International Journal of Analysis and Applications

Mathematical and Numerical Investigations for a Cholera Dynamics With a Seasonal Environment

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Abstract. We propose a mathematical model for the *vibrio cholerae* spread under the influence of a seasonal environment with two routes of infection. We proved the existence of a unique bounded positive solution, and that the system admits a global attractor set. The basic reproduction number \mathcal{R}_0 was calculated for both cases, the fixed and seasonal environment which permits to characterise both, the extinction and the persistence of the disease. We proved that the phage-free equilibrium point is globally asymptotically stable if $\mathcal{R}_0 \leq 1$, while the disease will be persist if $\mathcal{R}_0 > 1$. Finally, extensive numerical simulations are given to confirm the theoretical findings.

1. Introduction

Cholera is a highly contagious diarrheal disease caused by a Gram-negative bacillus: *vibrio cholerae*. This pathogenic bacterium has an exclusively digestive tropism and lives in a saprophytic state in water and estuaries. The bacterial strains responsible for cholera are transmitted either orally from water or food that it is contaminated with *vibrio cholerae* or by close contact with people infected with cholera. Cholera, known since Greek antiquity, was first time identified in the Ganges Delta, India. It remained there, for centuries, limited to Bangladesh, occasionally spilling over into the bordering territories of the Far East. The marked seasonality of cholera, or intra-annual variability,

Received: Oct. 3, 2023.

²⁰²⁰ Mathematics Subject Classification. 35B35, 35K57, 35Q92, 37N25, 92D30.

Key words and phrases. cholera model; environmental and horizontal transmission; basic reproduction number; global asymptotic stability.

and the simultaneous appearance of cases in different geographically distant places are at the origin of the search for "environmental or climatic forcing" to explain these parallel emergence or resurgence phenomena. and independent. Physical factors (i.e. extrinsic factors), such as water temperature, can explain the seasonality of disease either by exerting a direct influence on the abundance and/or toxicity of *vibrio cholerae* in the environment, or by exerting an indirect influence, for example, on reservoirs or even on parameters having an impact on the latter. Other physical parameters influencing water levels, such as precipitation, have been invoked to explain the distribution of cholera cases around the world. Indeed, floods and droughts not only affect the concentration of the bacteria in the environment but also its survival through effects on salinity, pH or the concentration of nutrients in the environment. The cholera/environment links are not only observed in the seasonal variability of cholera cases but also in the inter-annual variability, that is to say on an average time step of around 3 to 8 years.

The "Modeling" skill, if we take it in its broadest sense, refers for the mathematician to the fact of using a set of concepts, methods, mathematical theories that will make it possible to describe, understand and predict the evolution of phenomena external to mathematics. Modeling is a way to make the link between reality and mathematics. For several centuries, mathematics has not only been a tool extremely important for acting on and modifying nature, one of the main pillars of technique and technology, but also (and perhaps above all) a major instrument to understand it. In this sense, they are not only a source of utility but also of "truth". In particular, mathematical modeling is a way for studying the disease, predicting its behavior in the future, and then proposing suitable strategies. Several researchers worked on some mathematical models for several infectious diseases [1-6]). In particular, the modeling of the behavior of cholera bacteria in an aquatic environment [7] by proving the stability of both, the disease-free and the endemic steady sates by ignoring the human-to-human infection by vibrio cholerae. Later, in [8], the authors present the influence of phages in cholera control by extending the proposed model in [7] by adding a new compartment for phages in the model, and deduced that phages decrease the bacteria concentration of bacteria which reduces the infection. Several other mathematical models of cholera including the phages as compartments are developed and analysed [9, 10].

Note that seasonality in infectious is very repetitive [11]. In particular, each year with the return of cold weather, infectious diseases spread among the population. Although they are often temporary and harmless, they can nevertheless be much more serious, particularly in the weakest people. Cholera epidemics occur in a context marked by seasonal rains and tropical storms which have caused heavy flooding. Seasonal factors such as the monsoon or rainy season affect the development of an epidemic. We then talk about seasonality of cholera. Climate changes linked to global warming can interact with seasonal climatic factors, particularly through climatic anomalies (drought, floods) and be the cause of significant epidemic outbreaks Several sand simple mathematical models of infectious diseases that take into account of the seasonality were proposed [12–14]. In such mathematical models, the

basic reproduction number can be calculated either using the time-averaged system (autonomous) as in [15, 16] or other definition as in [1, 12, 17, 18] where all these definitions are different from the one defined for time-averaged system. In [19], the authors analysed the seasonal behaviour of an SVEIR epidemic model with vaccination. Similarly, in [20, 21], the authors studied the seasonal behaviour of some epidemic models related HIV and chikungunya virus spread. We aim in this paper to study the dynamics of *vibrio cholerae* in relation with phages and hosts when it is considered in both, fixed and seasonal environment and with a nonlinear general incidence rate. We calculated the basic reproduction number as the spectral radius of an integral operator. We analysed the global stability of the disease-free solution where we proved that it is globally asymptotically stable if $\mathcal{R}_0 < 1$. However, $\mathcal{R}_0 > 1$, we proved that the dynamics is persistent and so the disease-present solution converges to a limit cycle. We confirmed the theoretical findings by using an intense numerical examples.

The rest of this article is organized as follows. In Section 2, we present a generalised cholera epidemic model taking into of the seasonality. In Section 3, we concentrate on the case of fixed environment, and we calculated \mathcal{R}_0 and we studied the global analysis of both, the disease-free and the endemic equilibrium points. However, in section 4, we focus on the stability of phage-free and phage-present periodic solutions for the case of seasonal environment. Several numerical examples are given to confirm the theoretical findings in Section 5. Finally, in section 6, we provide some conclusions.

2. Generalised Cholera Epidemic Model

The mathematical model for vibrio cholerae spread that we proposed here is a compartmental one. Let t be the time variable, and we denote by S(t) and I(t) the quantities of susceptible and infected hosts, respectively. We denote also by V(t) and P(t) to be the quantities of vibrio cholerae and phages, respectively. Therefore, we are interested by the dynamical behaviors of susceptible, infected, vibrio cholerae, and phages. Therefore, the model is given by the fourth dimensional system of differential equations hereafter.

$$\dot{S}(t) = d(t)\Lambda_{1}(t) - \rho_{1}(t)f_{1}(I(t))S(t) - \rho_{2}(t)f_{2}(V(t))S(t) - d(t)S(t),
\dot{I}(t) = \rho_{1}(t)f_{1}(I(t))S(t) + \rho_{2}(t)f_{2}(V(t))S(t) - (\gamma(t) + d(t))I(t),
\dot{V}(t) = \eta(t)I(t) - \mu(t)V(t) - \rho_{3}(t)f_{3}(V(t))P(t),
\dot{P}(t) = \delta(t)\Lambda_{2}(t) + \theta(t)\rho_{3}(t)f_{3}(V(t))P(t) - \delta(t)P(t).$$
(2.1)

with initial conditions given by $S(0) = S_0$, $I(0) = I_0$, $V(0) = V_0$, and $P(0) = P_0$.

The susceptible hosts have a periodic recruited rate $d(t)\Lambda_1(t)$, and a periodic death rate d(t) and a periodic incidence rate $\rho_1(t)S(t)f_1(I(t)) + \rho_2(t)S(t)f_2(V(t))$, where $\rho_1(t)$ and $\rho_2(t)$ are the periodic contact rates. The periodic parameters $\mu(t)$ and $\delta(t)$ describe the periodic death rates of the *vibrio cholerae* and the phages, respectively. $\eta(t)$ is the periodic production rate from infected hosts to *vibrio cholerae*. The phages have a periodic proliferation rate given by $\delta(t)\Lambda_2(t) + \theta(t)\rho_3(t)f_3(V(t))P(t)$.



Figure 1. Diagram explaining the transition between the model compartments.

More details concerning the significance of the model parameters are given in Table 1.

Notation	Definition
S(t)	Periodic concentration of susceptible hosts
I(t)	Periodic concentration of infected hosts
V(t)	Periodic concentration of vibrio cholerae
P(t)	Periodic concentration of phages
$f_1(I)S$	Horizontal transmission described by the mass action
$f_2(V)S$	Environmental transmission described by the saturation incidence
$f_3(V)P$	Phage proliferation rate
Λ_1	Susceptible hosts periodic recruitment rate
Λ ₂	Phage periodic recruitment rate
μ	Periodic natural death rate of bacteria
d	Periodic natural death rates of susceptible and infected hosts
δ	Periodic death rate of phages
γ	Periodic removal rate of infected hosts other than natural death
η	Periodic shedding rate of bacteria from infected hosts
θ	Periodic burst size of bacteria (Concentration of phages produced per vibrio cholerae).

Table 1. Parameters and variables of system (2.1).

The incidence rates f_1 , f_2 and f_3 and the model parameters satisfy the following assumptions:

- **Assumption 2.1.** (A1) The functions f_i , i = 1, 2, 3 are bounded, non-negative $C^1(\mathbb{R}_+)$, concave and increasing satisfying $f_i(0) = 0$ for i = 1, 2, 3.
 - (2) The function $\Lambda_1(t)$, d(t), $\gamma(t)$, $\eta(t)$, $\delta(t)$, $\mu(t)$, $\rho_1(t)$, $\rho_2(t)$ and $\rho_3(t)$ are non-negative continuous bounded and *T*-periodic.

Assumption 2.1 means that the *vibrio cholerae*-to-host and host-to-host incidence rates increase when susceptible hosts number increase and that no *vibrio cholerae*-to-host nor host-to-host infection can be in the absence of infected hosts and *vibrio cholerae*, respectively.

Lemma 2.1. (1) The functions
$$f_i$$
, $i = 1, 2, 3$ satisfy $f'_i(\omega)\omega \le f_i(\omega) \le f'_i(0)\omega$, $\forall \omega > 0$.
(2) For all $\omega, \omega' \in \mathbb{R}_+$, one has $\left(\frac{\omega}{\omega'} - \frac{f_i(\omega)}{f_i(\omega')}\right) \times \left(\frac{f_i(\omega')}{f_i(\omega)} - 1\right) \le 0$, for all $i = 1, 2, 3$.

