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Study of an HIV-1 Model with Time Delays

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Abstract

We propose a mathematical model for HIV-1 infection with two time delays, one for the average latent period of cell infection and the other for the average time needed for the virus production after a virion enters a cell. The model examines a viral-therapy for controlling infections through recombining HIV-1 virus with a genetically modified virus. When only the intracellular delay is enrolled into model (1.13), the basic reproduction numbers R_0 and R_d are identified and their threshold properties are discussed. When $R_0 < 1$, the infection-free equilibrium E_0 is globally asymptotically stable. When $R_0 > 1$, E_0 becomes unstable and there occurs the single-infection equilibrium E_s. If $R_0 > 1$ and $R_d < 1$, E_s is asymptotically stable, while for $R_d > 1$, E_s loses its stability to the double-infection equilibrium. For the double-infection equilibrium E_d, we show how to determine its stability and existence of Hopf bifurcation. Some simulations are presented to demonstrate the theoretical results.

Further investigation is carried over by introducing the second time lag into model (2.1). We have identified the new basic reproduction numbers $\tilde{R}_0$ and $\tilde{R}_d$, and proved that for $\tilde{R}_0 < 1$ the infection-free equilibrium $\tilde{E}_0$ is globally asymptotically stable. If $\tilde{R}_0 > 1$ and $\tilde{R}_d < 1$, the single-infection equilibrium $\tilde{E}_s$ is asymptotically stable. For the double-infection equilibrium $\tilde{E}_d$, it has been found that there exist both Hopf and double Hopf bifurcations. These theoretical predictions are verified by using some numerical examples. Evidences indicate that the viral-therapy of recombining HIV-1 virus with a genetically modified virus may be effective in reducing the HIV-1 load, and larger delays may be able to help eradicate the virus.

Keywords

HIV-1 Model, Time Delay, Recombinant Virus, Stability of Equilibria, Lyapunov Function, LaSalle Invariance Principle, Hopf Bifurcation, Double Hopf Bifurcation, Limit Cycle.

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Last but not the least, I dedicate my thesis to my parents, family and friends. Their unconditional love and support are the source of my strength to hold on and overcome various difficulties.

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Chapter 1

Introduction

1.1 Overview

Recently, time-delay differential equation (DDE) has become an important tool in modeling real-life systems, especially in population dynamics. A simple but well-known delay differential equation in population dynamics is the evolution equation, given by

$$\tfrac{d}{dt}z(t) = R[z(t) - z(t-\tau)^2], \tag{1.1}$$

representing a system named after Belgian mathematician P.F. Verhulst [15] in the 19th century. Hutchinson's equation is another well-known delay logistic equation with a discrete delay, described by the following equation:

$$\tfrac{dx(t)}{dt} = \gamma x(t)[1 - x(t-\tau)/K], \tag{1.2}$$

which is also referred as Wright's equation. One can show [49] that if $\gamma\tau < 37/24$ and $x(0) > 0$, $x(t) \to K$ as $t \to \infty$. Then system (1.2) has a nonconstant periodic solution oscillating around $x = K$.

For immune response model (predator-prey model), the well-known time-delay differential equation is the Lotka–Volterra model. A modified form of the Lotka–Volterra model [2] is given by:

$$\begin{aligned} \frac{dx(t)}{dt} &= rx(t) - \frac{r}{K}x(t)x(t-\tau) - \alpha x(t)y(t) - H_x, \\ \frac{dy(t)}{dt} &= -cy(t) + \beta x(t)y(t) - H_y, \end{aligned} \tag{1.3}$$

where $x(t)$ and $y(t)$ represent the rates of change for prey population and predator population, respectively. r is the intrinsic growth rate of the prey and c is the death rate for the predator without prey. α measures the rate of consumption of prey by the predator and β measures the conversion of prey consumed into the predator reproduction rate. K is the carrying capacity. The constants H_x and H_y denote the rates of harvesting for the populations x and y, respectively. All the parameters are assumed to take positive values. Model (1.3) has been analyzed by Martin and Ruan [2], who showed that the time delay could induce instability, oscillations via Hopf bifurcation, and switching stability.

A more complicated model of immune response is HIV-1 infection model [21], described by

$$\begin{aligned} \frac{dx(t)}{dt} &= s - dx(t) - kv(t)x(t), \\ \frac{dy(t)}{dt} &= ke^{-\delta\tau}v(t-\tau)x(t-\tau) - \delta y(t) - py(t)z(t), \\ \frac{dv(t)}{dt} &= N\delta y(t) - \mu v(t), \\ \frac{dz(t)}{dt} &= cy(t)z(t) - bz(t), \end{aligned} \tag{1.4}$$

where $x(t)$, $y(t)$, $v(t)$ and $z(t)$ denote the concentrations of uninfected cells, infected cells, virus and concentration of cytotoxic T lymphocytes, respectively. The parameter s is the rate at which new target cells are generated. d is the death rate of the susceptible cells and k is the infection rate. The death rate of infected cells is δ, and the production rate of new virus particles is N as the lysis of infected cells occurs. Thus, on average, virus is instantaneously produced at rate $N\delta y(t)$. Also, virus particles are cleared from the system at rate μ per virion. p represents the strength of the lytic component and b is the death rate for cytotoxic T lymphocytes. Lastly, τ denotes the lag between the time when the virus contacts a target cell and the time when the cell becomes actively infected. For the above model, the stability conditions for uninfected steady state and infected steady state have been found. In addition, increasing either of the two delays will help to control HIV-1 infection. Details are shown in [21].

In recent decades, many researchers made contributions to the theory and applications of delay differential equations. The book of Bellman and Cooke [34] describes the basic theory for the DDEs, while Hale's work [23] focuses on the theory of DDEs with bounded delay. The book of Stépán [19] discusses the stability of the retarded DDEs. The theory and applications of DDEs in population models can be found in the book of Yang [49]. This dissertation also studies Hopf Bifurcation in DDEs. The theory of Hopf bifurcation in DDEs can be found in the book of Hassard et al [4]. There are many other researchers who developed theories and methodologies for studying DDEs.

To solve DDEs, computation is vital. There are several software packages for numerically solving delay differential equations and analyzing bifurcations of DDEs. dde23 developed by Shampine and Thompson in Matlab is a powerful tool for simulating retarded differential equations with fixed discrete delays. This method is an extension of the Matlab ODE solver ode23, so called the method of steps. The idea can be described by using the following simple example:

$$y'(t) = y(t-1) \quad \text{for} \quad t \geq 0, \tag{1.5}$$

with history $S(t) = 1$ for $t \leq 0$. For $0 \leq t \leq 1$, the above equation can be reduced to an initial value problem for an ODE with $y(t-1) = S(t-1)$ and $y(0) = 1$. For the next interval $1 \leq t \leq 2$, analytical solution is treated in the same way, but the numerical solution is more complicated. For numerically solving ODEs, ode23 combines Runge-Kutta methods with cubic Hermite interpolation. Runge-Kutta methods are more attractive since they are easy to start. With the given initial value, $y_0 = y(a)$ at $x_0 = a$, a distance $h_n = x_{n+1} - x_n$ is taken so that $y_n \approx y(x_n)$ and $y_{n+1} \approx y(x_{n+1})$. To obtain a more accurate approximation, the step size h_n needs be chosen as small as necessary. Different from Runge-Kutta methods which only work at mesh points, cubic Hermite interpolation provides an accurate numerical solution between mesh points. Thus, with such a method, we can obtain $y(t)$ everywhere in the interval. In this dissertation, new DDE models are developed for the HIV-1 infection. The models are used to study stability of equilibria and Hopf bifurcation.

1.2 Stability of equilibria and Lyapunov functions

The study of equilibria of nonlinear systems plays an important role in HIV-1 model. In order to be meaningful physically, an equilibrium point must satisfy a certain stability criterion. We begin the discussion on delay differential equations with continuous initial data. For a given constant $r \geq 0$, let $C = C([-r, 0], R^n)$ and, if $x : [-r, \alpha) \to R^n$, $\alpha > 0$, let $x_t \in C$, $t \in [0, \alpha)$, be defined by $x_t(\theta) = x(t + \theta)$, $\theta \in [-r, 0]$. For a given function $f : C \to R^n$, a DDE can be defined as

$$\dot{x} = f(x_t) \tag{1.6}$$

If $\varphi \in C$ is given, then a solution $x(t, \varphi)$ of (1.6) with initial value φ at $t = 0$ is a continuous function defined on an interval $[-r, \alpha)$, $\alpha > 0$, such that $x_0(\theta) = x(\theta, \varphi) = \varphi(\theta)$ for $\theta \in [-r, 0]$, $x(t, \varphi)$ has a continuous derivative on $(0, \alpha)$, a right hand derivative at $t = 0$ and satisfies (1.6) for $t \in [0, \alpha)$.

Definition 1.1 Suppose that 0 is an equilibrium point of (1.6); that is, a zero of f. The point 0 is said to be stable if, for any $\varepsilon > 0$, there exists a $\delta > 0$ such that for any $\varphi \in C$ with $|\varphi| < \delta$, we have $|x(t, \varphi)| < \varepsilon$ for $t \geq -r$. The point 0 is asymptotically stable if it is stable and there is $b > 0$ such that $|\varphi| < b$ implies that $|x(t, \varphi)| \to 0$ as $t \to \infty$. The point 0 is said to be a local attractor if there is a neighborhood U of 0 such that

$$\lim_{t\to\infty} \text{dist}(x(t, U), 0) = 0$$

that is, 0 attracts elements in U uniformly.

For linear retarded equation (1.6), $f : C \to R^n$ being a continuous linear functional, there is a solution of the form $ce^{\lambda t}$ for some nonzero n-vector c if and only if λ satisfies the following characteristic equation

$$\det D(\lambda) = \lambda I - f(e^{-\lambda I}) = 0. \tag{1.7}$$

The λ is called the eigenvalue of the linearized equation. Equation (1.7) may have infinitely many solutions, but there can be only a finite number in any vertical strip in the complex plane. This is a consequence of the analyticity of (1.7) in λ and the fact that $\text{Re}\lambda \to \infty$ if $|\lambda| \to \infty$.

The eigenvalues play an important role in studying stability of equilibria. If there is an eigenvalue with positive real part, then the origin is unstable. For asymptotic stability, it is necessary and sufficient to have Re$\lambda < 0$ for all eigenvalues.

The notion of global stability is usually attributed to Lyapunov. Lyapunov stability is concerned with the trajectories of a system when the initial state is near an equilibrium point. Two methods related to stability were developed in the early 1950's by Razumikhin (1956) and Krasovskii (1956).

Theorem 1.1 (Razumikhin, 1956) Suppose that $u, v, w : [0, \infty) \to [0, \infty)$ are continuous nondecreasing functions, $u(s)$, $v(s)$ are positive for $s > 0$, $u(0) = v(0) = 0$ and v strictly increasing. If there is a continuous function $V : R^n \to R$ such that $u(|x|) \le V(x) \le v(|x|)$, $x \in R^n$, and $\dot{V}(\varphi(0)) \le w(|\varphi(0)|)$, if $V(\varphi(\theta)) \le V(\varphi(0))$, $\theta \in [-r, 0]$, then the point 0 is stable. In addition, if there is a continuous nondecreasing function $p(s) > s$ for $s > 0$ such that

$$\dot{V}(\varphi(0)) \le w(|\varphi(0)|) \quad \text{if} \quad V(\varphi(\theta)) \le p(V(\varphi(0))), \quad \theta \in [-r, 0],$$

then 0 is asymptotically stable.

Theorem 1.2 (Krasovskii, 1956) Suppose that $u, v, w : [0, \infty) \to [0, \infty)$ are continuous nonnegative nondecreasing functions, $u(s)$, $v(s)$ positive for $s > 0$, $u(0) = v(0) = 0$. If there is a continuous function $V : C \to R$ such that

$$u(|\varphi(0)|) \le V(\varphi) \le v(|\varphi|), \quad \varphi \in C,$$

$$\dot{V}(\varphi) = \limsup_{t\to\infty} \tfrac{1}{t}[V(x_t(.,\varphi)) - V(\varphi)] \le -w(|\varphi(0)|)$$

then 0 is stable. If, in addition, $w(s) > 0$ for $s > 0$, then 0 is asymptotically stable.

Theorem 1.3 (Hale, 1963) Let V be a continuous scalar function on C with $\dot{V}(\varphi) \le 0$ for all $\varphi \in C$. If $U_a = \varphi \in C : V(\varphi) \le a$, $W_a = \varphi \in U_a : \dot{V}(\varphi) = 0$ and M is the maximal invariant set in W_a, then, for any $\varphi \in U_a$ for which $\gamma^+(\varphi)$ is bounded, we have $w(\varphi) \subset M$. (This theorem is a natural generalization of the classical LaSalle invariance principle for ODE.) (see [33])

1.3 Hopf bifurcation theorem

Hopf bifurcation theorem was developed in 1942 by E. Hopf ([33]) and actingly researched in the following several decades. The implication of the theorem is extraordinary, since it provides a powerful analytical tool for exploring properties of periodic solutions. Also, it has been found that Hopf bifrucation theorem can be formulated for both ODEs and DDEs, where the latter is mainly studied in this destruction.

Consider the following delay differential equation

$$\dot{x} = F(\alpha, x_t) \tag{1.8}$$

with $F : R \times C \to R^n$, F of class C^2, $F(\alpha, 0) = 0 \quad \forall \alpha \in R$ and $C = C([-r, 0], R^n)$ the space of continuous functions from $[-r, 0]$ into R^n. x_t is the function defined from $[-r, 0]$ into R^n by $x_t(\theta) = x(t + \theta)$, $r \geq 0$.

Definition 1.2 $(\alpha_0, 0) \in R \times C$ is called Hopf bifurcation point of equation (1.8) if every neighborhood of this point in $R \times C$ includes a point (α, φ), with $\varphi \neq 0$ such that φ is the initial value of a periodic solution, with period near a fixed positive number, of equation (1.8) for the value of α.

We assume that

(H_0) F is of class C^k, for $k \geq 2$, $F(\alpha, 0) = 0$ for each α, and the map $(\alpha, \varphi) \to D^k{}_\varphi F(\alpha, \varphi)$ sends bounded sets into bounded sets.

(H_1) The characteristic equation

$$\det \Delta(\alpha, \lambda) := \lambda Id - D_\varphi F(\alpha, 0) e^{\lambda(\cdot) Id} \tag{1.9}$$

of the linearized equation of (1.8) around the equilibrium $v = 0$:

$$\frac{dv(t)}{dt} = D_\varphi F(\alpha, 0) v_t \tag{1.10}$$

in $\alpha = \alpha_0 \geq 0$ has a simple pair of imaginary roots $\lambda_0 = \lambda(\alpha_0) = \pm i$, all the other roots λ satisfy $\lambda \neq m\lambda_0$ for $m = 0, 2, 3, 4, \ldots$.

(H_1) implies that the root λ_0 lies on a branch of roots $\lambda = \lambda(\alpha)$ of the equation (1.9), of class C^{k-1}.

(H_2) For $\lambda(\alpha)$ being the branch of roots passing through λ_0, we have

$$\frac{\partial}{\partial\alpha}\Re e\lambda(\alpha)|_{\alpha=\alpha_0} \neq 0 \tag{1.11}$$

Hopf Bifurcation Theorem. Under the assumptions (H_0), (H_1) and (H_2), there exist a constants R, $\delta > 0$, $\eta > 0$, functions $\alpha(c)$, $\omega(c)$ and a periodic function with period $\omega(c)$, $u^*(c)$ such that (i) all of these functions are of class C^1 with respect to c, for $c \in [0, R]$, $\alpha(0) = \alpha_0$, $\omega(0) = \omega_0$, $u^*(0) = 0$; (ii) $u^*(c)$ is a periodic solution of (1.8) for the parameter values $\alpha(c)$ and period $\omega(c)$; (iii) For $|\alpha - \alpha_0| < \delta$ and $|\omega - 2\pi| < \eta$, any $\omega-$periodic solution p, with $\|p\| < R$, of (1.8) for the parameter value α, there exists $c \in [0, R]$ such $\alpha = \alpha(c)$, $\omega = \omega(c)$ and p is, up to a phase shift, equal to $u^*(c)$.

1.4 About the Thesis

This thesis is focused on the study of a HIV-1 model. Particular attention is given to stability of equilibrium solutions and bifurcations. Recently reported results show that new drugs and new therapies can help to eradicate the HIV-1 virus. An intention to generalize the results motivated this research. It is expected that the models developed and the results obtained in this dissertation could enhance the research in modelling HIV-1 infection in host.

1.4.1 Higher dimensional HIV-1 therapy model with time delays

In recent years, mathematical modelling plays an important role in understanding HIV-1 in host. During the long history of research in HIV-1 problem, people usually focused on lower dimensional systems, which have less critical points, less coefficients and are easier for analysis. However, in order to understand well the HIV-1 infection, studying higher dimensional systems is necessary.

Moreover, most existing mathematical models for HIV-1 infection are described by ordinary differential equations (ODEs). However, in reality, we need consider the time effects during the infection. Therefore, analyzing delayed HIV-1 models can provide more valuable insight into HIV-1 pathogenesis. Simpler delayed HIV-1 systems are usually 2 or 3 dimension. In this dissertation, we will study a 5-dimensional HIV-1 model with time delays.

1.4.2 HIV-1 therapy model (ODE) of fighting a virus with another virus

By years of study, researchers have obtained much knowledge about the mechanism of the interactions of the components within a host and have thereby enhanced the progress in developing new drugs and designing optimal combination of existing therapies. Current therapies for AIDS employ inhibitors of the enzymes required for replication of HIV-1 to reduce the load. However, an alternative approaches, offered by genetic engineering, is to use recombinant virus capable of controlling infections of HIV [12, 16]. This method has been used to modify rhabdoviruses, which makes them capable of killing cells previously infected by HIV-1. The engineered virus codifies the coreceptor pair CD4 and CXCR4 of the host cell membrane and bind specifically to the protein complex gp120/41 of HIV-1 expressed on the surface of infected cells, where it causes a rapid cytopathic infection. This destruction of infected cells decreased by about 1000-fold HIV-1 load [32]. In the present study, evidences show that this treatment could be effective in reducing individual HIV-1 load.

To understand this approach of fighting a virus with a genetically modified virus, Revialla and Garcia-Ramos [42] proposed a mathematical model, which has been subjected to intensive studies in [46]. A standard and classic differential equation model for HIV infection can be described by the following system:

$$\begin{aligned} \dot{x} &= \lambda - dx - \beta xv, \\ \dot{y} &= \beta xv - ay, \\ \dot{v} &= ky - pv, \end{aligned} \tag{1.12}$$

where the dot indicates differentiation with respect to time t, $x(t)$, $y(t)$ and $v(t)$ are the densities of virus-free host cells, infected cells and a pathogen virus, respectively, at time t. The production rate and death rate for the healthy cells are λ and d. β is the constant rate at which a T-cell is contacted by the virus. It is also assumed that once cells are infected, they may die at rate a due to the action of either the virus

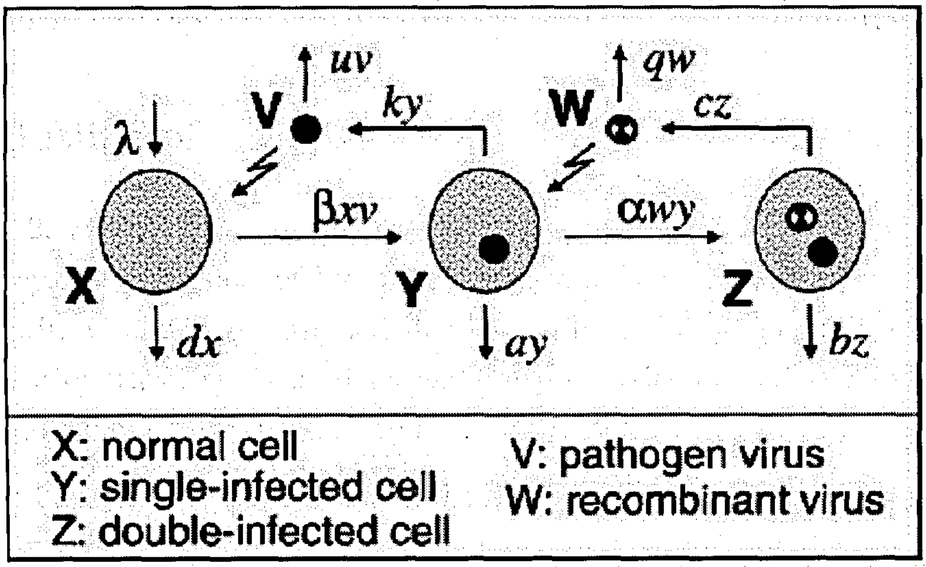

Figure 1.1: Model for a double viral infection.

or the immune system, and each produces the pathogens at a rate k during their life which on average has length $1/a$.

In [46, 42], a second virus is added into the model (1.12), which then becomes

$$\begin{aligned} \dot{x} &= \lambda - dx - \beta xv, \\ \dot{y} &= \beta xv - ay - \alpha wy, \\ \dot{z} &= \alpha wy - bz, \\ \dot{v} &= ky - pv, \\ \dot{w} &= cz - qw, \end{aligned} \tag{1.13}$$

where $w(t)$ and $z(t)$ are the recombinant (genetically modified) virus and double-infected cells. After second virus enrolled, once the recombinant infects cells previously infected by the pathogens, they can be turned into double-infected cells at a rate αwy, where recombinants are removed at a rate qw. The double infected cells die at a rate bz, and release recombinants at rate cz (see Figure 1.1).

The viral-therapy may have several benefits over present conventional treatment. It is expected to have no toxicity, no negative side effects, and no evolution of resistance. Another advantage is the simplicity of treatment. These advantages could make this viral-therapy an alternative to extend the survival of AIDS patients ([42]).

1.4.3 Outline of the thesis

In Chapter 2, we propose a mathematical model for HIV-1 infection with the intracellular delay. The method of Lyapunov function, LaSalle's invariant principle and Routh-Hurwitz Criterion are applied to analyze the stability of equilibrium solutions. Hopf bifurcation theorem is used to explore properties of periodic solutions. The effect of time delay is also investigated.

In Chapter 3, a modified mathematical model for HIV-1 infection is given, which has delays in cell infection and virus production. Besides the analysis for stability of equilibria and Hopf bifurcation, we will also develop an analytical approach to consider double-Hopf bifurcation in the model with multiple delays. Determining the critical parameter values for double Hopf bifurcation is illustrated using numerical examples. Conclusion and discussions are presented at the end of each chapter. The study in this thesis is intended to provide some useful information for medical treatment.

Chapter 2

HIV MODEL WITH INTRACELLULAR DELAY

2.1 Introduction

In this chapter, we introduce a time lag into model (1.13), since in the real situation, it takes time for the virus to contact a target cell and the contacted cells to be actively affected. This can be described by the eclipse phase of the virus life cycle. Further, we assume that the probability density that a cell still remains infected for τ time units after being contacted by the virus obeys an exponentially decay function. Therefore, following the line of [21, 22], model (1.13) can be modified to

$$\begin{aligned} x'(t) &= \lambda - dx(t) - \beta x(t)v(t), \\ y'(t) &= \beta e^{-a\tau}x(t-\tau)v(t-\tau) - ay(t) - \alpha w(t)y(t), \\ z'(t) &= \alpha w(t)y(t) - bz(t), \\ v'(t) &= ky(t) - pv(t), \\ w'(t) &= cz(t) - qw(t), \end{aligned} \tag{2.1}$$

where τ denotes the average time for a viral particle to go through the eclipse phase. Because the dimension of the system is higher than 2, system (2.1) may exhibit some interesting dynamic behaviors (Hopf bifurcation, limit cycles and even chaos), which would make the analysis of the system more complicated. Thus, the goal of this chapter focuses on equilibrium solutions and their bifurcations. In next section, we will justify the positivity and boundedness of solutions of (2.1). Also, in order to obtain biologically meaningful equilibria, the basic reproduction number R_0 will be fined. In Sections 2.3, 2.4 and 2.5, we analyze the stability of the three equilibria: disease-free equilibrium E_0 , single-infection equilibrium E_s and double-infection equilibrium E_d. In Section 2.6, two numerical examples are provided to demonstrate the theoretical predictions. The last section summarizes the results obtained in this chapter with some discussions.

2.2 Positivity, boundedness of solutions, equilibria and basic reproduction number

Because of biological reasons, all variables in system (2.1) must be non-negative. Therefore, given a non-negative initial value, the corresponding solution must remain non-negative. This can be verified as follows.

Let $X = C([-\tau, 0]; R^5)$ be the Banach space of continuous mapping from $[-\tau, 0]$ to R^5 equipped with the sup-norm. By the fundamental theory of FDEs (see, e.g. [23]), we know that there is a unique solution $(x(t), y(t), z(t), v(t), w(t))$ to system (2.1). It is biologically reasonable to consider the following initial conditions for (2.1):

$$(x(\theta), y(\theta), z(\theta), v(\theta), w(\theta)) \in X, \tag{2.2}$$

$$x(\theta) \geq 0, y(\theta) \geq 0, z(\theta) \geq 0, v(\theta) \geq 0, w(\theta) \geq 0, \quad \theta \in [-\tau, 0]. \tag{2.3}$$

From (2.1), we obtain

$$\begin{aligned}
x(t) &= x(0)e^{-\int_0^t (d+\beta v(\xi))d\xi} + \lambda \int_0^t e^{-\int_\eta^t (d+\beta v(\xi))d\xi} d\eta, \\
y(t) &= y(0)e^{-\int_0^t (a+\alpha w(\xi))d\xi} + \beta \int_0^t x(\eta-\tau)v(\eta-\tau)e^{-a\tau}e^{-\int_\eta^t (a+\alpha w(\xi))d\xi} d\eta, \\
z(t) &= z(0)e^{-bt} + \int_0^t \alpha w(\eta)y(\eta)e^{-b(t-\eta)} d\eta, \\
v(t) &= v(0)e^{-pt} + \int_0^t ky(\eta)e^{-p(t-\eta)} d\eta, \\
w(t) &= w(0)e^{-qt} + \int_0^t cz(\eta)e^{-q(t-\eta)} d\eta.
\end{aligned} \tag{2.4}$$

Positivity immediately follows from the non-negative initial conditions. To show the boundedness of the solutions of system (2.1), we define

$$B(t) = cke^{-a\tau}x(t) + cky(t+\tau) + ckz(t+\tau) + \tfrac{ac}{2}v(t+\tau) + \tfrac{bk}{2}w(t+\tau), \qquad (2.5)$$

where all the solutions are non-negative. Choosing $m = \min\{\frac{a}{2}, \frac{b}{2}, d, p, q\}$, it follows that the derivative of $B(t)$ with respective to time t along the solution of (2.1) is given by

$$\begin{aligned}
\tfrac{dB(t)}{dt}|_{(2.1)} &= cke^{-a\tau}[\lambda - dx(t) - \beta v(t)x(t)] \\
&\quad + ck\beta e^{-a\tau}v(t)x(t) - ckay(t+\tau) - ck\alpha w(t+\tau)y(t+\tau) \\
&\quad + ck\alpha w(t+\tau)y(t+\tau) - ckbz(t+\tau) \\
&\quad + \tfrac{ac}{2}ky(t+\tau) - \tfrac{ac}{2}pv(t+\tau) \\
&\quad + \tfrac{bk}{2}cz(t+\tau) - \tfrac{bk}{2}qw(t+\tau) \\
&= cke^{-a\tau}\lambda - cke^{-a\tau}dx(t) - \tfrac{a}{2}cky(t+\tau) - \tfrac{b}{2}ckz(t+\tau) \\
&\quad - \tfrac{ac}{2}pv(t+\tau) - \tfrac{bk}{2}qw(t+\tau) \\
&\leq cke^{-a\tau}\lambda - mB(t).
\end{aligned} \qquad (2.6)$$

This implies that $B(t)$ is bounded, so are $x(t)$, $y(t)$, $z(t)$, $v(t)$ and $w(t)$. System (2.1) has three possible biologically meaningful equilibria: disease-free equilibrium E_0, single-infection equilibrium E_s and double-infection equilibrium E_d, given below:

$$\begin{aligned}
E_0 &= (\tfrac{\lambda}{d}, 0, 0, 0, 0), \\
E_s &= (\tfrac{ap}{\beta ke^{-a\tau}}, \tfrac{\lambda e^{-a\tau}}{a} - \tfrac{dp}{\beta k}, 0, \tfrac{\lambda ke^{-a\tau}}{ap} - \tfrac{d}{\beta}, 0), \\
E_d &= (\tfrac{\lambda\alpha cp}{d\alpha cp+\beta bkq}, \tfrac{bq}{\alpha c}, \tfrac{q(\alpha\beta\lambda cke^{-a\tau}-\beta abkq-\alpha acdp)}{\alpha c(\beta bkq+\alpha cdp)}, \tfrac{bkq}{\alpha cp}, \tfrac{\alpha\beta\lambda cke^{-a\tau}-\beta abkq-\alpha acdp}{\alpha(\beta bkq+\alpha cdp)}).
\end{aligned} \qquad (2.7)$$

From biological meaning of the basic reproduction number (see [42]), we define

$$R_0 = \tfrac{k\beta\lambda}{adp}e^{-a\tau}. \qquad (2.8)$$

If $R_0 < 1$, E_0 is the only biologically meaningful equilibrium. If $R_0 > 1$, there is another biologically meaningful equilibrium E_s (single-infection equilibrium). The double-infection equilibrium E_d exists (biologically meaningful) if and only if $R_d > 1$, where

$$R_d = \frac{c\alpha}{bq}\left(\frac{\lambda e^{-a\tau}}{a} - \frac{dp}{k\beta}\right) = \frac{cdp\alpha}{bkq\beta}(R_0 - 1). \tag{2.9}$$

Hence

$$R_d > 1 \iff R_0 > 1 + \frac{bkq\beta}{cdp\alpha}. \tag{2.10}$$

2.3 Stability of the disease-free equilibrium E_0

The linearized system of (2.1) at the disease-free equilibrium E_0 is

$$\begin{aligned}
x'(t) &= -dx(t) - \frac{\beta\lambda}{d}v(t),\\
y'(t) &= \beta e^{-a\tau}\frac{\lambda}{d}v(t-\tau) - ay(t),\\
z'(t) &= -bz(t),\\
v'(t) &= ky(t) - pv(t),\\
w'(t) &= cz(t) - qw(t),
\end{aligned} \tag{2.11}$$

for which the characteristic equation is given by

$$D(\xi,\tau) = (\xi+d)(\xi+b)(\xi+q)[(\xi+a)(\xi+p) - k\beta e^{-a\tau}\frac{\lambda}{d}e^{-\xi\tau}] = 0. \tag{2.12}$$

Obviously, it suffices to only consider the quadratic factor,

$$(\xi+a)(\xi+p) - k\beta e^{-a\tau}\frac{\lambda}{d}e^{-\xi\tau} = \xi^2 + (a+p)\xi + ap - k\beta e^{-a\tau}\frac{\lambda}{d}e^{-\xi\tau}. \tag{2.13}$$

Note that $\xi = 0$ is not a root of equation (2.13) if $R_0 < 1$, since

$$ap - k\beta e^{-a\tau}\frac{\lambda}{d} = ap(1 - R_0) > 0. \tag{2.14}$$

When $\tau = 0$, equation (2.13) becomes

$$\xi^2 + (a+p)\xi + ap - k\beta\frac{\lambda}{d} = 0. \tag{2.15}$$

In order for the two roots of Equation (2.15) to have negative real part, it requires

$$ap - k\beta\frac{\lambda}{d} > 0, \tag{2.16}$$

which is equivalent to

$$R_0(\tau = 0) < 1. \tag{2.17}$$

Thus, when $R_0 < 1$, all roots of Equation (2.15) have negative real part. From [36], we know that all roots of Equation (2.13) depend continuously on τ. In [10], the assumption (ii),

$$\limsup\{|Q_m(\xi,\tau)/P_n(\xi,\tau)| : |\xi| \to \infty, \Re(\xi) \geq 0\} < 1 \quad \text{for} \quad \text{any} \quad \tau \tag{2.18}$$

holds here, where

$$P_n(\xi,\tau) + Q_m(\xi,\tau)e^{-\xi\tau} = D(\xi,\tau).$$

This condition ensures that there are no roots exist in the infinity (see [10]), and hence $Re(\xi) < +\infty$ for any root of (2.13). As a result, the only possibility for the roots of Equation (2.13) to enter into the right half of complex plane is to cross the imaginary axis when τ increases. Thus, we define $\xi = i\omega \quad (\omega > 0)$ to be a purely imaginary root of (2.13). Then we get

$$-\omega^2 + i\omega(a+p) + ap - k\beta e^{-a\tau}\frac{\lambda}{d}e^{-i\omega\tau} = 0. \tag{2.19}$$

Taking moduli of Equation (2.19) gives

$$H(\omega^2) := \omega^4 + (a^2+p^2)\omega^2 + a^2p^2 - (k\beta e^{-a\tau}\frac{\lambda}{d})^2 = 0. \tag{2.20}$$

Clearly, $H(\omega^2)$ has no positive real roots if $R_0 < 1$. Therefore, all roots of (2.13) have negative (positive) real parts if $R_0 < 1 \quad (R_0 > 1)$.

