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The effect of vector control strategy against dengue transmission between mosquitoes and human

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Abstract. With the consideration of the mechanism of prevention and control for the spread of dengue fever, a mathematical model of dengue fever dynamical transmission between mosquitoes and humans, incorporating a vector control strategy of impulsive culling of mosquitoes, is proposed in this paper. By using the comparison principle, Floquet theory and some of analytical methods, we obtain the basic reproductive number $\mathcal{R}_0$ for this infectious disease, which illustrates the stability of the disease-free periodic solution and the uniform persistence of the disease. Further, the explicit conditions determining the backward or forward bifurcation are obtained and we show that the culling rate ϕ has a major effect on the occurrence of backward bifurcation. Finally, numerical simulations are given to verify the correctness of theoretical results and the highest efficiency of vector control strategy.

Keywords: dengue fever, impulsive culling, extinction, uniform persistence, bifurcation.

2010 Mathematics Subject Classification: 34A37, 34D23, 92D30.

1 Introduction

Dengue fever is a fast emerging pandemic-prone viral disease in many parts of the world, which was first discovered in Cairo of Egypt, Indonesia-Jakarta and Philadelphia 1779 and was named arthritis fever and break-bone fever according to clinical symptoms [8, 18]. Dengue fever is a re-emergent disease affecting people in more than 100 countries in the tropical and subtropical areas. The symptoms of the disease are characterized by high fever, frontal headache, pain behind the eyes, joint pains, nausea, vomiting etc [27,33]. Every year, 500,000 cases reports of dengue are received by the World Health Organization (WHO), with more than 2.5 billion people at risk. It is well know that dengue fever is a mosquito-borne infectious disease, the female mosquitoes of *Aedes aegypti* and *Aedes albopictus* are the prominent carriers of dengue fever virus of *Flaviviridae* family [7,33]. The infected mosquitoes transfer infection on biting susceptible persons, and then susceptible mosquito bites an infected person, it gets infected.

The control and hence eradication of infectious diseases is one of the major concerns in the study of mathematical epidemiology [1,2,11,21,31] and the references therein. In the past nearly

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twenty years, the prevention and control of the spread of dengue fever (or other vector-borne diseases) are also caused extensive attention of many scholars (see, for instance, [5,12,13,24] and the references therein). Especially, Esteva et al. [24] proposed a host–vector dengue fever model with varying total population size and obtained the global asymptotic stability of equilibria for this model. Derouich et al. [10] introduced a mathematical model to simulate the succession of dengue with variable human populations, and analysed the stability of equilibria for this model. Garba et al. [16] structured a basic single strain dengue model, which incorporates the dynamics of exposed humans and vectors, and obtained the basic reproduction number and the phenomenon of backward bifurcation, where the stable disease-free equilibrium coexists with a stable endemic equilibrium. Further, they also extended the model to incorporate an imperfect vaccine against the spread of dengue. For more research results also can be found in [3,9,14,15,19,28–30] and the references therein.

Dengue vaccination research and development are began in 1940s, but no specific vaccine and treatment are available for this vector-borne disease in recent years due to the limited appreciation of global disease burden and the potential markets. Therefore, how to prevent, control and put an end to the spread of dengue fever have always been hot issues in medicine and mathematical epidemiology. Considering mosquitoes are the principal vectors in spread of the disease, hence vector population control through insecticides is the possible ways to prevent human population from dengue fever virus. Based on this idea, significant advances were made by Macdonald [25] who proposed that the most effective control strategy against vector-borne infections is to kill adult mosquitoes. From a theoretical perspective, many mathematical models have been developed to describe the control of vector population. Examples can be found in [26] where they studied the effects of awareness and mosquito control on dengue fever, and indicated that the sufficiently large amount of vector control is required to control the disease. And in [4], Amaku et al. considered the impact of vector-control strategies on the human prevalence of dengue. Other examples also can be found in [17,20] and the references therein, to just a few.

A noticed fact is that most of above mathematical models considering control measures on vector population invariably assume that the pesticides affect vector population continuously. Generally, however, the culling of vector population is usually put in practice at discrete certain times. So for this reason, Xu et al. [34] presented a mathematical model to describe the transmission of West Nile virus between vector mosquitoes and birds, incorporating a control strategy of culling mosquitoes and defined by impulsive differential equations.

Motivated by these facts, we propose, in this paper, a mathematical model of dengue with saturation and bilinear incidence, and impulsive culling of mosquitoes. The dynamical behaviour of this model was investigated and the influence of impulsive vector control for the preventing of the disease was discussed. The rest of the paper is structured as follows. We formulate a mathematical model and give some useful lemmas in Section 2. Some threshold value conditions of the disease-free periodic solution are presented in Section 3 to control the disease. We discuss the uniform persistence of the disease in Section 4 and also provide a explicit conditions determining the backward or forward bifurcation in Section 5. Finally, we give the numerical simulation and discussion in the last section.