- *Proof.* (1) For all i = 1, 2, 3, let $\omega, \omega' \in \mathbb{R}_+$, and the function $g_1(\omega) = f_i(\omega) \omega f'_i(\omega)$. Since $f'_i(\omega) \ge 0$ and $f''_i(\omega) \le 0$ then $g'_1(\omega) = -\omega f''_i(\omega) \ge 0$ and $g_1(\omega) \ge g_1(0) = 0$. Therefore, $f_i(\omega) \ge \omega f'_i(\omega)$. Similarly, let $g_2(\omega) = f_i(\omega) \omega f'_i(0)$ then $g'_2(\omega) = f'_i(\omega) f'_i(0) \le 0$. Thus $g_2(\omega) \le g_2(0) = 0$ and $f_i(\omega) \le \omega f'_i(0)$.
 - (2) Let the function $g_3(\omega) = \frac{f_i(\omega)}{\omega}$, $g'_3(\omega) = \frac{f'_i(\omega)\omega f_i(\omega)}{\omega^2} \leq 0$ which means that g_3 is decreasing. Since the function f_i is increasing then $(g_3(\omega) g_3(\omega')) \times (f_i(\omega) f_i(\omega'))$ is always negative. Then

$$(g_{3}(\omega) - g_{3}(\omega')) \times (f_{i}(\omega) - f_{i}(\omega')) = \left(\frac{f_{i}(\omega)}{\omega} - \frac{f_{i}(\omega')}{\omega'}\right) \times (f_{i}(\omega) - f_{i}(\omega'))$$
$$= \frac{f_{i}(\omega')f_{i}(\omega)}{\omega} \left(\frac{\omega}{\omega'} - \frac{f_{i}(\omega)}{f_{i}(\omega')}\right) \times \left(\frac{f_{i}(\omega')}{f_{i}(\omega)} - 1\right)$$
$$\leq 0.$$

3. Case of Fixed Environment

In this section, we assume that all parameters are positive constant reflecting the case of fixed environment. Therefore, we obtain the the autonomous form of the dynamics (2.1).

$$\begin{aligned} \dot{S}(t) &= d\Lambda_1 - \rho_1 f_1(I(t)) S(t) - \rho_2 f_2(V(t)) S(t) - dS(t), \\ \dot{I}(t) &= \rho_1 f_1(I(t)) S(t) + \rho_2 f_2(V(t)) S(t) - (\gamma + d) I(t), \\ \dot{V}(t) &= \eta I(t) - \mu V(t) - \rho_3 f_3(V(t)) P(t), \\ \dot{P}(t) &= \delta\Lambda_2 + \theta \rho_3 f_3(V(t)) P(t) - \delta P(t). \end{aligned}$$
(3.1)

with initial conditions $S(0) = S_0$, $I(0) = I_0$, $V(0) = V_0$ and $P(0) = P_0$.

3.1. **Basic properties.** In this subsection, we give some classical properties for epidemiological models. Let $\sigma = \min(\mu, \delta)$, then we obtain the following results. Lemma 3.1. The bounded set

$$\Sigma = \left\{ (S, I, V, P) \in \mathbb{R}^4_+ : S + I \le \Lambda_1, \theta V + P \le \Lambda_2 + \frac{\eta \theta}{\sigma} \Lambda_1 \right\}$$

is a positively invariant and attractor of the dynamics (3.1).

Proof. Assume that S = 0 then $\dot{S} = d\Lambda_1 > 0$. Assume that I = 0 then $\dot{I} = \rho_2 f_2(V) S \ge 0$. Assume that V = 0 then $\dot{P} = \eta I \ge 0$. Assume that P = 0 then $\dot{P} = \delta \Lambda_2 > 0$. Consider $T_1(t) = S(t) + I(t) - \Lambda_1$ and $T_2(t) = \theta V(t) + P(t) - \frac{\eta \theta \Lambda_1}{\sigma} - \Lambda_2$. Then, one has $\dot{T}_1(t) \le d\Lambda_1 - d(S(t) + I(t)) = -dT_1(t)$. Hence, $T_1(t) \leq T_1(0)e^{-dt}$. Then, $T_1(t) \leq 0$ if $T_1(0) \leq 0$. Similarly, one has

$$\dot{T}_{2}(t) = \theta \eta I(t) - \theta \mu V(t) + \delta \Lambda_{2} - \delta P(t) \le \theta \eta \Lambda_{1} - \sigma \left(\theta V(t) + P(t) - \Lambda_{2} \right) = -\sigma T_{2}(t)$$

Then $T_2(t) \leq T_2(0)e^{-\sigma t}$. Hence, $T_2(t) \leq 0$ if $T_2(0) \leq 0$. Thus, Σ is an invariant set for the dynamics (2.1) since all compartments are non-negative.

3.2. Basic reproduction number and steady states. As our model has several compartments, the next-generation matrix method [22-24] will be used to calculate the basic reproduction number as follows.

$$F = \begin{pmatrix} \rho_1 f'_1(0)\Lambda_1 & \rho_2 f'_2(0)\Lambda_1 & 0\\ 0 & 0 & 0\\ 0 & 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} (\gamma + d) & 0 & 0\\ -\eta & \mu + \rho_3 f'_3(0)\Lambda_2 & 0\\ 0 & 0 & \delta \end{pmatrix}.$$
 Then, the inverse matrix of V is given by

$$V^{-1} = \begin{pmatrix} \frac{1}{(\gamma+d)} & 0 & 0\\ \frac{\eta}{(\gamma+d)(\mu+\rho_3 f_3'(0)\Lambda_2)} & \frac{1}{\mu+\rho_3 f_3'(0)\Lambda_2} & 0\\ 0 & 0 & \frac{1}{\delta} & \lambda \end{pmatrix}$$

and the next-generation matrix is given by

$$FV^{-1} = \begin{pmatrix} \frac{\rho_1 f_1'(0)\Lambda_1}{(\gamma+d)} + \frac{\eta\rho_2 f_2'(0)\Lambda_1}{(\gamma+d)(\mu+\rho_3 f_3'(0)\Lambda_2)} & \frac{\rho_2 f_2'(0)\Lambda_1}{(\mu+\rho_3 f_3'(0)\Lambda_2)} & 0\\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}.$$

Thus, the spectral radius of FV^{-1} which is the basic reproduction number is expressed by:

$$\mathcal{R}_{0} = \frac{\rho_{1}f_{1}'(0)\Lambda_{1}}{(\gamma+d)} + \frac{\eta\rho_{2}f_{2}'(0)\Lambda_{1}}{(\gamma+d)(\mu+\rho_{3}f_{3}'(0)\Lambda_{2})} \\
= \frac{(\mu+\rho_{3}f_{3}'(0)\Lambda_{2})\rho_{1}f_{1}'(0) + \eta\rho_{2}f_{2}'(0)}{(\gamma+d)(\mu+\rho_{3}f_{3}'(0)\Lambda_{2})}\Lambda_{1}.$$
(3.2)

• If $\mathcal{R}_0 \leq 1$, then (3.1) admits only $E_0 = (\Lambda_1, 0, 0, \Lambda_2)$ as a steady state. Lemma 3.2.

• If $\mathcal{R}_0 > 1$, then the autonomous dynamics (3.1) admits two steady states; E_0 and an endemic steady state $E^* = (S^*, I^*, V^*, P^*)$.

Proof. Consider E = (S, I, V, P) to be a steady state then it satisfies:

$$0 = d\Lambda_{1} - \rho_{1}f_{1}(I)S - \rho_{2}f_{2}(V)S - dS,$$

$$0 = \rho_{1}f_{1}(I)S + \rho_{2}f_{2}(V)S - (\gamma + d)I,$$

$$0 = \eta I - \mu V - \rho_{3}f_{3}(V)P,$$

$$0 = \delta\Lambda_{2} + \theta\rho_{3}f_{3}(V)P - \delta P.$$
(3.3)

From Eq (3.3) we obtain the *vibrio cholerae*-free steady state $E_0 = (\Lambda_1, 0, 0, \Lambda_2)$. Furthermore, we have

$$\begin{cases}
P = \frac{\delta\Lambda_2}{\delta - \theta\rho_3 f_3(V)}, \\
I = \frac{\mu V + \rho_3 f_3(V)P}{\eta} = \frac{\mu}{\eta} V + \frac{\delta\Lambda_2 \rho_3 f_3(V)}{\eta(\delta - \theta\rho_3 f_3(V))}, \\
S = \Lambda_1 - \frac{\gamma + d}{d}I = \Lambda_1 - \frac{\mu(\gamma + d)}{d\eta} V - \frac{(\gamma + d)\delta\Lambda_2 \rho_3 f_3(V)}{d\eta(\delta - \theta\rho_3 f_3(V))}, \\
(\gamma + d)I = \rho_1 f_1(I)S + \rho_2 f_2(V)S.
\end{cases}$$
(3.4)

We define the function

$$g(V) = \frac{\rho_{1}f_{1}(I)S + \rho_{2}f_{2}(V)S - (\gamma + d)I}{V} \\ = \left(\rho_{1}\frac{f_{1}\left(\frac{\mu}{\eta}V + \frac{\delta\Lambda_{2}\rho_{3}f_{3}(V)}{\eta(\delta - \theta\rho_{3}f_{3}(V))}\right)}{V} + \rho_{2}\frac{f_{2}(V)}{V} \right) \left(\Lambda_{1} - \frac{\mu(\gamma + d)}{d\eta}V - \frac{\delta(\gamma + d)\Lambda_{2}\rho_{3}f_{3}(V)}{d\eta(\delta - \theta\rho_{3}f_{3}(V))}\right)$$
(3.5)
$$-\frac{\mu(\gamma + d)}{\eta} - \frac{\delta(\gamma + d)\Lambda_{2}\rho_{3}f_{3}(V)}{\eta V(\delta - \theta\rho_{3}f_{3}(V))}.$$

Then, we obtain

$$\lim_{V \to 0^{+}} g(V) = \left(\rho_{1} \frac{\mu}{\eta} f_{1}'(0) + \frac{\rho_{1} \rho_{3} \Lambda_{2}}{\eta} f_{1}'(0) f_{3}'(0) + \rho_{2} f_{2}'(0) \right) \Lambda_{1} - \frac{\mu(\gamma + d)}{\eta} - \frac{(\gamma + d) \Lambda_{2} \rho_{3} f_{3}'(0)}{\eta} \\ = \frac{\mu(\gamma + d)}{\eta} \left(\frac{\rho_{1} f_{1}'(0) \Lambda_{1}}{(\gamma + d)} + \frac{\eta \rho_{2} f_{2}'(0) \Lambda_{1}}{\mu(\gamma + d)} + \frac{\rho_{3} f_{3}'(0) \Lambda_{2}}{\mu} - 1 \right) + \frac{\rho_{1} \rho_{3}}{\eta} f_{1}'(0) f_{3}'(0) \Lambda_{1} \Lambda_{2}$$
(3.6)
$$= \frac{\mu(\gamma + d)}{\eta} (\mathcal{R}_{0} - 1) + \frac{\rho_{1} \rho_{3}}{\eta} f_{1}'(0) f_{3}'(0) \Lambda_{1} \Lambda_{2} > 0 \text{ since } \mathcal{R}_{0} > 1.$$