Summarizing the above results, we have the following theorem.

Theorem 2.1 When $R_0 < 1$, the disease-free equilibrium E_0 is locally asymptotically stable; at $R_0 = 1$, E_0 becomes unstable and the single-infection equilibrium E_s occurs.

Furthermore, for global stability, we have the following result.

Theorem 2.2 If $R_0 < 1$, the disease-free equilibrium E_0 is globally asymptotically stable, implying that none of the two virus can invade regardless of the initial load.

Proof: We choose the following Lyapunov function:

$$\begin{aligned} V &= \tfrac{e^{-a\tau}}{2}(x(t) - \tfrac{\lambda}{d})^2 + \tfrac{\lambda}{d}y(t) + \tfrac{\lambda}{d}z(t) + \tfrac{a\lambda}{dk}v(t) \\ &\quad + \tfrac{b\lambda}{cd}w(t) + \tfrac{\lambda}{d}\beta e^{-a\tau}\int_{t-\tau}^{t} x(\eta)v(\eta)d\eta. \end{aligned} \tag{2.21}$$

Using non-negativity of the solution and $R_0 < 1$, the derivative of V with respective to time t along the solution of system (2.1) can be manipulated as

$$\begin{aligned} \tfrac{dV}{dt}|_{(2.1)} &= e^{-a\tau}(x(t) - \tfrac{\lambda}{d})[\lambda - dx(t) - \beta v(t)(x(t) - \tfrac{\lambda}{d})] \\ &\quad - e^{-a\tau}(x(t) - \tfrac{\lambda}{d})\beta v(t)\tfrac{\lambda}{d} + \tfrac{\lambda}{d}\beta e^{-a\tau}x(t-\tau)v(t-\tau) \\ &\quad - \tfrac{a\lambda}{d}y(t) - \tfrac{\alpha\lambda}{d}w(t)y(t) + \tfrac{\lambda}{d}\alpha w(t)y(t) - \tfrac{\lambda}{d}bz(t) \\ &\quad + \tfrac{a\lambda}{d}y(t) - \tfrac{a\lambda}{dk}pv(t) + \tfrac{b\lambda}{d}z(t) - \tfrac{b\lambda}{cd}qw(t) \\ &\quad + \tfrac{\lambda}{d}\beta e^{-a\tau}[x(t) - \tfrac{\lambda}{d}]v(t) + \tfrac{\lambda}{d}\beta e^{-a\tau}\tfrac{\lambda}{d}v(t) - \tfrac{\lambda}{d}\beta e^{-a\tau}x(t-\tau)v(t-\tau) \\ &= -e^{-a\tau}(x(t) - \tfrac{\lambda}{d})^2(d + \beta v(t)) - [\tfrac{a\lambda}{dk}p - \tfrac{\lambda}{d}\beta e^{-a\tau}\tfrac{\lambda}{d}]v(t) - \tfrac{b\lambda}{cd}qw(t) \\ &= -e^{-a\tau}(x(t) - \tfrac{\lambda}{d})^2(d + \beta v(t)) - \tfrac{ap\lambda}{dk}[1 - R_0]v(t) - \tfrac{b\lambda}{cd}qw(t) \\ &\leq -de^{-a\tau}(x(t) - \tfrac{\lambda}{d})^2. \end{aligned} \tag{2.22}$$

Thus, by LaSalle's invariance principle [24], we conclude that E_0 is globally asymptotically stable. □

2.4 Stability of the single-infection equilibrium E_s

From the analysis in the previous section, we know that the single-infection equilibrium E_s occurs when $R_0 > 1$. Thus, in order to study the stability of E_s, we assume

$R_0 > 1$ in this section. The linearized system of (2.1) at E_s is

$$\begin{aligned}
x'(t) &= -\tfrac{k\beta\lambda}{ap}e^{-a\tau}x(t) - \tfrac{ap}{k}e^{a\tau}v(t),\\
y'(t) &= \beta e^{-a\tau}(\tfrac{k\lambda}{ap}e^{-a\tau} - \tfrac{d}{\beta})x(t-\tau) + \tfrac{ap}{k}v(t-\tau)\\
&\quad -ay(t) - \alpha w(t)(\tfrac{\lambda}{a}e^{-a\tau} - \tfrac{dp}{k\beta}),\\
z'(t) &= \alpha w(t)(\tfrac{\lambda}{a}e^{-a\tau} - \tfrac{dp}{k\beta}) - bz(t),\\
v'(t) &= ky(t) - pv(t),\\
w'(t) &= cz(t) - qw(t),
\end{aligned} \tag{2.23}$$

with the corresponding characteristic equation:

$$\begin{aligned}
&\{(\xi + \tfrac{k\beta\lambda}{ap}e^{-a\tau})[(\xi+a)(\xi+p) - k(\tfrac{ap}{k}e^{-\xi\tau})] + \beta e^{-a\tau}(\tfrac{k\lambda}{ap}e^{-a\tau} - \tfrac{d}{\beta})e^{-\xi\tau})k(\tfrac{ap}{k}e^{-a\tau})\}\\
&\times[(\xi+b)(\xi+q) - c\alpha(\tfrac{\lambda}{a}e^{-a\tau} - \tfrac{dp}{k\beta})] = 0.
\end{aligned} \tag{2.24}$$

The above characteristic equation consists of two factors:

$$(\xi+b)(\xi+q) - c\alpha(\tfrac{\lambda}{a}e^{-a\tau} - \tfrac{dp}{k\beta}) = \xi^2 + (b+q)\xi + bq - c\alpha(\tfrac{\lambda}{a}e^{-a\tau} - \tfrac{dp}{k\beta}) \tag{2.25}$$

and

$$\begin{aligned}
&(\xi + \tfrac{k\beta\lambda}{ap}e^{-a\tau})[(\xi+a)(\xi+p) - k(\tfrac{ap}{k}e^{-\xi\tau})] + \beta e^{-a\tau}(\tfrac{k\lambda}{ap}e^{-a\tau} - \tfrac{d}{\beta})e^{-\xi\tau})k(\tfrac{ap}{ke^{-a\tau}}),\\
&= \xi^3 + (a+p+\tfrac{k\beta\lambda}{ap}e^{-a\tau})\xi^2 + [\tfrac{k\beta\lambda}{ap}e^{-a\tau}(a+p) + ap]\xi + k\beta\lambda e^{-a\tau} - ap(\xi+d)e^{-\xi\tau}.
\end{aligned} \tag{2.26}$$

For the quadratic factor (2.25), it is easy to verify that its two roots have negative real part if and only if $R_d < 1$. For the cubic factor (2.26), we rewrite it as

$$\xi^3 + a_2(\tau)\xi^2 + a_1(\tau)\xi + a_0(\tau) - (c_1\xi + c_2)e^{-\xi\tau} = 0, \tag{2.27}$$

where

$$\begin{aligned} a_2(\tau) &= a+p+\tfrac{k\beta\lambda}{ap}e^{-a\tau}, \\ a_1(\tau) &= \tfrac{k\beta\lambda}{ap}e^{-a\tau}(a+p)+ap, \\ a_0(\tau) &= k\beta\lambda e^{-a\tau}, \\ c_1 &= ap, \\ c_2 &= apd. \end{aligned} \tag{2.28}$$

It is easy to see that $\xi = 0$ is not a root of (2.27) if $R_0 > 1$, since

$$a_0(\tau) - c_2 = k\beta\lambda e^{-a\tau} - apd = apd(R_0 - 1) > 0 \tag{2.29}$$

When $\tau = 0$, (2.27) becomes

$$\xi^3 + a_2(0)\xi^2 + (a_1(0) - c_1)\xi + a_0(0) - c_2 = 0. \tag{2.30}$$

Applying the Routh-Hurwitz crition (see [13]), we know that all roots of (2.30) have negative real part, because

$$\begin{aligned} &a_2(0) = a+p+\tfrac{k\beta\lambda}{ap} > 0, \\ &a_1(0) - c_1 = ap + \tfrac{k\beta\lambda}{ap}(a+p) - ap = \tfrac{k\beta\lambda}{ap}(a+p) > 0, \\ &a_0(0) - c_2 = k\beta\lambda - apd = apd(R_0(\tau=0) - 1) > 0, \end{aligned}$$

and

$$\begin{aligned} a_2(0)[a_1(0) - c_1] - [a_0(0) - c_2] &= (a+p+\tfrac{k\beta\lambda}{ap})[\tfrac{k\beta\lambda}{ap}(a+p)] - (k\beta\lambda - apd) \\ &= (\tfrac{k\beta\lambda}{ap})^2(a+p) + \tfrac{k\beta\lambda}{ap}(a^2+ap+p^2) + apd > 0. \end{aligned}$$

Therefore, for $\tau = 0$, all roots of (2.27) have negative real part. From [36], we know that all roots of Equation (2.27) depend continuously on τ. Also, (2.18) holds for this case, and hence $Re(\xi) < +\infty$ for any root of (2.27). As a result, the roots of Equation (2.27) can only enter into the right half in complex plane by crossing the imaginary axis when τ increases. Thus, we define $\xi = i\omega$ ($\omega > 0$) to be a purely imaginary root of (2.27), and then obtain

$$-i\omega^3 - a_2(\tau)\omega^2 + a_1(\tau)i\omega + a_0(\tau) - (c_1 i\omega + c_2)e^{-i\omega\tau} = 0, \tag{2.31}$$

Taking moduli of the above equation results in

$$H(\omega^2) := \omega^6 + [a_2(\tau)^2 - 2a_1(\tau)]\omega^4 + [a_1(\tau)^2 - 2a_0(\tau)a_2(\tau) - c_1^2]\omega^2 + a_0(\tau)^2 - c_2^2 = 0. \tag{2.32}$$

Since

$$\begin{aligned} &a_2(\tau)^2 - 2a_1(\tau) = a^2 + p^2 + (\tfrac{k\beta\lambda}{ap}e^{-a\tau})^2 > 0, \\ &a_1(\tau)^2 - 2a_0(\tau)a_2(\tau) - c_1^2 = (\tfrac{k\beta\lambda}{ap}e^{-a\tau})^2(a^2 + p^2) > 0, \\ &a_0(\tau)^2 - c_2^2 = (k\beta\lambda e^{-a\tau} + apd)apd(R_0 - 1) > 0, \end{aligned} \tag{2.33}$$

the function $H(\omega^2)$ is monotonically increasing for $0 \le \omega^2 < \infty$ with $H(0) > 0$. This implies that Equation (2.32) does not have positive roots if $R_0 > 1$. As a result, all roots of (2.27) have negative real part for $\tau > 0$ if $R_0 > 1$.

Summarizing the above results, we have the following theorem.

Theorem 2.3 If $1 < R_0 < 1 + \frac{bkq\beta}{cdp\alpha}$, the single-infection equilibrium E_s is asymptotically stable, implying that the recombinant virus cannot survive but the pathogen virus can; when $R_0 = 1 + \frac{bkq\beta}{cdp\alpha}$ (i.e., $R_d = 1$), E_s becomes unstable and the recombinant virus may persist.

2.5 Stability of the double-infection equilibrium E_d: Existence of Hopf bifurcation

When $R_0 > 1 + \frac{bkq\beta}{cdp\alpha}$ (i.e., $R_d > 1$), the single-infection equilibrium E_s becomes unstable and the double-infection equilibrium E_d comes into existence. To discuss the stability of E_d, we assume $R_d > 1$ in this section. The linearized system of (2.1) at $E_d = (x_d, y_d, z_d, v_d, w_d)$ is

$$\begin{aligned}
x'(t) &= -(d+\beta v_d)x(t) - \beta x_d v(t),\\
y'(t) &= \beta e^{-a\tau} v_d x(t-\tau) - (a+\alpha w_d)y(t) + \beta e^{-a\tau} x_d v(t-\tau) - \alpha y_d w(t),\\
z'(t) &= \alpha w_d y(t) - bz(t) + \alpha y_d w(t),\\
v'(t) &= ky(t) - pv(t),\\
w'(t) &= cz(t) - qw(t).
\end{aligned} \tag{2.34}$$

Letting $m_d = d + \beta v_d$, $m_a = a + p$ and $m_b = b + q$. Using the facts that $c\alpha y_d = bq$ and $k\beta e^{-a\tau} x_d = p(\alpha w_d + a)$, we obtain the characteristic equation of (2.34), given by

$$\begin{aligned}
D(\xi) := \xi^5 + A_4(\tau)\xi^4 + A_3(\tau)\xi^3 + A_2(\tau)\xi^2 + A_1(\tau)\xi + A_0\\
-(B_3(\tau)\xi^3 + B_2(\tau)\xi^2 + B_1(\tau)\xi)e^{-\xi\tau} = 0,
\end{aligned} \tag{2.35}$$

where

$$\begin{aligned}
A_4(\tau) &= m_a + m_b + m_d + \alpha w_d,\\
A_3(\tau) &= ap + m_a m_d + (m_a + m_d)m_b + (p + m_b + m_d)\alpha w_d,\\
A_2(\tau) &= apm_d + m_b(ap + m_a m_d) + (bq + m_b m_d + pm_b + pm_d)\alpha w_d,\\
A_1(\tau) &= apm_b m_d + (bqm_d + pbq + pm_b m_d)\alpha w_d,\\
A_0 &= \alpha bpqw_d m_d,\\
B_3(\tau) &= p(\alpha w_d + a),\\
B_2(\tau) &= (d + m_b)(\alpha w_d + a)p,\\
B_1(\tau) &= dm_b(\alpha w_d + a)p,
\end{aligned} \tag{2.36}$$

When $\tau = 0$, it has been shown in [46] that there exists an $R_2 > R_1$ such that when $R_0 \in (R_1, R_2)$, E_d is asymptotically stable, implying that all roots of (2.35) have negative real part. Unlike for E_0 and E_s where the characteristic equations can be factorized into lower degree polynomials, we are unable to factorize the characteristic equation (2.35). Hence, it is very challenging to determine the stability of E_d by the procedure as shown in Sections 2.3 and 2.4. In what follows, we let $R(\omega)$ and $S(\omega)$ respectively be the real and imaginary parts of $D(i\omega)$, given by

$$\begin{aligned} R(\omega) = & \tfrac{1}{\alpha^2 cp(d\alpha cp+\beta bkq)}\Big\{\omega^4[\alpha\beta^2b^2q^2k^2+\alpha^2c\beta pbq(p+b+q+2d)k \\ & +\alpha^3c^2p^2d(b+q+p+d)]-\omega^2[\alpha p\beta^2b^2q^2(b+q)k^2 \\ & +\alpha^2bcp\beta q(2bdp+2dqp-bqa)k+\alpha^3dc^2p^2(dbp+dqp-bqa)] \\ & -a^2bp^3qd^2\alpha^2c^2-2a^2b^2p^2q^2d\alpha c\beta k-a^2b^3pq^3\beta^2k^2 \\ & +\Big[\omega^4\alpha^3c^2p\beta\lambda k-\omega^2[\alpha^2\beta^2bq\lambda c(p+b+q)k^2 \\ & +\alpha^3c^2p\beta\lambda(qd+pb+bd+bq+pq+dp)k]+ab^2pq^2\beta^2\alpha\lambda ck^2 \\ & +abp^2qd\alpha^2c^2\beta\lambda k-\cos(\tau\omega)\omega^2\alpha^3\beta\lambda c^2kp^2(d+b+q) \\ & -\sin(\tau\omega)p^2\alpha^3\beta\lambda c^2k[\omega^3-\omega d(b+q)]\Big]e^{-a\tau}\Big\}, \end{aligned} \tag{2.37}$$

$$\begin{aligned} S(\omega) = & \tfrac{1}{\alpha cp(d\alpha cp+\beta bkq)}\Big\{\omega\Big[\omega^4(\alpha cp\beta bqk+\alpha^2c^2p^2d)-\omega^2[\beta^2b^2q^2(p+b+q)k^2 \\ & +\alpha cpb\beta q(pb+pq+2dp+2bd+2qd)k \\ & +\alpha^2c^2p^2d(bp+pq+bd+qd+dp)] \\ & -b^3q^3\beta^2ak^2-b^2q^2\alpha cp\beta ak(2d+p) \\ & -bqd\alpha^2c^2ap^2(d+p)+\Big[-\omega^2[\alpha^2c^2p\beta\lambda(p+b+q+d)k+\beta^2bq\alpha\lambda ck^2] \\ & +bq\beta^2\alpha\lambda c(bq+bp+pq)k^2+p\alpha^2c^2\beta\lambda(bpq+bdp+dpq+bdq)k \\ & +\cos(\tau\omega)p^2\alpha^2\beta\lambda c^2k(db+dq-\omega^2) \\ & +\sin(\tau\omega)\omega\alpha^2\beta\lambda c^2kp^2(b+d+q)\Big]e^{-a\tau}\Big]\Big\}. \end{aligned} \tag{2.38}$$

To obtain the critical point at which a Hopf bifurcation takes place, we need solve the following equtions for τ and ω

$$R(\omega)=0 \quad \text{and} \quad S(\omega)=0, \tag{2.39}$$

where τ is our bifurcation parameter. Solving (2.39) yields two solutions for τ: $\tau=\tau_{s1}$

and $\tau = \tau_{s2}$, which are given in Appendix. Then, substituting these two solutions into any one of the above equations, we get the solutions for ω. We choose a positive value for $\tau = \tau_{s1}$ or $\tau = \tau_{s2}$ and the corresponding value of ω as the critical value, from which the corresponding value of R_d can be determined. Hence, all the critical values of parameters τ, ω and R_d are expressed in terms of $\alpha, \beta, \lambda, a, b, c, d, k, p, q$, denoted by τ_h, ω_h and R_h.

Following lecture notes in [48], there are three additional conditions which need be satisfied

$$R(\omega) = 0 \quad \Rightarrow \quad S(\omega) < 0 \quad \text{for} \quad \tau < \tau_h \tag{2.40}$$

$$\frac{\partial D(\xi,\tau)}{\partial \xi} |_{\xi=\omega_h i, \tau=\tau_h} \neq 0 \tag{2.41}$$

and

$$Re\frac{d\xi}{d\tau} |_{\xi=\omega_h i, \tau=\tau_h} < 0. \tag{2.42}$$

If the conditions (2.40), (2.41) and (2.42) hold, then we conclude that (2.35) has a pair of purely imaginary roots when $\tau = \tau_h$ or $(R = R_h)$, implying existence of a Hopf bifurcation. Therefore, when $1 < R_d < R_h$, the equilibrium solution E_d is stable. At the critical point $\tau = \tau_h$ $(R_d = R_h)$, E_d loses its stability and bifurcates into a family of limit cycles.

2.6 Numerical Simulation

In this section, we present two numerical examples to illustrate the theoretical results obtained in previous sections.

Example 1. For this example, we choose τ as the bifurcation parameter and set $\lambda = 0.24$, $d = 0.004$, $\beta = 0.004$, $a = 0.33$, $\alpha = 0.004$, $b = 2$, $k = 50$, $p = 2$, $c = 2000$, $q = 2$. Note that these parameter values have been used in computer simulation in [46] for the model without delay. Then,

$$\begin{aligned} R_0 &= 18.1818e^{-0.33\tau}, \\ R_d &= 0.08(18.1818e^{-0.33\tau} - 1). \end{aligned} \tag{2.43}$$

The disease-free equilibrium E_0 now is given by

$$E_0 = (60, 0, 0, 0, 0), \tag{2.44}$$

which is stable for $\tau > 8.7892$, as shown in Figure 2.1. When $\tau < 8.7892$, $R_0 > 1$, implying that E_0 is unstable and the single-infection equilibrium E_s occurs, given by

$$E_s = (3.3e^{0.33\tau}, 0.7273e^{-0.33\tau} - 0.04, 0, 18.1818e^{-0.33\tau} - 1, 0), \tag{2.45}$$

which is stable for $0.9022 < \tau < 8.7892$. See Figure 2.2 for the simulated results when $\tau = 4$. Further decreasing τ to pass the critical value $\tau = 0.9022$ will cause E_s to lose its stability, giving rise to the double-infection equilibrium,

$$E_d = (4.4444, 0.5, 0.1111e^{-0.33\tau} - 0.0825, 12.5, 111.11e^{-0.33\tau} - 82.5). \tag{2.46}$$

The corresponding characteristic equation (2.35) at E_d for this example becomes

$$\begin{aligned} D(\xi) \;=\;& \xi^5 + (6.054 + 0.4444e^{-0.33\tau})\xi^4 + (8,324 + 2.6907e^{-0.33\tau})\xi^3 \\ &+(-0.888 + 5.4773e^{-0.33\tau})\xi^2 + (-0.07656 + 0.2951e^{-0.33\tau})\xi \\ &+0.129e^{-0.33\tau} - 0.14256 - [(0.8889e^{-0.33\tau})\xi^3 \\ &+(3.5591e^{-0.33\tau})\xi^2 + (0.0142e^{-0.33\tau})\xi]e^{-\xi\tau} = 0. \end{aligned} \tag{2.47}$$

Let $R(\omega)$ and $S(\omega)$ be the real and imaginary parts of $D(i\omega)$, i.e.,

$$\begin{aligned} R(\omega) \;=\;& (6.054 + 0.4444e^{-0.33\tau})\omega^4 - (-0.888 + 5.4773e^{-0.33\tau})\omega^2 \\ &+0.192e^{-0.33\tau} - 0.14256 + (0.8889e^{-0.33\tau})\omega^3 \sin(\omega\tau) \\ &+(3.5591e^{-0.33\tau})\omega^2 \cos(\omega\tau) - (0.0142e^{-0.33\tau})\omega \sin(\omega\tau), \end{aligned} \tag{2.48}$$

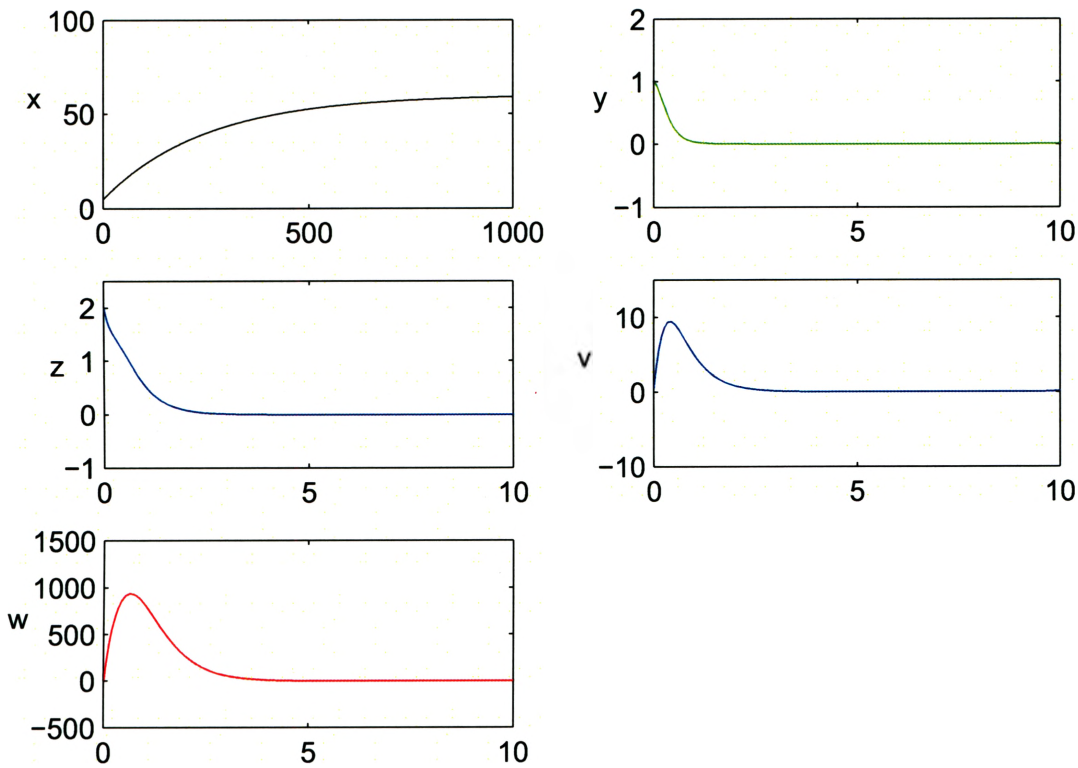

Figure 2.1: Simulated time history of system (2.1) for $\lambda = 0.24$, $\alpha = \beta = d = 0.004$, $k = 50$, $a = 0.33$, $c = 2000$, $b = p = q = 2$, $\tau = 9$ with the initial condition: $x(0) = 5.0$, $y(0) = 1.0$, $z(0) = 2.0$, $v(0) = 0.5$, $w(0) = 4.0$, converging to the stable equilibrium solution $E_0 = (60, 0, 0, 0, 0)$.

$$\begin{aligned} S(\omega) &= \omega^5 - (8.324 + 2.691e^{-0.33\tau})\omega^3 + (-0.07656 + 0.2951e^{-0.33\tau})\omega \\ &\quad +(0.8889e^{-0.33\tau})\omega^3\cos(\omega\tau) - (3.5591e^{-0.33\tau})\omega^2\sin(\omega\tau) \\ &\quad -(0.0142e^{-0.33\tau})\omega\cos(\omega\tau). \end{aligned} \tag{2.49}$$

Then, in order to determine the stability of E_d, we first solve the two equations,

$$R(\omega) = 0 \quad \text{and} \quad S(\omega) = 0. \tag{2.50}$$

A numerical scheme is applied to find the real solution of (2.50), given by

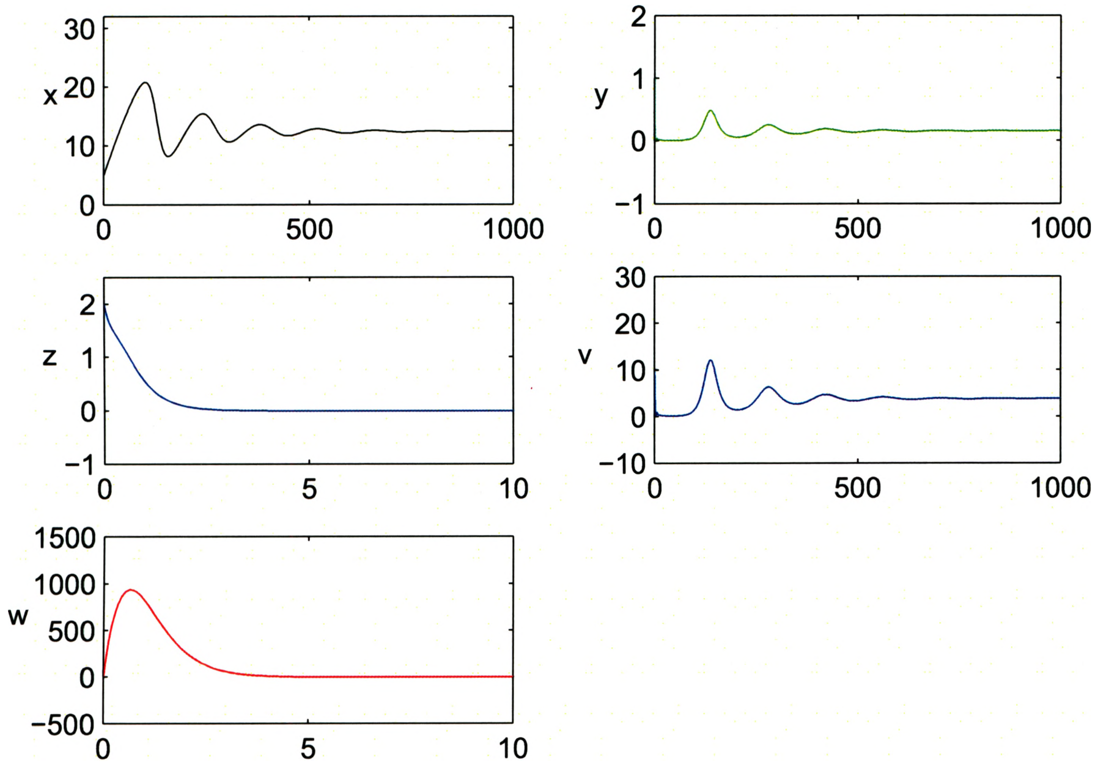

Figure 2.2: Simulated time history of system (2.1) for $\lambda = 0.24$, $\alpha = \beta = d = 0.004$, $k = 50$, $a = 0.33$, $c = 2000$, $b = p = q = 2$, $\tau = 4$ with the initial condition: $x(0) = 5.0$, $y(0) = 1.0$, $z(0) = 2.0$, $v(0) = 0.5$, $w(0) = 4.0$, converging to the stable equilibrium solution $E_s = (12.3533, 0.1543, 0, 3.857, 0)$.

$$(\tau, \omega) = (0.8712406304, 0.1451313875). \tag{2.51}$$

Hence, $\tau_h = 0.8712406304$ is the critical value, giving a corresponding value $R_h := R_d(\tau = \tau_h) = 1.011097469$. It is easy to verify that for $\tau < \tau_h$,

$$R(\omega) = 0 \quad \Rightarrow \quad S(\omega) < 0. \tag{2.52}$$

It can also be shown that other two conditions are satisfied:

$$\frac{\partial D(\xi,\tau)}{\partial \xi}\Big|_{\xi=0.1451313875i, \tau=0.8712406304} = -0.3642551096 + 1.623717248i \neq 0 \tag{2.53}$$

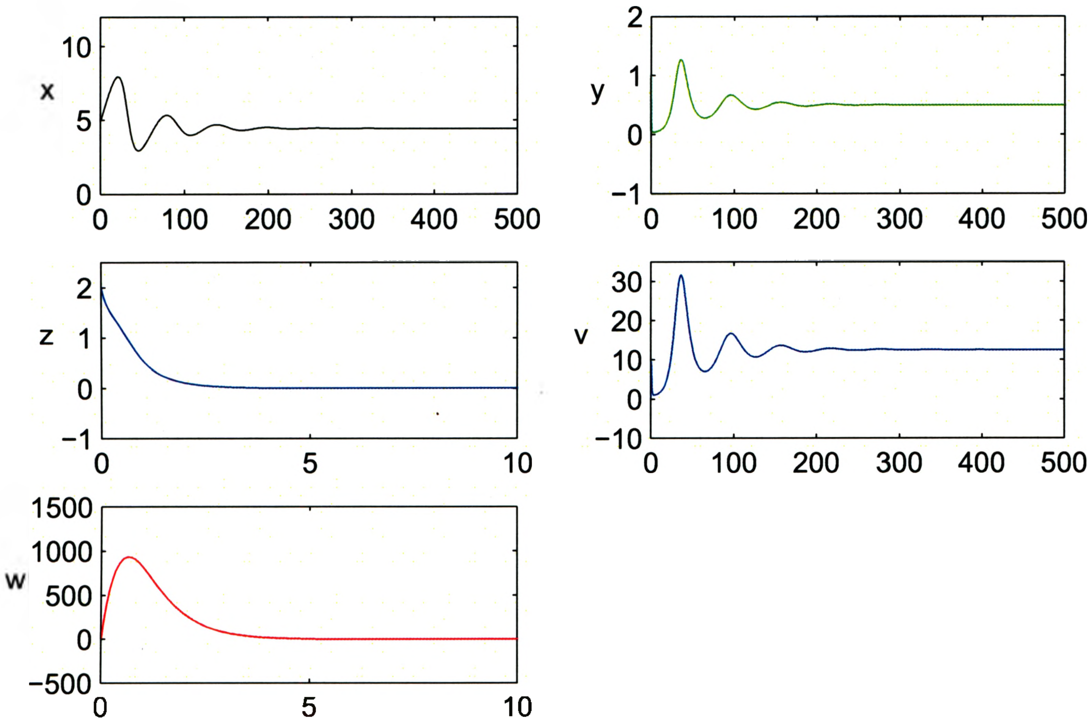

Figure 2.3: Simulated time history of system (2.1) for $\lambda = 0.24$, $\alpha = \beta = d = 0.004$, $k = 50$, $a = 0.33$, $c = 2000$, $b = p = q = 2$, $\tau = 0.89$ with the initial condition: $x(0) = 5.0$, $y(0) = 1.0$, $z(0) = 2.0$, $v(0) = 0.5$, $w(0) = 4.0$, converging to the stable equilibrium solution $E_d = (4.4444, 0.5, 0.0003, 12.5, 0.3333)$.

and

$$Re\frac{d\xi}{d\tau}\,|_{\xi=0.1451313875i,\tau=0.8712406304} = -0.4331822741 < 0. \tag{2.54}$$

Thus, the roots of (2.47) have positive real part when $\tau < \tau_h$ $(R > R_h)$, and (2.47) has a pair of purely imaginary roots when $\tau = \tau_h (R = R_h)$, implying existence of a Hopf bifurcation. Therefore, we conclude that when $0.8712406304 < \tau < 0.9022$, the equilibrium solution E_d is stable. At the critical point, $\tau = \tau_h$ $(R = R_h)$, E_d loses its stability through a Hopf bifurcation (see Figure 2.3 and 2.4).

