrow\left(\frac{E}{E^*}=\frac{I}{I^*}\right).$$

Let $r = \frac{E}{E^*} = \frac{I}{I^*}$, then $E = rE^*$ and $I = rI^*$.
For the endemic equilibrium, I get

$$\begin{aligned} DS_{in} &= \left(D + m_S + p\right)S^* + \beta S^* I^*, \\ pS^* &= \left(D + m_V\right)V^* + \theta\beta V^* I^*, \\ \beta I^*\left(S^* + \theta V^*\right) &= \left(D + m_E + \varepsilon\right)E^*, \\ \varepsilon E^* &= \left(D + m_I + \gamma\right)I^*. \end{aligned}$$

Then I obtain

$$pS^* = \left(D + m_V\right)V^* + \theta\beta V^* I^*, r = 1$$

and therefore $I = I^*$ and $E = E^*$. Finally

$$\dot{\mathcal{V}}\left(S,V,E,I,R\right) = 0 \Leftrightarrow \left(S = S^*, V = V^*, E = E^*, I = I^*, R = R^*\right).$$

Thus, the largest invariant set contained in $\{(S,V,E,I,R) \mid \dot{\mathcal{V}} = 0\}$ is $\left\{E^* = \left(S^*, V^*, E^*, I^*, R^*\right)\right\}$. Then the global stability of the disease-persistence equilibrium $E^* = \left(S^*, V^*, E^*, I^*, R^*\right)$ follows according to the Lasalle invariance principle (see for an application) [11,16].

Consider the case where the dilution rate is large enough compared to the natural mortality rates of all individuals which is the most considered in applied cases. Then by neglecting all mortality rates m_S, m_V, m_E, m_I and m_R, one obtains:

Corollary 2:

• $\Omega_3 = \left\{\left(S,V,E,I,R\right) \in \mathbb{R}_+^5 \ / \ S + V + E + I + R = S_{in}; S \le \frac{DS_{in}}{D+p}, V \le \frac{pS_{in}}{D+p}\right\}$ is a positive invariant attractor set of all solutions of system (1).

• If $R > 1$, then the disease-persistence equilibrium $E^* = \left(S^*, V^*, E^*, I^*, R^*\right)$ is globally asymptotically stable and the disease-free equilibrium $\bar{E} = \left(\frac{DS_{in}}{D+p}, \frac{pS_{in}}{D+p}, 0, 0, 0\right)$ is unstable.

• If $\mathcal{R} \le 1$, then the disease-persistence equilibrium E^* is unstable and the disease-free equilibrium $\bar{E}$ is globally asymptotically stable.

Numerical Simulations

We performed numerical simulations for system (1). Four cases were considered. Two of them performing the global stability of the disease-free equilibrium $\bar{E}$ when $\mathcal{R} \le 1$. The other two tests perform the global stability of the disease-persistence equilibrium $E^* = \left(S^*, V^*, E^*, I^*, R^*\right)$ when $R > 1$ (Figure 2 and 3) [17-23].

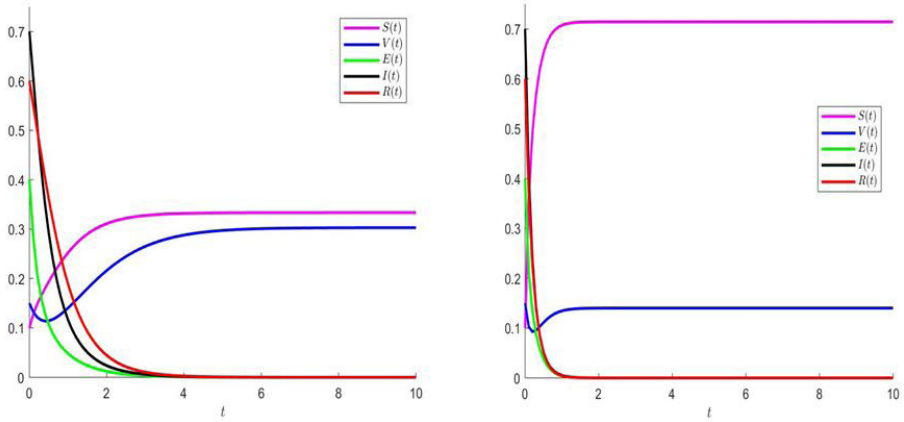

Figure 3: (*S(t), V(t), E(t), I(t), R(t)*) behaviours for (left)

$S_{in}=1; D=1; m_S=1; m_V=0.1; m_E=1; m_I=1; m_R=1; p=1; \beta=5; \theta=0.3; \varepsilon=3; \gamma=1, \mathcal{R}=0.4242\leq 1$ and for (right) S_{in}=1;D=5;m_S=1; m_V=0.1;m_E=1;m_I=1;m_R=1;p=1;β=5;θ=0.3;ε=3;γ=1,R=0.1801≤1. The solution of system (1) converge asymptotically to $\bar{E}$. Only Susceptible and Vaccinated compartiments persist, the other compartments vanish (Figure 4).

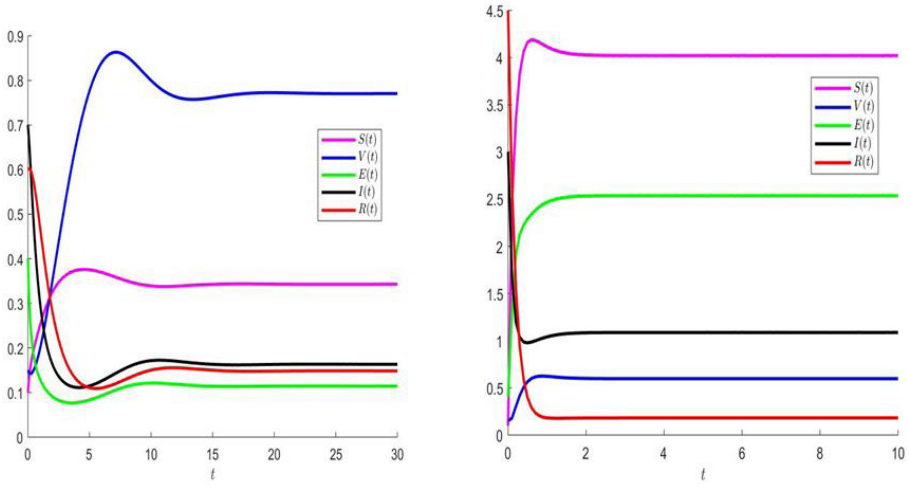

Figure 4: (*S(t), V(t), E(t), I(t), R(t)*) behaviours for (left) and for (right)

$$S_{in}=10; D=0.1; m_S=1; m_V=0.1; m_E=1; m_I=1; m_R=1; p=1; \beta=5; \theta=0.3; \varepsilon=3; \gamma=1, \mathcal{R}=2.0740>1$$

The solution of system (1) converge asymptotically to E^*. All compartiments persist.

Conclusion

A mathematical 5D dynamical system modelling an SVEIR model of infectious disease transmission in a chemostat is proposed. A profound qualitative analysis is given. The analysis of the local and global stability of equilibrium points is carried out. It is proved that if $R > 1$, then the disease-persistence (endemic) equilibrium is globally asymptotically stable. However, if $\mathcal{R}\leq 1$, then the disease-free equilibrium is globally asymptotically stable in $\mathbb{R}^5$.

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