Let us define \overline{V} to be the solution of $\delta - \theta \rho_3 f_3(V) = 0$. Since f_3 is an increasing function, $f_3(0) = 0$ and $f_3(\frac{\Lambda_2}{\theta} + \frac{\eta \Lambda_1}{\sigma}) > \frac{\delta}{\theta \rho_3}$, then \overline{V} exists and is unique. Now, one has

$$\lim_{V \to \bar{V}^-} \frac{\delta(\gamma + d)\Lambda_2 \rho_3 f_3(V)}{\eta(\delta - \theta \rho_3 f_3(V))} = -\infty$$

then,

$$\lim_{V\to \bar{V}^-}g(V)<0.$$

The derivative of the function g is given by

$$\begin{split} g'(V) &= \left[\rho_{1} \frac{\left(\frac{\mu}{\eta}V + \frac{\delta^{2} \Lambda_{2} \rho_{3} f_{3}^{\prime}(V)V}{\eta(\delta - \theta \rho_{3} f_{3}(V))^{2}}\right) f_{1}^{\prime} \left(\frac{\mu}{\eta}V + \frac{\delta \Lambda_{2} \rho_{3} f_{3}(V)}{\eta(\delta - \theta \rho_{3} f_{3}(V))}\right) - f_{1} \left(\frac{\mu}{\eta}V + \frac{\delta \Lambda_{2} \rho_{3} f_{3}(V)}{\eta(\delta - \theta \rho_{3} f_{3}(V))}\right) \\ &+ \rho_{2} \frac{(V f_{2}^{\prime}(V) - f_{2}(V))}{V^{2}} \right] \times \left(\Lambda_{1} - \frac{\mu(\gamma + d)}{d\eta}V - \frac{\delta(\gamma + d)\Lambda_{2} \rho_{3} f_{3}(V)}{d\eta(\delta - \theta \rho_{3} f_{3}(V))}\right) \\ &- \left(\rho_{1} \frac{f_{1} \left(\frac{\mu}{\eta}V + \frac{\delta \Lambda_{2} \rho_{3} f_{3}(V)}{\eta(\delta - \theta \rho_{3} f_{3}(V))}\right)}{V^{2}} + \rho_{2} \frac{f_{2}(V)}{V} \right) \times \left(\frac{\mu(\gamma + d)}{d\eta} + \frac{\delta(\gamma + d)\Lambda_{2} \rho_{3}}{d\eta} \frac{\delta f_{3}^{\prime}(V)}{(\delta - \theta \rho_{3} f_{3}(V))^{2}} \right) \\ &- \frac{\delta(\gamma + d)\Lambda_{2} \rho_{3}}{\eta} \frac{\delta(V f_{3}^{\prime}(V) - f_{3}(V)) + \theta \rho_{3} f_{3}^{2}(V))}{V^{2}} + \rho_{2} \frac{\delta \Lambda_{2} \rho_{3} f_{3}(V)}{\eta(\delta - \theta \rho_{3} f_{3}(V))} - f_{1} \left(\frac{\mu}{\eta}V + \frac{\delta \Lambda_{2} \rho_{3} f_{3}(V)}{\eta(\delta - \theta \rho_{3} f_{3}(V))}\right) \\ &+ \rho_{2} \frac{(V f_{2}^{\prime}(V) - f_{2}(V))}{V^{2}} \right] \times \left(\Lambda_{1} - \frac{\mu(\gamma + d)}{d\eta}V - \frac{\delta(\gamma + d)\Lambda_{2} \rho_{3}}{d\eta(\delta - \theta \rho_{3} f_{3}(V))} \right) \\ &- \left(\rho_{1} \frac{f_{1} \left(\frac{\mu}{\eta}V + \frac{\delta \Lambda_{2} \rho_{3} f_{3}(V)}{\eta(\delta - \theta \rho_{3} f_{3}(V))}\right)}{V^{2}} + \rho_{2} \frac{f_{2}(V)}{V} \right) \times \left(\frac{\mu(\gamma + d)}{d\eta} + \frac{\delta(\gamma + d)\Lambda_{2} \rho_{3}}{d\eta(\delta - \theta \rho_{3} f_{3}(V))} \right) \\ &- \frac{\delta(\gamma + d)\Lambda_{2} \rho_{3}}{\eta} \frac{\delta(V f_{3}^{\prime}(V) - f_{3}(V)) + \theta \rho_{3} f_{3}^{2}(V))}{V^{2}} \right). \end{split}$$

By Assumption 2.1 and Lemma 2.1, we have $\begin{pmatrix} \frac{\mu}{\eta}V + \frac{\delta\Lambda_2\rho_3f_3(V)}{\eta(\delta - \theta\rho_3f_3(V))} \end{pmatrix} f_1' \left(\frac{\mu}{\eta}V + \frac{\delta\Lambda_2\rho_3f_3(V)}{\eta(\delta - \theta\rho_3f_3(V))} \right) - f_1 \left(\frac{\mu}{\eta}V + \frac{\delta\Lambda_2\rho_3f_3(V)}{\eta(\delta - \theta\rho_3f_3(V))} \right) \leq 0,$ $Vf_2'(V) - f_2(V) \leq 0 \text{ and } (Vf_3'(V) - f_3(V)) \leq 0.$ Therefore, we deduce that $g'(V) \leq 0$ for all $V \in (0, \bar{V}).$ Then, the function g(V) admits a unique root $V^* \in (0, \bar{V}).$ Therefore, one obtains

$$\begin{cases}
P^* = \frac{\delta\Lambda_2}{\delta - \theta\rho_3 f_3(V^*)}, \\
I^* = \frac{\mu}{\eta}V^* + \frac{\delta\Lambda_2\rho_3 f_3(V^*)}{\eta(\delta - \theta\rho_3 f_3(V^*))}, \\
S^* = \Lambda_1 - \frac{\mu(\gamma + d)}{d\eta}V^* + \frac{(\gamma + d)\delta\Lambda_2\rho_3 f_3(V^*)}{d\eta(\delta - \theta\rho_3 f_3(V^*))}.
\end{cases}$$
(3.8)

Therefore, the infected equilibrium $E^* = (S^*, I^*, V^*, P^*)$ exists and is unique if $\mathcal{R}_0 > 1$.

3.3. **Local analysis.** We aim, in this section, to analyse the local stability of the equilibria of the dynamics (3.1).

Theorem 3.1. In the case where $\mathcal{R}_0 < 1$, the phage-free E_0 is locally asymptotically stable, and in the case where $\mathcal{R}_0 > 1$, E_0 is unstable.

Proof. The linearisation of the dynamics (3.1) at the steady state E_0 is:

$$J_{0} = \begin{pmatrix} -d & -\rho_{1}f_{1}'(0)\Lambda_{1} & -\rho_{2}f_{2}'(0)\Lambda_{1} & 0\\ 0 & \rho_{1}f_{1}'(0)\Lambda_{1} - \gamma - d & \rho_{2}f_{2}'(0)\Lambda_{1} & 0\\ 0 & \eta & -(\mu + \rho_{3}f_{3}'(0)\Lambda_{2}) & 0\\ 0 & 0 & \rho_{3}f_{3}'(0)\Lambda_{2} & -\delta \end{pmatrix}$$

 J_0 admits four eigenvalues; $\lambda_1 = -d < 0$ and $\lambda_2 = -\delta < 0$. λ_3 and λ_4 are eigenvalues of the sub-matrix

$$M_{0} := \begin{pmatrix} \rho_{1}f_{1}'(0)\Lambda_{1} - \gamma - d & \rho_{2}f_{2}'(0)\Lambda_{1} \\ \eta & -(\mu + \rho_{3}f_{3}'(0)\Lambda_{2}) \end{pmatrix}$$

The trace of the matrix M_0 is:

$$\begin{aligned} \operatorname{tr}(M_0) &= \rho_1 f_1'(0) \Lambda_1 - \gamma - d - (\mu + \rho_3 f_3'(0) \Lambda_2) \\ &\leq -(\mu + \rho_3 f_3'(0) \Lambda_2) - (\gamma + d) \Big(1 - \frac{\rho_1 f_1'(0) \Lambda_1}{\gamma + d} - \frac{\rho_2 f_2'(0) \Lambda_1}{(\gamma + d)(\mu + \rho_3 f_3'(0) \Lambda_2)} \Big) \\ &= -(\mu + \rho_3 f_3'(0) \Lambda_2) - (\gamma + d) \Big(1 - \mathcal{R}_0 \Big) \end{aligned}$$

and the determinant of M_0 is:

$$det(M_0) = -(\rho_1 f'_1(0)\Lambda_1 - \gamma - d) \left(\mu + \rho_3 f'_3(0)\Lambda_2\right) - \eta \rho_2 f'_2(0)\Lambda_1$$

= $-(\gamma + d) \left(\mu + \rho_3 f'_3(0)\Lambda_2\right) \left(\frac{\rho_1 f'_1(0)\Lambda_1}{(\gamma + d)} - 1 + \frac{\eta \rho_2 f'_2(0)\Lambda_1}{(\gamma + d)(\mu + \rho_3 f'_3(0)\Lambda_2)}\right)$
= $-(\gamma + d) \left(\mu + \rho_3 f'_3(0)\Lambda_2\right) \left(\mathcal{R}_0 - 1\right).$

Then, E_0 is locally asymptotically stable once $\mathcal{R}_0 < 1$, however, it is unstable once $\mathcal{R}_0 > 1$.

Theorem 3.2. If $\mathcal{R}_0 > 1$, therefore E^* is locally asymptotically stable.

Proof. The linearisation of the dynamics (3.1) at the steady state $E^* = (S^*, I^*, V^*, P^*)$ is:

$$J^{*} = \begin{pmatrix} -d - \rho_{1}f_{1}(I^{*}) - \rho_{2}f_{2}(V^{*}) & -\rho_{1}f_{1}'(I^{*})S^{*} & -\rho_{2}f_{2}'(V^{*})S^{*} & 0\\ \rho_{1}f_{1}(I^{*}) + \rho_{2}f_{2}(V^{*}) & \rho_{1}f_{1}'(I^{*})S^{*} - (d + \gamma) & \rho_{2}f_{2}'(V^{*})S^{*} & 0\\ 0 & \eta & -(\mu + \rho_{3}f_{3}'(V^{*})P^{*}) & -\rho_{3}f_{3}(V^{*})\\ 0 & 0 & \theta\rho_{3}f_{3}'(V^{*})P^{*} & \theta\rho_{3}f_{3}(V^{*}) - \delta \end{pmatrix}.$$

The characteristic polynomial is then given by:

$$\begin{split} Q(\lambda) &= \begin{vmatrix} -(\lambda+d) & -(\lambda+d+\gamma) & 0 & 0 \\ \rho_1 f_1(l^*) + \rho_2 f_2(V^*) & -\lambda + \rho_1 f_1'(l^*) S^* - (d+\gamma) & \rho_2 f_2'(V^*) S^* & 0 \\ 0 & \eta & -\lambda - (\mu + \rho_3 f_3'(V^*) P^*) & -\rho_3 f_3(V^*) \\ 0 & 0 & \theta \rho_3 f_3'(V^*) P^* & -\lambda + \theta \rho_3 f_3(V^*) - \delta \end{vmatrix} \\ &= -(\lambda+d) \begin{vmatrix} -\lambda + \rho_1 f_1'(l^*) S^* - (d+\gamma) & \rho_2 f_2'(V^*) S^* & 0 \\ \eta & -\lambda - (\mu + \rho_3 f_3'(V^*) P^*) & -\rho_3 f_3(V^*) \\ 0 & \theta \rho_3 f_3'(V^*) P^* & -\lambda + \theta \rho_3 f_3(V^*) - \delta \end{vmatrix} \\ &+ (\lambda+d+\gamma) \begin{vmatrix} \rho_1 f_1(l^*) + \rho_2 f_2(V^*) & \rho_2 f_2'(V^*) S^* & 0 \\ 0 & -\lambda - (\mu + \rho_3 f_3'(V^*) P^*) & -\rho_3 f_3(V^*) \\ 0 & \theta \rho_3 f_3'(V^*) P^* & -\lambda + \theta \rho_3 f_3(V^*) - \delta \end{vmatrix} \\ &= -(\lambda+d) \Big[(-\lambda + \rho_1 f_1'(l^*) S^* - (d+\gamma)) \Big((-\lambda - (\mu + \rho_3 f_3'(V^*) P^*)) (-\lambda + \theta \rho_3 f_3(V^*) - \delta) \\ &+ \theta \rho_3 f_3'(V^*) P^* \rho_3 f_3(V^*) \Big) - \eta \rho_2 f_2'(V^*) S^* (-\lambda + \theta \rho_3 f_3(V^*) - \delta) \Big] + (\lambda+d+\gamma) (\rho_1 f_1(l^*) + \rho_2 f_2(V^*)) \\ & ((-\lambda - (\mu + \rho_3 f_3'(V^*) P^*)) (-\lambda + \theta \rho_3 f_3(V^*) - \delta) + \theta \rho_3 f_3'(V^*) P^* \rho_3 f_3(V^*) \Big). \end{split}$$