Example 2. Now we select d as our bifurcation parameter and set $\tau = 0.5$. Then,

$$\begin{aligned} R_0 &= \frac{0.06166}{d}, \\ R_d &= 20d(\frac{0.06166}{d} - 1), \end{aligned} \tag{2.55}$$

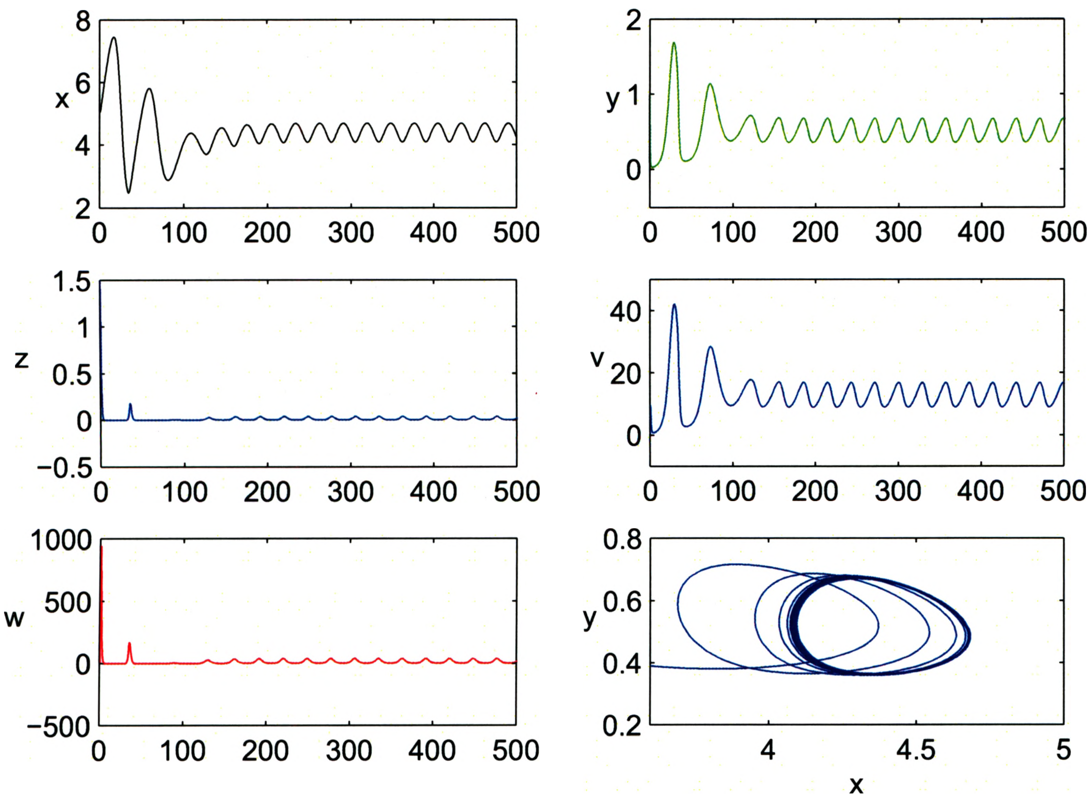

Figure 2.4: Simulated time history of system (2.1) for $\lambda = 0.24$, $\alpha = \beta = d = 0.004$, $k = 50$, $a = 0.33$, $c = 2000$, $b = p = q = 2$, $\tau = 0.4$ with the initial condition: $x(0) = 5.0$, $y(0) = 1.0$, $z(0) = 2.0$, $v(0) = 0.5$, $w(0) = 4.0$, converging to a periodic solution. The bottom right graph is the phase portrait projected on $x - y$ plane indicating a limit cycle.

and the disease-free equilibrium E_0 becomes

$$E_0 = (\tfrac{0.24}{d}, 0, 0, 0, 0), \tag{2.56}$$

which is stable for $d > 0.06166$. When $d < 0.06166$, $R_0 > 1$, causing E_0 to lose its stability and bifurcate into the single-infection equilibrium:

$$E_s = (3.8929, 0.61665 - 10d, 0, 15.41625 - 250d, 0). \tag{2.57}$$

It follows from Theorem (2.3) that E_s is stable when $0.011665 < d < 0.06166$. Further decreasing d to pass the critical value $d = 0.011665$ will cause E_s to become unstable and there occurs the double-infection equilibrium:

$$E_d = (\tfrac{3.84}{0.8+16d}, 0.5, \tfrac{0.25(0.6159-5.28d)}{0.8+16d}, 12.5, \tfrac{250(0.6159-5.28d)}{0.8+16d}). \tag{2.58}$$

The corresponding characteristic equation (2.35) for this example can be written as

$$\begin{aligned} D(\xi) &= \xi^5 + (6.38 + d + \tfrac{0.6159-5.28d}{0.8+16d})\xi^4 + (10.2965 + 6.33d + \tfrac{(6.05+d)(0.6159-5.28d)}{0.8+16d})\xi^3 \\ &\quad +(9.98d + 3.139 + \tfrac{(12.3+6d)(0.61595.28d)}{0.8+16d})\xi^2 + (2.64d + 0.132 \\ &\quad + \tfrac{(16d+0.6)(0.6159-5.28d)}{0.8+16d})\xi + \tfrac{8(0.61595.28d)(d+0.5)}{0.8+16d} \\ &\quad -[(\tfrac{2(0.6159-5.28d)}{0.8+16d} + 0.66)\xi^3 + 2(d+4)(\tfrac{0.6159-5.28d}{0.8+16d} + 0.33)\xi^2 \\ &\quad +8d(\tfrac{0.6159-5.28d}{0.8+16d} + 0.33)\xi]e^{-0.5\xi} = 0. \end{aligned} \tag{2.59}$$

Let $R(\omega)$ and $S(\omega)$ be the real and imaginary parts of $D(i\omega)$, i.e.,

$$\begin{aligned} R(\omega) &= (6.38 + d + \tfrac{0.6159-5.28d}{0.8+16d})\omega^4 - (9.98d + 3.139 + \tfrac{(12.3+6d)(0.61595.28d)}{0.8+16d})\omega^2 \\ &\quad \tfrac{8(0.61595.28d)(d+0.5)}{0.8+16d} + (\tfrac{2(0.6159-5.28d)}{0.8+16d} + 0.66)\omega^3 \sin(0.5\omega) \\ &\quad +2(d+4)(\tfrac{0.6159-5.28d}{0.8+16d} + 0.33)\omega^2 \cos(0.5\omega) \\ &\quad -8d(\tfrac{0.6159-5.28d}{0.8+16d} + 0.33)\omega \sin(0.5\omega), \end{aligned} \tag{2.60}$$

$$\begin{aligned} S(\omega) &= \omega^5 - (10.2965 + 6.33d + \tfrac{(6.05+d)(0.6159-5.28d)}{0.8+16d})\omega^3 + (2.64d + 0.132 \\ &\quad +\tfrac{(16d+0.6)(0.6159-5.28d)}{0.8+16d})\omega - 8d(\tfrac{0.6159-5.28d}{0.8+16d} + 0.33)\omega \cos(\omega\tau) \\ &\quad +(\tfrac{2(0.6159-5.28d)}{0.8+16d} + 0.66)\omega^3 \cos(\omega\tau) \\ &\quad -2(d+4)(\tfrac{0.6159-5.28d}{0.8+16d} + 0.33)\omega^2 \sin(\omega\tau). \end{aligned} \tag{2.61}$$

Similarly, solving the two equations

$$R(\omega) = 0 \quad \text{and} \quad S(\omega) = 0, \tag{2.62}$$

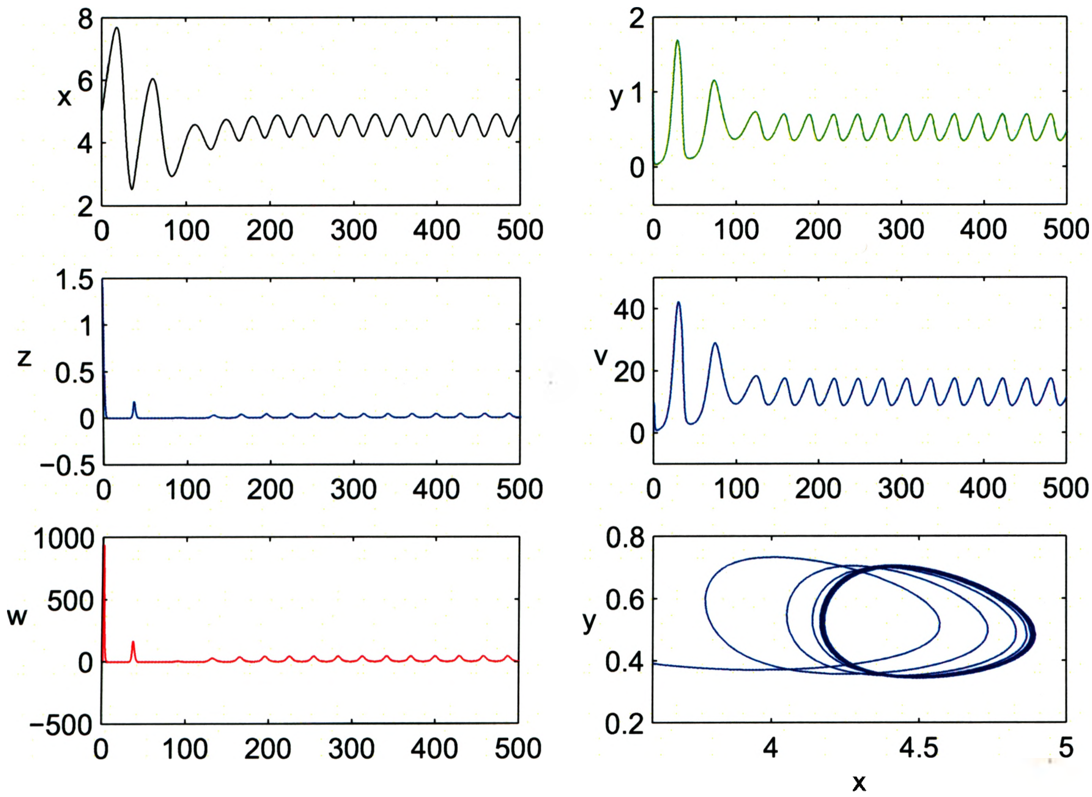

Figure 2.5: Simulated time history of system (2.1) for $\lambda = 0.24$, $\alpha = \beta = 0.004$, $k = 50$, $a = 0.33$, $c = 2000$, $b = p = q = 2$, $\tau = 0.5$, $d = 0.002$ with the initial condition: $x(0) = 5.0$, $y(0) = 1.0$, $z(0) = 2.0$, $v(0) = 0.5$, $w(0) = 4.0$, converging to a periodic solution. The bottom right graph is the phase portrait projected on $x - y$ plane indicating a limit cycle.

we get the critical value $d_h = 0.01106282794$, and the corresponding value $R_h = R_d(d = d_h) = 1.012043375$. It is easy to prove that for $d < d_h$,

$$R(\omega) = 0 \quad \Rightarrow \quad S(\omega) < 0. \tag{2.63}$$

We can also verify that

$$\frac{\partial D(\xi,\tau)}{\partial \xi} \,|_{\xi=0.1503251517i, d=0.01106282794} = -0.4371876370 + 1.701468428i \neq 0 \tag{2.64}$$

and

$$Re\frac{d\xi}{d\tau} \,|_{\xi=0.1503251517i, d=0.01106282794} = -27.01142970 < 0 \tag{2.65}$$

Therefore, all roots of (2.59) have positive real part when $d < d_h$ ($R > R_h$), and (2.59) has a pair of purely imaginary root at $d = d_h$ ($R_d = R_h$), implying existence of a Hopf bifurcation. Therefore, we conclude that when $0.01106282794 < d < 0.011665$, the equilibrium solution E_d is stable. At the critical point, $d = d_h$ ($R_d = R_h$), E_d loses its stability through Hopf bifurcation, leading to a family of limit cycles, as shown in Figure 2.5.

2.7 Conclusion and discussion

In this chapter, we have studied a HIV-1 infection model with intracellular delay, described by (2.1). We have fully analyzed the stability of the infection-free equilibrium E_0, and derived the condition for the local stability of the single-infection equilibrium E_s. For the double-infection equilibrium E_d, we demonstrated how to determine the stability of E_d and existence of Hopf bifurcation.

However, Due to difficulty in constructing a suitable Lyapunov function for the single-infection equilibrium E_s, we didn't obtain its global stability. In addition, the characteristic equations for double-infection equilibrium E_d cannot be factorized into lower degree polynomials, so it is very challenging to obtain the symbolic solution for ω.

In our simulations, we use the same data used as in [46], so we are able to catch sight of the effect of delay by comparing with the results in [46]. In [46], the simulation results show that

E_0 is stable when $d < 0.192$,

E_0 is unstable and E_s is stable when $0.052 < d < 0.192$,

E_s is unstable and E_d is stable when $0.024 < d < 0.052$,

At $d_h = 0.024$ ($R_h = 7.891$), E_d loses its stability through Hopf bifurcation.

It is obvious that the critical values obtained in Example 2 are all larger than the above ones. An implication of this observation is that the intracellular delay τ plays a positive role in preventing the virus. When all other parameters are fixed, a larger value of τ can bring R_0 to a level lower than 1, making the infection free equilibrium globally asymptotically stable. Therefore, viral-therapy of recombining HIV-1 virus with a generally modified virus can effectively reduce the HIV-1 load in patients, and larger intracellular delay is able to help eradicate the virus.

In reality, there also exists a time period between the time when the virus has penetrated into a cell and the time when the new virions are created within the cell and are released from the cell. Thus, another time lag may should be considered in model (2.1), which will be studied in next chapter.

Chapter 3

DELAYS IN CELL INFECTION AND VIRUS PRODUCTION ON HIV-1 DYNAMICS

3.1 Introduction

In this chapter, we shall introduce a second time lag to model (2.1). There is a virus production period for new virions to be produced within and released from the infected cells. This is because the virus production process within a cell consists of several stages: (i) uncoating of viral RNA, (ii) reverse transcription of viral RNA into DNA, (iii) transport of the newly made DNA into the nucleus, (iv) integration of the viral DNA into the chromosome, (v) production of viral RNA and protein, and (vi) creation of new virus from these newly synthesized RNA molecules and proteins (see [25]).

When both delays are present, model (1.13) can be written as

$$\begin{aligned}
x'(t) &= \lambda - dx(t) - \beta x(t)v(t), \\
y'(t) &= \beta e^{-a\tau_1} x(t-\tau_1)v(t-\tau_1) - ay(t) - \alpha w(t)y(t), \\
z'(t) &= \alpha w(t)y(t) - bz(t), \\
v'(t) &= ke^{-\tilde{a}\tau_2} y(t-\tau_2) - pv(t), \\
w'(t) &= cz(t) - qw(t),
\end{aligned} \tag{3.1}$$

where τ_1 and τ_2 represent the latent period and virus production period, respectively. When the second delay is introduced, the dynamic analysis of model (3.1) becomes much more involved. In Section 3.2, we will prove the positivity and boundedness of solutions of system (3.1). Also, the basic reproduction number $\tilde{R}_0$ will be fined. In Sections 3.3, 3.4 and 3.5, we analyze the stability of three equilibria: disease-free equilibrium $\tilde{E}_0$, single-infection equilibrium $\tilde{E}_s$ and double-infection equilibrium $\tilde{E}_d$. In Section 3.6, simulation results are given to illustrate the theoretical predictions. The last section concludes this chapter with some discussions.

3.2 Well-posedness and basic reproduction number

To show the well-posedness, we define $\tilde{X} := C([-\max(\tau_1, \tau_2), 0]; R^5)$, which is the Banach space of continuous mapping from $[-\max(\tau_1, \tau_2), 0]$ to R^5 equipped with the sup-norm. It is biologically reasonable to consider the following initial conditions for system (3.1):

$$(x(\theta), y(\theta), z(\theta), v(\theta), w(\theta)) \in \tilde{X}, \tag{3.2}$$

$$x(\theta) \geq 0, y(\theta) \geq 0, z(\theta) \geq 0, v(\theta) \geq 0, w(\theta) \geq 0, \quad \theta \in [-\max(\tau_1, \tau_2), 0]. \tag{3.3}$$

It can be shown using the fundamental theory of FDEs (see, e.g. [23]) that there is a unique solution $(x(t), y(t), z(t), v(t), w(t))$ to system (3.1). The following theorem establishes the non-negativity and boundedness of solutions to (3.1-3.3).

Theorem 3.1 Let $(x(t), y(t), z(t), v(t), w(t))$ be a solution of system (3.1) satisfying the conditions (3.2) and (3.3). Then $x(t)$, $y(t)$, $z(t)$, $v(t)$ and $w(t)$ are all non-negative and bounded for all $t \geq 0$ at which the solution exists.

Proof: From (3.1), we obtain

$$\begin{aligned}
x(t) &= x(0)e^{-\int_0^t (d+\beta v(\xi))d\xi} + \lambda \int_0^t e^{-\int_\eta^t (d+\beta v(\xi))d\xi} d\eta, \\
y(t) &= y(0)e^{-\int_0^t (a+\alpha w(\xi))d\xi} + \beta \int_0^t x(\eta-\tau_1)v(\eta-\tau_1)e^{-a\tau_1}e^{-\int_\eta^t (a+\alpha w(\xi))d\xi} d\eta, \\
z(t) &= z(0)e^{-bt} + \int_0^t \alpha w(\eta)y(\eta)e^{-b(t-\eta)}d\eta, \\
v(t) &= v(0)e^{-pt} + \int_0^t ky(\eta-\tau_2)e^{-p(t-\eta)}e^{-\tilde{a}\tau_2}d\eta, \\
w(t) &= w(0)e^{-qt} + \int_0^t cz(\eta)e^{-q(t-\eta)}d\eta.
\end{aligned} \tag{3.4}$$

which clearly show that $x(t)$, $y(t)$, $z(t)$, $v(t)$ and $w(t)$ are all non-negative for all $t \geq 0$, as long as (3.3) is satisfied

For boundedness of the solution, we let

$$\tilde{B}(t) = cke^{-a\tau_1}x(t) + cky(t+\tau_1) + ckz(t+\tau_1) + \tfrac{ac}{2}e^{\tilde{a}\tau_2}v(t+\tau_1+\tau_2) + \tfrac{bk}{2}w(t+\tau_1), \tag{3.5}$$

where all the solutions are non-negative. Thus, differentiating $\tilde{B}(t)$ with respect to time along the solution of (3.1) yields

$$\begin{aligned}
\tfrac{d\tilde{B}}{dt}|_{(3.1)} &= cke^{-a\tau_1}[\lambda - dx(t) - \beta v(t)x(t)] \\
&\quad + ck\beta e^{-a\tau_1}v(t)x(t) - ckay(t+\tau_1) - ck\alpha w(t+\tau_1)y(t+\tau_1) \\
&\quad + ck\alpha w(t+\tau_1)y(t+\tau_1) - ckbz(t+\tau_1) \\
&\quad + \tfrac{ac}{2}ky(t+\tau_1) - \tfrac{ac}{2}pv(t+\tau_1+\tau_2)e^{\tilde{a}\tau_2} \\
&\quad + \tfrac{bk}{2}cz(t+\tau_1) - \tfrac{bk}{2}qw(t+\tau_1) \\
&= cke^{-a\tau}\lambda - cke^{-a\tau_1}dx(t) - \tfrac{a}{2}cky(t+\tau_1) - \tfrac{b}{2}ckz(t+\tau_1) \\
&\quad - \tfrac{ac}{2}pv(t+\tau_1+\tau_2)e^{\tilde{a}\tau_2} - \tfrac{bk}{2}qw(t+\tau_1) \\
&\leq cke^{-a\tau_1}\lambda - \tilde{m}B(t),
\end{aligned} \tag{3.6}$$

where $\tilde{m} = \min\{\frac{a}{2}, \frac{b}{2}, d, p, q\}$. □

Similarly, system (3.1) has three possible biologically meaningful equilibria:

$$\begin{aligned}
\tilde{E}_0 &= (\tfrac{\lambda}{d}, 0, 0, 0, 0),\\
\tilde{E}_s &= (\tfrac{ap}{\beta k e^{-a\tau_1-\tilde{a}\tau_2}}, \tfrac{\lambda e^{-a\tau_1}}{a} - \tfrac{dp}{\beta k e^{-\tilde{a}\tau_2}}, 0, \tfrac{\lambda k e^{-a\tau_1-\tilde{a}\tau_2}}{ap} - \tfrac{d}{\beta}, 0),\\
\tilde{E}_d &= (\tfrac{\lambda\alpha cp}{d\alpha cp+\beta bkqe^{-\tilde{a}\tau_2}}, \tfrac{bq}{\alpha c}, \tfrac{q(\alpha\beta\lambda cke^{-a\tau_1-\tilde{a}\tau_2}-\beta abkqe^{-\tilde{a}\tau_2}-\alpha acdp)}{\alpha c(\beta bkqe^{-\tilde{a}\tau_2}+\alpha cdp)}, \tfrac{bkqe^{-\tilde{a}\tau_2}}{\alpha cp},\\
&\quad \tfrac{\alpha\beta\lambda cke^{-a\tau_1-\tilde{a}\tau_2}-\beta abkqe^{-\tilde{a}\tau_2}-\alpha acdp}{\alpha(\beta bkqe^{-\tilde{a}\tau_2}+\alpha cdp)}),
\end{aligned} \tag{3.7}$$

where the basic reproduction number is defined as

$$\tilde{R}_0 = \frac{k\beta\lambda}{adp} e^{-a\tau_1-\tilde{a}\tau_2}, \tag{3.8}$$

and for convenience, we let

$$\tilde{R}_d = \frac{c\alpha}{bq}\left(\frac{\lambda e^{-a\tau_1}}{a} - \frac{dp}{k\beta}e^{\tilde{a}\tau_2}\right) = \frac{cdp\alpha}{bkq\beta}e^{\tilde{a}\tau_2}(\tilde{R}_0 - 1). \tag{3.9}$$

$\tilde{E}_0$ is the only biologically meaningful equilibrium when $\tilde{R}_0 < 1$. For $\tilde{R}_0 > 1$, there is another biologically meaningful equilibrium $\tilde{E}_s$ (single-infection equilibrium). The double-infection equilibrium $\tilde{E}_d$ exists if and only if $\tilde{R}_d > 1$.

3.3 Stability of the infection-free equilibrium $\tilde{E}_0$

Let $r = \frac{\tau_2}{\tau_1}$. Then, system (3.1) can be reduced to the following system with dimensionless time $\frac{t}{\tau_1}$, which, for simplicity, is again denoted by t:

$$\begin{aligned}
\frac{dx(t)}{dt} &= \tau_1(\lambda - dx(t) - \beta x(t)v(t)),\\
\frac{dy(t)}{dt} &= \tau_1(\beta e^{-a\tau_1}x(t-1)v(t-1) - ay(t) - \alpha w(t)y(t)),\\
\frac{dz(t)}{dt} &= \tau_1(\alpha w(t)y(t) - bz(t)),\\
\frac{dv(t)}{dt} &= \tau_1(ke^{-\tilde{a}\tau_2}y(t-r) - pv(t)),\\
\frac{dw(t)}{dt} &= \tau_1(cz(t) - qw(t)).
\end{aligned} \tag{3.10}$$

Linearizing (3.10) at $\tilde{E}_0$ yields

$$\begin{aligned} x'(t) &= \tau_1(-dx(t) - \tfrac{\beta\lambda}{d}v(t)),\\ y'(t) &= \tau_1(\beta e^{-a\tau_1}\tfrac{\lambda}{d}v(t-1) - ay(t)),\\ z'(t) &= -bz(t)\tau_1,\\ v'(t) &= \tau_1(ke^{-\tilde{a}\tau_2}y(t-r) - pv(t)),\\ w'(t) &= \tau_1(cz(t) - qw(t)), \end{aligned} \tag{3.11}$$

whose characteristic equation is

$$(\xi + d\tfrac{\tau_2}{r})(\xi + b\tfrac{\tau_2}{r})(\xi + q\tfrac{\tau_2}{r})[(\xi + a\tfrac{\tau_2}{r})(\xi + p\tfrac{\tau_2}{r}) - k\beta(\tfrac{\tau_2}{r})^2 e^{-a\frac{\tau_2}{r}(1+r\frac{\tilde{a}}{a})}\tfrac{\lambda}{d}e^{-\xi(r+1)}] = 0. \tag{3.12}$$

Let

$$\begin{aligned} &\bar{d} = d\tfrac{\tau_2}{r}, \quad \bar{b} = b\tfrac{\tau_2}{r}, \quad \bar{q} = q\tfrac{\tau_2}{r}, \quad \bar{c} = c\tfrac{\tau_2}{r}, \quad \bar{a} = a\tfrac{\tau_2}{r}, \quad \bar{p} = p\tfrac{\tau_2}{r},\\ &\bar{\alpha} = \alpha\tfrac{\tau_2}{r}, \quad \bar{\beta} = \beta\tfrac{\tau_2}{r}, \quad \bar{\lambda} = \lambda\tfrac{\tau_2}{r}, \quad \bar{\tau} = 1 + r\tfrac{\tilde{a}}{a} \quad \text{and} \quad \tau = r+1. \end{aligned} \tag{3.13}$$

Then (3.12) can be rewritten as

$$(\xi + \bar{d})(\xi + \bar{b})(\xi + \bar{q})[(\xi + \bar{a})(\xi + \bar{p}) - k\bar{\beta}e^{-\bar{a}\bar{\tau}}\tfrac{\bar{\lambda}}{d}e^{-\xi\tau}] = 0. \tag{3.14}$$

Hence, only the quadratic factor,

$$\xi^2 + (\bar{a} + \bar{p})\xi + \bar{a}\bar{p} - k\bar{\beta}e^{-\bar{a}\bar{\tau}}\tfrac{\bar{\lambda}}{d}e^{-\xi\tau} = 0, \tag{3.15}$$

need be considered. Since

$$\bar{a}\bar{p} - k\bar{\beta}e^{-\bar{a}\bar{\tau}}\tfrac{\bar{\lambda}}{d} = \bar{a}\bar{p}(1 - \tilde{R}_0) > 0, \tag{3.16}$$

$\xi = 0$ is not a root of Equation (3.15), implying that the roots of (3.15) can only cross the imaginary axis with non-zero real part. Note that when $\tau = 0$, equation (3.15) becomes

$$\xi^2 + (\bar{a} + \bar{p})\xi + \bar{a}\bar{p} - k\bar{\beta}e^{-\bar{a}\bar{\tau}}\tfrac{\bar{\lambda}}{d} = 0, \tag{3.17}$$

whose roots have negative real part if $\bar{a}\bar{p} - k\bar{\beta}e^{-\bar{a}\bar{\tau}}\frac{\bar{\lambda}}{d} > 0$, which is equivalent to $\tilde{R}_0 < 1$.