2 Model formulation and preliminaries

In this section, we propose a mathematical model of dengue fever with impulsive culling mosquitoes. For convenience, we separate human population into three classes: susceptible S_h, infectious I_h, recovered R_h, and female mosquitoes are divided into two classes: uninfected S_m, infectious

I_m. For establishing this model, we come up with the following assumptions.

(A_1) The human population is recruited at the rate of $\mu_h K$, K is the maximum size of people and μ_h is natural death rate, and because dengue fever also causes mortality in humans, we assume that d_h is the disease-induced death rate for humans, γ_h is the recovery rate of humans, N_h is the total size of human population.

(A_2) Assuming that Λ_m is the recruitment rate of mosquitoes, N_m is the total number of mosquitoes and μ_m is the natural birth/death rate of mosquitoes.

(A_3) Average biting rate of mosquitoes is b, ρ_{hm} and ρ_{mh} are the transmission probabilities from human to mosquitoes and from mosquitoes to human respectively. We assume that the incidence of infected mosquito to susceptible humans is the saturation incidence due to the "psychological" effect or the inhibition effect, and assume that the incidence of infected humans to susceptible mosquito is bilinear incidence since it is not impacted by these issues. They are given by

$$\frac{b\rho_{hm} I_m(t) S_h(t)}{1+\alpha I_m}, \qquad b\rho_{mh} I_h(t) S_m(t),$$

respectively, where α is positively constant.

(A_4) We suppose that impulsive culling of infectious and susceptible mosquitoes happens at a rate ϕ.

Based on the above assumptions, we have the following mathematical model with impulsive control

$$\begin{cases} \left.\begin{aligned} \frac{\mathrm{d}S_h(t)}{\mathrm{d}t} &= \mu_h K - \frac{b\rho_{hm} I_m(t) S_h(t)}{1+\alpha I_m} - \mu_h S_h(t) \\ \frac{\mathrm{d}I_h(t)}{\mathrm{d}t} &= \frac{b\rho_{hm} I_m(t) S_h(t)}{1+\alpha I_m} - (\mu_h + d_h + \gamma_h) I_h(t) \\ \frac{\mathrm{d}R_h(t)}{\mathrm{d}t} &= \gamma_h I_h(t) - \mu_h R_h(t) \\ \frac{\mathrm{d}S_m(t)}{\mathrm{d}t} &= \Lambda_m - b\rho_{mh} I_h(t) S_m(t) - \mu_m S_m(t) \\ \frac{\mathrm{d}I_m(t)}{\mathrm{d}t} &= b\rho_{mh} I_h(t) S_m(t) - \mu_m I_m(t) \end{aligned}\right\} t \neq nT, \\ \left.\begin{aligned} S_h(t^+) &= S_h(t) \\ I_h(t^+) &= I_h(t) \\ R_h(t^+) &= R_h(t) \\ S_m(t^+) &= (1-\phi) S_m(t) \\ I_m(t^+) &= (1-\phi) I_m(t) \end{aligned}\right\} t = nT,\ n = 1, 2, \ldots \end{cases} \tag{2.1}$$

From the first to fifth equations of model (2.1), we obtain that the total numbers of humans and vectors at time t satisfy

$$\frac{\mathrm{d}N_h(t)}{\mathrm{d}t} = \mu_h K - \mu_h N_h(t) - d_h I_h(t), \qquad \frac{\mathrm{d}N_m(t)}{\mathrm{d}t} = \Lambda_m - \mu_h N_m(t).$$

Obviously, from the above two equations, it is easy to get

$$\frac{\mu_h K}{\mu_h + d_h} \leq \liminf_{t\to+\infty} N_h(t) \leq \limsup_{t\to+\infty} N_h(t) \leq K, \qquad \lim_{t\to+\infty} N_m(t) = \frac{\Lambda_m}{\mu_m}. \tag{2.2}$$

Table 2.1: Parameter values for model (2.1)

Param.	Description	Range	Source
$\mu_h K$	Recruitment rate of human population	0.36	Garba S.M. [16]
Λ_m	Recruitment rate of mosquitoes (day^{-1})	28	Estimate
b	Bites per mosquito (day^{-1})	0.5	Garba S.M. [16]
α	Saturation constant	$(0,1)$	Estimate
ρ_{hm}	Transmission rate of mosquito to human (day^{-1})	$2.6071e^{-5} \sim 4.0018e^{-4}$	Pandey [28]
ρ_{mh}	Transmission rate of human to mosquito (day^{-1})	$5.6478e^{-5} \sim 7.3135e^{-4}$	Pandey [28]
μ_h	The natural death rate of human (day)	$1/25000$	Garba S.M. [16]
μ_m	The natural death rate of mosquito (day^{-1})	$0.0378 \sim 0.0781$	Pandey [28]
d_h	The diseased death rate of human (day^{-1})	$1e^{-3}$	Amaku M. [4]
γ_h	The rate of recovery in human (day^{-1})	$0.1521 \sim 0.4440$	Pandey [28]
ϕ	The culling rate for mosquitoes (day^{-1})	$0 \sim 1$	Estimate