The characteristic polynomial $Q(\lambda) = 0$ if, and only if

$$\begin{bmatrix} (\lambda + d + \gamma)(\rho_1 f_1(I^*) + \rho_2 f_2(V^*)) - (\lambda + d)(\lambda + (d + \gamma) - \rho_1 f_1'(I^*)S^*) \\ ((\lambda + (\mu + \rho_3 f_3'(V^*)P^*))(X + \delta - \theta\rho_3 f_3(V^*)) + \theta\rho_3 f_3'(V^*)P^*\rho_3 f_3(V^*)) \end{bmatrix}$$

= $\eta\rho_2 f_2'(V^*)S^*(\lambda + d)(\lambda + \delta - \theta\rho_3 f_3(V^*))$

or if

$$= \frac{\eta \rho_2 f_2'(V^*) S^*(\lambda + d)(\lambda + d + \gamma) - \rho_1 f_1'(I^*) S^*)}{\left((\lambda + (\mu + \rho_3 f_3'(V^*)P^*))(\lambda + \delta - \theta \rho_3 f_3(V^*)) + \theta \rho_3 f_3'(V^*)P^* \rho_3 f_3(V^*)\right)}.$$

Suppose that the eigenvalue λ is with positive real part. Therefore, since

$$\left((d+\gamma)-\rho_1 f_1'(I^*)S^*\right) \ge \left((d+\gamma)-\rho_1 \frac{f_1(I^*)}{I^*}S^*\right) = \frac{\rho_2 S^* f_2(V^*)}{I^*} \ge \frac{\rho_2 S^* f_2'(V^*)V^*}{I^*}$$

and

$$\frac{V^*}{I^*} \geq \frac{\eta}{(\mu + \rho_3 P^* f_3'(V^*))}$$

then, by considering the left-hand side, we obtain

$$\left| (\lambda + d + \gamma)(\rho_1 f_1(I^*) + \rho_2 f_2(V^*)) + (\lambda + d)(X + (d + \gamma) - \rho_1 f_1'(I^*)S^*) \right|$$

> $((d + \gamma) - \rho_1 f_1'(I^*)S^*)|\lambda + d + \gamma| \ge \frac{\rho_2 S^* f_2(V^*)}{I^*}|\lambda + d + \gamma| \ge \frac{\eta \rho_2 S^* f_2'(V^*)}{(\mu + \rho_3 P^* f_3'(V^*))}|\lambda + d + \gamma|$ (3.9)

however, by considering the right-hand side, we obtain

$$\left| \frac{\eta \rho_{2} f_{2}'(V^{*}) S^{*}(\lambda + d)(\lambda + \delta - \theta \rho_{3} f_{3}(V^{*}))}{\left((\lambda + (\mu + \rho_{3} f_{3}'(V^{*})P^{*}))(\lambda + \delta - \theta \rho_{3} f_{3}(V^{*})) + \theta \rho_{3} f_{3}'(V^{*})P^{*} \rho_{3} f_{3}(V^{*}) \right)} \right|$$

$$< \left| \frac{\eta \rho_{2} f_{2}'(V^{*}) S^{*}(\lambda + d)(\lambda + \delta - \theta \rho_{3} f_{3}(V^{*}))}{\left((\lambda + (\mu + \rho_{3} f_{3}'(V^{*})P^{*}))(\lambda + \delta - \theta \rho_{3} f_{3}(V^{*})) \right)} \right|$$

$$= \eta \rho_{2} f_{2}'(V^{*}) S^{*} \left| \frac{(\lambda + d)}{\left((\lambda + (\mu + \rho_{3} f_{3}'(V^{*})P^{*})) \right)} \right|$$

$$\leq \frac{\eta \rho_{2} S^{*} f_{2}'(V^{*})}{(\mu + \rho_{3} P^{*} f_{3}'(V^{*}))} |\lambda + d + \gamma|.$$
(3.10)

This is a contradiction and then λ has non-positive real-part and then the endemic equilibrium point E^* should be locally asymptotically stable.

3.4. **Global analysis.** Our aim, in this section, is to prove the global stability of the equilibria of the dynamics (3.1). Consider the function $G(x) = x - 1 - \ln x$ that we will use is this section.

Theorem 3.3. E_0 is a globally asymptotically stable steady state if $\mathcal{R}_0 \leq 1$.

Proof. Let us define the Lyapunov function $L_0(S, I, V, P)$ given by:

$$L_0(S, I, V, P) = S - \Lambda_1 - \int_{\Lambda_1}^S \frac{\Lambda_1}{v} dv + I + \frac{\rho_2 f_2'(0)\Lambda_1}{\mu + \rho_3 f_3'(0)\Lambda_2} \left(V + \frac{\Lambda_2}{\theta} G\left(\frac{P}{\Lambda_2}\right)\right).$$

Note that $L_0(S, I, V, P) > 0$ for all S, I, V, P > 0 and $L_0(\Lambda_1, 0, 0, \Lambda_2) = 0$. Furthermore, we have

$$\begin{split} \dot{L}_{0} &= \left(1 - \frac{\Lambda_{1}}{S}\right) \left(d\Lambda_{1} - dS - \rho_{1}f_{1}(I)S - \rho_{2}If_{2}(V)S\right) + \rho_{1}f_{1}(I)S + \rho_{2}If_{2}(V)S - (\gamma + d)I \\ &+ \frac{\rho_{2}f_{2}'(0)\Lambda_{1}}{\mu + \rho_{3}f_{3}'(0)\Lambda_{2}} \left(\eta I - \mu V - \rho_{3}f_{3}(V)P + \frac{1}{\theta}(1 - \frac{\Lambda_{2}}{P})(\delta\Lambda_{2} + \theta\rho_{3}f_{3}(V)P - \delta P)\right) \right) \\ &= \left(1 - \frac{\Lambda_{1}}{S}\right) (d\Lambda_{1} - dS) + \rho_{1}\Lambda_{1}f(I) + \rho_{2}\Lambda_{1}f_{2}(V) - (\gamma + d)I \\ &+ \frac{\rho_{2}f_{2}'(0)\Lambda_{1}}{\mu + \rho_{3}f_{3}'(0)\Lambda_{2}} \left(\eta I + \frac{1}{\theta}(1 - \frac{\Lambda_{2}}{P})(\delta\Lambda_{2} - \delta P) - \mu V - \rho_{3}f_{3}(V)\Lambda_{2}\right) \\ &= \left(1 - \frac{\Lambda_{1}}{S}\right) (d\Lambda_{1} - dS) + \rho_{1}\Lambda_{1}f(I) + \rho_{2}\Lambda_{1}f_{2}(V) - (\gamma + d)I \\ &+ \frac{\rho_{2}f_{2}'(0)\Lambda_{1}}{\mu + \rho_{3}f_{3}'(0)\Lambda_{2}} \left(\eta I + \frac{1}{\theta}(1 - \frac{\Lambda_{2}}{P})(\delta\Lambda_{2} - \delta P)\right) - \frac{\rho_{2}f_{2}'(0)\Lambda_{1}\rho_{3}f_{3}(V)\Lambda_{2}}{\mu + \rho_{3}f_{3}'(0)\Lambda_{2}} \\ &\leq -d\frac{(S - \Lambda_{1})^{2}}{S} - \frac{\rho_{2}f_{2}'(0)\Lambda_{1}}{\mu + \rho_{3}f_{3}'(0)\Lambda_{2}} \frac{\delta}{\theta} \frac{(P - \Lambda_{2})^{2}}{P} + (\gamma + d)(\mathcal{R}_{0} - 1)I. \end{split}$$

If $\mathcal{R}_0 \leq 1$, thus $\dot{L}_0 \leq 0$, $\forall S, I, V, P > 0$. Let $W_0 = \{(S, I, V, P) : \dot{L}_0 = 0\} = \{E_0\}$. Using LaSalle's invariance principle [25], one can deduces that E_0 is globally asymptotically stable if $\mathcal{R}_0 \leq 1$.

Theorem 3.4. E^* is globally asymptotically stable for the dynamics (3.1) once $\mathcal{R}_0 > 1$.

Proof. Let us define the Lyapunov function $L_1(S, I, V, P)$ given by:

$$L_1(S, I, V, P) = S - S^* - \int_{S^*}^{S} \frac{f(S^*)}{f(v)} dv + I^* G(\frac{I}{I^*}) + \frac{\rho_1 S^* f_1(I^*)}{\eta I^*} V^* G(\frac{V}{V^*}) + \frac{\rho_1 S^* f_1(I^*)}{\theta \eta I^*} P^* G(\frac{P}{P^*}).$$

Clearly, $L_1(S, I, V, P) > 0$ for all variables S, I, V, P > 0 and $L_1(S^*, I^*, V^*, P^*) = 0$. The derivative of L_1 with respect to time is given by:

$$\begin{split} \dot{L}_{1} &= \left(1 - \frac{S^{*}}{S}\right) \left(d\Lambda_{1} - \rho_{1}f_{1}(I)S - \rho_{2}f_{2}(V)S - dS\right) + \left(1 - \frac{I^{*}}{I}\right) \left(\rho_{1}f_{1}(I)S + \rho_{2}f_{2}(V)S - (\gamma + d)I\right) \\ &+ \frac{\rho_{1}S^{*}f_{1}(I^{*})}{\eta I^{*}} \left(1 - \frac{V^{*}}{V}\right) \left(\eta I - \mu V - \rho_{3}f_{3}(V)P\right) + \frac{\rho_{1}S^{*}f_{1}(I^{*})}{\theta \eta I^{*}} \left(1 - \frac{P^{*}}{P}\right) \left(\delta\Lambda_{2} + \theta\rho_{3}f_{3}(V)P - \delta P\right) \\ &= \left(1 - \frac{S^{*}}{S}\right) \left(d\Lambda_{1} - dS\right) + \rho_{1}f_{1}(I)S^{*} + \rho_{2}f_{2}(V)S^{*} - \rho_{1}f_{1}(I)\frac{I^{*}}{I}S - \rho_{2}f_{2}(V)\frac{I^{*}}{I}S - (\gamma + d)I + (\gamma + d)I^{*} \\ &+ \frac{\rho_{1}S^{*}f_{1}(I^{*})}{I^{*}}I - \frac{\rho_{1}S^{*}f_{1}(I^{*})}{\eta I^{*}}\mu V - I\frac{V^{*}}{V}\frac{\rho_{1}S^{*}f_{1}(I^{*})}{I^{*}} + \mu V^{*}\frac{\rho_{1}S^{*}f_{1}(I^{*})}{\eta I^{*}} \\ &+ \rho_{3}f_{3}(V)P\frac{V^{*}}{V}\frac{\rho_{1}S^{*}f_{1}(I^{*})}{\eta I^{*}} - \rho_{3}f_{3}(V)P^{*}\frac{\rho_{1}S^{*}f_{1}(I^{*})}{\eta I^{*}} + \frac{\rho_{1}S^{*}f_{1}(I^{*})}{\theta \eta I^{*}}\left(1 - \frac{P^{*}}{P}\right)\left(\delta\Lambda_{2} - \delta P\right) \end{split}$$