Since the roots of Equation (3.15) depend continuously on τ, they can only possibly enter into the right half of complex plane through crossing the imaginary axis (see, e.g. [10]). Thus, let $\xi = i\tilde{\omega}$ be a purely imaginary root of (3.15) with $\tilde{\omega} > 0$. Then, (3.15) becomes

$$-\tilde{\omega}^2 + i\tilde{\omega}(\bar{a} + \bar{p}) + \bar{a}\bar{p} - k\bar{\beta}e^{-\bar{a}\tau}\tfrac{\lambda}{d}e^{-i\tilde{\omega}\tau} = 0. \tag{3.18}$$

Taking moduli of (3.18) yields

$$\tilde{\omega}^4 + (\bar{a}^2 + \bar{p}^2)\tilde{\omega}^2 + \bar{a}^2\bar{p}^2 - (k\bar{\beta}e^{-\bar{a}\tau}\tfrac{\lambda}{d})^2 = 0, \tag{3.19}$$

which has no positive root for $\tilde{\omega}^2$ if $\tilde{R}_0 < 1$, implying that all roots of (3.15) remain in the left half of complex plane for all $\tau > 0$ as long as $\tilde{R}_0 < 1$. On the other hand, it is easy to see that (3.15) has a positive root when $\tilde{R}_0 > 1$.

Summarizing the above results, we obtain the following theorem.

Theorem 3.2 When $\tilde{R}_0 < 1$, the disease-free equilibrium $\tilde{E}_0$ is locally asymptotically stable; at $\tilde{R}_0 = 1$, $\tilde{E}_0$ becomes unstable and the single-infection equilibrium $\tilde{E}_s$ occurs.

Moreover, by applying the fluctuation lemma (see, e.g. [22]), we can prove that the infection-free equilibrium $\tilde{E}_0$ is also globally attractive for $\tilde{R}_0 < 1$. For this purpose, we first introduce some basic notations. For a continuous and bounded function $f : [0, \infty) \to R$, let

$$f_\infty \triangleq \liminf_{t\to\infty} f(t), \quad f^\infty \triangleq \limsup_{t\to\infty} f(t). \tag{3.20}$$

Now, let $(x(t), y(t), z(t), v(t), w(t))$ be any solution of system (3.1) - (3.3). By Theorem 3.1, we know

$$\begin{aligned} &0 \leqslant x_\infty \leqslant x^\infty < \infty, \\ &0 \leqslant y_\infty \leqslant y^\infty < \infty, \\ &0 \leqslant z_\infty \leqslant z^\infty < \infty, \\ &0 \leqslant v_\infty \leqslant v^\infty < \infty, \\ &0 \leqslant w_\infty \leqslant w^\infty < \infty. \end{aligned} \tag{3.21}$$

Applying the fluctuation lemma (see [45]), there exists a sequence t_n with $t_n \to \infty$ as

$n \to \infty$ such that

$$x(t_n) \to x^\infty \quad \text{and} \quad x'(t_n) \to 0 \quad \text{as} \quad n \to \infty. \tag{3.22}$$

From the first equation of system (3.1), we get

$$\dot{x}(t_n) + dx(t_n) + \beta x(t_n)v(t_n) = \lambda. \tag{3.23}$$

Letting $n \to \infty$ in the above equation leads to the following estimate

$$dx^\infty \leq (d + \beta v_\infty)x^\infty \leq \lambda. \tag{3.24}$$

Using a similar argument to the rest of the equations in (3.1) gives

$$ay^\infty \leq (a + \alpha w_\infty)y^\infty \leq \beta e^{-a\tau_1}x^\infty v^\infty, \tag{3.25}$$

$$bz^\infty \leq \alpha w^\infty y^\infty, \tag{3.26}$$

$$pv^\infty \leq ke^{-\tilde{a}\tau_2}y^\infty, \tag{3.27}$$

$$qw^\infty \leq cz^\infty. \tag{3.28}$$

We claim that $y^\infty = 0$. Otherwise, $v^\infty > 0$ by (3.25). It then follows from (3.24), (3.25) and (3.27) that

$$pv^\infty \leq ke^{-\tilde{a}\tau_2}y^\infty \leq \tfrac{k\beta}{a}e^{-a\tau_1-\tilde{a}\tau_2}x^\infty v^\infty \leq \tfrac{k\beta\lambda}{ad}e^{-a\tau_1-\tilde{a}\tau_2}v^\infty, \tag{3.29}$$

yielding

$$p \leq \tfrac{k\beta\lambda}{ad}e^{-a\tau_1-\tilde{a}\tau_2} \Rightarrow \tilde{R}_0 \geq 1, \tag{3.30}$$

which contradicts the assumption $\tilde{R}_0 < 1$. So, $y^\infty = 0$, which in turn implies $z^\infty = 0$, $v^\infty = 0$ and $w^\infty = 0$ by Equations (3.26)-(3.28). Therefore, we conclude that $y(t) \to 0$ as $t \to \infty$ by using the relation $0 \leq y_\infty \leq y^\infty$. Similarly, $z(t)$, $v(t)$ and $w(t)$ all approach 0 as $t \to \infty$. Finally, applying the theory of asymptotical autonomous system (see, e.g. [5]) to the first equation of (3.1) with $v(t) \to 0$, we obtain that $\lim_{t\to\infty} x(t) = \frac{\lambda}{d}$. Summarizing the above, result yields the following theorem.

Theorem 3.3 The disease-free equilibrium $\tilde{E}_0$ is globally asymptotically stable when $\tilde{R}_0 < 1$.

3.4 Stability of the single-infection equilibrium $\tilde{E}_s$

In this section, we assume $\tilde{R}_0 \geq 1$. At $\tilde{R}_0 = 1$, $\tilde{E}_0$ loses its stability and the single-infection equilibrium $\tilde{E}_s$ comes into existence. To study the stability of $\tilde{E}_s$, we linearize system of (3.1) at $\tilde{E}_s$ to obtain

$$\begin{aligned}
x'(t) &= \tau_1(-\tfrac{k\beta\lambda}{ap}e^{-a\tau_1-\tilde{a}\tau_2}x(t) - \tfrac{ap}{k}e^{a\tau_1+\tilde{a}\tau_2}v(t)),\\
y'(t) &= \tau_1\{\beta e^{-a\tau_1}(\tfrac{k\lambda}{ap}e^{-a\tau_1-\tilde{a}\tau_2} - \tfrac{d}{\beta})x(t-1) + \tfrac{ap}{k}e^{\tilde{a}\tau_2}v(t-1)\\
&\quad -ay(t) - \alpha w(t)(\tfrac{\lambda}{a}e^{-a\tau_1} - \tfrac{dp}{k\beta}e^{\tilde{a}\tau_2})\},\\
z'(t) &= \tau_1(\alpha w(t)(\tfrac{\lambda}{a}e^{-a\tau_1} - \tfrac{dp}{k\beta}e^{\tilde{a}\tau_2}) - bz(t)),\\
v'(t) &= \tau_1(ke^{-\tilde{a}\tau_2}y(t-r) - pv(t)),\\
w'(t) &= \tau_1(cz(t) - qw(t)).
\end{aligned} \tag{3.31}$$

The characteristic equation of (3.31) is

$$\begin{aligned}
&\{(\xi + \tfrac{\bar{k}\bar{\beta}\bar{\lambda}}{\bar{a}\bar{p}}e^{-\bar{a}\bar{\tau}})[(\xi+\bar{a})(\xi+\bar{p}) - \bar{a}\bar{p}e^{-\xi\tau}] + \bar{\beta}e^{-\bar{a}\bar{\tau}}(\tfrac{\bar{k}\bar{\lambda}}{\bar{a}\bar{p}}e^{-\bar{a}\bar{\tau}} - \tfrac{\bar{d}}{\bar{\beta}})e^{-\xi\tau}\bar{k}(\tfrac{\bar{a}\bar{p}}{\bar{k}}e^{-\bar{a}\bar{\tau}})\}\\
&\times[(\xi+\bar{b})(\xi+\bar{q}) - \bar{c}\bar{\alpha}(\tfrac{\bar{\lambda}}{\bar{a}}e^{-a\tau_1} - \tfrac{\bar{d}\bar{p}}{k\beta}e^{\tilde{a}\tau_2})] = 0,
\end{aligned} \tag{3.32}$$

which has two factors:

$$(\xi+\bar{b})(\xi+\bar{q}) - \bar{c}\bar{\alpha}(\tfrac{\bar{\lambda}}{\bar{a}}e^{-a\tau_1} - \tfrac{\bar{d}\bar{p}}{k\beta}e^{\tilde{a}\tau_2}) = \xi^2 + (\bar{b}+\bar{q})\xi + \bar{b}\bar{q} - \bar{c}\bar{\alpha}(\tfrac{\bar{\lambda}}{\bar{a}}e^{-a\tau_1} - \tfrac{\bar{d}\bar{p}}{k\beta}e^{\tilde{a}\tau_2}) \tag{3.33}$$

and

$$\begin{aligned}
&(\xi + \tfrac{\bar{k}\bar{\beta}\bar{\lambda}}{\bar{a}\bar{p}}e^{-\bar{a}\bar{\tau}})[(\xi+\bar{a})(\xi+\bar{p}) - \bar{a}\bar{p}e^{-\xi\tau}] + \bar{\beta}e^{-\bar{a}\bar{\tau}}(\tfrac{\bar{k}\bar{\lambda}}{\bar{a}\bar{p}}e^{-\bar{a}\bar{\tau}} - \tfrac{\bar{d}}{\bar{\beta}})e^{-\xi\tau}\bar{k}(\tfrac{\bar{a}\bar{p}}{\bar{k}}e^{-\bar{a}\bar{\tau}})\\
&= \xi^3 + (\bar{a}+\bar{p}+\tfrac{\bar{k}\bar{\beta}\bar{\lambda}}{\bar{a}\bar{p}}e^{-\bar{a}\bar{\tau}})\xi^2 + [\tfrac{\bar{k}\bar{\beta}\bar{\lambda}}{\bar{a}\bar{p}}e^{-\bar{a}\bar{\tau}}(\bar{a}+\bar{p}) + \bar{a}\bar{p}]\xi + \bar{k}\bar{\beta}\bar{\lambda}e^{-\bar{a}\bar{\tau}} - \bar{a}\bar{p}(\xi+\bar{d})e^{-\xi\tau}.
\end{aligned} \tag{3.34}$$

It is clear that the quadratic factor has two roots with negative real part since $\tilde{R}_d < 1$. For the cubic factor (3.34), we may rewrite it as

$$\xi^3 + \tilde{a}_2(\bar{\tau})\xi^2 + \tilde{a}_1(\bar{\tau})\xi + \tilde{a}_0(\bar{\tau}) - (\tilde{c}_1\xi + \tilde{c}_2)e^{-\xi\tau} = 0, \tag{3.35}$$

where

$$\begin{aligned} \tilde{a}_2(\bar{\tau}) &= \bar{a} + \bar{p} + \tfrac{\bar{k}\bar{\beta}\bar{\lambda}}{\bar{a}\bar{p}} e^{-\bar{a}\bar{\tau}}, \\ \tilde{a}_1(\bar{\tau}) &= \tfrac{\bar{k}\bar{\beta}\bar{\lambda}}{\bar{a}\bar{p}} e^{-\bar{a}\bar{\tau}}(\bar{a}+\bar{p}) + \bar{a}\bar{p}, \\ \tilde{a}_0(\bar{\tau}) &= \bar{k}\bar{\beta}\bar{\lambda}e^{-\bar{a}\bar{\tau}}, \\ \tilde{c}_1 &= \bar{a}\bar{p}, \\ \tilde{c}_2 &= \bar{a}\bar{p}\bar{d}. \end{aligned} \tag{3.36}$$

Because

$$\tilde{a}_0(\bar{\tau}) - \tilde{c}_2 = \bar{k}\bar{\beta}\bar{\lambda}e^{-\bar{a}\bar{\tau}} - \bar{a}\bar{p}\bar{d} = \bar{a}\bar{p}\bar{d}(\tilde{R}_0 - 1) > 0, \tag{3.37}$$

when $\tilde{R}_0 > 1$, so $\xi = 0$ is not a root of Equation (3.35). Next, we show that when $\tau = 0$, all roots of (3.35) have negative real part. Indeed, if $\tau = 0$, (3.35) becomes

$$\xi^3 + \tilde{a}_2(\bar{\tau})\xi^2 + (\tilde{a}_1(\bar{\tau}) - c_1)\xi + \tilde{a}_0(\bar{\tau}) - \tilde{c}_2 = 0. \tag{3.38}$$

Note that when $\tilde{R}_0 > 1$,

$$\begin{aligned} &\tilde{a}_2(\bar{\tau}) = \bar{a} + \bar{p} + \tfrac{\bar{k}\bar{\beta}\bar{\lambda}}{\bar{a}\bar{p}} e^{-\bar{a}\bar{\tau}} > 0, \\ &\tilde{a}_1(\bar{\tau}) - \tilde{c}_1 = \tfrac{\bar{k}\bar{\beta}\bar{\lambda}}{\bar{a}\bar{p}} e^{-\bar{a}\bar{\tau}}(\bar{a}+\bar{p}) + \bar{a}\bar{p} - \bar{a}\bar{p} = \tfrac{\bar{k}\bar{\beta}\bar{\lambda}}{\bar{a}\bar{p}} e^{-\bar{a}\bar{\tau}}(\bar{a}+\bar{p} > 0, \\ &\tilde{a}_0(\bar{\tau}) - \tilde{c}_2 = \bar{k}\bar{\beta}\bar{\lambda}e^{-\bar{a}\bar{\tau}} - \bar{a}\bar{p}\bar{d} = \bar{a}\bar{p}\bar{d}(\tilde{R}_0 - 1) > 0, \\ &\tilde{a}_2(\bar{\tau})[\tilde{a}_1(\bar{\tau}) - \tilde{c}_1] - [\tilde{a}_0(\bar{\tau}) - \tilde{c}_2] \\ &\qquad = (\bar{a} + \bar{p} + \tfrac{\bar{k}\bar{\beta}\bar{\lambda}}{\bar{a}\bar{p}} e^{-\bar{a}\bar{\tau}})[\tfrac{\bar{k}\bar{\beta}\bar{\lambda}}{\bar{a}\bar{p}} e^{-\bar{a}\bar{\tau}}(\bar{a}+\bar{p})] - (\bar{k}\bar{\beta}\bar{\lambda}e^{-\bar{a}\bar{\tau}} - \bar{a}\bar{p}\bar{d}) \\ &\qquad = (\tfrac{\bar{k}\bar{\beta}\bar{\lambda}}{\bar{a}\bar{p}})^2(\bar{a}+\bar{p}) + \tfrac{\bar{k}\bar{\beta}\bar{\lambda}}{\bar{a}\bar{p}}(\bar{a}^2 + \bar{a}\bar{p} + \bar{p}^2) + \bar{a}\bar{p}\bar{d} > 0. \end{aligned} \tag{3.39}$$

By Routh-Hurwitz criterion (see [13]), we know that all roots of (3.38) have negative real part. Note that all roots of (3.35) depend continuously on τ (see [36]). Also, (2.18) holds, so $Re(\xi) < +\infty$ for any root of (3.35). As a result, the roots of Equation (3.35) are only able to enter into the right half of complex plane by crossing the imaginary axis when τ increases. Similarly, let $\xi = i\tilde{\omega}$ ($\tilde{\omega} > 0$) be a purely imaginary root of (3.35). Then

$$-i\tilde{\omega}^3 - \tilde{a}_2(\bar{\tau})\tilde{\omega}^2 + \tilde{a}_1(\bar{\tau})i\tilde{\omega} + \tilde{a}_0(\bar{\tau}) - (\tilde{c}_1 i\tilde{\omega} + \tilde{c}_2)e^{-i\tilde{\omega}\tau} = 0, \tag{3.40}$$

Taking moduli of the above equation gives

$$\tilde{H}(\tilde{\omega}^2) := \tilde{\omega}^6 + (\tilde{a}_2(\bar{\tau})^2 - 2\tilde{a}_1(\bar{\tau}))\tilde{\omega}^4 + (\tilde{a}_1(\bar{\tau})^2 - 2\tilde{a}_0(\bar{\tau})\tilde{a}_2(\bar{\tau}) - \tilde{c}_1^2)\tilde{\omega}^2 + \tilde{a}_0(\bar{\tau})^2 - \tilde{c}_2^2 = 0, \tag{3.41}$$

where

$$\begin{aligned} &\tilde{a}_2(\bar{\tau})^2 - 2\tilde{a}_1(\bar{\tau}) = \bar{a}^2 + \bar{p}^2 + (\tfrac{\bar{k}\bar{\beta}\bar{\lambda}}{\bar{a}\bar{p}}e^{-\bar{a}\bar{\tau}})^2 > 0, \\ &\tilde{a}_1(\bar{\tau})^2 - 2\tilde{a}_0(\bar{\tau})\tilde{a}_2(\bar{\tau}) - \tilde{c}_1^2 = (\tfrac{\bar{k}\bar{\beta}\bar{\lambda}}{\bar{a}\bar{p}}e^{-\bar{a}\bar{\tau}})^2(\bar{a}^2 + \bar{p}^2) > 0, \\ &\tilde{a}_0(\bar{\tau})^2 - \tilde{c}_2^2 = (\bar{k}\bar{\beta}\bar{\lambda}e^{-\bar{a}\bar{\tau}} + \bar{a}\bar{p}\bar{d})\bar{a}\bar{p}\bar{d}(\tilde{R}_0 - 1) > 0. \end{aligned} \tag{3.42}$$

It is obvious that the function $\tilde{H}(\tilde{\omega}^2)$ is monotonically increasing for $0 \le \tilde{\omega}^2 < \infty$ with $\tilde{H}(0) > 0$, implying that Equation (3.35) has no positive roots for $\tilde{R}_0 > 1$. Therefore, all roots of (3.35) have negative real part for all $\tau > 0$ if $\tilde{R}_0 > 1$.

Summarizing the above results, we have the following theorem.

Theorem 3.4 When $1 < \tilde{R}_0 < 1 + \frac{bkq\beta}{cdp\alpha}e^{-\bar{a}\tau_2}$, the single-infection equilibrium $\tilde{E}_s$ is asymptotically stable; at $\tilde{R}_0 = 1 + \frac{bkq\beta}{cdp\alpha}e^{-\bar{a}\tau_2}$ (i.e., $\tilde{R}_d = 1$), $\tilde{E}_s$ becomes unstable and bifurcates into $\tilde{E}_d$.

3.5 Stability of the double-infection equilibrium $\tilde{E}_d$: Existence of Hopf and double Hopf bifurcations

To discuss the stability of double-infection equilibrium $\tilde{E}_d$, we assume $\tilde{R}_d > 1$, since it is the necessary condition for the existence of $\tilde{E}_d$. The linearized system of (3.1) at $\tilde{E}_d = (\tilde{x}_d, \tilde{y}_d, \tilde{z}_d, \tilde{v}_d, \tilde{w}_d)$ is

$$
\begin{aligned}
x'(t) &= -(d+\beta\tilde{v}_d)x(t) - \beta\tilde{x}_d v(t),\\
y'(t) &= \beta e^{-a\tau_1}\tilde{v}_d x(t-\tau_1) - (a+\alpha\tilde{w}_d)y(t) + \beta e^{-a\tau_1}\tilde{x}_d v(t-\tau_1) - \alpha\tilde{y}_d w(t),\\
z'(t) &= \alpha\tilde{w}_d y(t) - bz(t) + \alpha\tilde{y}_d w(t),\\
v'(t) &= ke^{-\tilde{a}\tau_2}y(t-\tau_2) - pv(t),\\
w'(t) &= cz(t) - qw(t).
\end{aligned}
\tag{3.43}
$$

Let $\tilde{m}_d = d + \beta\tilde{v}_d$, $\tilde{m}_a = a + p$ and $\tilde{m}_b = b + q$. Using the facts that $c\alpha\tilde{y}_d = bq$ and $k\beta e^{-a\tau_1-\tilde{a}\tau_2}\tilde{x}_d = p(\alpha\tilde{w}_d + a)$, the characteristic equation of (3.43) can be written as

$$
\begin{aligned}
D(\xi) := \xi^5 + \tilde{A}_4(\tau)\xi^4 + \tilde{A}_3(\tau)\xi^3 + \tilde{A}_2(\tau)\xi^2 + \tilde{A}_1(\tau)\xi + \tilde{A}_0 \\
-(\tilde{B}_3(\tau)\xi^3 + \tilde{B}_2(\tau)\xi^2 + \tilde{B}_1(\tau)\xi)e^{-\xi(\tau_1+\tau_2)} = 0,
\end{aligned}
\tag{3.44}
$$

where

$$
\begin{aligned}
\tilde{A}_4(\tau) &= \tilde{m}_a + \tilde{m}_b + \tilde{m}_d + \alpha\tilde{w}_d,\\
\tilde{A}_3(\tau) &= ap + \tilde{m}_a\tilde{m}_d + (\tilde{m}_a + \tilde{m}_d)\tilde{m}_b + (p + \tilde{m}_b + \tilde{m}_d)\alpha\tilde{w}_d,\\
\tilde{A}_2(\tau) &= ap\tilde{m}_d + \tilde{m}_b(ap + \tilde{m}_a\tilde{m}_d) + (bq + \tilde{m}_b\tilde{m}_d + p\tilde{m}_b + p\tilde{m}_d)\alpha\tilde{w}_d,\\
\tilde{A}_1(\tau) &= ap\tilde{m}_b\tilde{m}_d + (bq\tilde{m}_d + pbq + p\tilde{m}_b\tilde{m}_d)\alpha\tilde{w}_d,\\
\tilde{A}_0 &= \alpha bpq\tilde{w}_d\tilde{m}_d,\\
\tilde{B}_3(\tau) &= p(\alpha\tilde{w}_d + a),\\
\tilde{B}_2(\tau) &= (d + \tilde{m}_b)(\alpha\tilde{w}_d + a)p,\\
\tilde{B}_1(\tau) &= d\tilde{m}_b(\alpha\tilde{w}_d + a)p.
\end{aligned}
\tag{3.45}
$$

Similarly, letting $\tilde{R}(\omega)$ and $\tilde{S}(\omega)$ be the real and imaginary parts of $D(i\omega)$ yields

$$
\begin{aligned}
\tilde{R}(\omega) \;=\; & -\frac{1}{\alpha^2(cdp\alpha+\beta bkqe^{-\tilde{a}\tau_2})cp}\{-\alpha^3c^2p^2d\omega^4(p+d+b+q)\\
& +\omega^2\alpha^3c^2dp^2(bdp+qdp-baq)+a^2bp^3qc^2d^2\alpha^2\\
& +e^{-\tilde{a}\tau_2}[-\omega^4\alpha^2cp\beta bkq(p+b+q+2d)+\omega^2\alpha^2bcp\beta kq(2bdp+2qdp-bqa)\\
& +2a^2b^2p^2q^2cd\alpha\beta k]+e^{-2\tilde{a}\tau_2}[-w^4\alpha\beta^2b^2k^2q^2+\omega^2\alpha p\beta^2b^2k^2q^2(b+q)\\
& +a^2b^3pq^3\beta^2k^2]+e^{-a\tau_1-\tilde{a}\tau_2}[-\omega^4\alpha^3c^2p\beta\lambda k\\
& +\omega^2\alpha^3c^2p\beta\lambda k(bq+db+dq+pb+pq+dp)-abp^2qc^2d\alpha^2\beta\lambda k\\
& +\cos((\tau_1+\tau_2)\omega)\omega^2\alpha^3\beta\lambda c^2kp^2(b+d+q)\\
& +\sin((\tau_1+\tau_2)\omega)p^2\alpha^3\beta\lambda c^2k(\omega^3-\omega db-\omega dq)]\\
& +e^{-a\tau_1-2\tilde{a}\tau_2}[\omega^2\alpha^2\beta^2bk^2q\lambda c(b+q+p)-ab^2pq^2\beta^2k^2\alpha\lambda c]\},
\end{aligned}
\tag{3.46}
$$

and

$$
\begin{aligned}
\tilde{S}(\omega) \;=\; & \frac{1}{\alpha cp(cdp\alpha+\beta bkqe^{-\tilde{a}\tau_2})}\{\omega\{\omega^4\alpha^2c^2p^2d-\omega^2c^2dp^2\alpha^2(dp+dq+db+bp+pq)\\
& -bqc^2dp^2\alpha^2a(p+d)+e^{-\tilde{a}\tau_2}[\omega^4\alpha cp\beta bkq\\
& -\omega^2cp\alpha\beta bkq(2pd+2dq+2bd+pq+bp)\\
& -b^2q^2cp\alpha\beta ak(2d+p)]+e^{-a\tau_1-\tilde{a}\tau_2}[-\omega^2\alpha^2c^2p\beta\lambda k(p+b+q+d)\\
& +p\alpha^2c^2\beta\lambda k(bpq+bdp+dpq+bdq)\\
& +\cos((\tau_1+\tau_2)\omega)p^2\alpha^2\beta\lambda c^2k(-\omega^2+db+dq)\\
& +\sin((\tau_1+\tau_2)\omega)\omega\alpha^2\beta\lambda c^2kp^2(b+d+q)]\\
& -e^{-2\tilde{a}\tau_2}[\omega^2\beta^2b^2k^2q^2(b+p+q)+b^3q^3\beta^2k^2a]\\
& +e^{-a\tau_1-2\tilde{a}\tau_2}\beta^2bk^2q\alpha\lambda c[-\omega^2+bq+pq+bp]\}\}.
\end{aligned}
\tag{3.47}
$$

Then, in order to determine the stability of $\tilde{E}_d$, we solve the following two equations for τ_1 and ω:

$$\tilde{R}(\omega)=0 \quad \text{and} \quad \tilde{S}(\omega)=0, \tag{3.48}$$

where τ_1 is our bifurcation parameter. The two equations in (3.48) have two solutions for τ_1: $\tau_1 = \tau_{11}$ and $\tau_1 = \tau_{12}$, listed in Appendix. The solutions for ω can be obtained by substituting the two solutions of τ_1 into any one of the above equations. Also, we need choose the positive value for $\tau_1 = \tau_{11}$ or $\tau_1 = \tau_{12}$ and the corresponding value for ω to determine the value of $\tilde{R}_d$. Hence, all the critical parameter values τ_1, ω and $\tilde{R}_d$ are expressed in terms of $\alpha, \beta, \lambda, a, b, c, d, k, p, q$, called $\tilde{\tau}_h$, ω_h and $\tilde{R}_h$.

Same as the discussion in the previous chapter, if other three conditions need be satisfied (see [48]),

$$\tilde{R}(\omega) = 0 \quad \Rightarrow \quad \tilde{S}(\omega) < 0 \quad \text{for} \quad \tau_1 < \tilde{\tau}_h, \tag{3.49}$$

$$\frac{\partial D(\xi,\tau_1)}{\partial \xi} \Big|_{\xi=\omega_h i, \tau_1=\tilde{\tau}_h} \neq 0 \tag{3.50}$$

and

$$Re\frac{d\xi}{d\tau} \Big|_{\xi=\omega_h i, \tau_1=\tilde{\tau}_h} < 0, \tag{3.51}$$

then (3.44) has a pair of purely imaginary roots when $\tau_1 = \tilde{\tau}_h(\tilde{R}_d = \tilde{R}_h)$, implying existence of Hopf bifurcation. Therefore, when $1 < \tilde{R}_d < \tilde{R}_h$, the equilibrium solution $\tilde{E}_d$ is stable. At the critical point, $\tau_1 = \tilde{\tau}_h$ $(\tilde{R}_d = \tilde{R}_h)$, $\tilde{E}_d$ loses its stability through Hopf bifurcation, leading to bifurcation of a family of limit cycles.

Finally, we show that there exists double Hopf bifurcation in system (3.1). In order to have double Hopf bifurcation, the corresponding characteristic equation (3.44) need have two pairs of purely imaginary eigenvalues. We choose τ_1, a, λ as our bifurcation parameters. λ is solved from the first equation of (3.48) to yield

$$\begin{aligned}
\lambda \; = \; & -\{-w^4\alpha^3c^2p^2d(b+d+p+q)+\omega^2\alpha^3dc^2p^2(bdp+dpq-baq)+a^2bp^3qd^2\alpha^2c^2 \\
& -e^{-\tilde{a}\tau_2}[\omega^4\alpha^2cp\beta bkq(p+b+q+2d)+\omega^2\alpha^2bcp\beta kq(-2bdp+baq-2dpq) \\
& -2a^2b^2p^2q^2d\alpha c\beta k]+e^{-2\tilde{a}\tau_2}[-\omega^4\alpha\beta^2b^2k^2q^2+\omega^2\alpha p\beta^2b^2k^2q^2(b+q) \\
& +a^2b^3pq^3\beta^2k^2]\}/\{ck\alpha\beta\{e^{-a\tau_1-\tilde{a}\tau_2}[-c\alpha^2p\omega^4+\omega^2c\alpha^2p \\
& \times(bq+bp+pq+dp+db+dq)+c\alpha^2\cos((\tau_1+\tau_2)\omega)\omega^2p^2(b+q+d) \\
& +c\alpha^2\sin((\tau_1+\tau_2)\omega)p^2(\omega^3-db\omega-\omega dq)-cabp^2qd\alpha] \\
& +e^{-a\tau_1-2\tilde{a}\tau_2}[\omega^2k\alpha\beta bq(b++p+q)-kab^2pq^2\beta]\}\}.
\end{aligned} \tag{3.52}$$

Then, substituting the above λ into the second equation of (3.48) and assuming $\pm\omega_1$ and $\pm\omega_2$ being the two pairs of purely imaginary eigenvalues yields two equations: $\tilde{S}_{d1}(\omega_1)=0$ and $\tilde{S}_{d2}(\omega_2)=0$, given in Appendix. Also, note that the critical point giving rise to double Hopf bifurcation requires $a_+=a_-=a_c$. By solving a_c and setting $\omega_2:\omega_1=\omega_r$. The new equations are obtained for τ_1, ω_1 and ω_r as

$$\begin{aligned}
\tilde{S}_{dd1}(\omega_r,a_c) &= \tilde{F}(\tau_1,\omega_1), \\
\tilde{S}_{dd2}(\omega_r,a_c) &= \tilde{F}(\tau_1,\omega_r\omega_1),
\end{aligned} \tag{3.53}$$

where $\tilde{F}(\tau_1,\omega_1)$ is shown in Appendix. If (3.53) has real positive solution for ω_1 and τ_1, called ω_{1c} and τ_{1c}, all the critical values of the bifurcation parameters can be determined as: $(\tau_1,a,\lambda)=(\tau_{1c},a_c,\lambda_c)$. Moreover, the two pairs of purely imaginary eigenvalues for the characteristic equation (3.44) are $(\pm\omega_{1c},\pm(\omega_r\times\omega_{1c}))$, implying existence of double Hopf bifurcation.

3.6 Numerical Simulation

In this section, numerical simulations are performed to verify the theoretical results obtained in the previous sections.

3.6.1 Periodic Solutions

Firstly, two examples are given to show that there exist periodic solutions in system (3.1).