Therefore, from biological considerations, we only need to analyze the dynamical behavior of model (2.1) in the region

$$\Omega = \left\{(S_h, I_h, R_h, S_m, I_m) \in \mathbb{R}^5_+ \mid 0 \le S_h(t) + I_h(t) + R_h(t) \le K, 0 \le S_m(t) + I_m(t) \le \frac{\Lambda_m}{\mu_m}\right\},$$

where $\mathbb{R}^5_+ = \{(x_1, \dots, x_5) : x_i \ge 0, i = 1, \dots, 5\}$. Obviously, Ω is positively invariant with respect to model (2.1).

Now, let $Q(t)$ be a bounded, continuous, cooperative and irreducible $j \times j$ matrix function and $Q(t) = Q(t+\omega)$, $P = \operatorname{diag}\{p_1, p_2, \dots, p_j\}$. Consider the following impulsive differential equation

$$\begin{cases} \dfrac{\mathrm{d}x(t)}{\mathrm{d}t} = Q(t)x(t), & t \ne nT, \\ x(t^+) = Px(t), & t = nT,\ n = 1, 2, \dots. \end{cases} \tag{2.3}$$

Let $\Phi_{Q(\cdot)}(t)$ be the fundamental solution matrix of system (2.3) and $\rho(\Phi_{Q(\cdot)}(\omega))$ be the spectral radius of $\Phi_{Q(\cdot)}(\omega)$. By the Perron–Frobenius theorem, $\rho(\Phi_{Q(\cdot)}(\omega))$ is the principle eigenvalue of $\Phi_{Q(\cdot)}(\omega)$ in the sense that it is simple and admits an eigenvector $v^* \gg 0$. Then, similar to Lemma 2.1 in [32, 35], we have the following result.

Lemma 2.1. *Let $\mu = \ln\{\rho(P\Phi_{Q(\cdot)}(\omega))\}/\omega$, then there exists a positive ω-periodic function $v(t)$ such that $e^{\mu t}v(t)$ is a solution of system* (2.3).

Proof. Let $v^* \gg 0$ be a eigenvector of $\rho(P\Phi_{Q(\cdot)}(\omega))$. By the change of variable

$$\begin{cases} x(t) = e^{\mu t}v(t), & t \ne nT, \\ x(t^+) = e^{\mu t}v(t^+), & t = nT,\ n = 1, 2, \dots, \end{cases}$$

we have

$$\begin{cases} \dfrac{\mathrm{d}v(t)}{\mathrm{d}t} = (Q(t) - \mu I)v(t), & t \ne nT, \\ v(t^+) = Pv(t), & t = nT,\ n = 1, 2, \dots \end{cases}$$

Then, $v(t) := \Phi_{(Q(\cdot)-\mu I)}(t)Pv^*$ is a positive solution of system (2.3). Obviously, $e^{\mu t}P\Phi_{(Q(\cdot)-\mu I)}(t) = P\Phi_{Q(\cdot)}(t)$. Moreover,

$$v(\omega) = P\Phi_{Q(\cdot)-\mu I}(\omega)v^* = e^{-\mu\omega}P\Phi_{Q(\cdot)}(\omega)v^* = e^{-\mu\omega}\rho(P\Phi_Q(\omega))v^* = v^* = v(0^+).$$

Thus, $v(t)$ is a positive ω-periodic function. So, $x(t) = e^{\mu t}v(t)$ is a solution of system (2.3). This completes the proof. □

The following Lemma 2.2 is from [23], although very simple, but very useful.

Lemma 2.2. *Consider the following impulsive differential equation*

$$\begin{cases} \left.\begin{aligned} \frac{\mathrm{d}x_1(t)}{\mathrm{d}t} &= a - bx_1(t) \\ \frac{\mathrm{d}x_2(t)}{\mathrm{d}t} &= c - dx_1(t) \end{aligned}\right\} t \neq nT, \\ \left.\begin{aligned} x_1(t^+) &= x_1(t) \\ x_2(t^+) &= (1-p)x_2(t) \end{aligned}\right\} t = nT,\ n = 1,2,\ldots, \end{cases} \tag{2.4}$$

where a, b, c, d are positive constants and $p \in (0,1)$. Then equation (2.4) has a unique positive periodic solution $(\widetilde{x}_1(t), \widetilde{x}_2(t))$ which is globally asymptotically stable, where

$$\widetilde{x}_1(t) = \frac{a}{b}, \qquad \widetilde{x}_2(t) = \left(1 - \frac{pe^{(-d(t-nT))}}{1-(1-p)e^{-dT}}\right)\frac{c}{d}, \qquad nT < t \leq (n+1)T.$$