Since the steady state E^* satisfies

$$\begin{aligned}
d\Lambda_{1} &= \rho_{1}f_{1}(I^{*})S^{*} + \rho_{2}f_{2}(V^{*})S^{*} + dS^{*}, \\
\rho_{1}f_{1}(I^{*})S^{*} + \rho_{2}f_{2}(V^{*})S^{*} &= (\gamma + d)I^{*}, \\
\mu V^{*} &= \eta I^{*} - \rho_{3}f_{3}(V^{*})P^{*}, \\
\delta\Lambda_{2} &= \delta P^{*} - \theta\rho_{3}f_{3}(V^{*})P^{*},
\end{aligned}$$
(3.11)

we get

$$\begin{split} \dot{L}_{1} &= -d \frac{(S-S^{*})^{2}}{S} + \rho_{1}f_{1}(l^{*})S^{*} + \rho_{2}f_{2}(V^{*})S^{*} \\ &- \rho_{1}f_{1}(l^{*})S^{*}\frac{S^{*}}{S} - \rho_{2}f_{2}(V^{*})S^{*}\frac{S^{*}}{S} + \rho_{1}f_{1}(l)S^{*} + \rho_{2}f_{2}(V)S^{*} - \rho_{1}f_{1}(l)\frac{l^{*}}{l}S \\ &- \rho_{2}f_{2}(V)\frac{l^{*}}{l}S - \rho_{1}f_{1}(l^{*})S^{*}\frac{l}{l^{*}} - \rho_{2}f_{2}(V^{*})S^{*}\frac{l}{l^{*}} + \rho_{1}f_{1}(l^{*})S^{*} + \rho_{2}f_{2}(V^{*})S^{*} \\ &+ \frac{\rho_{1}S^{*}f_{1}(l^{*})}{l^{*}}l - \rho_{1}S^{*}f_{1}(l^{*})\frac{V}{V^{*}} - \frac{\rho_{1}S^{*}f_{1}(l^{*})}{\eta l^{*}}\rho_{3}f_{3}(V^{*})P^{*}\frac{V}{V^{*}} - l\frac{V^{*}}{V}\frac{\rho_{1}S^{*}f_{1}(l^{*})}{l^{*}} \\ &+ \rho_{1}S^{*}f_{1}(l^{*}) + \rho_{3}f_{3}(V^{*})P^{*}\frac{\rho_{1}S^{*}f_{1}(l^{*})}{\eta l^{*}} - \rho_{3}f_{3}(V)P^{*}\frac{\rho_{1}S^{*}f_{1}(l^{*})}{\eta l^{*}} \\ &+ \rho_{3}f_{3}(V)P\frac{V^{*}}{V}\frac{\rho_{1}S^{*}f_{1}(l^{*})}{\eta l^{*}} - \rho_{3}f_{3}(V)P^{*}\frac{\rho_{1}S^{*}f_{1}(l^{*})}{\eta l^{*}} \\ &- \frac{\delta\rho_{1}S^{*}f_{1}(l^{*})}{\theta\eta l^{*}}\frac{(P-P^{*})^{2}}{P} - \frac{\rho_{1}S^{*}f_{1}(l^{*})}{\eta l^{*}}\rho_{3}f_{3}(V^{*})P^{*} + \frac{\rho_{1}S^{*}f_{1}(l^{*})}{\eta l^{*}}\rho_{3}f_{3}(V^{*})\frac{P^{*}}{P}P^{*} \\ &\leq -d\frac{(S-S^{*})^{2}}{S} - \frac{\delta\rho_{1}S^{*}f_{1}(l^{*})}{\theta\eta l^{*}}\frac{(P-P^{*})^{2}}{P} \\ &+ \rho_{1}f_{1}(l^{*})S^{*}\left(5 - \frac{S^{*}}{S} - \frac{f_{1}(l)}{f_{1}(l^{*})}\frac{l^{*}}{l}\frac{S}{S^{*}} - \frac{V}{V^{*}} - \frac{lV^{*}}{Vl^{*}} - \frac{f_{1}(l^{*})}{f_{1}(l)}\right) \\ &+ \rho_{2}f_{2}(V^{*})S^{*}\left(4 - \frac{S^{*}}{S} - \frac{l^{*}}{l}\frac{f_{2}(V)S}{f_{2}(V^{*})S^{*}} - \frac{l}{l^{*}} - \frac{f_{2}(V^{*})}{f_{2}(V)}\right). \end{split}$$

Using the rule that

$$\frac{1}{n}\sum_{i=1}^{n}a_{i} \geq \sqrt[n]{\prod_{i=1}^{n}a_{i}},$$
(3.12)

we get

$$\frac{1}{5} \left(\frac{S^*}{S} + \frac{f_1(I)}{f_1(I^*)} \frac{I^*}{I} \frac{S}{S^*} + \frac{V}{V^*} + \frac{IV^*}{VI^*} + \frac{f_1(I^*)}{f_1(I)} \right) \ge 1$$

and

$$\frac{1}{4} \left(\frac{S^*}{S} + \frac{I^*}{I} \frac{f_2(V)S}{f_2(V^*)S^*} + \frac{I}{I^*} + \frac{f_2(V^*)}{f_2(V)} \right) \ge 1.$$

Thus, $\dot{L}_1 \leq 0, \forall S, I, V, P > 0$ and $\dot{L}_1 = 0$ iff $S = S^*, I = I^*, V = V^*$ and $P = P^*$. One can deduce easily that E^* is globally stable by using the LaSalle's invariance principle [25].

4. Case of Seasonal Environment

Let return to the main dynamics (2.1) for a seasonal environment. For any continuous, positive T-periodic function g(t), we define $g^u = \max_{t \in [0,T)} g(t)$ and $g' = \min_{t \in [0,T)} g(t)$.

4.1. **Preliminary.** Let A(t) to be a *T*-periodic $m \times m$ matrix continuous function that it is irreducible and cooperative. Let $\beta_A(t)$ to be the fundamental matrix with positive entries, solution of

$$\dot{w}(t) = A(t)w(t). \tag{4.1}$$

Let us denote the spectral radius of the matrix $\beta_A(T)$ by $r(\beta_A(T))$. By using the Perron-Frobenius theorem, one can define $r(\beta_A(T))$ to be the principal eigenvalue of $\beta_A(T)$. According to [26], we have:

Lemma 4.1. [26]. (4.1) admits a positive *T*-periodic function x(t) such that $w(t) = x(t)e^{at}$ with $a = \frac{1}{T} \ln(r(\beta_A(T))).$

In order to define the disease-free periodic trajectory of model (2.1), let us consider the subsystem

$$\begin{cases} \dot{S}(t) = d(t)\Lambda_1(t) - d(t)S(t), \\ \dot{P}(t) = \delta(t)\Lambda_2(t) - \delta(t)P(t). \end{cases}$$

$$(4.2)$$

with the initial condition $(S_0, P_0) \in \mathbb{R}^2_+$. The dynamics (4.2) has a unique *T*-periodic trajectory $(S^*(t), P^*(t))$ such that $S^*(t) > 0$ and $P^*(t) > 0$. This solution is globally attractive in \mathbb{R}^2_+ ; therefore, the dynamics (2.1) admits a unique disease-free periodic trajectory $(S^*(t), 0, 0, P^*(t))$.

Let us define $\sigma(t) = \min_{t \geq 0}(\mu(t), \delta(t))$ and then we have

Proposition 4.1. The compact set

$$\Sigma^{u} = \left\{ (S, I, V, P) \in \mathbb{R}^{4}_{+} / S + I \leq \Lambda^{u}_{1}; \theta V + P \leq \frac{\theta^{u} \eta^{u}}{\sigma^{l}} \Lambda^{u}_{1} + \frac{\delta^{u}}{\sigma^{l}} \Lambda^{u}_{2} \right\}$$

is a positively invariant and attractor of trajectories of dynamics (2.1) with

$$\lim_{t \to \infty} S(t) + I(t) - S^{*}(t) = 0,$$

$$\lim_{t \to \infty} \theta(t)V(t) + P(t) - P^{*}(t) = 0.$$
(4.3)

Proof. Using the dynamics (2.1), we obtain

$$\begin{split} \dot{S}(t) + \dot{I}(t) &= d(t)\Lambda_1(t) - d(t)(S(t) + I(t)) \\ &\leq d(t) \Big(\Lambda_1^u - (S(t) + I(t))\Big) \leq 0, \text{ if } S(t) + I(t) \geq \Lambda_1^u \end{split}$$

and

$$\begin{split} \theta(t)\dot{V}(t) + \dot{P}(t) = & \theta(t)\eta(t)I(t) - \theta(t)\mu(t)V(t) + \delta(t)\Lambda_2(t) - \delta(t)P(t) \\ & \leq \theta^u \eta^u \Lambda_1^u + \delta^u \Lambda_2^u - \theta(t)\sigma(t)V(t) - \sigma(t)P(t) \\ & \leq \theta^u \eta^u \Lambda_1^u + \delta^u \Lambda_2^u - \sigma^I(\theta(t)V(t) + P(t)). \end{split}$$

Let $Z_1(t) = S(t) + I(t)$ and $Z_2(t) = \theta(t)V(t) + P(t)$. For $x_1(t) = Z_1(t) - S^*(t)$, $t \ge 0$, it follows that $\dot{x}_1(t) = -d(t)x_1(t)$, and thus $\lim_{t \to \infty} x_1(t) = \lim_{t \to \infty} (Z_1(t) - S^*(t)) = 0$. By the same way, let $x_2(t) = Z_2(t) - P^*(t)$, $t \ge 0$, then $\dot{x}_2(t) \le -\sigma(t)x_2(t)$, and thus $\lim_{t \to \infty} x_2(t) = \lim_{t \to \infty} (Z_2(t) - P^*(t)) = 0$. \Box

In section 4.2, we aim to define the basic reproduction number; \mathcal{R}_0 , the disease-free and then its global stability for $\mathcal{R}_0 \leq 1$. Later, in section 4.3, we aim to prove that compartments I(t) and V(t) persists if $\mathcal{R}_0 > 1$.

4.2. **Disease-free trajectory.** By using the definition of \mathcal{R}_0 given by the theory in [18].

$$\mathcal{F}(t,Y) = \begin{pmatrix} \rho_1(t)f_1(l(t))S(t) + \rho_2(t)f_2(V(t))S(t) \\ \eta(t)l(t) \\ 0 \\ 0 \end{pmatrix}, \\ 0 \\ \mathcal{V}^-(t,Y) = \begin{pmatrix} (\gamma(t) + d(t))l(t) \\ \mu(t)V(t) + \rho_3(t)f_3(V(t))P(t) \\ \rho_1(t)f_1(l(t))S(t) + \rho_2(t)f_2(V(t))S(t) + d(t)S(t) \\ \delta(t)P(t) \end{pmatrix},$$

and

$$\mathcal{V}^{+}(t,Y) = \begin{pmatrix} 0 \\ 0 \\ d(t)\Lambda_{1}(t) \\ \delta(t)\Lambda_{2}(t) + \theta(t)\rho_{3}(t)f_{3}(V(t))P(t) \end{pmatrix}$$

Our aim is to satisfy conditions (A1)-(A7) in [18, Section 1]. The dynamics (2.1) can take the form hereafter:

$$\dot{Y} = \mathcal{F}(t,Y) - \mathcal{V}(t,Y) = \mathcal{F}(t,Y) - \mathcal{V}^{-}(t,Y) + \mathcal{V}^{+}(t,Y).$$
(4.4)

Thus, the first five conditions (A1)–(A5) are satisfied.