Example 1. Again, setting $\lambda = 0.24$, $d = 0.004$, $\beta = 0.004$, $a = \bar{a} = 0.33$, $\alpha = 0.004$, $b = 2$, $k = 50$, $p = 2$, $c = 2000$, $q = 2$, $\tau_2 = 0.5$ and choosing τ_1 as the bifurcation parameter, we have

$$\begin{aligned} \tilde{R}_0 &= 18.1818e^{-0.33(\tau_1+0.5)}, \\ \tilde{R}_d &= 0.09435144952(18.1818e^{-0.33(\tau_1+0.5)} - 1). \end{aligned} \tag{3.54}$$

Then, the disease-free equilibrium $\tilde{E}_0$ is

$$\tilde{E}_0 = (60, 0, 0, 0, 0), \tag{3.55}$$

which is stable for $\tau_1 > 8.289157860$. Numerical simulated solution result for $\tau_1 = 9$, shown in Figure 3.1, converges to $\tilde{E}_0$. If $\tau_1 < 8.289157860$ ($\tilde{R}_0 > 1$), $\tilde{E}_0$ is unstable and the single-infection equilibrium is emerged, given by,

$$\tilde{E}_s = (3.3e^{0.33(\tau_1+0.5)}, 0.7273e^{-0.33\tau_1} - 0.03391574816, 0, 18.1818e^{-0.33(\tau_1+0.5)} - 1, 0), \tag{3.56}$$

which is stable for $0.8622168041 < \tau_1 < 8.289157860$, as shown in Figure 3.2. When $\tau_1 < 0.8622168041$, the double-infection equilibrium $\tilde{E}_d$ comes into exist, given by

$$\begin{aligned} \tilde{E}_d = (&5.173006325, 0.5, 0.1293251581e^{-0.33(\tau_1+0.5)} - 0.0825, \\ &10.59867130, 129.32515e^{-0.33(\tau_1+0.5)} - 82.5), \end{aligned} \tag{3.57}$$

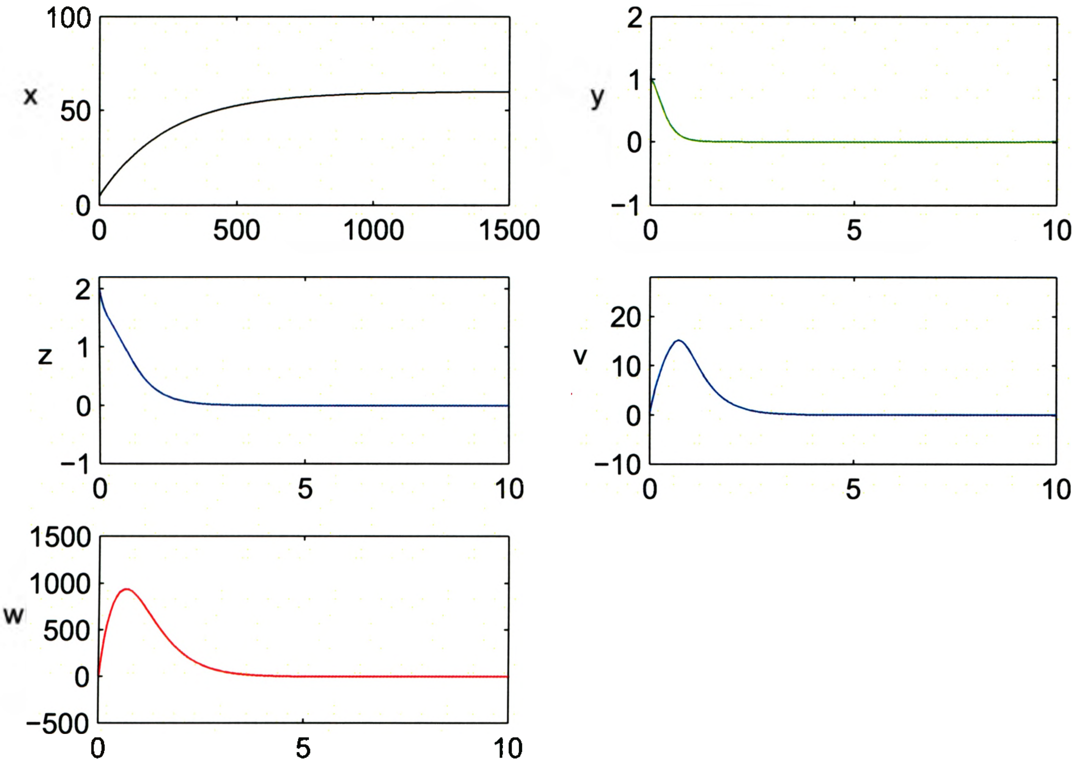

Figure 3.1: Simulated time history of system (3.1) for $\lambda = 0.24$, $\alpha = \beta = d = 0.004$, $k = 50$, $a = \bar{a} = 0.33$, $c = 2000$, $b = p = q = 2$, $\tau_2 = 0.5$, $\tau_1 = 9$ with the initial condition: $x(0) = 5.0$, $y(0) = 1.0$, $z(0) = 2.0$, $v(0) = 0.5$, $w(0) = 4.0$, converging to the stable equilibrium solution $\tilde{E}_0 = (60, 0, 0, 0, 0)$.

for which the characteristic equation (3.44) becomes

$$\begin{aligned} D(\xi) \;=\; & \xi^5 + (6.046394685 + 0.5173006324e^{-0.33(\tau_1+0.5)})\xi^4 \\ & +(8.278368114 + 3.12780379e^{-0.33(\tau_1+0.5)})\xi^3 \\ & +(-0.948842518 + 6.351607588e^{-0.33(\tau_1+0.5)})\xi^2 \\ & +(-2.701240984 + 4.426405059e^{-0.33(\tau_1+0.5)})\xi \\ & +15.83999999e^{-0.33(\tau_1+0.5)} \\ & -10.10476243 - [(1.034601265e^{-0.33(\tau_1+0.5)})\xi^3 \\ & +(4.142543464e^{-0.33(\tau_1+0.5)})\xi^2 \\ & +(0.1655362024e - 1e^{-0.33(\tau_1+0.5)})\xi]e^{-\xi(\tau_1+0.5)} = 0. \end{aligned} \tag{3.58}$$

Letting $\tilde{R}(\omega)$ and $\tilde{S}(\omega)$ be the real and imaginary parts of $D(i\omega)$, we have

$$\begin{aligned}\tilde{R}(\omega) &= (6.046394685 + .5173006324e^{-0.33(\tau_1+0.5)})\omega^4 \\ &-(-.948842518 + 6.351607588e^{-0.33(\tau_1+0.5)})\omega^2 \\ &+15.83999999e^{-0.33(\tau_1+0.5)} - 10.10476243 \\ &-(1.034601265e^{-0.33(\tau_1+0.5)})\omega^3 \sin(\omega(\tau_1+0.5)) \\ &-(4.14254346e^{-0.33(\tau_1+0.5)})\omega^2 \cos(\omega(\tau_1+0.5)) \\ &+(0.1655362024e^{-0.33(\tau_1+0.5)})\omega \sin(\omega(\tau_1+0.5)),\end{aligned} \tag{3.59}$$

$$\begin{aligned}\tilde{S}(\omega) &= \omega^5 - (8.278368114 + 3.127803794e^{-0.33(\tau_1+0.5)})\omega^3 \\ &+(-2.701240984 + 4.426405059e^{-0.33(\tau_1+0.5)})\omega \\ &-(1.034601265e^{-0.33(\tau_1+0.5)})\omega^3 \cos(\omega(\tau_1+0.5)) \\ &+(4.14254346e^{-0.33(\tau_1+0.5)})\omega^2 \sin(\omega(\tau_1+0.5)) \\ &+(0.1655362024e - e^{-0.33(\tau_1+0.5)})\omega \cos(\omega(\tau_1+0.5)).\end{aligned} \tag{3.60}$$

Similarly, numerically solving the two equations,

$$\tilde{R}(\omega) = 0 \quad \text{and} \quad \tilde{S}(\omega) = 0, \tag{3.61}$$

we obtain

$$(\tau_1, \omega) = (0.823938730, 0.1509390973). \tag{3.62}$$

Therefore, we have the critical value $\tilde{\tau}_h = 0.823938730$ giving a corresponding value $\tilde{R}_h = \tilde{R}_d(\tau_1 = \tilde{\tau}_h) = 1.013911267$. Also, it can be shown that when $\tau_1 < \tilde{\tau}_h$, the other three conditions are satisfied:

$$\tilde{R}(\omega) = 0 \quad \Rightarrow \quad \tilde{S}(\omega) < 0, \tag{3.63}$$

$$\frac{\partial D(\xi,\tau_1)}{\partial \xi} |_{\xi=0.1509390973i, \tau_1=0.823938730} = -0.3375687425 + 1.648144850i \neq 0 \tag{3.64}$$

and

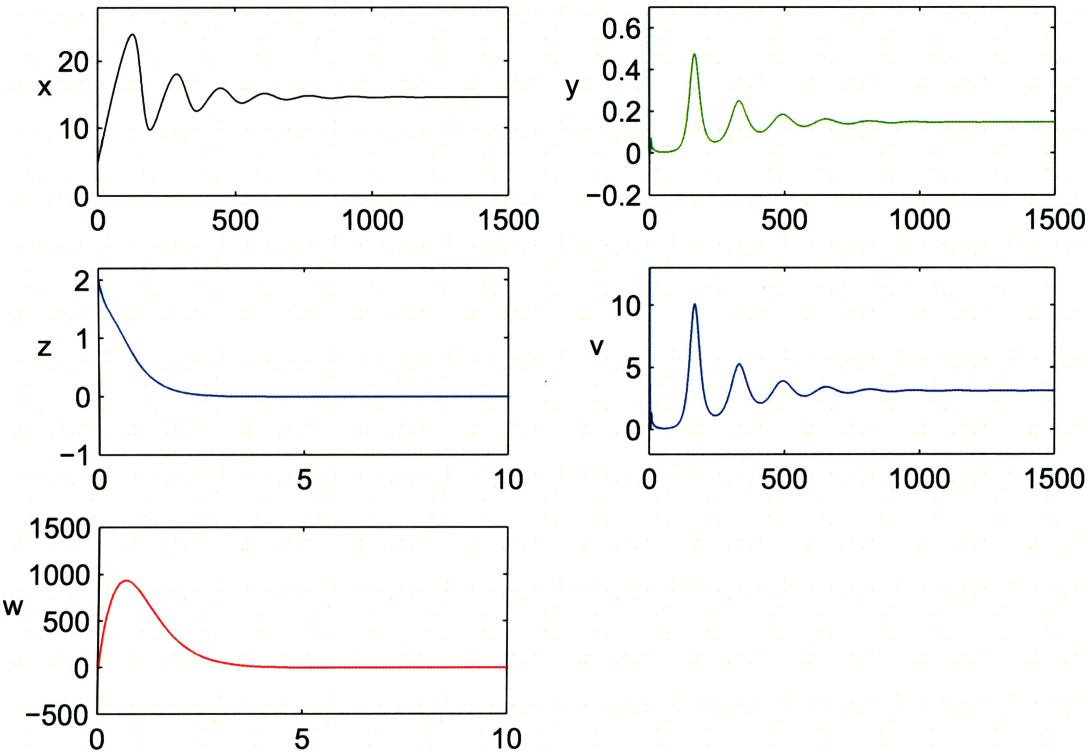

Figure 3.2: Simulated time history of system (3.1) for $\lambda = 0.24$, $\alpha = \beta = d = 0.004$, $k = 50$, $a = \bar{a} = 0.33$, $c = 2000$, $b = p = q = 2$, $\tau_1 = 4$ and $\tau_2 = 0.5$ with the initial condition: $x(0) = 5.0$, $y(0) = 1.0$, $z(0) = 2.0$, $v(0) = 0.5$, $w(0) = 4.0$, converging to the stable equilibrium solution $\tilde{E}_s = (14.5694, 0.1604, 0, 3.1182, 0)$.

$$Re\frac{d\xi}{d\tau}\,|_{\xi=0.1509390973i,\tau_1=0.823938730} = -0.317987439570544 < 0 \tag{3.65}$$

Therefore, the roots of (3.58) have non-negative real part when $\tau_1 < \tilde{\tau}_h$ ($\tilde{R}_d > \tilde{R}_h$), and (3.58) has a pair of purely imaginary roots when $\tau_1 = \tilde{\tau}_h$ ($\tilde{R}_d = \tilde{R}_h$), implying existence of a Hopf bifurcation. Therefore, we conclude that when $0.823938730 < \tau_1 < 0.8622168041$, the equilibrium solution $\tilde{E}_d$ is stable (see Figure 3.3). At the critical point, $\tau_1 = \tilde{\tau}_h$ ($R_d = \tilde{R}_h$), $\tilde{E}_d$ loses its stability through Hopf bifurcation, leading to bifurcation of a family of limit cycles, as shown in Figure 3.4.

Example 2. We choose τ_2 as our bifurcation parameter and set $\tau_1 = 0.4$. Thus,

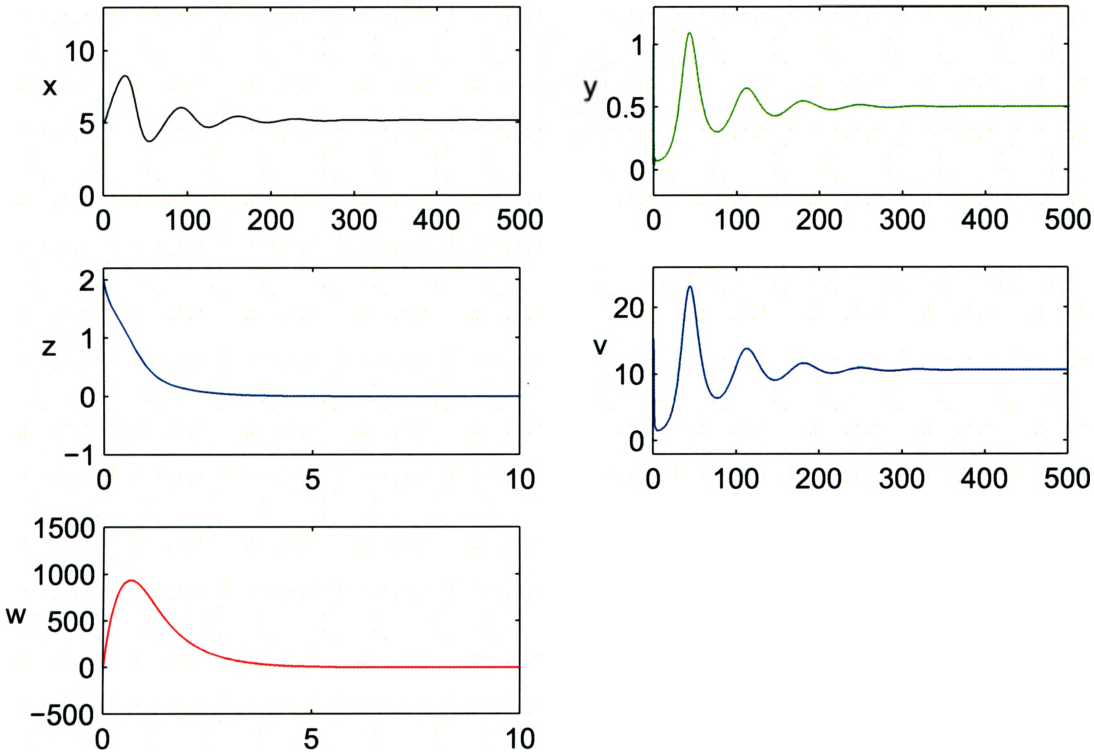

Figure 3.3: Simulated time history of system (3.1) for $\lambda = 0.24$, $\alpha = \beta = d = 0.004$, $k = 50$, $a = \bar{a} = 0.33$, $c = 2000$, $b = p = q = 2$, $\tau_1 = 0.85$ and $\tau_2 = 0.5$ with the initial condition: $x(0) = 5.0$, $y(0) = 1.0$, $z(0) = 2.0$, $v(0) = 0.5$, $w(0) = 4.0$, converging to the stable equilibrium solution $\tilde{E}_d = (5.173, 0.5, 0.0003, 10.5987, 0.3333)$.

$$\begin{aligned} \tilde{R}_0 &= 18.1818e^{-0.33(\tau_2+0.4)}, \\ \tilde{R}_d &= 0.08e^{-0.33\tau_2}(18.1818e^{-0.33(\tau_2+0.4)} - 1). \end{aligned} \tag{3.66}$$

The disease-free equilibrium $\tilde{E}_0$ becomes

$$\tilde{E}_0 = (60, 0, 0, 0, 0), \tag{3.67}$$

which is stable for $\tau_2 > 8.389157861$. When $\tau_2 < 8.389157861$, $\tilde{R}_0 > 1$, for which $\tilde{E}_0$

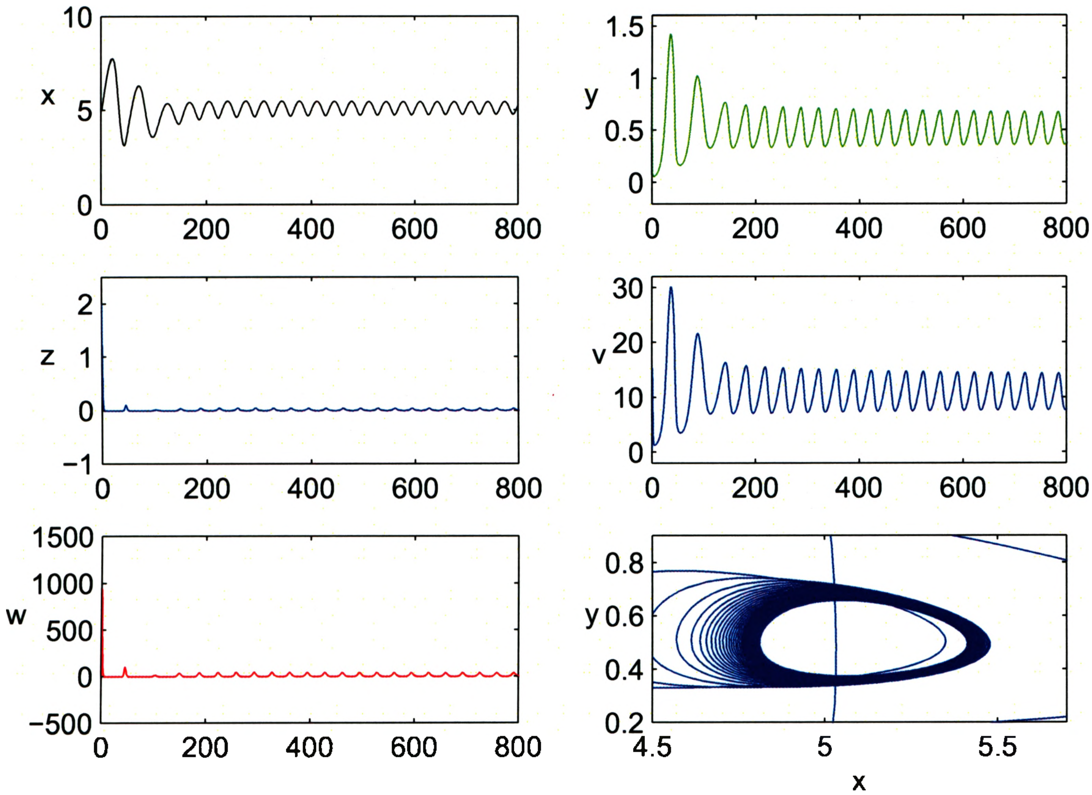

Figure 3.4: Simulated time history of system (3.1) for $\lambda = 0.24$, $\alpha = \beta = d = 0.004$, $k = 50$, $a = \bar{a} = 0.33$, $c = 2000$, $b = p = q = 2$, $\tau_1 = 0.4$ and $\tau_2 = 0.5$ with the initial condition: $x(0) = 5.0$, $y(0) = 1.0$, $z(0) = 2.0$, $v(0) = 0.5$, $w(0) = 4.0$, converging to a periodic solution. The bottom right graph is the phase portrait projected on $x - y$ plane indicating a limit cycle.

is unstable and the single-infection equilibrium bifurcates, given by

$$\tilde{E}_s = (3.3e^{0.33(\tau_2+0.4)}, 0.6373389056 - 0.04e^{0.33\tau_2}, 0, 18.1818e^{-0.33(\tau_2+0.4)} - 1, 0), \tag{3.68}$$

which is stable for $3.738097521 < \tau_2 < 8.389157861$. Further decreasing τ_2 to pass the critical value $\tau_2 = 3.738097521$ causes $\tilde{E}_s$ to be unstable and appearing of the double-infection equilibrium:

$$\begin{aligned}\tilde{E}_d = (&\tfrac{3.84}{0.064+0.8e^{-0.33\tau_2}}, 0.5, \tfrac{0.25(0.384e^{-0.33(\tau_2+0.4)}-0.264e^{-0.33\tau_2}-0.2112)}{0.064+0.8e^{-0.33\tau_2}},\\ &12.5e^{-0.33\tau_2}, \tfrac{250(0.384e^{-0.33(\tau_2+0.4)}-0.264e^{-0.33\tau_2}-0.2112)}{0.064+0.8e^{-0.33\tau_2}}).\end{aligned} \tag{3.69}$$

The corresponding characteristic equation (3.44) for the above $\tilde{E}_d$ becomes

$$\begin{aligned} D(\xi) &= \xi^5 + (6.334 + 0.5e^{-0.33\tau_2} + \tfrac{0.384e^{-0.33(\tau_2+0.4)} - 0.264e^{-0.33\tau_2} - 0.2112}{0.064+0.8e^{-0.33\tau_2}})\xi^4 \\ &+(10.00532 + .3165e^{-0.33\tau_2} \\ &+\tfrac{(6.004+0.5e^{-0.33\tau_2})(0.384e^{-0.33(\tau_2+0.4)}-0.264e^{-0.33\tau_2}-0.2112)}{0.064+0.8e^{-0.33\tau_2}})\xi^3 \\ &+(2.67992 + 0.499e^{-0.33\tau_2} \\ &+\tfrac{(12.024+0.3e^{-0.33\tau_2})(0.384e^{-0.33(\tau_2+0.4)}-0.264e^{-0.33\tau_2}-0.2112)}{0.064+0.8e^{-0.33\tau_2}})\xi^2 \\ &+(0.1056 + 0.132e^{-0.33\tau_2} \\ &+\tfrac{(8.048+0.6e^{-0.33\tau_2})(0.384e^{-0.33(\tau_2+0.4)}-0.264e^{-0.33\tau_2}-0.2112)}{0.064+0.8e^{-0.33\tau_2}})\xi \\ &+\tfrac{660(0.4+0.5e^{-0.33\tau_2})(0.384e^{-0.33(\tau_2+0.4)}-0.264e^{-0.33\tau_2}-0.2112)}{0.064+0.8e^{-0.33\tau_2}} \\ &-[(\tfrac{2(0.33+(0.384e^{-0.33(\tau_2+0.4)}-0.264e^{-0.33\tau_2}-0.2112)}{0.064+0.8e^{-0.33\tau_2}})\xi^3 \\ &+(\tfrac{8.008(0.33+(0.384e^{-0.33(\tau_2+0.4)}-0.264e^{-0.33\tau_2}-0.2112)}{0.064+0.8e^{-0.33\tau_2}})\xi^2 \\ &+(\tfrac{0.032(0.33+(0.384e^{-0.33(\tau_2+0.4)}-0.264e^{-0.33\tau_2}-0.2112)}{0.064+0.8e^{-0.33\tau_2}})\xi]e^{-0.33\xi(\tau_2+0.4)} = 0. \end{aligned} \tag{3.70}$$

Let $\tilde{R}(\omega)$ and $\tilde{S}(\omega)$ be the real and imaginary parts of $D(i\omega)$. Then solving the two equations,

$$R(\omega) = 0 \quad \text{and} \quad S(\omega) = 0, \tag{3.71}$$

we obtain $\tilde{\tau}_{2h} = 2.622465483$ as our critical value, giving a corresponding value $\tilde{R}_h := \tilde{R}_d(\tilde{\tau}_2 = \tau_{2h}) = 1.084598722$. It is easy to show that when $\tau_2 < \tilde{\tau}_h$,

$$\tilde{R}(\omega) = 0 \quad \Rightarrow \quad \tilde{S}(\omega) < 0. \tag{3.72}$$

Further, we can verify that

$$\frac{\partial D(\xi,\tau)}{\partial \xi} \,|_{\xi=0.2915019517i,\tau_2=2.622465483} = -0.6623825246 + 1.865961951i \neq 0 \tag{3.73}$$

and

$$Re\frac{d\xi}{d\tau} \,|_{\xi=0.2915019517i,\tau_2=2.622465483} = -0.0517127986976842 < 0. \tag{3.74}$$

Thus, all roots of (3.70) have non-negative real part for $\tau_2 < \tilde{\tau}_{2h}$ ($\tilde{R}_d > \tilde{R}_h$), and (3.70)

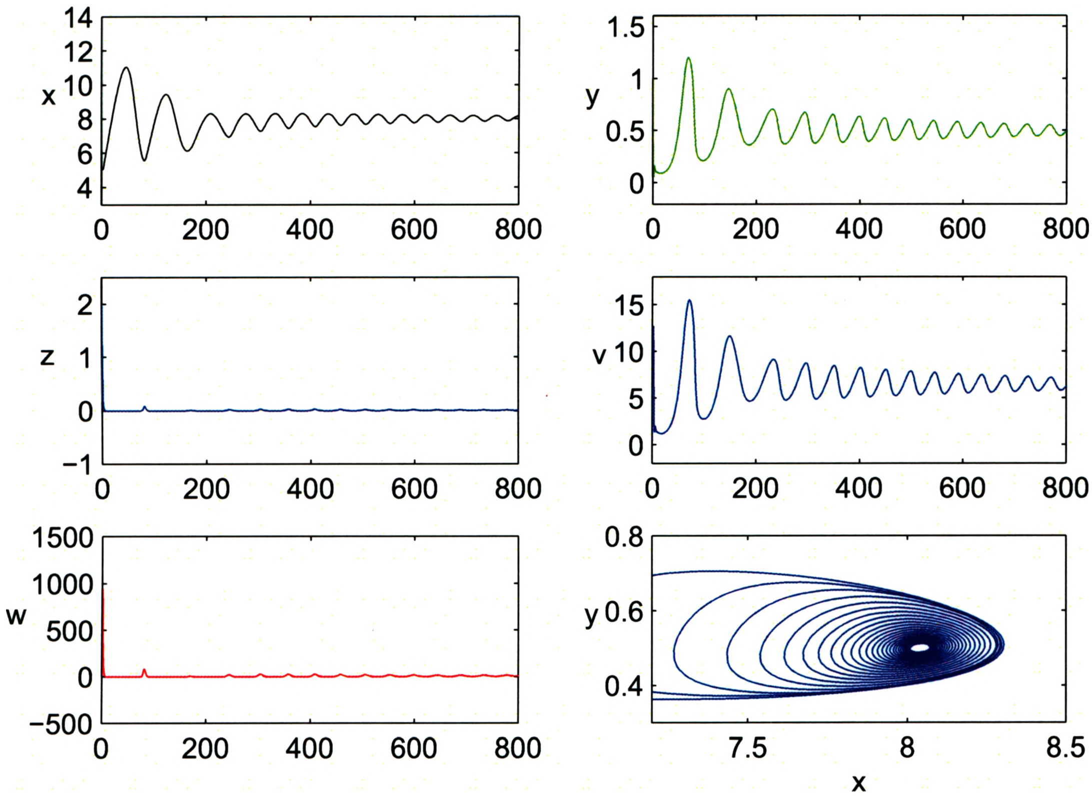

Figure 3.5: Simulated time history of system (3.1) for $\lambda = 0.24$, $\alpha = \beta = d = 0.004$, $k = 50$, $a = \bar{a} = 0.33$, $c = 2000$, $b = p = q = 2$, $\tau_1 = 0.4$, $\tau_2 = 2$ with the initial condition: $x(0) = 5.0$, $y(0) = 1.0$, $z(0) = 2.0$, $v(0) = 0.5$, $w(0) = 4.0$, converging to a periodic solution. The bottom right graph is the phase portrait projected on $x - y$ plane indicating a limit cycle.

has a pair of purely imaginary roots when $\tau_2 = \tilde{\tau}_{2h}$ $(\tilde{R}_d = \tilde{R}_h)$, implying existence of Hopf bifurcation. Therefore, when $2.622465483 < \tau_2 < 3.738097521$, the equilibrium solution $\tilde{E}_d$ is stable. At the critical point, $\tau_2 = \tilde{\tau}_{2h}$, $\tilde{E}_d$ loses its stability through a Hopf bifurcation, leading to bifurcation of a family of limit cycles, as shown in Figure 3.5.

3.6.2 Quasi-periodic Solutions

For quasi-periodic solutions, we present two cases: a resonant case and a non-resonant case. For convenience, we fix $d = 0.002$, $\beta = 0.004$, $\bar{a} = 0.33$, $\alpha = 0.004$, $b = 2$, $k = 50$, $p = 2$, $c = 2000$, $q = 2$, $\tau_2 = 3$ and choose τ_1, a, λ as the bifurcation parameters.

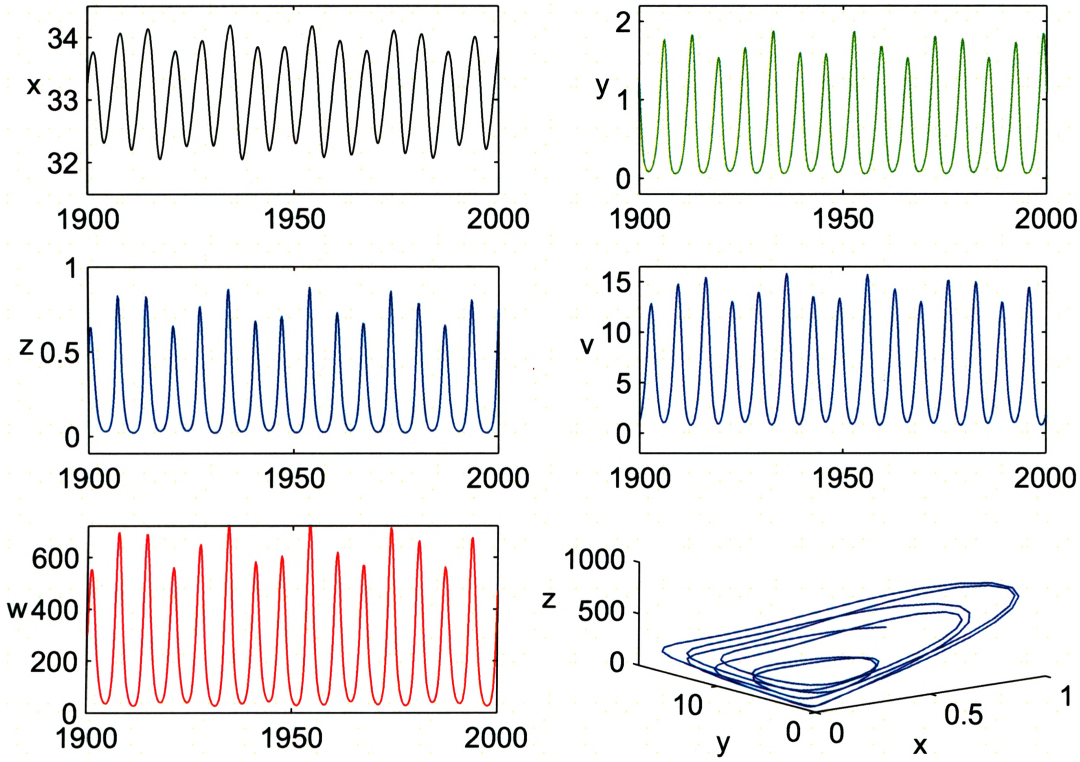

Figure 3.6: Simulated time history of system (3.1) for $\lambda = 0.83$, $\alpha = \beta = 0.004$, $d = 0.002$, $k = 50$, $a = 0.03$, $\bar{a} = 0.33$, $c = 2000$, $b = p = q = 2$, $\tau_1 = 16.03$, $\tau_2 = 3$ with the initial condition: $x(0) = 5.0$, $y(0) = 1.0$, $z(0) = 2.0$, $v(0) = 0.5$, $w(0) = 4.0$.