3 Stability of the disease-free periodic solution

In this section, we discuss the existence and stability of the disease-free periodic solution of model (2.1), in which infected individuals are completely absent. That is, $I_h(t) = 0$ and $I_m(t) = 0$. In this case, model (2.1) reduces to the following subsystem

$$\begin{cases} \left.\begin{aligned} \frac{\mathrm{d}S_h(t)}{\mathrm{d}t} &= \mu_h K - \mu_h S_h(t) \\ \frac{\mathrm{d}R_h(t)}{\mathrm{d}t} &= -\mu_h R_h(t) \\ \frac{\mathrm{d}S_m(t)}{\mathrm{d}t} &= \Lambda_m - \mu_m S_m(t) \end{aligned}\right\} t \neq nT, \\ \left.\begin{aligned} S_h(t^+) &= S_h(t) \\ R_h(t^+) &= R_h(t) \\ S_m(t^+) &= (1-\phi)S_m(t) \end{aligned}\right\} t = nT,\ n = 1,2,\ldots. \end{cases} \tag{3.1}$$

Obviously, from the second equation of model (3.1), we have $\lim_{t\to+\infty} R_h(t) = 0$. In view of Lemma 2.2, model (3.1) has a unique disease-free periodic solution $(\widetilde{S}_h(t), 0, \widetilde{S}_m(t))$ which is globally asymptotically stable, where

$$\widetilde{S}_h(t) = K, \quad \widetilde{S}_m(t) = \frac{\Lambda_m}{\mu_m}\left(1 - \frac{\phi e^{-\mu_m(t-nT)}}{1-(1-\phi)e^{-\mu_m T}}\right), \qquad nT < t \leq (n+1)T. \tag{3.2}$$

Therefore, model (2.1) admits a unique disease-free periodic solution $(\widetilde{S}_h(t), 0, 0, \widetilde{S}_m(t), 0)$.

For discussion of the stability of disease-free periodic solution of model (2.1), we define the following matrix functions

$$F = \begin{pmatrix} 0 & \rho_{hm} b\widetilde{S}_h(t) \\ \rho_{mh} b\widetilde{S}_m(t) & 0 \end{pmatrix}, \qquad V = \begin{pmatrix} \mu_h + \gamma_h + d_h & 0 \\ 0 & \mu_m \end{pmatrix}.$$

Let $A(t)$ be an $n \times n$ matrix function, $\Phi_{A(\cdot)}(t)$ be the fundamental solution matrix of the linear ordinary differential system $\mathrm{d}X(t)/\mathrm{d}t = A(t)X(t)$, and $\rho(\Phi_{A(\cdot)}(T))$ be the spectral radius of $\Phi_{A(\cdot)}(T)$. Let $S_h(t) = s_h(t) + \widetilde{S}_h(t), I_h(t) = i_h(t), R_h(t) = r_h(t), S_m(t) = s_m(t) + \widetilde{S}_m(t), I_m(t) = i_m(t)$ and $X(t) = (i_h(t), i_m(t), s_h(t), s_m(t), r_h(t))^{\mathcal{T}}$, where $C^{\mathcal{T}}$ denotes the transpose of C. Then model (2.1) becomes

$$\begin{cases} \dfrac{\mathrm{d}X(t)}{\mathrm{d}t} = A(t)X(t), & t \neq nT, \\ X(t^+) = PX(t), & t = nT, \ n = 1, 2, \ldots, \end{cases} \tag{3.3}$$

where

$$A(t) = \begin{pmatrix} F - V & \mathbf{0} \\ -J & M \end{pmatrix}, \qquad P = \begin{pmatrix} P_1 & \mathbf{0} \\ \mathbf{0} & P_2 \end{pmatrix}, \qquad P_1 = \begin{pmatrix} 1 & 0 \\ 0 & 1-\phi \end{pmatrix},$$

and

$$J = \begin{pmatrix} 0 & -\rho_{hm} b \widetilde{S}_h(t) \\ -\rho_{mh} b \widetilde{S}_m(t) & 0 \\ \gamma_h & 0 \end{pmatrix}, \quad M = \begin{pmatrix} -\mu_h & 0 & 0 \\ 0 & -\mu_m & 0 \\ 0 & 0 & -\mu_h \end{pmatrix}, \quad P_2 = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1-\phi & 0 \\ 0 & 0 & 1 \end{pmatrix}.$$

Obviously, the monodromy matrix of model (3.3) equals

$$\begin{pmatrix} P_1 & \mathbf{0} \\ \mathbf{0} & P_2 \end{pmatrix} \begin{pmatrix} \Phi_{F-V}(T) & \mathbf{0} \\ * & \Phi_M(T) \end{pmatrix},$$

where $*$ stands for a non-zero block matrix. Further, the Floquet multiplier of model (2.1) is the eigenvalue of $\rho(P_1\Phi_{F-V}(T))$ and $\rho(\Phi_M(T))$. We can easily get the following theorem if $\mathcal{R}_0 = \rho(P_1\Phi_{F-V}(T)) < 1$.