The dynamics (4.4) has a disease-free periodic solution $Y^*(t) = (0, 0, S^*(t), P^*(t))$. Let $f(t, Y(t)) = \mathcal{F}(t, Y) - \mathcal{V}^-(t, Y) + \mathcal{V}^+(t, Y)$ and $M(t) = \left(\frac{\partial f_i(t, Y^*(t))}{\partial Y_j}\right)_{3 \le i, j \le 4}$ where $f_i(t, Y(t))$ and Y_i are the *i*-th components of f(t, Y(t)) and Y, respectively. A simple calculation give us $M(t) = \begin{pmatrix} -d(t) & 0 \\ 0 & -\delta(t) \end{pmatrix}$ and thus $r(\beta_M(T)) < 1$. Therefore, the trajectory $Y^*(t)$ is linearly asymptotically stable in $\Omega_s = \{(0, 0, S, P) \in R^4_+\}$. Therefore, the condition (A6) in [18, Section 1] is also fulfilled. Let us define $\mathbf{F}(t)$ and $\mathbf{V}(t)$ to be two matrices defined by $\mathbf{F}(t) = \left(\frac{\partial \mathcal{F}_i(t, Y^*(t))}{\partial Y_i}\right)_{t < 1}$ and

$$\mathbf{V}(t) = \left(\frac{\partial \mathcal{V}_i(t, Y^*(t))}{\partial Y_j}\right)_{1 \le i,j \le 2} \text{ where } \mathcal{F}_i(t, Y) \text{ and } \mathcal{V}_i(t, Y) \text{ are the } i\text{-th components of } \mathcal{F}(t, Y) \text{ and } \mathcal{F}_i(t, Y) \text{ and } \mathcal{V}_i(t, Y) \text{ are the } i\text{-th components of } \mathcal{F}(t, Y) \text{ and } \mathcal{F}_i(t, Y) \text{ and } \mathcal{V}_i(t, Y) \text{ are the } i\text{-th components of } \mathcal{F}(t, Y) \text{ and } \mathcal{F}_i(t, Y) \text{ and } \mathcal{V}_i(t, Y) \text{ are the } i\text{-th components of } \mathcal{F}(t, Y) \text{ and } \mathcal{F}_i(t, Y) \text{ and } \mathcal{V}_i(t, Y) \text{ are the } i\text{-th components of } \mathcal{F}(t, Y) \text{ and } \mathcal{F}_i(t, Y) \text{ are the } i\text{-th components of } \mathcal{F}(t, Y) \text{ and } \mathcal{F}_i(t, Y) \text{ and } \mathcal{F}_i(t, Y) \text{ are the } i\text{-th components of } \mathcal{F}(t, Y) \text{ and } \mathcal{F}_i(t, Y) \text{ are the } i\text{-th components of } \mathcal{F}_i(t, Y) \text{ and } \mathcal{F}_i(t, Y)$$

 $\mathcal{V}(t, Y)$, respectively. A simple calculation by using (4.4) give us the expressions of matrices $\mathbf{F}(t)$ and $\mathbf{V}(t)$ as the following:

$$\mathbf{F}(t) = \begin{pmatrix} \rho_1(t)f_1'(0)S^*(t) & \rho_2(t)f_2'(0)S^*(t) \\ \eta(t) & 0 \end{pmatrix}, \mathbf{V}(t) = \begin{pmatrix} \gamma(t) + d(t) & 0 \\ 0 & \mu(t) + \rho_3(t)f_3'(0)P^*(t) \end{pmatrix}.$$

Consider $Z(t_1, t_2)$ to be the two by two matrix solution of the system $\frac{d}{dt}Z(t_1, t_2) = -\mathbf{V}(t_1)Z(t_1, t_2)$ for any $t_1 \ge t_2$, with $Z(t_1, t_1) = I_2$, i.e., the 2 × 2 identity matrix. Therefore, condition (A7) is also fulfilled.

Denote by C_T the ordered Banach space of T-periodic functions that are defined on $\mathbb{R} \mapsto \mathbb{R}^2$, with the maximum norm $\|.\|_{\infty}$ and the positive cone $C_T^+ = \{\psi \in C_T : \psi(s) \ge 0, \text{ for any } s \in \mathbb{R}\}$. Consider the linear operator $K : C_T \to C_T$ given by

$$(K\phi)(\omega) = \int_0^\infty Z(\omega, \omega - z) \mathbf{F}(\omega - z) \phi(\omega - z) dz, \quad \forall \omega \in \mathbb{R}, \phi \in C_T$$
(4.5)

Therefore, the basic reproduction number, \mathcal{R}_0 , of dynamics (2.1) is given by $\mathcal{R}_0 = r(K)$.

Thus, the local stability of the disease-free periodic trajectory, $\mathcal{E}_0(t) = (S^*(t), 0, 0, P^*(t))$, of the dynamics (2.1) with respect to \mathcal{R}_0 is given hereafter.

Theorem 4.1. [18, Theorem 2.2]

- $\mathcal{R}_0 < 1 \Leftrightarrow r(\beta_{F-V}(T)) < 1.$
- $\mathcal{R}_0 = 1 \Leftrightarrow r(\beta_{F-V}(T)) = 1.$
- $\mathcal{R}_0 > 1 \Leftrightarrow r(\beta_{F-V}(T)) > 1.$

Then, $\mathcal{E}_0(t)$ is asymptotically stable if $\mathcal{R}_0 < 1$, however, it is unstable if $\mathcal{R}_0 > 1$.

Theorem 4.2. $\mathcal{E}_0(t)$ is globally asymptotically stable if $\mathcal{R}_0 < 1$. It is unstable if $\mathcal{R}_0 > 1$.

Proof. By Theorem 4.1, one has $\mathcal{E}_0(t)$ is locally stable if $\mathcal{R}_0 < 1$ however it is unstable if $\mathcal{R}_0 > 1$. Therefore, it remains to satisfy the global attractivity of $\mathcal{E}_0(t)$ once $\mathcal{R}_0 < 1$. Using (4.3) in Proposition 4.1, for any $\delta_1 > 0$, $\exists T_1 > 0$ such that $S(t) + I(t) \leq S^*(t) + \delta_1$ and $\theta(t)V(t) + P(t) \leq P^*(t) + \delta_1$ for $t > T_1$. Therefore, $S(t) \leq S^*(t) + \delta_1$ and $P(t) \leq P^*(t) + \delta_1$; and

$$\begin{cases} \dot{I}(t) \leq \rho_1(t)f_1(I(t))(S^*(t) + \delta_1) + \rho_2(t)f_2(V(t))(S^*(t) + \delta_1) - (\gamma(t) + d(t))I(t), \\ \dot{V}(t) \leq \eta(t)I(t) - \mu(t)V(t) - \rho_3(t)f_3(V(t))(P^*(t) + \delta_1) \end{cases}$$
(4.6)

for $t > T_1$. Let $M_2(t)$ be the two by two matrix function given hereafter

$$M_2(t) = \begin{pmatrix} \rho_2(t)f_1'(I(t))(S^*(t) + \delta_1) & \rho_1(t)f_2'(V(t))(S^*(t) + \delta_1) \\ \eta(t) & 0 \end{pmatrix}.$$
 (4.7)

using the equivalences in Theorem 4.1, one has $r(\varphi_{F-V}(T)) < 1$. By choosing $\delta_1 > 0$ satisfying $r(\varphi_{F-V+\delta_1M_2}(T)) < 1$ and we consider the dynamics hereafter,

$$\begin{cases} \dot{I}(t) = \rho_1(t)f_1(\bar{I}(t))(S^*(t) + \delta_1) + \rho_2(t)f_2(\bar{V}(t))(S^*(t) + \delta_1) - (\gamma(t) + d(t))\bar{I}(t), \\ \dot{V}(t) = \eta(t)\bar{I}(t) - \mu(t)\bar{V}(t) - \rho_3(t)f_3(\bar{V}(t))(P^*(t) + \delta_1). \end{cases}$$
(4.8)

Using Lemma 4.1, there exists a positive *T*-periodic function $x_1(t)$ such that $w(t) \le x_1(t)e^{a_1t}$ with $w(t) = \begin{pmatrix} I(t) \\ V(t) \end{pmatrix}$ and $a_1 = \frac{1}{T} \ln (r(\varphi_{F-V+\delta_1M_2}(T)) < 0$. Thus, $\lim_{t\to\infty} I(t) = 0$ and $\lim_{t\to\infty} V(t) = 0$. Furthermore, we have that $\lim_{t\to\infty} S(t) - S^*(t) = \lim_{t\to\infty} Z_1(t) - I(t) - S^*(t) = 0$ and $\lim_{t\to\infty} P(t) - P^*(t) = \lim_{t\to\infty} Z_2(t) - \theta(t)V(t) - P^*(t) = 0$. Then, we deduce that the disease-free periodic trajectory $\mathcal{E}_0(t)$ is globally attractive.

4.3. **Endemic trajectory**. Note that the dynamics (2.1) admits Σ^u as an invariant compact set. Let $Y_0 = (S^0, I^0, V^0, P^0)$ and $Y_1 = (S^*(0), 0, 0, P^*(0))$. Define $\mathcal{P} : \mathbb{R}^4_+ \to \mathbb{R}^4_+$ to be the Poincaré map related to the dynamics (2.1) with $Y_0 \mapsto u(T, Y^0)$, where $u(t, Y^0)$ is the unique solution of dynamics (2.1) and initial condition $u(0, Y^0) = Y^0 \in \mathbb{R}^4_+$. Let us define

$$\Omega = \left\{ (S, I, V, P) \in \mathbb{R}_+^4 \right\}, \ \Omega_0 = Int(\mathbb{R}_+^4) \text{ and } \partial\Omega_0 = \Omega \setminus \Omega_0.$$

 Ω and Ω_0 are both positively invariant. ${\cal P}$ is point dissipative. Define

$$M_{\partial} = \left\{ (Y_0) \in \partial \Omega_0 : \mathcal{P}^k(Y_0) \in \partial \Omega_0, \text{ for any } k \ge 0 \right\}.$$

By using the persistence theory given in [27] (also in [26, Theorem 2.3]), we have

$$M_{\partial} = \{ (S, 0, 0, P), \ S \ge 0, P \ge 0 \}.$$
(4.9)

It is easy to see that $M_{\partial} \supseteq \{(S, 0, 0, P), S \ge 0, P \ge 0\}$.

To prove that $M_{\partial} \setminus \{(S, 0, 0, P), S \ge 0, P \ge 0\} = \emptyset$, consider $(Y_0) \in M_{\partial} \setminus \{(S, 0, 0, P), S \ge 0, P \ge 0\}$. If $V^0 = 0$ and $0 < I^0$, then I(t) > 0 for all t > 0. Then $\dot{V}(t)_{|t=0} = \delta(0)I^0 > 0$. If $V^0 > 0$ and $I^0 = 0$, then V(t) > 0 and S(t) > 0 for all t > 0. Thus, for all t > 0, we obtain

$$I(t) = \left[I^0 + \int_0^t (\rho_1(\omega)S(\omega)f_1(I(\omega)) + \rho_2S(\omega)f(V(\omega)))e^{\int_0^\omega (\gamma(u) + d(u))du} d\omega\right]e^{-\int_0^t (\gamma(u) + d(u))du} > 0$$

for all t > 0. This means that $Y(t) \notin \partial \Omega_0$ for $0 < t \ll 1$. Therefore, Ω_0 is positively invariant from which we deduce (4.9). Using the previous discussion, we deduce that there exists one fixed point Y_1 of \mathcal{P} in M_{∂} . We deduce, therefore, the uniform persistence of the disease as follows.