Resonant case. We choose $\omega_1 : \omega_2 = \omega_r = 1 : 2$, so system (3.53) is reduced to

$$\begin{aligned} \tilde{S}_{dd1}(\omega_r, a_c) &= \tilde{F}_1, \\ \tilde{S}_{dd2}(\omega_r, a_c) &= \tilde{F}_2, \end{aligned} \tag{3.75}$$

where $\tilde{F}_1, \tilde{F}_2$ are given in Appendix. The numerical solution for the above two equations is $(\tau_1, \omega_1) = (16.0283293568469, 0.548085462867220)$. Therefore, at the critical point, a double Hopf bifurcation occurs and all the critical values of the bifurcation parameters can be determined as: $(\tau_1, a, \lambda) = (16.028, 0.0347, 0.8326)$. The two pairs of purely imaginary eigenvalues for the characteristic equation are $(\pm 0.5481, \pm 1.0962)$, implying existence of double Hopf bifurcation. The simulated solutions for this case are shown in Figure 3.6.

Non-resonance case. We choose $\omega_1 : \omega_2 = \omega_r = 1 : \sqrt{2}$. Similarly, by using the two equations in (3.53), we obtain the numerical solution for (τ_1, ω_1), given by

$$(\tau_1, \omega_1) = (43.8987067132056, -0.398679840517696). \tag{3.76}$$

Therefore, at the above critical point a double Hopf bifurcation occurs. All the critical values of the bifurcation parameters can be determined as:

$$(\tau_1, a, \lambda) = (43.8987067132056, 0.0865744881680455, 7.48065701077655). \tag{3.77}$$

The two pairs of purely imaginary eigenvalues for the characteristic equation are

$$(\pm 0.398679840517696, \pm 0.563818437504870) \tag{3.78}$$

The simulation results are shown in Figure 3.7.

3.7 Conclusion and discussion

In this chapter, we have analysed an HIV-1 infection model with two concentrated delays. We have identified the basic reproduction number $\tilde{R}_0$, and proved that if $\tilde{R}_0 < 1$, the infection-free equilibrium $\tilde{E}_0$ is globally asymptotically stable; if $< 1\tilde{R}_0 < 1 + \frac{bkq\beta}{cdp\alpha}e^{-\bar{a}\tau_2}$, the single-infection equilibrium $\tilde{E}_s$ is asymptotically stable. For the double-infection equilibrium $\tilde{E}_d$, we have showed how to determine the stability, existence of Hopf and double Hopf bifurcations.

Due to difficulty in constructing a suitable Lyapunov function for the single-infection equilibrium $\tilde{E}_s$, we didn't obtain its global stability. Moreover, the characteristic equation for the double-infection equilibrium $\tilde{E}_d$ can not be factorized into lower degree polynomials, so it is not possible to provide explicit stability conditions.

Comparing with the results for single delay in Chapter 2, the results obtained in this chapter are more significant. With large τ_2 and all other fixed parameters, the the critical values of τ_1 are smaller than the ones obtained in Chapter 2. This implies that increasing τ_2 also decreases $\tilde{R}_0$, which determines whether or not the HIV-1 virus in host will be persistent or will go to extinction. In other words, both prolonging the latent period and slowing down the virus production process can help control the HIV-1 infection.

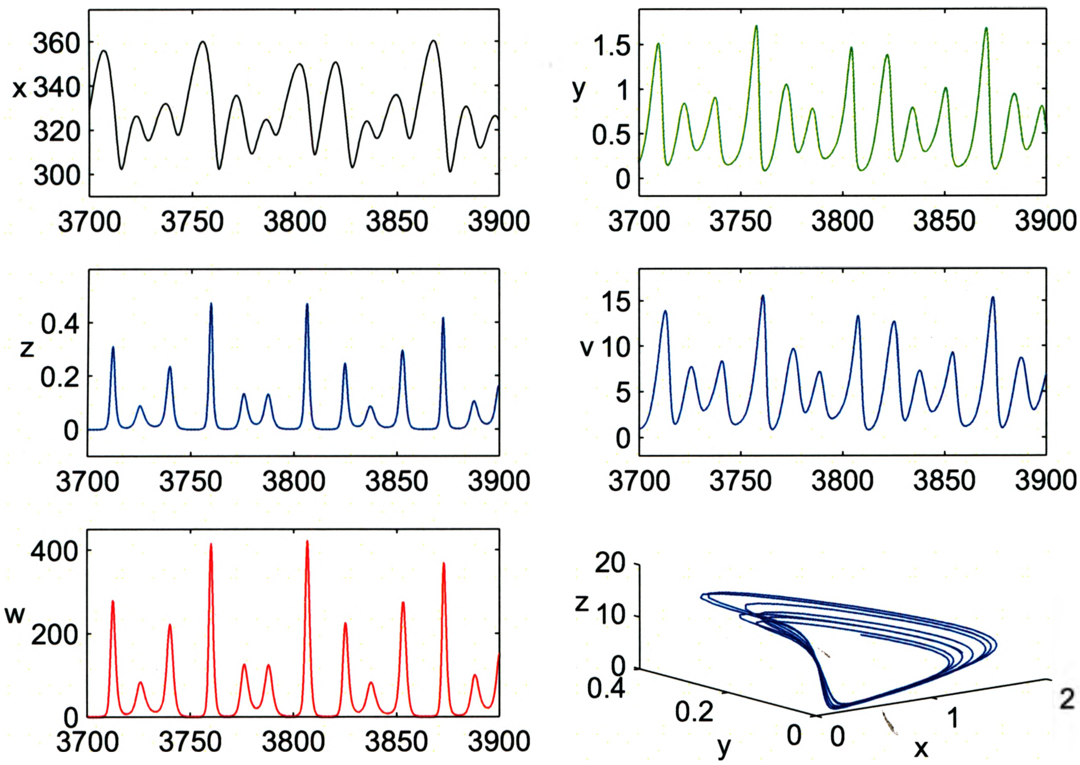

Figure 3.7: Simulated time history of system (3.1) for $\lambda = 7.4807$, $\alpha = \beta = 0.004$, $d = 0.002$, $k = 50$, $a = 0.0865744881680455$, $\bar{a} = 0.33$, $c = 2000$, $b = p = q = 2$, $\tau_1 = 43.8987$, $\tau_2 = 3$ with the initial condition: $x(0) = 5.0$, $y(0) = 1.0$, $z(0) = 2.0$, $v(0) = 0.5$, $w(0) = 4.0$.

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Appendix A

Since Equations (2.37) and (2.38) can be directly obtained by setting $\tau_2 = 0$ in Equations (3.46) and (3.47), we have $\tau_{s1} = \tau_{11}|_{\tau_2=0}$ and $\tau_{s2} = \tau_{12}|_{\tau_2=0}$. Thus, we only need list τ_{11} and τ_{12} as following:

$$\begin{aligned} \tau_{11} &= \tfrac{1}{a}\ln\{\tfrac{\tau_{11n}}{\tau_{1d}}\}, \\ \tau_{12} &= \tfrac{1}{a}\ln\{\tfrac{\tau_{12n}}{\tau_{1d}}\}, \end{aligned} \tag{A.1}$$

where

$$\begin{aligned} \tau_{1d} = \; & (d\alpha cp + \beta bkqe^{-\tilde{a}\tau_2})\Big\{e^{-\tilde{a}\tau_2}\Big[2bkq\beta pc\alpha^3\omega^8 d + 2bkq\beta pc\alpha^3 d(p^2 + b^2 + 2bq \\ & +q^2)\omega^6 - 2bckpq\alpha^2\beta(-p^2 d\alpha q^2 - 2p^2 q\alpha bd - p^2 q\alpha \dot{a} b + p^2 qa^2 b - p^2 b^2 d\alpha \\ & -pbq^2 a\alpha + pq^2 a^2 b - pb^2 qa\alpha - 2pq\alpha bad + pqb^2 a^2 + 2pqba^2 d - 2\alpha badq^2 \\ & -2b^2 ad\alpha q)\omega^4 - 2a^2 b^2 ckpq^2\alpha^2\beta(-2bdp^2 - bq\alpha p + abpq - q\alpha bd \\ & -2dqp^2)\omega^2 + 2b^3 kq^3\beta c\alpha p^3 a^4 d\Big] + e^{-2\tilde{a}\tau_2}\Big[b^2 k^2 q^2\beta^2\omega^8\alpha^2 \\ & +b^2 k^2 q^2\beta^2\alpha^2(2bq + q^2 + p^2 + b^2)\omega^6 - -b^2 k^2 q^2\alpha\beta^2(-2\alpha qbap \\ & -2\alpha q^2 ba - \alpha b^2 p^2 + 2a^2 bpq - 2\alpha qb^2 a - \alpha q^2 p^2 - 2\alpha qbp^2)\omega^4 \\ & +a^2 b^3 k^2 q^3\alpha\beta^2(bq\alpha + 2qp^2 + 2bp^2)\omega^2 + b^4 k^2 q^4\beta^2 a^4 p^2\Big] \\ & +p^2 c^2\alpha^4\omega^1 0 + p^2 c^2\alpha^4(2bq + d^2 + p^2 + q^2 + b^2)\omega^8 + p^2 c^2\alpha^4(2bqp^2 \end{aligned}$$

$$+p^2d^2 + q^2p^2 + b^2p^2 + 2d^2bq + d^2q^2 + d^2b^2 + 2bq^2a + 2b^2qa)\omega^6$$
$$-p^2c^2\alpha^3(-2\alpha bqp^2d^2 - \alpha q^2p^2d^2 - \alpha b^2p^2d^2 + 2pb^2qa^2d$$
$$-2\alpha pb^2qad - 2\alpha b^2qad^2 + 2pbq^2a^2d - 2\alpha pbq^2ad - 2\alpha bq^2ad^2$$
$$+2pbqa^2d^2 - 2\alpha p^2bqad + 2p^2bqa^2d - 2\alpha pbqad^2 - \alpha b^2q^2a^2$$
$$-2\alpha b^2qap^2 - 2\alpha bq^2ap^2)\omega^4 - a^2bqp^2c^2\alpha^3(-\alpha qbp^2 - 2bp^2d^2$$
$$-2bqp\alpha d + 2bpqad - bq\alpha d^2 - 2qp^2d^2)\omega^2 + b^2q^2c^2\alpha^2p^4a^4d^2\Big\},$$

and

$$\tau_{11n} = (\beta\alpha c\lambda k e^{-\tilde{a}\tau_2})[\tau_{n1} + \sqrt{-\alpha^2\omega^2\tau_{n2}}],$$
$$\tau_{12n} = (\beta\alpha c\lambda k e^{-\tilde{a}\tau_2})[\tau_{n1} - \sqrt{-\alpha^2\omega^2\tau_{n2}}],$$

with

$$\tau_{n1} = e^{-\tilde{a}\tau_2}\Big[b^2ckpq^2\alpha^2\beta(p^2\alpha - ap^2 + \alpha qp - apq + p\alpha b - ap\alpha$$
$$+2\alpha pd - 2apd + a^2p - bap + 2\alpha qd + 2\alpha bd - 2\alpha ad)\omega^4 - ab^2ckpq^2\alpha^2 beta$$
$$\times(-bp^2\alpha - 2bp^2d + bp^2a - 2\alpha pbq + 2bapq - 2\alpha pbd + 2bapd - 2\alpha bqd$$
$$-p^2\alpha q - 2qp^2d + p^2qa + 2p^2ad - 2\alpha pqd + 2pqad)\omega^2$$
$$+2\beta\alpha ckb^3q^3p^3a^3d\Big] + e^{-2\tilde{a}\tau_2}\Big[-b^3k^2q^3\alpha\beta^2(-\alpha b - \alpha q + \alpha a - p\alpha + ap)\omega^4$$
$$-ab^3k^2q^3\alpha\beta^2(-\alpha bq - p\alpha b - bp^2 + bap - \alpha qp - qp^2 + apq + ap^2)\omega^2$$
$$+\beta^2k^2b^4q^4p^2a^3\Big] - \alpha^4c^2bqp^2(-b - q + a)\omega^6 + bc^2p^2q\alpha^3(p^2\alpha q + bp^2\alpha$$
$$+\alpha p^2d - \alpha ap^2 - p^2ad + \alpha pqd - pqad - ap\alpha d + \alpha pd^2 + \alpha pbd - bapd$$
$$+a^2pd - apd^2 + \alpha qd^2 + q\alpha ba + \alpha bd^2 - \alpha ad^2)\omega^4 - ac^2bp^2q\alpha^3(-\alpha bqp^2$$
$$-b\alpha p^2d + bp^2ad - bp^2d^2 - 2p\alpha bqd + 2bpqad - p\alpha bd^2 + bapd^2 - \alpha bqd^2$$
$$-\alpha p^2dq + p^2qad - qp^2d^2 + p^2ad^2 - p\alpha d^2q + pqad^2)\omega^2 + \alpha^2c^2b^2q^2p^4a^3d^2,$$

$$
\begin{aligned}
\tau_{n2} \;=\;& e^{-\tilde{a}\tau_2}\Big[4p^3c^3\alpha^5bkbetaqd\omega^{14}+2bc^3kp^3q\alpha^4\beta([4\alpha b^2d-\alpha pbq+bapq\\
&+4bdq\alpha+3\alpha p^2d+4\alpha q^2d+2\alpha d^3]\omega^{12}-2bc^3kp^3q\alpha^4\beta[\alpha qpb^3\\
&-2\alpha pbqad-4\alpha qb^3d-4\alpha qbd^3-2\alpha q^4d-\alpha p^4d-\alpha q^2p^2b+\alpha q^2pb^2\\
&+\alpha qp^3b-4\alpha q^3bd-6\alpha p^2b^2d-qpb^3a+qp^2b^2a+q^2p^2ba-qp^3ba\\
&+q^2pba^2-q^2pb^2a+qp^2ba^2-qp^3ba-q^3pba+qpb^2a^2-3\alpha p^2d^3\\
&-3bpqd^2a+2qp^2bad-4\alpha q^2bad-4\alpha qb^2ad-\alpha qpb^2a-6\alpha qp^2bd\\
&-\alpha qp^2ba-\alpha q^2pba+3\alpha pbqd^2-2\alpha qpb^2d-2\alpha q^2pbd-4\alpha q^2d^3\\
&-4\alpha b^2d^3-2\alpha b^4d+2qpb^2ad+2q^2pbad+2bpqa^2d-\alpha qp^2b^2+\alpha q^3pb\\
&-6\alpha q^2p^2d-6\alpha q^2b^2d]\omega^{10}-2bc^3kp^3q\alpha^4\beta[\alpha qpb^3-2\alpha pbqad-4\alpha qb^3d\\
&-4\alpha qbd^3-2\alpha q^4d-\alpha p^4d-\alpha q^2p^2b+\alpha q^2pb^2+\alpha qp^3b-4\alpha q^3bd\\
&-6\alpha p^2b^2d-qpb^3a+qp^2b^2a+q^2p^2ba+q^2pba^2-q^2pb^2a+qp^2ba^2\\
&-q^3pba+qpb^2a^2-3\alpha p^2d^3-3bpqd^2a+2qp^2bad-4\alpha q^2bad-4\alpha qb^2ad\\
&-\alpha qpb^2a-6\alpha qp^2bd-\alpha qp^2ba-\alpha q^2pba+3\alpha pbqd^2-2\alpha qpb^2d\\
&-2\alpha q^2pbd-4\alpha q^2d^3-4\alpha b^2d^3-2\alpha b^4d+2qpb^2ad+2q^2pbad+2bpqa^2d\\
&-\alpha qp^2b^2+\alpha q^3pb-6\alpha q^2p^2d-6\alpha q^2b^2d]\omega^8-2bc^3kp^3q\alpha^3\beta\\
&\times[-2\alpha^2q^2p^4d-2\alpha^2p^4b^2d-3\alpha^2p^2b^4d-3\alpha^2q^2pbad^2-4\alpha^2q^2p^2bad\\
&-3\alpha q^3pd^2ba+2\alpha q^2p^3bad+2\alpha qp^3b^2ad+4\alpha q^2pbd^3a-2\alpha^2q^3pbad\\
&-3\alpha^2qpb^2ad^2-2\alpha^2q^2pdb^2a-3\alpha^2qp^2bad^2+2\alpha q^3pba^2d-2\alpha^2q^3p^2b^2\\
&+\alpha^2q^3p^3b+3\alpha^2qp^3bd^2+\alpha q^3p^2ba^2+\alpha qp^2b^3a^2+3\alpha^2qpb^3d^2\\
&-\alpha q^3p^3ba-\alpha^2q^3pb^2a+2\alpha q^3p^2b^2a-4\alpha^2q^3pb^2d+\alpha q^3pb^2a^2\\
&+2\alpha q^2p^2b^3a-4\alpha^2q^2pb^3d+\alpha q^2pb^3a^2-\alpha^2q^4pba-\alpha q^2p^3b^2a-2\alpha^2qp^4bd\\
&-3\alpha^2qp^2b^2d^2-4\alpha^2qpb^2d^3-4\alpha^2q^2pbd^3-\alpha^2q^3p^2ba-\alpha^2qp^2b^3a\\
&-8\alpha^2qp^2bd^3-4\alpha^2qb^2ad^3-4\alpha^2q^2bad^3-4\alpha^2q^4bad-8\alpha^2q^3b^2ad\\
&-8\alpha^2q^2b^3ad-4\alpha^2qb^4ad+\alpha q^2p^4ba-\alpha qp^3b^3a-3\alpha^2q^2p^2bd^2\\
&+3\alpha^2q^2pb^2d^2-\alpha^2qpb^4a+\alpha q^4p^2ba+\alpha qp^2b^4a+2\alpha qpb^3a^2d\\
&-4\alpha^2qpbad^3-3\alpha qpd^2b^3a-4\alpha^2qp^2b^2ad+4\alpha q^2pb^3ad-2\alpha^2qpb^3ad\\
&+2\alpha q^4pbad+2\alpha qp^4bad+4\alpha q^3pb^2ad+3\alpha q^2p^2d^2ba+3\alpha qp^2d^2b^2a\\
&+4\alpha q^2p^2b^2ad+3\alpha q^2pba^2d^2+4\alpha qpb^2d^3a-2\alpha q^2p^2ba^2d-\alpha^2p^4d^3\\
&-2\alpha^2b^4d^3-2\alpha^2q^4d^3+4\alpha qp^2bd^3a-\alpha^2qp^2b^4-\alpha^2q^2p^4b-4\alpha^2qb^3d^3\\
&-\alpha^2q^4p^2b+3\alpha qp^2ba^2d^2+2\alpha q^2pb^2a^2d-3\alpha qp^3bd^2a-6\alpha^2q^2b^2d^3\\
&-6\alpha^2p^2b^2d^3+2\alpha q^3p^2bad+2\alpha qp^2b^3ad-3\alpha q^2pd^2b^2a+4\alpha qpba^2d^3\\
&+2\alpha qpb^4ad+3\alpha qpb^2a^2d^2-2\alpha^2qp^3b^2d+3\alpha^2q^3pbd^2-2\alpha^2q^4pbd\\
&-q^2p^2b^2a^2d-2\alpha^2qpb^4d+\alpha q^4pba^2-\alpha^2q^2p^2b^2a-\alpha^2q^2pb^3a+\alpha qpb^4a^2\\
&+\alpha q^2p^2b^2a^2-2\alpha^2q^2p^3bd-6\alpha^2qp^2b^3d-9\alpha^2q^2p^2b^2d-6\alpha^2q^3p^2bd\\
&+\alpha qp^4b^2a-6\alpha^2q^2p^2d^3-4\alpha^2q^3bd^3-2\alpha qp^2b^2a^2d+\alpha^2qp^3b^3-\alpha^2qp^4b^2\\
&-3\alpha^2q^4p^2d-2\alpha^2q^2p^2b^3+\alpha^2q^2p^3b^2]\omega^6-2bc^3kp^3q\alpha^3\beta[4\alpha q^3pb^3a^2d
\end{aligned}
$$

$$-2\alpha^2q^4pb^2ad+2\alpha q^4p^3bad+3\alpha bp^4d^2aq^2+4\alpha^2b^2q^2ap^3d-2\alpha^2bq^2ap^4d$$
$$+2\alpha bp^4aq^3d+2\alpha b^2p^4aq^2d-6\alpha q^3p^2b^2a^2d-6\alpha^2q^3p^2b^2ad-2\alpha^2q^2pb^4ad$$
$$-2\alpha^2qp^3bad^3-4\alpha^2q^3pbad^3-6\alpha q^2p^2b^3a^2d+2\alpha q^2pb^4a^2d-4\alpha^2qpb^3ad^3$$
$$-4\alpha q^2p^2ba^2d^3+4\alpha qp^2b^3d^3a+2\alpha q^4pb^2a^2d-4\alpha^2q^4p^2bad+3\alpha qp^2b^4d^2a$$
$$+2\alpha qp^3b^4ad-2\alpha^2qp^4b^2ad-4\alpha^2q^4pbd^3-2\alpha^2b^2p^3dq^3+2\alpha b^3p^4aq^2$$
$$-2\alpha^2b^4p^3dq+\alpha^2b^2q^2ap^4-\alpha b^2q^2p^4a^2+\alpha bq^4p^4a-2\alpha^2b^3q^2p^3d$$
$$-4\alpha^2bq^2p^3d^3-4\alpha^2b^2p^3d^3q-3\alpha^2bp^4d^2q^2-2\alpha^2b^2p^4q^2d-2\alpha^2bp^4q^3d$$
$$+2\alpha b^2q^3p^4a-2\alpha^2bq^4p^3d-\alpha^2q^2pb^4a^2-\alpha^2q^2p^2b^4a-8\alpha^2q^3pb^2d^3$$
$$-3\alpha^2q^3p^2b^2d^2-\alpha^2q^3p^2b^2a^2-10\alpha^2q^2p^2b^2d^3+\alpha q^3p^2b^2a^3-3\alpha^2q^4p^2bd^2$$
$$+6\alpha^2q^2p^3b^2d^2+\alpha q^4p^2b^2a^2+2\alpha^2b^3q^2p^3a-2\alpha q^2p^3b^3a^2-8\alpha^2qp^2b^3d^3$$
$$-8\alpha^2q^3p^2bd^3-4\alpha^2qp^4bd^3-8\alpha^2q^2pb^3d^3-3\alpha^2q^2p^2b^3d^2+2\alpha q^3pb^3a^3$$
$$-\alpha q^2p^3b^2a^3+\alpha qp^4b^4a+3\alpha^2q^3p^3bd^2+3\alpha^2qp^3b^3d^2-2\alpha q^3p^3b^2a^2$$
$$-3\alpha^2qp^4b^2d^2+\alpha^2q^2p^3b^2a^2-2\alpha^2q^3p^2b^3a-\alpha^2q^4p^2b^2a+\alpha q^2pb^4a^3$$
$$-2\alpha^2qp^4b^3d+2\alpha q^3p^2b^3a^2+\alpha q^2p^2b^4a^2-2\alpha^2b^3p^4q^2-\alpha^2bq^4p^4$$
$$-2\alpha^2q^3b^2p^4-\alpha^2p^4b^4d-3\alpha^2p^2b^4d^3-2\alpha^2b^2p^4d^3-\alpha^2q^4p^4d-2\alpha^2q^2p^4d^3$$
$$-3\alpha^2q^4p^2d^3-\alpha^2qp^4b^4-2\alpha^2q^2pb^3a^2d+4\alpha qpb^4d^3a+\alpha^2q^2p^2b^2a^2d$$
$$-3\alpha^2q^2pb^3ad^2-6\alpha q^2p^3b^2a^2d-3\alpha^2q^3pb^2ad^2+3\alpha qp^4b^2d^2a+4\alpha qp^3b^2d^3a$$
$$+4\alpha q^2p^3bd^3a-2\alpha^2qp^2b^2ad^3+3\alpha q^4p^2bd^2a+4\alpha q^3p^2bd^3a+2\alpha q^2pb^3a^3d$$
$$-2\alpha^2q^2p^2bad^3+4\alpha q^3pba^2d^3+2\alpha qp^3ba^2d^3+4\alpha qpb^3a^2d^3-3\alpha^2q^4pbad^2$$
$$-3\alpha^2q^3p^2bad^2-2\alpha^2qp^4bad^2-3\alpha^2qp^2b^3ad^2+4\alpha qp^4bd^3a-3\alpha q^2p^2b^2a^2d^2$$
$$+2\alpha qp^3b^2a^2d^2+3\alpha qpb^4a^2d^2-2\alpha qp^2b^4a^2d-2\alpha^2qp^3b^2ad^2-3\alpha^2qpb^4ad^2$$
$$-2\alpha^2q^3pb^2a^2d-4\alpha qp^2b^2a^2d^3-4\alpha^2q^3pb^3ad-6\alpha^2q^2p^2b^3ad+3\alpha q^3pb^2a^2d^2$$
$$+2\alpha q^3pb^2a^3d+3\alpha q^4pba^2d^2+2\alpha q^2p^3ba^2d^2+3\alpha q^2pb^3a^2d^2-4\alpha^2q^2pb^2ad^3$$
$$+4\alpha q^2pb^2a^2d^3-9\alpha q^2p^3b^2ad^2-2\alpha q^4p^2ba^2d-3\alpha qp^3b^3d^2a+8\alpha q^2pb^3ad^3$$
$$+8\alpha q^3pb^2ad^3+4\alpha q^2p^2b^2ad^3+2\alpha qp^4b^3ad-3\alpha q^3p^3bd^2a+4\alpha q^4pbd^3a$$
$$-2\alpha^2q^3pb^3a^2-\alpha^2q^2p^2b^3a^2-3\alpha^2qp^2b^4d^2-4\alpha^2qpb^4d^3+\alpha q^4pb^2a^3+2q^3p^3b^2a^2d$$
$$-\alpha^2q^4pb^2a^2+2\alpha^2q^3p^3b^2a+\alpha q^2p^2b^3a^3-4\alpha^2qb^4ad^3-4\alpha^2bq^4ad^3+2\alpha qp^4ba^2d^2$$
$$-2\alpha^2q^4b^2a^2d-2\alpha^2q^2b^4a^2d-8\alpha^2b^3q^2ad^3-8\alpha^2q^3b^2ad^3-4\alpha^2q^3b^3a^2d$$
$$+3q^2p^2b^3a^2d^2+2q^2p^2b^3a^3d+3q^3p^2b^2a^2d^2+2q^2p^3b^2a^3d+3q^2p^3b^2a^2d^2$$
$$+3q^2p^2b^2a^3d^2+2q^3p^2b^2a^3d+2q^2p^3b^3a^2d-4\alpha^2qp^2b^4ad+3\alpha q^3p^2ba^2d^2$$
$$+3\alpha qp^2b^3a^2d^2-2\alpha^2bq^2p^3ad^2]\omega^4-2a^2b^2c^3dkp^5q^2\alpha^3\beta[\alpha^2qb^3d^2+2\alpha^2q^2b^2d^2$$
$$+b^3qa^2p^2+bq^3a^2p^2+2q^2p^2b^2a^2-4\alpha q^3bad^2-2\alpha q^3p^2d^2-4\alpha qb^3ad^2$$
$$-4\alpha qpd^2b^3-4\alpha q^3pd^2b+\alpha^2q^3pdb-3\alpha qp^2db^3+\alpha^2qpdb^3-3\alpha q^3p^2db$$
$$+2\alpha^2q^2pdb^2-8\alpha q^2pd^2b^2+3qpdb^3a^2+6q^2pdb^2a^2+3q^3pdba^2+3q^3p^2bad$$
$$+3q^2p^2ba^2d-6\alpha q^2p^2d^2b-6\alpha q^2p^2db^2-2\alpha p^2b^3d^2-3\alpha qp^2db^2a-4\alpha qpdb^3a$$
$$-8\alpha q^2pdb^2a-4\alpha q^3pdba-4\alpha q^2pd^2ba-3\alpha q^2p^2dba-4\alpha qpd^2ab^2+\alpha^2q^3bd^2$$
$$-8ab^2d^2q^2\alpha-4\alpha q^2p^2b^2a-2\alpha q^3p^2ba-2\alpha qp^2b^3a-6\alpha qp^2d^2b^2+4q^3pbad^2$$