Theorem 3.1. *If $\mathcal{R}_0 = \rho(P_1\Phi_{F-V}(T)) < 1$ holds, then model (2.1) admits a disease-free periodic solution $(\widetilde{S}_h(t), 0, 0, \widetilde{S}_m(t), 0)$ which is locally asymptotically stable.*

The following Theorem 3.2 is on the global asymptotic stability of the disease-free periodic solution of model (2.1).

Theorem 3.2. *If $\mathcal{R}_0 < 1$ holds, then the disease-free periodic solution $(\widetilde{S}_h(t), 0, 0, \widetilde{S}_m(t), 0)$ of model (2.1) is globally asymptotically stable.*

Proof. From Theorem 3.1, we have verified the local asymptotic stability of the disease-free periodic solution of model (2.1). So we only need to prove the global attractivity of this solution. By $\mathcal{R}_0 = \rho(P_1\Phi_{(F-V)}(T)) < 1$, we can choose small enough constant $\epsilon > 0$, such that $\rho(P_1\Phi_{(F-V-G(\epsilon))}(T)) < 1$, where

$$G(\epsilon) = \begin{pmatrix} 0 & b\rho_{hm}\epsilon \\ b\rho_{mh}\epsilon & 0 \end{pmatrix}.$$

From the first, fourth, sixth and ninth equations of model (2.1), one has

$$\begin{cases} \left.\begin{aligned} \dfrac{\mathrm{d}S_h(t)}{\mathrm{d}t} &\le \mu_h K - \mu_h S_h(t) \\ \dfrac{\mathrm{d}S_m(t)}{\mathrm{d}t} &\le \Lambda_m - \mu_m S_m(t) \end{aligned}\right\} t \neq nT, \\ \left.\begin{aligned} S_h(t^+) &= S_h(t) \\ S_m(t^+) &= (1-\phi) S_m(t) \end{aligned}\right\} t = nT, \ n = 1, 2, \ldots \end{cases}$$

Consider the auxiliary system

$$\begin{cases} \left.\begin{aligned} \frac{d\omega_1(t)}{dt} &= \mu_h K - \mu_h \omega_1(t) \\ \frac{d\omega_2(t)}{dt} &= \Lambda_m - \mu_m \omega_2(t) \end{aligned}\right\} t \neq nT, \\ \left.\begin{aligned} \omega_1(t^+) &= \omega_1(t) \\ \omega_2(t^+) &= (1-\phi)\omega_2(t) \end{aligned}\right\} t = nT,\ n = 1, 2, \ldots \end{cases} \tag{3.4}$$

By Lemma 2.2, model (3.4) has a unique positively periodic solution $(\widetilde{\omega}_1(t), \widetilde{\omega}_2(t))$ which is globally asymptotically stable, where

$$\widetilde{\omega}_1(t) = K = \widetilde{S}_h(t), \quad \widetilde{\omega}_2(t) = \frac{\Lambda_m}{\mu_m}\left(1 - \frac{\phi e^{(-\mu_m(t-nT))}}{1-(1-\phi)e^{(-\mu_m T)}}\right) = \widetilde{S}_m(t), \quad nT < t \leq (n+1)T.$$

Let $(S_h(t), I_h(t), R_h(t), S_m(t), I_m(t))$ be a solution of model (2.1) with $S_h(0^+) = S_h^0 \geq 0$, $S_m(0^+) = S_m^0 \geq 0$, and $(\omega_1(t), \omega_2(t))$ be a solution of model (3.4) with the initial value $\omega_1(0^+) = S_h^0$, $\omega_2(0^+) = S_m^0$. By the comparison theorem of impulsive differential equations (more detail see Lakshmikantham et al. [6,23]), there exists an integer $n_1 > 0$ such that

$$S_h(t) \leq \omega_1(t) \leq \widetilde{\omega}_1(t) + \frac{\epsilon}{2}, \qquad S_m(t) \leq \omega_2(t) \leq \widetilde{\omega}_2(t) + \frac{\epsilon}{2}, \qquad nT < t \leq (n+1)T,\ n \geq n_1.$$

That is,

$$S_h(t) \leq \omega_1(t) \leq \widetilde{S}_h(t) + \epsilon, \qquad S_m(t) \leq \omega_2(t) \leq \widetilde{S}_m(t) + \epsilon, \qquad nT < t \leq (n+1)T,\ n \geq n_1. \tag{3.5}$$