Theorem 4.3. Assume that $\mathcal{R}_0 > 1$. The dynamics (2.1) admits at least one periodic solution such that there exists $\gamma > 0$ that satisfies $\forall Y_0 \in \mathbb{R}_+ \times Int(\mathbb{R}^2_+) \times \mathbb{R}_+$ and

$$\liminf_{t\to\infty} I(t) \ge \gamma > 0$$

Proof. We aim to prove that \mathcal{P} is uniformly persistent with respect to $(\Omega_0, \partial \Omega_0)$ which permits to prove that the solution of the dynamics (2.1) is uniformly persistent with respect to $(\Omega_0, \partial \Omega_0)$ by using [27, Theorem 3.1.1]. From Theorem 4.1, we have $r(\varphi_{F-V}(T)) > 1$. Therefore, there exists $\eta > 0$ such that $r(\varphi_{F-V-\eta M_2}(T)) > 1$. Define the system of equations:

$$\begin{cases} \dot{S}_{\alpha}(t) = d(t)\Lambda_{1}(t) - d(t)S_{\alpha}(t) - (\rho_{1}(t)f_{1}(\alpha) + \rho_{2}(t)f_{2}(\alpha))S_{\alpha}(t), \\ \dot{P}_{\alpha}(t) = \delta(t)\Lambda_{2}(t) - \delta(t)P_{\alpha}(t) + \theta(t)\rho_{3}(t)f_{3}(\alpha)P_{\alpha}(t). \end{cases}$$
(4.10)

 \mathcal{P} associated with the dynamics (4.10) admits a unique fixed point $(\bar{S}^0_{\alpha}, \bar{P}^0_{\alpha})$ which is globally attractive in \mathbb{R}^2_+ . By using the implicit function theorem, $\alpha \mapsto (\bar{S}^0_{\alpha}, \bar{P}^0_{\alpha})$ is continuous. Thus, $\alpha > 0$ can be chosen small enough such that $\bar{S}_{\alpha}(t) > \bar{S}(t) - \eta$, and $\bar{P}_{\alpha}(t) > \bar{P}(t) - \eta$, $\forall t > 0$. Using the continuity property of the solution with respect to the initial condition, $\exists \alpha^*$ such that $Y_0 \in \Omega_0$ with $||Y_0 - u(t, Y_1)|| \leq \alpha^*$; then

$$||u(t, Y_0) - u(t, Y_1)|| < \alpha \text{ for } 0 \le t \le T.$$

We prove by contradiction that

$$\limsup_{k \to \infty} d(\mathcal{P}^k(Y_0), Y_1) \ge \alpha^* \ \forall \ Y_0 \in \Omega_0.$$
(4.11)

Suppose that $\limsup_{k\to\infty} d(\mathcal{P}^k(Y_0), Y_1) < \alpha^*$ for some $Y_0 \in \Omega_0$. We can assume that $d(\mathcal{P}^k(Y_0), Y_1) < \alpha^*$ for all k > 0. Therefore

$$||u(t, \mathcal{P}^{k}(Y_{0})) - u(t, Y_{1})|| < \alpha \ \forall \ k > 0 \text{ and } 0 \le t \le T.$$

For $t \ge 0$, let $t = kT + t_1$, where $t_1 \in [0, T)$ and $k = \lfloor \frac{t}{T} \rfloor$. Therefore

$$\|u(t, Y_0) - u(t, Y_1)\| = \|u(t_1, \mathcal{P}^k(Y_0)) - u(t_1, Y_1)\| < lpha ext{ for all } t \ge 0.$$

Set $(S(t), I(t), V(t), P(t)) = u(t, Y_0)$. Therefore $0 \le I(t), V(t) \le \alpha, t \ge 0$ and

$$\begin{cases} \dot{S}(t) \geq d(t)\Lambda_1(t) - d(t)S(t) - (\rho_1(t)f_1(\alpha) + \rho_2(t)f_2(\alpha))S(t), \\ \dot{P}(t) \geq \delta(t)\Lambda_2(t) - \delta(t)P(t). \end{cases}$$

$$(4.12)$$

 \mathcal{P} applied to the dynamics (4.10) admits a fixed point \bar{S}^{0}_{α} that it is globally attractive with $\bar{S}_{\alpha}(t) > \bar{S}(t) - \eta$, and $\bar{P}_{\alpha}(t) > \bar{P}(t) - \eta$; then, $\exists T_{2} > 0$ such that $S(t) > \bar{S}(t) - \eta$ and $P(t) > \bar{P}(t) - \eta$ for $t > T_{2}$. Then, for $t > T_{2}$, we have

$$\begin{cases} \dot{I}(t) \geq \rho_1(t)f_1(I(t))(\bar{S}(t) - \eta) + \rho_2(t)f_2(V(t))(\bar{S}(t) - \eta) - (\gamma(t) + d(t))I(t), \\ \dot{V}(t) = \eta(t)I(t) - \mu(t)V(t) - \rho_3(t)f_3(V(t))P(t). \end{cases}$$

$$(4.13)$$

Since $r(\varphi_{F-V-\eta M_2}(T)) > 1$, then by using Lemma 4.1, there exists a positive *T*-periodic function $x_2(t)$ such that $J(t) \ge e^{a_2 t} x_2(t)$ where $a_2 = \frac{1}{T} \ln r (\varphi_{F-V-\eta M_2}(T)) > 0$, then $\lim_{t\to\infty} I(t) = \infty$ which contradicts the boundedness of the solution. Therefore, (4.11) is satisfied and \mathcal{P} is weakly uniformly persistent with respect to $(\Omega_0, \partial \Omega_0)$. By applying Proposition 4.1, \mathcal{P} has a global attractor. We deduce that Y_1 is an isolated invariant set inside Ω and that $W^s(Y_1) \cap \Omega_0 = \emptyset$. All trajectories inside

 M_{∂} converges to Y_1 which is acyclic in M_{∂} . Applying [27, Theorem 1.3.1 and Remark 1.3.1], we deduce that \mathcal{P} is uniformly persistent with respect to $(\Omega_0, \partial\Omega_0)$. Moreover, by using [27, Theorem 1.3.6], \mathcal{P} has a fixed point $\tilde{Y}_0 = (\tilde{S}^0, \tilde{I}^0, \tilde{V}^0, \tilde{P}^0) \in \Omega_0$ with $\tilde{Y}_0 \in R_+ \times Int(R_+^2) \times R_+$.

Suppose that $\tilde{S}^0 = 0$. From the first equation of the dynamics (2.1), $\tilde{S}(t)$ satisfies

$$\tilde{S}(t) = d(t)\Lambda_1(t) - \rho_1(t)f_1(\tilde{I}(t))\tilde{S}(t) - \rho_2(t)f_2(\tilde{V}(t))\tilde{S}(t) - d(t)\tilde{S}(t),$$
(4.14)

where $\tilde{S}^0 = \tilde{S}(nT) = 0, n = 1, 2, 3, \cdots$. By using Proposition 4.1, $\forall \delta_3 > 0, \exists T_3 > 0$ such that $\tilde{I}(t) \leq \Lambda_1^u + \delta_3$ and $\tilde{V}(t) \leq \frac{\theta^u \eta^u}{\theta' \sigma'} \Lambda_1^u + \frac{\delta^u}{\theta' \sigma'} \Lambda_2^u + \delta_3$ for $t > T_3$. Then, by Lemma 2.1, we obtain

$$\tilde{\tilde{S}}(t) \ge d(t)\Lambda_1(t) - d(t)\tilde{S}(t) - \left(\rho_1(t)(\Lambda_1^u + \delta_3)f_1'(0) + \rho_2(t)\left(\frac{\Lambda_2^u}{k'} + \frac{\delta^u k'' \Lambda_1^u}{k'm_a'} + \delta_3\right)f_2'(0)\right)\tilde{S}(t), \text{ for } t \ge T_3.$$
(4.15)

 $\exists \bar{n} \text{ such that } nT > T_3 \text{ for all } n > \bar{n}.$ Therefore

$$\tilde{S}(nT) \ge \left[\tilde{S}^{0} + \int_{0}^{nT} d(\omega)\Lambda_{1}(\omega)e^{\int_{0}^{\omega} \left(\rho_{1}(u)(\Lambda_{1}^{u} + \delta_{3})f_{1}'(0) + \rho_{2}(u)\left(\frac{\Lambda_{2}^{u}}{k^{l}} + \frac{\delta^{u}k^{u}\Lambda_{1}^{u}}{k^{l}m_{a}^{l}} + \delta_{3}\right)f_{2}'(0) + d(u)\right)du} d\omega\right] \\ \times e^{-\int_{0}^{nT} \left(\rho_{1}(u)(\Lambda_{1}^{u} + \delta_{3})f_{1}'(0) + \rho_{2}(u)\left(\frac{\Lambda_{2}^{u}}{k^{l}} + \frac{\delta^{u}k^{u}\Lambda_{1}^{u}}{k^{l}m_{a}^{l}} + \delta_{3}\right)f_{2}'(0) + d(u)\right)du}$$

for all $n > \bar{n}$ which contradicts the fact that $\tilde{S}(nT) = 0$. Then, $\tilde{S}^0 > 0$ and \tilde{Y}_0 is a positive *T*-periodic solution of the dynamics (2.1).

5. Numerical Examples

Let us consider Holling type-II functions as examples that can describe the incidence rates in the dynamics (2.1). These function satisfy Assumption 2.1.

$$f_1(I) = \frac{I}{\kappa_1 + I}, f_2(V) = \frac{V}{\kappa_2 + V}, f_3(V) = \frac{V}{\kappa_3 + V}$$

Here κ_1,κ_2 and κ_3 are non-negative constants. The periodic functions are given by

$$\begin{cases} d(t) = d^{0}(1 + d^{1}\cos(2\pi(t+\phi))), & \gamma(t) = \gamma^{0}(1 + \gamma^{1}\cos(2\pi(t+\phi))), \\ \eta(t) = \eta^{0}(1 + \eta^{1}\cos(2\pi(t+\phi))), & \delta(t) = \delta^{0}(1 + \delta^{1}\cos(2\pi(t+\phi))), \\ \Lambda_{1}(t) = \Lambda_{1}^{0}(1 + \Lambda_{1}^{1}\cos(2\pi(t+\phi))), & \Lambda_{2}(t) = \Lambda_{2}^{0}(1 + \Lambda_{2}^{1}\cos(2\pi(t+\phi))), \\ \rho_{1}(t) = \rho_{1}^{0}(1 + \rho_{1}^{1}\cos(2\pi(t+\phi))), & \rho_{2}(t) = \rho_{2}^{0}(1 + \rho_{2}^{1}\cos(2\pi(t+\phi))), \\ \rho_{3}(t) = \rho_{3}^{0}(1 + \rho_{3}^{1}\cos(2\pi(t+\phi))), & \mu(t) = \mu^{0}(1 + \mu^{1}\cos(2\pi(t+\phi))) \end{cases}$$
(5.1)

with $|d^1|$, $|\gamma^1|$, $|\eta^1|$, $|\delta^1|$, $|\Lambda_1^1|$, $|\Lambda_2^1|$, $|\rho_1^1|$, $|\rho_2^1|$, $|\rho_3^1|$ and $|\mu^1|$ describe the seasonal cycles frequencies, however, ϕ describes the phase shift. The numerical values of d^0 , γ^0 , η^0 , δ^0 , Λ_1^0 , Λ_2^0 , ρ_1^0 , ρ_2^0 , ρ_3^0 and μ^0 are considered in Table 2. However, the values of d^1 , γ^1 , η^1 , δ^1 , Λ_1^1 , Λ_2^1 , ρ_1^1 , ρ_2^1 , ρ_3^1 and μ^1 are considered in Table 3.