$$+3qp^2b^3ad + 4qpb^2a^2d^2 + 4qp^2b^2ad^2 + 8q^2pb^2ad^2 + 6q^2p^2b^2ad + 4q^2pba^2d^2$$
$$+qp^2ba^2d^2 + 3qp^2b^2a^2d + 4q^2p^2bad^2 + 4qpb^3ad^2]\omega^2 + 2\alpha^3c^3b^3q^3p^7a^4d^3\beta k(b+q)^2\Big]$$
$$+e^{-2\tilde{a}\tau_2}\Big[2b^2k^2q^2\beta^2\alpha^4p^2c^2\omega^{14} + b^2k^2q^2\beta^2\alpha^4p^2c^2(4q^2+3p^2+6d^2+4b^2+4bq)\omega^{12}$$
$$-b^2c^2k^2p^2q^2\alpha^3\beta^2[6\alpha qpbd - 2\alpha qpba - 12\alpha qbd^2 + 2bpqa^2 - \alpha p^4 - 2\alpha q^4$$
$$-12\alpha d^2q^2 - 4\alpha qb^3 - 12\alpha d^2b^2 - 6\alpha q^2p^2 - 6\alpha qbp^2 - 4\alpha q^3b - 4\alpha qb^2a - 6bpqad$$
$$-2\alpha qpb^2 + 2qpb^2a - 2\alpha q^2pb - 4\alpha q^2ba + 2qp^2ba + 2q^2pba - 6\alpha b^2q^2 - 2\alpha b^4$$
$$-6\alpha b^2p^2 - 11\alpha p^2d^2]\omega^{10} - b^2c^2k^2p^2q^2\alpha^2\beta^2[-2\alpha^2q^2p^4 - 3\alpha^2q^4p^2 - 2\alpha^2b^2p^4$$
$$-6\alpha^2b^4d^2 - 5\alpha^2p^4d^2 - 3\alpha^2b^4p^2 - 6\alpha^2q^4d^2 - 12\alpha^2qb^3d^2 - 6\alpha^2bq^3p^2$$
$$+2\alpha qb^2p^3a - 12\alpha^2qb^2ad^2 + 2\alpha qpb^3a^2 - 2\alpha^2qbp^4 - 18\alpha^2q^2b^2d^2 + 6\alpha^2q^3pdb$$
$$-4\alpha^2qb^2ap^2 - 12\alpha^2q^3bd^2 + 6\alpha^2qpdb^3 - 9\alpha^2b^2q^2p^2 - 2\alpha qp^2b^2a^2 - q^2p^2b^2a^2$$
$$+2\alpha pbq^3a^2 - 2\alpha^2pbq^4 - 12\alpha^2q^2pbd^2 - 8\alpha^2q^2b^3a + 2\alpha q^2pb^2a^2 - 6\alpha^2q^2pbad$$
$$+4\alpha pb^2aq^3 - 6\alpha^2q^2p^2bd - 2\alpha^2q^2bp^3 - 6\alpha qbap^3d + 2\alpha pbaq^4 - 8\alpha^2b^2q^3a$$
$$-4\alpha^2bq^4a - 22\alpha^2p^2d^2b^2 + 6\alpha^2qbp^3d - 6\alpha^2qb^3p^2 - 4\alpha^2q^2bap^2 + 2\alpha qbp^4a$$
$$+6\alpha^2q^2pdb^2 - 22\alpha^2p^2d^2q^2 - 2\alpha^2qpb^3a + 2\alpha q^2bp^3a - 4\alpha^2qb^4a + 12\alpha qp^2bd^2a$$
$$-12\alpha^2qpbad^2 + 4\alpha q^2pb^3a + 2\alpha qpb^4a - 12\alpha^2q^2bad^2 - 2\alpha^2qpb^4 + 6\alpha qp^2ba^2d$$
$$-4\alpha^2pb^2q^3 - 2\alpha^2qb^2p^3 - 32\alpha^2qbp^2d^2 - 2\alpha^2pbq^3a + 6\alpha qpb^2a^2d - 2\alpha q^2p^2ba^2$$
$$+6\alpha q^2pba^2d - 6\alpha^2qp^2b^2d + 12\alpha qpba^2d^2 - 6\alpha^2qpb^2ad + 6\alpha qp^2db^2a - 6\alpha qpdb^3a$$
$$-6\alpha q^2pdb^2a - 6\alpha q^3pdba + 12\alpha q^2pd^2ba + 6\alpha q^2p^2dba + 12\alpha qpd^2ab^2 - 4\alpha^2q^2pb^3$$
$$-2\alpha^2q^2pb^2a + 4\alpha q^2p^2b^2a + 2\alpha q^3p^2ba + 2\alpha qp^2b^3a - 12\alpha^2qpb^2d^2 - 6\alpha^2qp^2bad]\omega^8$$
$$-b^2c^2k^2p^2q^2\alpha^2\beta^2[-2\alpha^2q^2p^4 - 3\alpha^2q^4p^2 - 2\alpha^2b^2p^4 - 6\alpha^2b^4d^2 - 4\alpha^2q^2bap^2$$
$$-5\alpha^2p^4d^2 - 3\alpha^2b^4p^2 - 6\alpha^2q^4d^2 - 12\alpha^2qb^3d^2 - 6\alpha^2bq^3p^2 + 2\alpha qb^2p^3a$$
$$-12\alpha^2qb^2ad^2 + 2\alpha qpb^3a^2 - 2\alpha^2qbp^4 - 18\alpha^2q^2b^2d^2 - 4\alpha^2qb^2ap^2 - 12\alpha^2q^3bd^2$$
$$+6\alpha^2qpdb^3 - 9\alpha^2b^2q^2p^2 - 2\alpha qp^2b^2a^2 - q^2p^2b^2a^2 + 2\alpha pbq^3a^2 - 2\alpha^2pbq^4$$
$$-12\alpha^2q^2pbd^2 - 8\alpha^2q^2b^3a + 2\alpha q^2pb^2a^2 + 4\alpha pb^2aq^3 - 6\alpha^2q^2p^2bd - 4\alpha^2bq^4a$$
$$-2\alpha^2q^2bp^3 - 6\alpha qbap^3d + 2\alpha pbaq^4 - 8\alpha^2b^2q^3a + 6\alpha^2qbp^3d - 6\alpha^2qb^3p^2$$
$$-22\alpha^2p^2d^2b^2 + 6\alpha^2q^3pdb - 6\alpha^2q^2pbad + 2\alpha qbp^4a + 6\alpha^2q^2pdb^2 - 4\alpha^2qb^4a$$
$$-22\alpha^2p^2d^2q^2 - 2\alpha^2qpb^3a + 2\alpha q^2bp^3a + 12\alpha qp^2bd^2a - 12\alpha^2qpbad^2$$
$$+4\alpha q^2pb^3a + 2\alpha qpb^4a - 12\alpha^2q^2bad^2 - 2\alpha^2qpb^4 + 6\alpha qp^2ba^2d - 4\alpha^2pb^2q^3$$
$$-2\alpha^2qb^2p^3 - 32\alpha^2qbp^2d^2 - 2\alpha^2pbq^3a + 6\alpha qpb^2a^2d + 12\alpha qpba^2d^2 - 2\alpha q^2p^2ba^2$$
$$+6\alpha q^2pba^2d - 6\alpha^2qp^2b^2d - 6\alpha^2qpb^2ad + 6\alpha qp^2db^2a - 6\alpha qpdb^3a$$
$$-6\alpha q^2pdb^2a - 6\alpha q^3pdba + 12\alpha q^2pd^2ba + 6\alpha q^2p^2dba + 12\alpha qpd^2ab^2 - 4\alpha^2q^2pb^3$$
$$-2\alpha^2q^2pb^2a + 4\alpha q^2p^2b^2a + 2\alpha q^3p^2ba + 2\alpha qp^2b^3a - 12\alpha^2qpb^2d^2 - 6\alpha^2qp^2bad]\omega^6$$
$$+b^2c^2k^2p^2q^2\alpha^2\beta^2[-54\alpha q^2b^3a^2p^3d + 5q^2p^2b^2\alpha^2a^2d^2 - 12\alpha q^2p^2b^2a^3d^2$$
$$+12\alpha^2q^3pb^3a^2d - 12\alpha q^3pb^2a^3d^2 - 6\alpha q^4pb^2a^3d - 6\alpha qb^3a^2p^4d + 2q^2b^3a^3p^4$$
$$+2q^3p^4b^3a^2 + p^2b^2q^4a^4 + q^2p^2b^4a^4 + q^2p^4b^4a^2 + 4q^3p^3b^3a^3 + 2q^2p^3b^3a^4 + 2q^3p^3b^2a^4$$
$$+2q^3p^2b^3a^4 + 2q^2p^3b^4a^3 + \alpha^2q^4b^2p^4 + \alpha^2q^2b^4p^4 + 5\alpha^2q^4p^4d^2 + 2\alpha^2b^3q^3p^4$$

$$+5\alpha^2b^4p^4d^2+6\alpha^2qb^3ap^4d+6\alpha^2qb^4ap^3d-12\alpha p^2b^2q^3a^2d^2-6\alpha q^3b^2p^3a^3$$
$$+\alpha^2b^2q^2p^4a^2+12\alpha^2q^3b^3a^2d^2+6\alpha^2q^2b^4a^2d^2+6\alpha^2q^4b^2a^2d^2-2\alpha q^2p^4b^2a^3$$
$$+6\alpha^2q^2p^3b^4d+4\alpha^2q^2p^3b^4a+36\alpha^2q^2p^3d^2b^3-2\alpha q^2p^4b^4a+20\alpha^2qb^3p^4d^2$$
$$+2\alpha^2qb^4ap^4+12\alpha^2qp^3d^2b^4+6\alpha^2qb^4p^4d-6\alpha q^2b^4p^3a^2-8\alpha q^2b^3p^4a^2$$
$$+8\alpha^2q^2b^3ap^4+2\alpha^2q^2b^4a^2p^2-18\alpha p^2b^2a^2dq^4+18\alpha^2q^2b^3p^4d-12\alpha bp^3d^2aq^4$$
$$+30\alpha^2b^2q^3ap^3d-6\alpha bq^4p^4ad+6\alpha^2bq^3ap^4d-6\alpha bq^3a^2p^4d-12\alpha b^2q^4ap^3d$$
$$-12\alpha bp^4d^2aq^3-54\alpha q^3b^2a^2p^3d+8\alpha^2b^3q^3ap^3-6\alpha bq^4a^2p^3d-48\alpha b^2p^3d^2aq^3$$
$$+42\alpha^2b^2q^3ap^2d^2-24\alpha pb^3q^3a^2d^2+24\alpha^2p^2b^3q^3ad-36\alpha p^2b^3q^3a^2d$$
$$+24\alpha^2pb^3q^3ad^2+12\alpha^2pb^2q^4ad^2-12\alpha pb^2q^4a^2d^2+12\alpha p^2bq^4a^2d^2-12\alpha q^2b^4p^3ad$$
$$-24\alpha q^3b^2p^4ad-24\alpha q^2b^3p^4ad-18\alpha q^2p^2b^3a^3d+20\alpha^2bq^3p^4d^2-24\alpha p^2b^3d^2aq^3$$
$$+6\alpha^2q^4b^2p^3d+8\alpha^2b^2q^3ap^4+36\alpha^2b^2p^3d^2q^3+18\alpha^2b^2q^3p^4d-6\alpha b^2q^4p^3a^2$$
$$-8\alpha q^3b^2p^4a^2+6\alpha^2bq^4p^4d-2\alpha b^2q^4p^4a+2\alpha^2bq^4ap^4+6\alpha^2b^4p^2d^2q^2$$
$$-4\alpha p^4b^3aq^3+30\alpha^2p^4d^2b^2q^2+12\alpha^2b^3q^3p^3d+12\alpha^2p^2b^3q^3d^2-12\alpha b^3q^3p^3a^2$$
$$+4\alpha^2q^3b^3a^2p^2-6\alpha q^2b^3p^3a^3+12\alpha^2b^2q^2p^4ad+12\alpha qp^2b^4a^2d^2-12\alpha q^2pb^4a^2d^2$$
$$-18\alpha q^3p^2b^2a^3d+12\alpha^2q^2p^2b^4ad+12\alpha^2q^4p^2b^2ad-48\alpha q^2p^3d^2b^3a$$
$$-6\alpha qb^4a^2p^3d-12\alpha qp^3d^2b^4a+10\alpha^2qb^4ap^2d^2-10\alpha qb^3a^2p^3d^2+30\alpha^2q^2b^3ap^3d$$
$$+42\alpha^2q^2b^3ap^2d^2+10\alpha^2qb^3ap^3d^2+20\alpha^2q^2b^2p^3ad^2-32\alpha q^2b^2p^3a^2d^2$$
$$-24\alpha q^2b^2p^4ad^2+10\alpha q^2bp^4a^2d^2+10\alpha qb^2p^4a^2d^2-18\alpha q^2b^2a^2p^4d$$
$$+12\alpha^2q^2pb^4ad^2-12\alpha q^3pb^3a^3d-12\alpha q^2p^2b^4ad^2-12\alpha q^2p^2b^3a^2d^2$$
$$-6\alpha qb^4p^4ad-18\alpha q^2p^2b^4a^2d-12\alpha qp^4d^2b^3a-12\alpha q^2pb^3a^3d^2-12\alpha p^2b^2q^4ad^2$$
$$+12\alpha^2q^3pb^2a^2d^2-6\alpha q^2pb^4a^3d+12\alpha^2q^2pb^3a^2d^2+6\alpha^2q^2pb^4a^2d$$
$$+6\alpha^2pb^2q^4a^2d+6\alpha^2q^4p^2d^2b^2+6q^3p^2b^2a^4d+24q^2p^3b^3a^3d+12q^2p^3b^3a^2d^2$$
$$+12q^3p^3b^2a^2d^2+12q^3p^2b^3a^3d+6q^2p^2b^4d^2a^2+24q^3p^3b^2a^3d+6q^2p^3b^2a^4d$$
$$+6q^2b^3p^4a^2d+6q^2b^2a^3p^4d+6q^3b^2p^4a^2d+2p^2b^2\alpha^2a^2q^4+6p^3b^2q^4a^2d$$
$$+6q^2p^3b^4a^2d+6q^2p^2b^4a^3d+6q^2p^4b^2a^2d^2+6q^2p^2b^2a^4d^2+6q^2p^2b^3a^4d$$
$$+4\alpha^2q^2p^3b^3a^2+4\alpha^2b^2p^3q^3a^2+12q^2p^2b^3a^3d^2+12q^3p^2b^2a^3d^2+6p^2b^2q^4d^2a^2$$
$$+4\alpha^2q^4b^2p^3a+12\alpha^2bp^3d^2q^4-12\alpha q^2p^3b^2a^3d+12q^3p^3b^3a^2d$$
$$-10\alpha bq^3a^2p^3d^2+6\alpha^2bq^4ap^3d+10\alpha^2bq^4ap^2d^2+12q^3p^2b^3d^2a^2+12q^2p^3b^2a^3d^2$$
$$+10\alpha^2bq^3ap^3d^2-24\alpha b^3q^3ap^3d+12q^2p^2b^3\alpha^2a^2d+6p^2b^2q^4a^3d$$
$$+6q^2p^3b^2\alpha^2a^2d+12q^3p^2b^2\alpha^2a^2d+b^2p^4a^2q^4+2p^3b^2q^4a^3+2q^3b^2a^3p^4]\omega^4$$
$$-b^3a^2c^2k^2p^4q^3\alpha^2\beta^2[\alpha^2qb^3d^2+2\alpha^2q^2b^2d^2+\alpha^2q^3bd^2+b^3qa^2p^2+bq^3a^2p^2$$
$$+2q^2p^2b^2a^2-12\alpha q^3bad^2-10\alpha q^3p^2d^2-12\alpha qb^3ad^2-30\alpha qp^2d^2b^2$$
$$-12\alpha qpd^2b^3-12\alpha q^3pd^2b-6\alpha qp^2db^3-6\alpha q^3p^2db-24\alpha q^2pd^2b^2+6qpdb^3a^2$$
$$+12q^2pdb^2a^2+6q^3pdba^2+6q^3p^2bad+12q^3pbad^2+6q^2p^2ba^2d-30\alpha q^2p^2d^2b$$
$$-12\alpha q^2p^2db^2-10\alpha p^2b^3d^2-6\alpha qp^2db^2a-6\alpha qpdb^3a-12\alpha q^2pdb^2a$$
$$-6\alpha q^3pdba-12\alpha q^2pd^2ba-6\alpha q^2p^2dba-12\alpha qpd^2ab^2-24ab^2d^2q^2\alpha$$
$$-4\alpha q^2p^2b^2a-2\alpha q^3p^2ba-2\alpha qp^2b^3a+6qp^2b^3ad+12qpb^2a^2d^2+12qp^2b^2ad^2$$
$$+24q^2pb^2ad^2+12q^2p^2b^2ad+12q^2pba^2d^2+qp^2ba^2d^2+6qp^2b^2a^2d+12q^2p^2bad^2$$

$$+12qpb^3ad^2]\omega^2+5\alpha^2c^2b^4q^4p^6a^4d^2\beta^2k^2(b+q)^2\Big]+e^{-3\bar{a}\tau_2}\Big[4b^3k^3q^3\beta^3\alpha^3pcd\omega^{12}$$
$$+2b^3ck^3pq^3\alpha^2\beta^3(4d\alpha b^2-bpq\alpha+bpqa+4bd\alpha q+4d\alpha p^2+4d\alpha q^2)\omega^{10}$$
$$-2b^3ck^3pq^3\alpha^2\beta^3[-2b^4d\alpha-2d\alpha q^4-2d\alpha p^4-4pq\alpha bad-4\alpha bdq^3-6q^2d\alpha b^2$$
$$-4q\alpha b^3d+p^3bq\alpha-p^3bqa-p^2bq^2\alpha-8p^2d\alpha q^2+p^2q^2ab-p^2b^2q\alpha+p^2qb^2a$$
$$+p^2qba^2-8p^2d\alpha b^2+pbq^3\alpha-pq^3ab+pb^2q^2\alpha-pb^2q^2a+pq^2ba^2+pb^3q\alpha$$
$$+pqb^2a^2-pqb^3a-4q^2\alpha bad-4q\alpha b^2ad-12p^2bd\alpha q-p^2qba\alpha+4p^2qbad$$
$$-4pq^2\alpha bd-pbq^2a\alpha+4pq^2bad-4pqd\alpha b^2-pb^2qa\alpha+4pqba^2d+4pqb^2ad]\omega^8$$
$$-2b^3ck^3pq^3\alpha\beta^3[-4p^2b^4d\alpha^2-4p^2bq^2\alpha a^2d-p^2q\alpha^2b^4+p^2q^2a^3b^2+4p^2q^3\alpha bad$$
$$-4p^2q^2\alpha^2bad+4p^3bq\alpha a^2d+4p^3q\alpha b^2ad-4p^3q\alpha^2bad+4p^2q^2\alpha b^2ad+8pq^3\alpha b^2ad$$
$$+4pbq^3\alpha a^2d-4pq^2\alpha^2b^2ad+p^2q^3\alpha ba^2-16p^2q^2b^2d\alpha^2-p^2q^2\alpha b^2a^2-p^2qb^3a\alpha^2$$
$$-12p^2q\alpha^2b^3d+p^2qb^3a^2\alpha+p^2b^4qa\alpha+p^2bq^4a\alpha-4pq^4\alpha^2bd-pq^4\alpha^2ab+pq^4\alpha ba^2$$
$$-pq^3\alpha^2b^2a-8pq^3b^2d\alpha^2+pq^3\alpha b^2a^2-pq^2b^3a\alpha^2-8pq^2\alpha^2b^3d+pq^2b^3a^2\alpha$$
$$-4pqb^4d\alpha^2+4pb^2q^2\alpha a^2d-p^4b^2\alpha^2q+8pq^2\alpha b^3ad+p^4b^2qa\alpha+p^4q\alpha ba^2+p^3q^3\alpha^2b$$
$$-p^4b\alpha^2q^2+pq\alpha b^4a^2+p^3q^2b^2a^2-4p^2q\alpha^2b^2ad+4p^3q^2\alpha bad-4pq\alpha^2b^3ad$$
$$+4pq\alpha b^4ad+p^3qb^3\alpha^2-p^3q^3ba\alpha-p^3b\alpha^2aq^2-4p^3q^2\alpha^2bd-3p^3q^2\alpha b^2a$$
$$+p^3q^2\alpha ba^2-4p^3qb^2d\alpha^2-p^3b^2\alpha^2aq+p^3q\alpha b^2a^2-p^3q\alpha b^3a-12p^2q^3\alpha^2bd$$
$$+4p^4q\alpha bad-4p^2b^2q\alpha a^2d+4pq^4\alpha bad+4p^2q\alpha b^3ad+2p^3q^2\alpha^2b^2+p^2q^3b^2a^2$$
$$-p^2q^3\alpha^2b^2-p^2q^4\alpha^2b-4p^2q^4\alpha^2d+p^2q^2b^3a^2-4pq^3\alpha^2bad-4b^4ad\alpha^2q-pq\alpha^2b^4a$$
$$+p^4bq^2a\alpha-p^4q\alpha^2ab-8p^4q\alpha^2bd-p^2q^2b^3\alpha^2-p^2q^3\alpha^2ab+4pb^3q\alpha a^2d$$
$$-4p^4q^2\alpha^2d-4\alpha^2badq^4-8\alpha^2b^2adq^3-8\alpha^2b^3adq^2-4p^4b^2d\alpha^2]\omega^6$$
$$-2b^3ck^3pq^3\alpha\beta^3[-4p^2b^4d\alpha^2-4p^2bq^2\alpha a^2d-p^2q\alpha^2b^4+p^2q^2a^3b^2+4p^2q^3\alpha bad$$
$$-4p^2q^2\alpha^2bad+4p^3bq\alpha a^2d+4p^3q\alpha b^2ad-4p^3q\alpha^2bad+4p^2q^2\alpha b^2ad$$
$$+8pq^3\alpha b^2ad+4pbq^3\alpha a^2d-4pq^2\alpha^2b^2ad+p^2q^3\alpha ba^2-16p^2q^2b^2d\alpha^2$$
$$-p^2q^2\alpha b^2a^2-p^2qb^3a\alpha^2-12p^2q\alpha^2b^3d+p^2qb^3a^2\alpha+p^2b^4qa\alpha+p^2bq^4a\alpha$$
$$-4pq^4\alpha^2bd-pq^4\alpha^2ab+pq^4\alpha ba^2-pq^3\alpha^2b^2a-8pq^3b^2d\alpha^2+pq^3\alpha b^2a^2$$
$$-pq^2b^3a\alpha^2-8pq^2\alpha^2b^3d+pq^2b^3a^2\alpha-pq\alpha^2b^4a-4pqb^4d\alpha^2+4pb^2q^2\alpha a^2d$$
$$-p^4b^2\alpha^2q+8pq^2\alpha b^3ad+p^4b^2qa\alpha+p^4q\alpha ba^2+p^3q^3\alpha^2b-p^4b\alpha^2q^2$$
$$+pq\alpha b^4a^2+p^3q^2b^2a^2-4p^2q\alpha^2b^2ad+4p^3q^2\alpha bad-4pq\alpha^2b^3ad+4pb^3q\alpha a^2d$$
$$+4pq\alpha b^4ad+p^3qb^3\alpha^2-p^3q^3ba\alpha-p^3b\alpha^2aq^2-4p^3q^2\alpha^2bd-3p^3q^2\alpha b^2a$$
$$+p^3q^2\alpha ba^2-4p^3qb^2d\alpha^2-p^3b^2\alpha^2aq+p^3q\alpha b^2a^2-p^3q\alpha b^3a-12p^2q^3\alpha^2bd$$
$$-p^2q^3\alpha^2ab+4p^4q\alpha bad-4p^2b^2q\alpha a^2d+4pq^4\alpha bad+4p^2q\alpha b^3ad+2p^3q^2\alpha^2b^2$$
$$+p^2q^3b^2a^2-p^2q^3\alpha^2b^2-p^2q^4\alpha^2b-4p^2q^4\alpha^2d+p^2q^2b^3a^2-4pq^3\alpha^2bad$$
$$-4b^4ad\alpha^2q+p^4bq^2a\alpha-p^4q\alpha^2ab-8p^4q\alpha^2bd-p^2q^2b^3\alpha^2-4p^4q^2\alpha^2d-4\alpha^2badq^4$$
$$-8\alpha^2b^2adq^3-8\alpha^2b^3adq^2-4p^4b^2d\alpha^2]\omega^4-2b^4a^2c(b+q)k^3p^3q^4\alpha\beta^3[-p^2b^2q\alpha$$
$$+p^2qb^2a-4p^2d\alpha b^2-pb^2qa\alpha-4pqd\alpha b^2+4pqb^2ad+pqb^2a^2-4q\alpha b^2ad-p^2bq^2\alpha$$
$$+p^2q^2ab-8p^2bd\alpha q-p^2qba\alpha+4p^2qbad+p^2qba^2-pbq^2a\alpha-4pq^2\alpha bd$$
$$+4pq^2bad+pq^2ba^2-4pq\alpha bad+4pqba^2d-4q^2\alpha bad-4p^2d\alpha q^2]\omega^2$$

$$
\begin{aligned}
&+4a^4b^5cdk^3p^5q^5\alpha\beta^3(b+q)^2\Big]+e^{-4\tilde{a}\tau_2}\Big[b^4k^4q^4\beta^4\alpha^2\omega^{12}+2b^4k^4q^4\beta^4\alpha^2\\
&\times(q^2+p^2+b^2+bq)\omega^{10}-b^4k^4q^4\alpha\beta^4[-2\alpha q^3b-2\alpha qb^3-\alpha q^4-\alpha b^4-\alpha p^4\\
&+2bpqa^2+2pbq^2a+2pb^2qa+2p^2qba-2q^2\alpha ba-6\alpha qbp^2-2pq^2\alpha b-2q\alpha b^2a\\
&-4p^2q^2\alpha-4\alpha b^2p^2-2pq\alpha ba-3\alpha q^2b^2-2\alpha qb^2p]\omega^8-2b^4k^4q^4\alpha\beta^4[-\alpha q^2b^2pa\\
&-\alpha qb^3ap-q^2\alpha bap^2-\alpha qbap^3-\alpha q^3bap-q\alpha b^2ap^2-\alpha q^4ba-4\alpha q^2b^2p^2\\
&-2\alpha q^2b^3a-2\alpha qbp^4-\alpha q^2bp^3-\alpha qb^2p^3-3\alpha qb^3p^2-qb^2p^2a^2+bqp^4a+qb^3pa^2\\
&-3\alpha q^3bp^2-2\alpha q^3b^2a+2q^2b^3pa+bqp^3a^2+q^2b^2p^2a+q^3bap^2-q^2bp^2a^2+qb^2p^3a\\
&-2pq^3\alpha b^2-2pq^2\alpha b^3+2q^3b^2pa-p^4q^2\alpha-p^2q^4\alpha+q^3bpa^2-\alpha b^4p^2+q^2b^2pa^2\\
&+q^4bpa-p^4b^2\alpha+q^2bp^3a+qb^3ap^2-\alpha q^4bp+qb^4pa-\alpha qb^4p-\alpha qb^4a]\omega^6\\
&+b^4k^4q^4\beta^4[p^2q^4b^2a^2+\alpha^2b^4p^4+\alpha^2q^4p^4+p^2q^2b^2a^4+p^2q^2b^4a^2+2p^2q^3b^3a^2\\
&+q^2p^2b^2\alpha^2a^2+2\alpha^2pb^2q^4a+2\alpha p^2bq^4a^2-2\alpha pb^2q^4a^2-2\alpha p^2b^2q^3a^2+4\alpha^2pb^3q^3a\\
&-4\alpha pb^3q^3a^2+4\alpha^2q^2b^2p^3a+2\alpha^2q^2pb^3a^2-2\alpha q^2pb^3a^3-2\alpha q^3pb^2a^3+2\alpha^2q^2pb^4a\\
&-2\alpha q^2pb^4a^2+2\alpha qp^2b^4a^2-2\alpha q^2p^2b^3a^2+2\alpha^2q^3pb^2a^2+8\alpha^2q^2b^3ap^2-6\alpha q^2b^2p^3a^2\\
&-4\alpha q^2b^2p^4a-2\alpha qp^3b^4a-2\alpha qp^4b^3a+2\alpha^2qb^4ap^2+8\alpha^2b^2q^3ap^2+2\alpha^2bq^4ap^2\\
&-2\alpha bp^3aq^4-2qb^3p^3a^2\alpha-2q^2b^4\alpha ap^2-2q^3bp^3a^2\alpha-2\alpha bp^4aq^3-4q^3b^3\alpha ap^2\\
&-2q^2b^2\alpha p^2a^3-8q^3b^2\alpha ap^3-2q^4b^2\alpha ap^2+2q^3bap^3\alpha^2+2qb^3ap^3\alpha^2+2q^2p^3b^3a^2\\
&+2q^2b\alpha p^4a^2-8q^2b^3\alpha ap^3+2qb^2\alpha p^4a^2+p^4q^2b^2a^2+2p^2q^3\alpha^2b^3+2q^3p^2b^2a^3\\
&+2q^2p^2b^3a^3+2q^3p^3b^2a^2+2q^2p^3b^2a^3+4\alpha^2bq^3p^4+6\alpha^2b^2p^3q^3+2\alpha^2bp^3q^4\\
&+6\alpha^2b^2q^2p^4+6\alpha^2q^2p^3b^3+4\alpha^2qb^3p^4+2\alpha^2qp^3b^4+2\alpha^2q^3b^3a^2+\alpha^2q^4b^2a^2\\
&+\alpha^2q^2b^4a^2+p^2q^2\alpha^2b^4+p^2q^4\alpha^2b^2]\omega^4-2a^2b^5k^4p^2q^5(b+q)\beta^4[-\alpha qb^2p\\
&-\alpha b^2p^2-q\alpha b^2a+pb^2qa-pq^2\alpha b+pbq^2a-pq\alpha ba+bpqa^2+p^2qba-q^2\alpha ba\\
&-2\alpha qbp^2-p^2q^2\alpha]\omega^2+a^4b^6k^4p^4q^6\beta^4(b+q)^2\Big]+p^4c^4\alpha^6\omega^{16}+p^4c^4\alpha^6\\
&(2bq+2q^2+p^2+2d^2+2b^2)\omega^{14}+p^4c^4\alpha^5(2\alpha b^2p^2+2p^2q^2\alpha+2p^2\alpha d^2\\
&-2pbdq\alpha+2pbadq+\alpha q^4+\alpha d^4+2q^2\alpha ba+2q\alpha b^2a+4\alpha d^2bq+4\alpha d^2q^2+4\alpha d^2b^2\\
&+3\alpha b^2q^2+2\alpha b^3q+2\alpha bq^3+\alpha b^4)\omega^{12}-p^4c^4\alpha^5(2pb^2qa^2d+2pbq^2a^2d\\
&-2\alpha pbq^2ad-2\alpha pbqad^2-2\alpha p^2bqad-2pb^3adq+2pbqa^2d^2-2pb^2q^2ad-2pd^3baq\\
&-2\alpha pb^2qad+2p^2bad^2q-2p^3badq+2p^2b^2aqd-2pq^3bad+2p^2badq^2+2p^2bqa^2d\\
&+2pabd^2q^2+2pab^2d^2q-4\alpha b^2qad^2-4\alpha bq^2ad^2-2\alpha pbd^2q^2-2\alpha p^2bq^2d\\
&+2\alpha p^3bdq+2\alpha pq^3bd+2\alpha pb^3dq+2\alpha pb^2q^2d+2\alpha pd^3bq-2\alpha p^2bq^2a-2\alpha pb^2d^2q\\
&-2\alpha p^2b^2qa-2\alpha p^2bqd^2-2\alpha p^2b^2dq-2\alpha b^4d^2-\alpha p^2b^4-2\alpha b^2d^4-2\alpha q^4d^2\\
&-2\alpha q^2d^4-\alpha p^2q^4-\alpha p^2d^4+2\alpha bqp^4-6\alpha q^2d^2b^2-4\alpha b^3q^2a-2\alpha bq^4a\\
&-2\alpha b^4qa-4\alpha bq^3d^2-2\alpha bqd^4-4\alpha b^3qd^2-4\alpha b^2q^3a-4\alpha p^2q^2d^2-4\alpha p^2b^2d^2)\omega^{10}\\
&-p^4c^4\alpha^4(-2\alpha p^3d^3baq-3\alpha^2q^2d^4b^2+2\alpha pd^4abq^2+q^2p^2b^2\alpha^2a^2\\
&+4\alpha p^2b^2q^3ad+4\alpha p^2b^3q^2ad-2\alpha^2pbqad^4+2\alpha pd^4ab^2q+2\alpha p^2d^3b^2aq-2\alpha pb^2q^2d^3a\\
&-2\alpha^2q^2bad^4-2qp^2b\alpha^2d^4-p^2b^2a^2d^2q^2+2\alpha^2pq^3d^3b+2\alpha^2pb^3d^3q+2\alpha^2p^3d^3bq\\
&-2\alpha^2pd^4bq^2-2\alpha^2p^2d^3b^2q-2\alpha^2p^2d^3bq^2-2\alpha^2pd^4b^2q+2\alpha pbqa^2d^4+2\alpha p^2bqa^2d^3\\
&+2\alpha pb^2qa^2d^3-2\alpha^2pbd^2q^4-4\alpha^2pb^2d^2q^3-4\alpha^2p^2b^2q^3d-2\alpha^2p^2bq^4d\\
&-4\alpha^2qb^4ad^2-8\alpha^2q^2b^3ad^2-4\alpha^2q^2pd^2b^3-2\alpha^2qpd^2b^4-2\alpha^2pb^2qad^3
\end{aligned}
$$