Further, from (3.5) and the second, fifth, seventh and tenth equations of model (2.1), we can get

$$\begin{cases} \left.\begin{aligned} \frac{dI_h(t)}{dt} &\leq b\rho_{hm}(\widetilde{S}_h(t) + \epsilon)I_m(t) - (\mu_h + \gamma_h + d_h)I_h \\ \frac{dI_m(t)}{dt} &\leq b\rho_{mh}(\widetilde{S}_m(t) + \epsilon)I_h(t) - \mu_m I_m \end{aligned}\right\} t \neq nT, \\ \left.\begin{aligned} I_h(t^+) &= I_h(t) \\ I_m(t^+) &= (1-\phi)I_m(t) \end{aligned}\right\} t = nT,\ n = n_1, n_1+1, \ldots \end{cases}$$

Now, we consider the following auxiliary system

$$\begin{cases} \frac{dY(t)}{dt} = (F - V + G(\epsilon))Y(t), & t \neq nT, \\ Y(t^+) = P_1 Y(t), & t = nT,\ n = n_1, n_1+1, \ldots, \end{cases} \tag{3.6}$$

where $Y = (y_1, y_2)^T$. From Lemma 2.1, model (3.6) has a positive T-periodic solution $Y^*(t)$ such that $Y(t) = Y^*(t)e^{\mu t}$, where $\mu = \{\ln \rho(\Phi_{(F-V+G(\epsilon))}(T))\}/T$. Condition $\rho(P_1\Phi_{(F-V-G(\epsilon))}(T)) < 1$ implies $\mu < 0$. So, $Y(t) \to 0$ as $t \to +\infty$. Therefore, it implies that

$$\lim_{t\to+\infty} I_h(t) = 0, \qquad \lim_{t\to+\infty} I_m(t) = 0. \tag{3.7}$$

From these, for any $\epsilon_1 > 0$, there exists an integer $n_2 \geq n_1$, such that $I_h(t) < \epsilon_1$ and $I_m(t) < \epsilon_1$ for $t \geq n_2 T$. From the first, fourth, sixth and ninth equations of model (2.1), it can be easily shown that

$$\begin{cases} \left.\begin{array}{l} \dfrac{\mathrm{d}S_h(t)}{\mathrm{d}t} \geq \mu_h K - \dfrac{b\rho_{hm}S_h(t)\epsilon_1}{1+\alpha\epsilon_1} - \mu_h S_h(t) \\ \dfrac{\mathrm{d}S_m(t)}{\mathrm{d}t} \geq \Lambda_m - b\rho_{mh}S_m(t)\epsilon_1 - \mu_m S_m(t) \end{array}\right\} t \neq nT, \\ \left.\begin{array}{l} S_h(t^+) = S_h(t) \\ S_m(t^+) = (1-\phi)S_m(t) \end{array}\right\} t = nT,\ n = 1, 2, \ldots \end{cases}$$

Consider the auxiliary system

$$\begin{cases} \left.\begin{array}{l} \dfrac{\mathrm{d}z_1(t)}{\mathrm{d}t} = \mu_h K - \left(\dfrac{b\rho_{hm}\epsilon_1}{1+\alpha\epsilon_1} + \mu_h\right) z_1(t) \\ \dfrac{\mathrm{d}z_2(t)}{\mathrm{d}t} = \Lambda_m - (b\rho_{mh}\epsilon_1 + \mu_m) z_2(t) \end{array}\right\} t \neq nT, \\ \left.\begin{array}{l} z_1(t^+) = z_1(t) \\ z_2(t^+) = (1-\phi)z_2(t) \end{array}\right\} t = nT,\ n = 1, 2, \ldots \end{cases} \tag{3.8}$$

By Lemma 2.2, system (3.8) exists a unique positively solution $(\widetilde{z}_1(t), \widetilde{z}_2(t))$ which is globally asymptotically stable, where

$$\begin{cases} \widetilde{z}_1(t) = \dfrac{\mu_h K}{\frac{b\rho_{hm}\epsilon_1}{1+\alpha\epsilon_1} + \mu_h}, \\ \widetilde{z}_2(t) = \dfrac{\Lambda_m}{b\rho_{mh}\epsilon_1 + \mu_m}\left(1 - \dfrac{\phi e^{-(b\rho_{mh}\epsilon_1+\mu_m)(t-nT)}}{1-(1-\phi)e^{-(b\rho_{mh}\epsilon_1+\mu_m)T}}\right), \quad nT < t \leq (n+1)T,\ n \geq n_2. \end{cases}$$

Then by the comparison theorem, there exists a integer $n_3 \geq n_2$ such that

$$S_h(t) \geq \widetilde{z}_1(t) - \epsilon_1, \qquad S_m(t) \geq \widetilde{z}_2(t) - \epsilon_1, \qquad nT < t \leq (n+1)T,\ n \geq n_3.$$