Three scenarios were consider here. The first one was allocated to the case of fixed environment. However, the second was allocated to the case where only the contact rates are seasonal. Finally, the last case were allocated to the case where all parameters are periodic. The numerical resolution was done using explicit Runge-Kutta formulas of orders 4 and 5 under Matlab.

Parameter	φ	d ⁰	γ^0	η^0	δ^0	Λ_1^0	Λ_2^0	$ ho_1^0$	$ ho_2^0$	$ ho_3^0$	μ^0	θ^0
Value	0	3	2.8	9	1.9	2	1	4	5	2.5	0.3	0.6

Table 2. Used values for d^0 , γ^0 , η^0 , δ^0 , Λ^0_1 , Λ^0_2 , ρ^0_1 , ρ^0_2 , ρ^0_3 and μ^0 .

Table 3. Used values for d^1 , γ^1 , η^1 , δ^1 , Λ_1^1 , Λ_2^1 , ρ_1^1 , ρ_2^1 , ρ_3^1 and μ^1 .

Parameter	d^1	γ^1	η^1	δ^1	Λ^1_1	Λ^1_2	$ ho_1^1$	$ ho_2^1$	$ ho_3^1$	μ^1	θ^1
Value	-0.1	0.2	0.3	0.3	0.2	0.5	0.2	0.1	-0.2	0.2	0.5

5.1. **Case of fixed environment.** Let us start by the simple case where there is no influence of the seasonality on the dynamics. Thus, we restrict our attention on the autonomous dynamics (3.1), i.e., all parameters are positive constants.

$$\begin{cases} \dot{S}(t) = d^{0}\Lambda_{1}^{0} - \frac{\rho_{1}^{0}I(t)}{\kappa_{1} + I(t)}S(t) - \frac{\rho_{2}^{0}V(t)}{\kappa_{2} + V(t)}S(t) - d^{0}S(t), \\ \dot{I}(t) = \frac{\rho_{1}^{0}I(t)}{\kappa_{1} + I(t)}S(t) + \frac{\rho_{2}^{0}V(t)}{\kappa_{2} + V(t)}S(t) - (\gamma^{0} + d^{0})I(t), \\ \dot{V}(t) = \eta^{0}I(t) - \mu^{0}V(t) - \frac{\rho_{3}^{0}V(t)}{\kappa_{3} + V(t)}P(t), \\ \dot{P}(t) = \delta^{0}\Lambda_{2}^{0} + \theta^{0}\frac{\rho_{3}^{0}V(t)}{\kappa_{3} + V(t)}P(t) - \delta^{0}P(t). \end{cases}$$
(5.2)

with an initial condition $(S^0, I^0, V^0, P^0) \in \mathbb{R}^4_+$.

In Figure 2, the calculated trajectories of dynamics (5.2) converge asymptotically to \mathcal{E}^* if $\mathcal{R}_0 > 1$. However, in Figure 3, the calculated trajectories of the dynamics (5.2) converge to the disease-free steady state \mathcal{E}_0 , then confirming the global asymptotic stability of \mathcal{E}_0 if $\mathcal{R}_0 \leq 1$.



Figure 2. Behavior of the dynamics (2.1) for $\kappa_1 = 4$, $\kappa_2 = 3$ and $\kappa_3 = 2$ then $\mathcal{R}_0 \approx 3.68 > 1$.



Figure 3. Behavior of the dynamics (2.1) for $\kappa_1 = 4$, $\kappa_2 = 3$ and $\kappa_3 = 2$ then $\mathcal{R}_0 \approx 3.68 > 1$.



Figure 4. Behavior of the dynamics (2.1) for $\kappa_1 = 9$, $\kappa_2 = 13$ and $\kappa_3 = 0.1$ then $\mathcal{R}_0 \approx 0.2 < 1$.



Figure 5. Behavior of the dynamics (2.1) for $\kappa_1 = 9$, $\kappa_2 = 13$ and $\kappa_3 = 0.1$ then $\mathcal{R}_0 \approx 0.2 < 1$.

5.2. **Case of seasonal contact.** The second was allocated to the case where only the contact rates, ρ_1 , ρ_2 and ρ_3 are seasonal functions. All the rest of parameters are fixed. We obtain the following system.

$$\begin{cases} \dot{S}(t) = d^{0}\Lambda_{1}^{0} - \frac{\rho_{1}(t)I(t)}{\kappa_{1} + I(t)}S(t) - \frac{\rho_{2}(t)V(t)}{\kappa_{2} + V(t)}S(t) - d^{0}S(t), \\ \dot{I}(t) = \frac{\rho_{1}(t)I(t)}{\kappa_{1} + I(t)}S(t) + \frac{\rho_{2}(t)V(t)}{\kappa_{2} + V(t)}S(t) - (\gamma^{0} + d^{0})I(t), \\ \dot{V}(t) = \eta^{0}I(t) - \mu^{0}V(t) - \frac{\rho_{3}(t)V(t)}{\kappa_{3} + V(t)}P(t), \\ \dot{P}(t) = \delta^{0}\Lambda_{2}^{0} + \theta^{0}\frac{\rho_{3}(t)V(t)}{\kappa_{3} + V(t)}P(t) - \delta^{0}P(t). \end{cases}$$
(5.3)

with the positive initial condition $(S^0, I^0, V^0, P^0) \in \mathbb{R}^4_+$.

We give the results of some numerical simulations confirming the stability of the steady states of system (5.3). The approximation of the basic reproduction number \mathcal{R}_0 was performed using the time-averaged system.

In Figure 4, the calculated trajectories of the dynamics (5.3) converge asymptotically to the periodic solution corresponding to the disease persistence. In Figure 5, we display a magnified view of the limit cycle for the case where $\mathcal{R}_0 > 1$. In Figure 6, the calculated trajectories of the dynamics (5.3) converge to the disease-free trajectory if $\mathcal{R}_0 < 1$.



Figure 6. Behavior of the dynamics (2.1) for $\kappa_1 = 4$, $\kappa_2 = 3$ and $\kappa_3 = 2$ then $\mathcal{R}_0 \approx 3.68 > 1$.



Figure 7. Magnified view of the limit cycle of the dynamics (2.1) for $\kappa_1 = 4$, $\kappa_2 = 3$ and $\kappa_3 = 2$ then $\mathcal{R}_0 \approx 3.68 > 1$.



Figure 8. Behavior of the dynamics (2.1) for $\kappa_1 = 4$, $\kappa_2 = 3$ and $\kappa_3 = 2$ then $\mathcal{R}_0 \approx 3.68 > 1$.



Figure 9. Behavior of the dynamics (2.1) for $\kappa_1 = 13$, $\kappa_2 = 9$ and $\kappa_3 = 0.1$ then $\mathcal{R}_0 \approx 0.2 < 1$.



Figure 10. Behavior of the dynamics (2.1) for $\kappa_1 = 13$, $\kappa_2 = 9$ and $\kappa_3 = 0.1$ then $\mathcal{R}_0 \approx 0.2 < 1$.

5.3. Case of periodic parameters. In the third step, we performed numerical simulations for the system (2.1) where all parameters were set as *T*-periodic functions. Thus the model is given by

$$\begin{aligned}
\dot{S}(t) &= d(t)\Lambda_{1}(t) - \frac{\rho_{1}(t)I(t)}{\kappa_{1} + I(t)}S(t) - \frac{\rho_{2}(t)V(t)}{\kappa_{2} + V(t)}S(t) - d(t)S(t), \\
\dot{I}(t) &= \frac{\rho_{1}(t)I(t)}{\kappa_{1} + I(t)}S(t) + \frac{\rho_{2}(t)V(t)}{\kappa_{2} + V(t)}S(t) - (\gamma(t) + d(t))I(t), \\
\dot{V}(t) &= \eta(t)I(t) - \mu(t)V(t) - \frac{\rho_{3}(t)V(t)}{\kappa_{3} + V(t)}P(t), \\
\dot{P}(t) &= \delta(t)\Lambda_{2}(t) + \theta(t)\frac{\rho_{3}(t)V(t)}{\kappa_{3} + V(t)}P(t) - \delta(t)P(t).
\end{aligned}$$
(5.4)

with the positive initial condition $(S^0, I^0, V^0, P^0) \in \mathbb{R}^4_+$.

We give the results of some numerical simulations confirming the stability of the steady states of system (5.4). The basic reproduction number \mathcal{R}_0 was approximated by using the time-averaged system.

In Figure 12, the calculated trajectories of the dynamics (5.4) converge asymptotically to the periodic solution corresponding to the disease persistence if $\mathcal{R}_0 > 1$. In Figures 11 and 13, we displayed a magnified view of the limit cycle for the case where $\mathcal{R}_0 > 1$. In Figure 14, different initial conditions were considered and for each one of them, the solution converge to the same periodic solution. In Figure 15, the calculated trajectories of the dynamics (5.4) converge to the disease-free periodic solution $\mathcal{E}_0(t) = (S^*(t), 0, 0, P^*(t))$ for the case where $\mathcal{R}_0 \leq 1$.



Figure 11. Magnified view of the limit cycle of the dynamics (2.1) for $\kappa_1 = 4$, $\kappa_2 = 3$ and $\kappa_3 = 2$ then $\mathcal{R}_0 \approx 3.68 > 1$.



Figure 12. Behavior of the dynamics (2.1) for $\kappa_1 = 4$, $\kappa_2 = 3$ and $\kappa_3 = 2$ then $\mathcal{R}_0 \approx 3.68 > 1$.



Figure 13. Behavior of the dynamics (2.1) for $\kappa_1 = 4$, $\kappa_2 = 3$ and $\kappa_3 = 2$ then $\mathcal{R}_0 \approx 3.68 > 1$.



Figure 14. Behavior of the dynamics (2.1) for $\kappa_1 = 13$, $\kappa_2 = 9$ and $\kappa_3 = 0.1$ then $\mathcal{R}_0 \approx 0.2 < 1$.



Figure 15. Behavior of the dynamics (2.1) for $\kappa_1 = 13$, $\kappa_2 = 9$ and $\kappa_3 = 0.1$ then $\mathcal{R}_0 \approx 0.2 < 1$.

6. Conclusions

In order to more understand the vibrio cholerae dynamics when describing the contamination of uninfected hosts, an important way is to take into account of both, contact with vibrio cholerae (vibrio cholerae-to-host transmission) and contact with infected hosts (host-to-host transmission). The marked seasonality of cholera, impose the consideration of this property when modelling its dynamics. In this article, we proposed and analysed a mathematical model for vibrio cholerae dynamics reflecting the seasonality observed in real life. The basic reproduction number was defined and the steady states of the dynamics were calculated for the first step when considering the autonomous dynamics. We characterised the existence and uniqueness of the steady states. We characterised also the stability conditions for these steady states. Later, we concentrated on the non-autonomous dynamics and we defined the basic reproduction number, \mathcal{R}_0 by using an integral operator. It is proved that once $\mathcal{R}_0 \leq 1$, all solution of the dynamics converge to the disease-free periodic trajectory and that the disease persists if $\mathcal{R}_0 > 1$. We performed the theoretical findings by some numerical examples using explicit Runge-Kutta formulas of orders 4 and 5 under Matlab for three cases, the autonomous dynamics, the seasonal contact dynamics and the fully seasonal dynamics. As it is seen in the numerical simulations and proved theoretically that for the first case, the solution converge to one of the equilibria of the dynamics (5.2) regarding Theorems 3.3 and 3.4. However, for the second and third cases, the solutions converge to a limit cycle regarding Theorems 4.2 and 4.3.

Conflicts of Interest: The authors declare that there are no conflicts of interest regarding the publication of this paper.

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