$$-2\alpha^2qp^2b^4d-4\alpha^2q^2p^2b^3d-2\alpha^2q^2b^3ap^2-2\alpha^2q^2bp^3d^2+2\alpha^2qbp^4d^2+2\alpha^2q^2b^2p^3d$$
$$-2\alpha^2qb^2p^3d^2-2\alpha^2qb^2p^4d-2\alpha^2q^2bp^4d+2\alpha^2qb^3p^3d-2\alpha^2qb^3p^2d^2-2\alpha^2qb^4ap^2$$
$$-8\alpha^2b^2q^3ad^2-4\alpha^2bq^4ad^2+2\alpha^2bq^3p^3d-2\alpha^2bq^3p^2d^2-3\alpha^2p^2d^2b^2q^2$$
$$-2\alpha^2b^2q^3ap^2+2\alpha pbq^2a^2d^3+4\alpha pb^2d^2aq^3+2\alpha q^2pb^3a^2d+2\alpha p^2bq^3a^2d$$
$$-2\alpha^2bq^4ap^2-2\alpha^2bq^3d^4-2\alpha^2b^3qd^4-2\alpha^2p^2b^2d^4-2q^2p^2\alpha^2d^4+2\alpha p^2d^3baq^2$$
$$+2\alpha p^2d^4baq-2qp^2b\alpha^2ad^3-2\alpha pq^3d^3ba-2\alpha^2pbq^2ad^3-2q^2p^2b^2\alpha^2ad$$
$$-2\alpha pb^3d^3aq-2\alpha^2q^4p^2d^2+2\alpha^2bq^3p^4+3\alpha^2b^2q^2p^4-2\alpha^2b^4p^2d^2+2\alpha^2qb^3p^4$$
$$-2\alpha^2q^3b^3a^2-\alpha^2q^4b^2a^2-\alpha^2q^2b^4a^2+2\alpha p^2bd^2aq^3+2\alpha pbq^4a^2d-2\alpha^2qb^2ap^2d^2$$
$$-2\alpha^2p^2bq^3ad+2\alpha p^2bq^4ad-2\alpha^2pb^2q^3ad+2\alpha pbd^2aq^4+2\alpha pb^2q^3a^2d$$
$$+2\alpha pbq^3a^2d^2-2\alpha^2pbq^4ad-2\alpha^2pbq^3ad^2+2\alpha qp^2b^4ad+2\alpha qp^2d^2b^3a$$
$$+2\alpha qp^2b^3a^2d-2\alpha^2qp^2b^3ad-2\alpha^2qpb^4ad+4\alpha q^2pd^2b^3a+2\alpha qpb^4a^2d+2\alpha qpd^2b^4a$$
$$+2\alpha qpb^3a^2d^2-2\alpha^2q^2pb^3ad-2\alpha^2qpb^3ad^2-2\alpha^2q^2pb^2ad^2+2\alpha q^2pb^2a^2d^2$$
$$-2\alpha q^2p^2ba^2d^2+2\alpha qb^2p^4ad+4\alpha q^2p^2b^2ad^2-2\alpha qp^2b^2a^2d^2+2\alpha q^2p^2b^2a^2d$$
$$-2\alpha q^2b^2ap^3d+2\alpha q^2bp^4ad+2\alpha q^2bp^3d^2a+2\alpha qbp^4d^2a+2\alpha qb^2p^3d^2a$$
$$-2\alpha^2q^2bap^2d^2-2\alpha qb^3ap^3d-2\alpha bq^3ap^3d-\alpha^2q^4d^4-\alpha^2b^4d^4+2\alpha^2pb^2q^2d^3$$
$$-2\alpha^2qb^2ad^4)\omega^8-p^4c^4\alpha^4(-4\alpha q^2b^3a^2p^3d+2q^2p^2b^2\alpha^2a^2d^2-4\alpha^2q^3pb^3a^2d$$
$$+2\alpha q^3pb^2a^3d^2+2\alpha q^4pb^2a^3d-2\alpha^2pq^4d^4b-2\alpha^2p^2q^4d^3b+4\alpha^2p^3b^2q^2d^3$$
$$-4\alpha^2pb^3q^2d^4-4\alpha^2pb^2q^3d^4+2\alpha^2p^3q^3d^3b-4\alpha^2b^3q^2ad^4-4\alpha^2b^2q^3ad^4$$
$$-2\alpha^2p^2b^2q^2d^4-2\alpha^2pb^4d^4q-2\alpha^2p^2b^4d^3q+2\alpha^2p^3b^3d^3q-2\alpha^2p^2b^3q^2d^3$$
$$-2\alpha^2p^2b^3qd^4-2\alpha^2p^2bq^3d^4-2\alpha^2p^3d^4b^2q-2\alpha^2p^3d^4bq^2-2\alpha^2p^4d^3b^2q$$
$$-2\alpha^2p^4d^3bq^2-2\alpha^2p^2b^2q^3d^3-2\alpha^2bq^4ad^4-2\alpha^2b^4qad^4+2p^2b^2q^3a^2d^3$$
$$+2p^2b^2q^2a^3d^3+2p^2b^3q^2a^2d^3-6\alpha p^2b^2q^3a^2d^2+\alpha^2b^2q^2p^4a^2+2p^3b^2q^2a^2d^3$$
$$-4\alpha^2q^3b^3a^2d^2-2\alpha^2q^2b^4a^2d^2-2\alpha^2q^4b^2a^2d^2-2\alpha^2q^2p^3d^2b^3-2\alpha qp^2b^4a^2d^2$$
$$+2\alpha^2qb^3p^4d^2-2\alpha^2qp^3d^2b^4-2\alpha^2qb^4p^4d-4\alpha^2q^2b^3p^4d+2\alpha^2q^2b^3ap^4$$
$$-\alpha^2q^2b^4a^2p^2+2\alpha p^2b^2a^2dq^4+2\alpha bp^3d^2aq^4+4\alpha^2b^2q^3ap^3d+2\alpha bq^4p^4ad$$
$$+2\alpha bp^4d^2aq^3-4\alpha q^3b^2a^2p^3d+4\alpha pb^3q^3a^2d^2-4\alpha^2p^2b^3q^3ad+4\alpha p^2b^3q^3a^2d$$
$$-2\alpha^2pb^2q^4ad^2+2\alpha pb^2q^4a^2d^2-2\alpha p^2bq^4a^2d^2+4\alpha q^3b^2p^4ad-4\alpha^2pb^3q^3ad^2$$
$$+4\alpha q^2b^3p^4ad+2\alpha q^2p^2b^3a^3d+2\alpha^2bq^3p^4d^2+2\alpha^2b^2q^3ap^4-2\alpha^2bq^4p^4d$$
$$-2\alpha^2b^2p^3d^2q^3-4\alpha^2b^2q^3p^4d+4\alpha^2p^4d^2b^2q^2-2\alpha^2q^3b^3a^2p^2+2\alpha^2b^2q^2p^4ad$$
$$-\alpha^2p^2q^4d^4+2\alpha q^2pb^4a^2d^2+2\alpha q^3p^2b^2a^3d-2\alpha^2q^2p^2b^4ad-2\alpha^2q^4p^2b^2ad$$
$$+2\alpha qp^3d^2b^4a-2\alpha^2qb^4ap^2d^2+4\alpha^2q^2b^3ap^3d+4\alpha^2q^2b^2p^3ad^2-6\alpha q^2b^2p^3a^2d^2$$
$$+2\alpha q^2b^2p^4ad^2-2\alpha q^2b^2a^2p^4d-2\alpha^2q^2pb^4ad^2+4\alpha q^3pb^3a^3d-6\alpha q^2p^2b^3a^2d^2$$
$$+2\alpha qb^4p^4ad+2\alpha q^2p^2b^4a^2d+2\alpha qp^4d^2b^3a+2\alpha q^2pb^3a^3d^2-2\alpha^2q^3pb^2a^2d^2$$
$$+2\alpha q^2pb^4a^3d-2\alpha^2q^2pb^3a^2d^2-2\alpha p^3b^3d^3aq-2\alpha^2pb^3qad^4-2\alpha^2pbq^3ad^4$$
$$-2\alpha^2p^2b^3qad^3-2\alpha^2p^2bq^3ad^3+2\alpha pb^2q^2a^2d^4+2\alpha pq^4d^4ab+2\alpha p^2b^4d^3aq$$
$$+2\alpha pbq^3a^2d^4+2\alpha p^2b^2q^2ad^4+2\alpha p^2b^3qa^2d^3+2\alpha p^2bq^3a^2d^3+2\alpha pb^3qa^2d^4$$
$$+2\alpha pb^3q^2a^2d^3+2\alpha pb^2q^3a^2d^3+2\alpha p^2b^3d^4aq+2\alpha pb^4d^4aq+2\alpha p^4d^4baq$$
$$+2\alpha p^3d^4ab^2q+2\alpha p^3d^4abq^2+2\alpha p^4d^3baq^2+4\alpha pb^3q^2ad^4+4\alpha pb^2q^3ad^4$$

$$
\begin{aligned}
&-6\alpha p^3b^2q^2ad^3+2\alpha p^2q^3d^4ba+2\alpha p^2q^4d^3ba-2\alpha p^2bq^2a^2d^4+2\alpha pbq^4a^2d^3\\
&-2\alpha p^2b^2a^2d^3q^2-2\alpha^2pb^4qad^3+2\alpha p^4d^3b^2aq+2\alpha pb^4qa^2d^3-2\alpha^2pb^2q^2ad^4\\
&-2\alpha^2pb^3ad^3q^2-2\alpha^2pb^2ad^3q^3-2\alpha p^3q^3d^3ba-2\alpha p^2b^2qa^2d^4-2\alpha^2pbq^4ad^3\\
&-2\alpha^2q^2pb^4a^2d-2\alpha^2pb^2q^4a^2d+2q^2p^3b^3a^2d^2+2q^3p^3b^2a^2d^2-p^2b^2\alpha^2a^2q^4\\
&-2\alpha^2bq^4ap^2d^2+2q^2p^3b^2a^3d^2+2q^2p^2b^3a^3d^2+2q^3p^2b^2a^3d^2-2\alpha^2bp^3d^2q^4\\
&-2\alpha q^2p^3b^2a^3d-2q^2p^2b^3\alpha^2a^2d+2q^2p^3b^2\alpha^2a^2d-2q^3p^2b^2\alpha^2a^2d\\
&-\alpha^2p^2b^4d^4)\omega^6+bc^4dp^4q\alpha^4(2\alpha p^2b^3a^2d^3-8\alpha qp^4b^2ad^2-8\alpha qp^4b^2a^2d\\
&+2\alpha^2q^3pbad^3-8\alpha q^2p^4bad^2-2\alpha q^3p^4bad-4\alpha q^3p^3abd^2+\alpha^2qp^2b^3a^2d\\
&+4\alpha^2qp^2b^2a^2d^2+2\alpha^2qpd^3b^2a^2+8q^2p^3d^2ba^3+4\alpha^2q^2p^2d^2ba^2-6\alpha q^2p^3dba^3\\
&+2\alpha^2q^2pd^3ba^2+qp^2d^3ba^4-2\alpha qpd^3b^2a^3-2\alpha q^2pd^3ba^3+4\alpha^2q^2p^3dba^2\\
&+q^3p^2dba^4+qp^2db^3a^4+2qp^3db^3a^3+qp^4d^3ba^2+2q^3p^3d^2ba^2+2qp^2b^3a^3d^2\\
&-2\alpha qp^4d^2ba^2+4\alpha^2q^3p^2bad^2-8\alpha q^2p^3d^3ba+8\alpha^2q^2p^3b^2ad+\alpha^2q^3d^3ba^2\\
&-2\alpha qp^4b^3a^2-2\alpha qp^4b^2a^3+\alpha^2qd^3b^3a^2+\alpha^2qp^4b^3d+2\alpha^2qp^4b^3a\\
&+6\alpha^2qp^4b^2d^2+2\alpha^2qp^3b^3d^2+2\alpha^2q^3p^3bd^2+2\alpha^2q^2p^2b^2d^3+2\alpha^2qp^4b^2a^2\\
&+6\alpha^2q^2p^4d^2b+6\alpha^2qp^3b^2d^3+6\alpha^2q^2p^3d^3b+2\alpha^2q^2d^3b^2a^2+\alpha^2q^3p^4bd\\
&-2\alpha p^4d^3b^2a+2q^2p^2d^2ba^4+2q^3p^2d^2ba^3+qp^4db^3a^2+\alpha^2q^3p^2dba^2+2qp^3d^2ba^4\\
&+2\alpha^2q^3pd^2ba^2+2q^2p^2db^2a^4-4\alpha q^2p^2d^3b^2a-2\alpha p^3b^3d^3a+2\alpha^2p^3q^3d^3\\
&+2qp^2d^2b^2a^4-2\alpha p^4d^2b^3a+2\alpha^2q^3p^4d^2+2p^2b^2a^2d^3q^2+2\alpha^2p^3b^3d^3\\
&+2\alpha^2b^3p^4d^2-2\alpha q^3p^4ba^2+2\alpha^2q^3p^4ba+2q^2p^3d^3ba^2-2\alpha q^2p^4ba^3+2q^2p^2d^3ba^3\\
&-12\alpha q^2p^3d^2ba^2+4\alpha^2q^2p^3d^2ba+2q^2p^4dba^3+2q^2p^3dba^4+2q^3p^3dba^3\\
&+2\alpha^2qp^2d^3b^2a-2\alpha qp^3d^2ba^3-6\alpha qp^2d^2b^2a^3+4\alpha^2q^3p^3dba-2\alpha q^3p^2d^3ba\\
&-8\alpha q^2p^4dba^2-6\alpha q^2p^2d^2ba^3+q^3p^4dba^2-6\alpha qp^3b^3a^2d-2\alpha qpb^3a^2d^3\\
&-6\alpha q^3p^2ba^2d^2-2\alpha q^2p^2ba^2d^3-4\alpha q^2pb^2a^2d^3-2\alpha qpb^3a^3d^2-4\alpha q^2pb^2a^3d^2\\
&+4\alpha^2qp^3b^3ad+2\alpha^2q^2p^2b^2a^2d-4\alpha q^2p^4b^2ad-12\alpha q^2p^3b^2a^2d-2\alpha q^3pba^2d^3\\
&-12\alpha q^2p^2b^2a^2d^2-12\alpha qp^3b^2a^2d^2-2\alpha qp^2b^2a^2d^3+2\alpha^2qp^4b^2da\\
&+2qp^3b^2a^2d^3+2qp^3b^3a^2d^2+4q^2p^2b^2a^3d^2+2qp^2b^2a^3d^3+8qp^3b^2a^3d^2\\
&+2\alpha^2q^2p^4ba^2+p^2b^3qa^2d^3+p^2bq^3a^2d^3+4q^2p^3b^2a^3d-2\alpha qp^4b^3ad-6\alpha qp^3b^2a^3d\\
&+4\alpha^2q^2pa^2b^2d^2+2\alpha^2q^2p^2bad^3-6\alpha qp^2b^3a^2d^2-2\alpha q^3pd^2ba^3-4\alpha qp^4d^3ba\\
&+2qp^3db^2a^4+4q^2b^2p^3a^2d^2+2q^2b^2a^2p^4d+2\alpha^2qpa^2b^3d^2+4\alpha^2qp^3b^2ad^2\\
&+2\alpha^2qpb^3ad^3+4\alpha^2q^2pb^2ad^3+4\alpha^2qp^3b^2a^2d+8\alpha^2q^2p^2d^2b^2a-2\alpha qp^4dba^3\\
&-8\alpha qp^3b^2ad^3+2\alpha^2q^2p^4dba-8\alpha q^2p^3d^2b^2a+2qp^3d^3ba^3-2\alpha qp^3d^3ba^2\\
&+2qp^4d^2ba^3-4\alpha qp^3d^2b^3a-2\alpha qp^2d^3b^3a+4\alpha^2qp^2d^2b^3a+2q^2p^4d^2ba^2\\
&+2qp^4d^2b^2a^2+2qp^4db^2a^3-2\alpha qp^2d^3ba^3-6\alpha q^3p^3dba^2-4\alpha q^2b^2a^2p^4-2\alpha p^3q^3d^3a\\
&-2\alpha p^4d^2aq^3+2\alpha^2b^2q^2p^4d+4\alpha^2q^2b^2p^3d^2+\alpha^2p^2b^3qd^3+\alpha^2p^2bq^3d^3\\
&+4\alpha^2b^2q^2p^4a+2\alpha p^2q^3a^2d^3-2\alpha p^4d^3aq^2)\omega^4-p^6c^4\alpha^4b^2a^2d^2q^2(2qp^2a^2d\\
&-2\alpha q^2pd^2-2\alpha p^2bad-2\alpha pbd^2a-2\alpha q^2ad^2-2\alpha q^2ap^2+2qp^2d^2a+d^2q^2\alpha^2\\
&+p^2d^2a^2+2qpa^2d^2+2q^2pd^2a+2q^2pa^2d+2p^2q^2ad-4\alpha qpbd^2+2qp^2b\alpha^2
\end{aligned}
$$

$$-2\alpha pb^2d^2 - 2\alpha p^2b^2d - 4\alpha qp^2bd - 2\alpha b^2ad^2 - 2\alpha qp^2ad - 2\alpha qpd^2a - 2\alpha b^2ap^2$$
$$+2p^2b^2ad + 2pb^2d^2a + 2p^2bd^2a + 2pba^2d^2 + 2pb^2a^2d + 2p^2ba^2d - 4\alpha q^2pad$$
$$+\alpha^2p^2b^2 - 4\alpha p^2baq + 2\alpha^2q^2pd + 4qbp^2ad + 4pbad^2q + 2\alpha^2pb^2d + q^2p^2a^2$$
$$+4\alpha^2qpbd + q^2p^2\alpha^2 - 2\alpha q^2p^2d + 2qp^2ba^2 - 8\alpha qpbad + 4qpdba^2 - 4\alpha pb^2ad$$
$$+2\alpha^2qbd^2 - 4\alpha qbd^2a + p^2b^2a^2 + d^2b^2\alpha^2)\omega^2.$$

$$\tilde{F}(\tau_1,\omega_1) = \frac{\tilde{S}_{dd1n}}{\tilde{S}_{dd1d}} \quad , \qquad \text{(A.2)}$$

where

$$\tilde{S}_{dd1d} = \Big[\alpha cp(d\alpha cp + betabkqe^{-\tilde{a}\tau_2})\Big]\Big\{\beta bkq(bapq - b\omega^2\alpha - \omega^2\alpha q$$
$$-\alpha\omega^2p)e^{-a\tau_1 - 2\tilde{a}\tau_2} + \Big[cp\alpha[(-pb\alpha - p\alpha q - \alpha db - \alpha bq$$
$$-\alpha dq)\omega^2 + pabqd] + \sin((\tau_1+\tau_2)\omega)c\alpha^2\omega p^2(-\omega^2 + db + dq)$$
$$-\cos((\tau_1+\tau_2)\omega)c\alpha^2\omega^2p^2(d+b+q)\Big]e^{-a\tau_1 - \tilde{a}\tau_2}\Big\}$$

and

$$\tilde{S}_{dd1n} = \omega\Big\{e^{-a\tau_1-\tilde{a}\tau_2}\Big[w^8\alpha^4c^3p^3d + w^6d\alpha^4c^3p^3(p^2+d^2+bq+b^2+q^2) + w^4d\alpha^3c^3p^3$$
$$\times[d^2\alpha p^2 + b^2\alpha qa + q^2\alpha ba + pdabq - d\alpha pbq + bp^2q\alpha + bqd^2\alpha + d^2\alpha q^2$$
$$+\alpha p^2b^2 + \alpha p^2q^2 + d^2\alpha b^2] - w^2d\alpha^3c^3p^3[-b^2qd^2\alpha a - bqd^2\alpha pa$$
$$-pq^2d\alpha ba - bq^2d^2\alpha a - b^2p^2q\alpha a - bp^2q^2\alpha a - bp^2q\alpha ad + d^2p^2abq$$
$$+p^2a^2bqd + d^2pb^2aq + d^2pq^2ab - 2bd^2\alpha p^2q - b^2p^2q\alpha d$$
$$+b^2pa^2qd + p^2b^2daq + p^2q^2dab + q^2pa^2bd + d^2pa^2bq - b^2d\alpha pqa$$
$$-bp^2q^2\alpha d - b^2qd^2\alpha p - bq^2d^2\alpha p - b^2d^2\alpha p^2 - p^2q^2d^2\alpha]$$
$$+a^2bd^3\alpha^3c^3p^5q(b+q) + \cos((\tau_1+\tau_2)\omega)[w^6\alpha^4c^3p^5d + w^4c^3dp^4\alpha^4(d^2p$$
$$+2bpq + b^2p + q^2p + bqa) - w^2c^3dp^4\alpha^3(-\alpha pb^2qa - d^2bq\alpha a - \alpha pdabq$$
$$-\alpha pbq^2a - 2bqd^2\alpha p - \alpha d^2pb^2 - \alpha q^2d^2p + pda^2bq) + a^2bd^3\alpha^3c^3p^5q(b+q)]$$
$$+\sin((\tau_1+\tau_2)\omega)[-\alpha^4c^3p^4dw^7 - \alpha^4c^3p^4d(d^2+2bq+b^2+q^2)w^5 - \alpha^4c^3p^4d$$
$$\times(b^2qa + 2d^2bq + b^2d^2 - pbqa + d^2q^2 + q^2ba)w^3 + abc^3d^2p^4q\alpha^3(-db\alpha$$
$$-\alpha pb + bap + dap - dq\alpha - p\alpha q + pqa)]\Big] + e^{-a\tau_1-2\tilde{a}\tau_2}\Big[w^8\alpha^3c^2p^2betabkq$$
$$+w^6bq\alpha^3c^2p^2\beta k(p^2+3d^2+bq+b^2+q^2) + w^4bq\alpha^2c^2p^2\beta k[3d^2\alpha p^2 + \alpha b^2qa$$
$$+\alpha q^2ba + 2pdabq - 2d\alpha pbq + bp^2q\alpha + 3d^2bq\alpha + 3\alpha q^2d^2 + \alpha p^2b^2 + \alpha p^2q^2$$

$$+3\alpha b^2d^2] - w^2bq\alpha^2c^2p^2\beta k[-3\alpha d^2b^2qa - 3bqd^2\alpha pa - 3\alpha d^2bq^2a - b^2p^2q\alpha a$$
$$-bp^2q^2\alpha a - 2bp^2q\alpha ad + 3d^2p^2abq + 2p^2a^2bqd + 3d^2pb^2aq + 3d^2pq^2ab$$
$$+2pdb^2a^2q + 2p^2b^2daq + 2p^2q^2dab + 2pdq^2a^2b + 3pd^2a^2bq - 2\alpha pdb^2qa$$
$$-2\alpha pdbq^2a - 6bd^2\alpha p^2q - 2b^2p^2q\alpha d - 2bp^2q^2\alpha d - 3b^2qd^2\alpha p - 3bq^2d^2\alpha p$$
$$-3b^2d^2\alpha p^2 - 3p^2q^2d^2\alpha] + 3a^2b^2p^4\beta kq^2d^2\alpha^2c^2(b+q) + \sin((\tau_1+\tau_2)\omega)$$
$$\times[-\alpha^3c^2p^3\beta bkqw^7 - w^5bc^2kp^3\alpha^3\beta q(q^2+2bq+b^2-pd+2d^2)$$
$$-w^3\alpha^3c^2p^3\beta bkq(-pdb^2+b^2aq+2b^2d^2-bpaq-2bpqd+baq^2+4d^2bq$$
$$-bqda - pdq^2 + 2d^2q^2) + wab^2c^2dkp^3q^2\alpha^2\beta(-2bd\alpha - b\alpha p + 2bpa + 2pda$$
$$-2d\alpha q - p\alpha q + 2paq)] + \cos((\tau_1+\tau_2)\omega)[w^6bc^2\alpha^3p^3\beta kq(p+d)$$
$$+w^4\alpha^3c^2p^3\beta bkq(pb^2+db^2+2bpq+baq+2dbq+pq^2+2d^2p+dq^2)$$
$$-w^2bc^2kp^3q\alpha^2\beta(-2q^2\alpha d^2p - q^2\alpha bad - q^2\alpha bpa - q\alpha db^2a$$
$$-2q\alpha bd^2a - q\alpha pdab - 4d^2bq\alpha p - q\alpha pb^2a + 2qpba^2d - 2d^2pb^2\alpha)$$
$$+2a^2b^2p^4\beta kq^2d^2\alpha^2c^2(b+q)]\Big] + e^{-a\tau_1-3\tilde{a}\tau_2}\Big[3b^2q^2\beta^2k^2cp\alpha^2dw^6$$
$$+w^4b^2q^2\beta^2k^2cp\alpha[3q^2\alpha d + pbqa + 3p^2\alpha d - bq\alpha p + 3bq\alpha d + 3b^2\alpha d]$$
$$-w^2b^2q^2\beta^2k^2cp\alpha[3bq^2apd + 3b^2qapd + 3qpba^2d + 3p^2bqad - bp^2q\alpha a$$
$$+b^2pa^2q + q^2pa^2b + p^2b^2qa + p^2q^2ba + p^2a^2bq - 3b^2q\alpha dp - 3bq^2\alpha dp$$
$$-3b^2d\alpha p^2 - 6bd\alpha p^2q - b^2p^2q\alpha - bp^2q^2\alpha - 3p^2q^2d\alpha - 3q\alpha db^2a - q\alpha pb^2a$$
$$-q^2\alpha bpa - 3q\alpha pdab - 3q^2\alpha bad] + 3a^2b^3d\alpha cp^3q^3\beta^2k^2(b+q)$$
$$+\sin((\tau_1+\tau_2)\omega)[-w^5b^2c\alpha^2p^2\beta^2k^2q^2(-p+d) + w^3b^2ck^2p^2q^2\alpha^2\beta^2(b^2p$$
$$-b^2d + 2bpq - 2bqd + baq + pq^2 - dq^2) + wab^3ck^2p^2q^3\alpha\beta^2(pba - bd\alpha + pqa$$
$$+pad - q\alpha d)] + \cos((\tau_1+\tau_2)\omega)[w^6b^2ck^2p^2q^2\alpha^2\beta^2 + w^4b^2c\alpha^2p^2\beta^2k^2q^2$$
$$\times(pd+q^2+b^2+2bq) - w^2b^2ck^2p^2q^2\alpha\beta^2(-pq^2\alpha d - 2pbq\alpha d + qpba^2$$
$$-pb^2\alpha d - q^2\alpha ba - q\alpha bad - q\alpha b^2a) + a^2b^3d\alpha cp^3q^3\beta^2k^2(b+q)]\Big]$$
$$+e^{-a\tau_1-4\tilde{a}\tau_2}\Big[w^6\beta^3b^3k^3q^3\alpha + w^4\beta^3b^3k^3q^3\alpha(bq+b^2+q^2+p^2) - w^2b^3k^3q^3\beta^3$$
$$\times(-qba\alpha p - qb^2\alpha p - q^2b\alpha p + qbp^2a - 2qbp^2\alpha - q\alpha b^2a - q^2p^2\alpha$$
$$-q^2\alpha ba - b^2p^2\alpha + q^2bap + qb^2ap + qpba^2) + a^2b^4p^2\beta^3k^3q^4(b+q)\Big]\Big\}. \tag{A.3}$$

$$\begin{aligned}
\tilde{S}_{dd1}(\omega_r, a_c) = \tilde{F}_1 \; = \; & 1.6\omega\Big\{ -3.305\omega^8 - \omega^6(5.285 + 7.93\times 10^{-15}a) \\
& -\omega^4(157.6 - 365.2a) + \omega^2(1890a^2 + 2370a - 1.070) \\
& -\cos(0.1\omega(3+10\tau_1))\Big[1.35010^1\omega^6 + \omega^4(216.2 + 2.642a) \\
& -\omega^2(624.5a^2 - 216.4a - 0.02) + 5a^2\Big] \\
& +\sin(0.1\omega(3+10\tau_1))\Big[6.610\omega^7 + \omega^5(105.2 + 1.586\times 10^{-14}a) \\
& +\omega^3(5.170a - 9.570) + \omega(0.4330a - 2502a^2)\Big] - 118.4a^2\Big\} \\
& /\Big[42.32\omega^2\cos(0.1\omega(3+10\tau_1)) + \omega\sin(0.1\omega(3+10\tau_1)) \\
& \times[10.57\omega^2 - 0.08459] - 5.287\omega^4 + 64.94\omega^2 - 500a\Big].
\end{aligned} \tag{A.4}$$

$$\begin{aligned}
\tilde{S}_{dd2}(\omega_r, a_c) = \tilde{F}_2 \; = \; & 3.2\omega\Big\{ -21.15\omega^8 + 21.15\omega^7 sin((0.2(3+10\tau_1))\omega) \\
& -\omega^6\Big[21.6\cos((0.2(3+10\tau_1))\omega) + 1.269\times 10^{-14}a + 84.56\Big] \\
& +\sin((0.2(3+10\tau_1))\omega)\omega^5\Big[84.12 + 1.269\times 10^{-14}a\Big] \\
& -\omega^4\Big[\cos((0.2(3+10\tau_1))\omega)[86.5 + 10.57a] + 63.06 + 146.1a\Big] \\
& +\sin((0.2(3+10\tau_1))\omega)\omega^3\Big[10.34a - 1.914\Big] \\
& +\omega^2\Big[\cos((0.2(3+10\tau_1))\omega)[62.45a^2 - 21.64a - 0.002] \\
& +189.0a^2 + 237a + 1.07\Big] \\
& +\sin((0.2(3+10\tau_1))\omega)\omega\Big[-125.1a^2 + 0.02165a\Big] \\
& -0.1250\cos((0.2(3+10\tau_1))\omega)a^2 - 2.960a^2\Big\} \\
& /\Big\{-2.115\omega^4 + 2.114\omega^3\sin((0.2(3+10\tau_1))\omega) \\
& +\omega^2\Big[4.232\cos((0.2(3+10\tau_1))\omega) + 6.495\Big] \\
& -0.0423\omega\sin((0.2(3+10\tau_1))\omega) - 12.50a\Big\}.
\end{aligned} \tag{A.5}$$