Since ϵ_1 is arbitrarily small, it follows from the above inequality and (3.5) that $\widetilde{z}_1(t) \to \widetilde{S}_h(t)$, $\widetilde{z}_2(t) \to \widetilde{S}_m(t)$ as $t \to +\infty$. Therefore,

$$\lim_{t\to+\infty} S_h(t) = \widetilde{S}_h(t), \qquad \lim_{t\to+\infty} S_m(t) = \widetilde{S}_m(t). \tag{3.9}$$

Finally, from the second equation of model (2.1), we have $\lim_{t\to+\infty} R_h(t) = 0$. From this and (3.7), (3.9), we have that the disease-free periodic solution of model (2.1) is globally attractive. The proof is complete. □

4 Uniform persistence of the disease

In this section, we turn to the uniform persistence of the disease for model (2.1).

Theorem 4.1. *If $\mathcal{R}_0 = \rho(P_1\Phi_{F-V}(T)) > 1$ holds, then the disease of model (2.1) is uniform persistent, namely, there exists a constant $\eta > 0$ such that $\liminf_{t\to+\infty} I_i(t) \geq \eta$, $i = h, m$.*

Proof. From $\mathcal{R}_0 = \rho(P_1\Phi_{F-V}(T)) > 1$, we can chose small enough positive constants η, ϵ_1 and ϵ_2 such that

$$\rho(P_1\Phi_{(F(\eta,\epsilon_1,\epsilon_2)-V)}(T)) > 1, \tag{4.1}$$

where

$$F(\eta,\epsilon_1,\epsilon_2) = \begin{pmatrix} 0 & b\frac{\rho_{hm}(\widetilde{S}_h(t)-\epsilon_1-\epsilon_2)}{1+\alpha\eta} \\ b\rho_{mh}(\widetilde{S}_m(t)-\epsilon_1-\epsilon_2) & 0 \end{pmatrix},$$

and $(\widetilde{S}_h(t), \widetilde{S}_m(t))$ are given by (3.2).

Firstly, we prove

$$\limsup_{t\to+\infty} I_i(t) \geq \eta, \qquad i=h,m. \tag{4.2}$$

Otherwise, there exists a $t_1 > 0$ such that $I_h(t) < \eta$ or $I_m(t) < \eta$ for all $t \geq t_1$. Without loss generality, we suppose that $I_h(t) < \eta$ and $I_m(t) < \eta$ for all $t \geq t_1$. By the first, fourth, sixth and ninth equations of model (2.1), we have

$$\begin{cases} \left.\begin{aligned} \frac{\mathrm{d}S_h(t)}{\mathrm{d}t} &\geq \mu_h K - \frac{b\rho_{hm}S_h(t)\eta}{1+\alpha\eta} - \mu_h S_h(t) \\ \frac{\mathrm{d}S_m(t)}{\mathrm{d}t} &\geq \Lambda_m - b\rho_{mh}S_m(t)\eta - \mu_m S_m(t) \end{aligned}\right\} t \neq nT, \\ \left.\begin{aligned} S_h(t^+) &= S_h(t) \\ S_m(t^+) &= (1-\phi)S_m(t) \end{aligned}\right\} t = nT,\ n=1,2,\ldots \end{cases}$$

Consider the auxiliary system

$$\begin{cases} \left.\begin{aligned} \frac{\mathrm{d}u_1(t)}{\mathrm{d}t} &= \mu_h K - \frac{b\rho_{hm}u_1(t)\eta}{1+\alpha\eta} - \mu_h u_1(t) \\ \frac{\mathrm{d}u_2(t)}{\mathrm{d}t} &= \Lambda_m - b\rho_{mh}u_2(t)\eta - \mu_m u_2(t) \end{aligned}\right\} t \neq nT, \\ \left.\begin{aligned} u_1(t^+) &= u_1(t) \\ u_2(t^+) &= (1-\phi)u_2(t) \end{aligned}\right\} t = nT,\ n=1,2,\ldots \end{cases} \tag{4.3}$$

By Lemma 2.2, system (4.3) exists a unique positive solution $(\widetilde{u}_1(t), \widetilde{u}_2(t))$ and which is globally asymptotically stable, where

$$\widetilde{u}_1(t) = \frac{\mu_h K}{\frac{b\rho_{hm}\eta}{1+\alpha\eta} + \mu_h}, \quad \widetilde{u}_2(t) = \frac{\Lambda_m}{b\rho_{mh}\eta + \mu_m}\left(1 - \frac{\phi e^{-(b\rho_{mh}\eta+\mu_m)(t-nT)}}{1-(1-\phi)e^{-(b\rho_{mh}\eta+\mu_m)T}}\right), \quad nT < t \leq (n+1)T.$$

Obviously,

$$\lim_{\eta\to 0}(\widetilde{u}_1(t), \widetilde{u}_2(t)) = (\widetilde{S}_h(t), \widetilde{S}_m(t)).$$

Thus, there exists a positive constant $\widetilde{\eta}_1$ small enough for the above ϵ_1, such that $\widetilde{u}_1(t) \geq \widetilde{S}_h(t) - \epsilon_1$ and $\widetilde{u}_2(t) \geq \widetilde{S}_m(t) - \epsilon_1$ for $\eta < \widetilde{\eta}_1$. By the comparison principle, there exists $t_2 \geq t_1$ for the above $\epsilon_2 > 0$ such that

$$S_h(t) \geq u_1(t) > \widetilde{S}_h(t) - \epsilon_1 - \epsilon_2,\ S_m(t) \geq u_2(t) > \widetilde{S}_m(t) - \epsilon_1 - \epsilon_2, \qquad t \geq t_2.$$

From the second, fifth, seventh and tenth equations of model (2.1), we have

$$\begin{cases} \left.\begin{aligned} \frac{\mathrm{d}I_h(t)}{\mathrm{d}t} &\geq \frac{b\rho_{hm}I_m(t)(\widetilde{S}_h(t)-\epsilon_1-\epsilon_2)}{1+\alpha\eta} - (\mu_h+d_h+\gamma)I_h(t) \\ \frac{\mathrm{d}I_m(t)}{\mathrm{d}t} &\geq b\rho_{mh}I_h(t)(\widetilde{S}_m(t)-\epsilon_1-\epsilon_2) - \mu_m I_m \end{aligned}\right\} t \neq nT, \\ \left.\begin{aligned} I_h(t^+) &= I_h(t) \\ I_m(t^+) &= (1-\phi)I_m(t) \end{aligned}\right\} t = nT,\ n=1,2,\ldots \end{cases}$$

Considering the following auxiliary system

$$\begin{cases} \dfrac{\mathrm{d}Z(t)}{\mathrm{d}t} = (F(\eta,\epsilon_1,\epsilon_2) - V)Z(t), & t \neq nT, \\ Z(t^+) = P_1 Z(t), & t = nT, n = 1,2,\dots, \end{cases} \tag{4.4}$$

where $Z = (z_1, z_2)^{\mathcal{T}}$. From Lemma 2.1, system (4.4) has a positive T-periodic solution $\widetilde{Z}(t)$ such that $Z(t) = \widetilde{Z}(t)e^{\mu_1 t}$, where $\mu_1 = \{\ln \rho(\Phi_{(F(\eta,\epsilon_1,\epsilon_2)-V)}(T))\}/T$. Further, from the condition (4.1), we get $\mu_1 > 0$. Thus $Z(t) \to +\infty$, as $t \to +\infty$. That is,

$$\lim_{t\to+\infty} I_h(t) = +\infty, \qquad \lim_{t\to+\infty} I_m(t) = +\infty. \tag{4.5}$$

These contradict the boundedness of $I_h(t)$ and $I_m(t)$. So (4.2) is valid.

In the following, we prove that $\liminf_{t\to+\infty} I_i(t) \geq \eta$, $i = h,\ m$. From the above discussion, we consider only the following two possibilities:

(i) $I_i(t) \geq \eta$ for all large t, $i = h,\ m$;

(ii) $I_i(t)$ oscillates about η for all large t, $i = h,\ m$.

If case (i) holds, then we have completely the result. Next, we turn to case (ii).

Owing to $\limsup_{t\to+\infty} I_i(t) \geq \eta$, there exists a $t_1 \in (m_1 T, (m_1+1)T]$ and $t_2 \in (m_2 T, (m_2+1)T]$ such that $I_i(t_1) \geq \eta$, $I_i(t_2) \geq \eta$, $i = h,\ m$, where $m_2 - m_1 \geq 0$ is finite. Then we will consider the solution of the following equation from model (2.1) in the time interval $[t_1, t_2]$. From the second equation of model (2.1), one have

$$\frac{\mathrm{d}I_h(t)}{\mathrm{d}t} \geq -(\mu_h + d_h + \gamma)I_h(t).$$

Integrating the above equation from t_1 to t, we get

$$I_h(t) \geq I_h(t_1)e^{-(\mu_h+d_h+\gamma)(t-t_1)} \geq \eta e^{-(\mu_h+d_h+\gamma)(m_2-m_1+1)T}.$$

Moreover, from the fifth and tenth equations of model (2.1), it follows that

$$\begin{cases} \dfrac{\mathrm{d}I_m(t)}{\mathrm{d}t} \geq -\mu_m I_m(t), & t \neq nT, \\ I_m(t^+) = (1-\phi)I_m(t), & t = nT,\ n = 1,2,\dots \end{cases}$$

And, integrating the equation from t_1 to t, we have

$$I_m(t) \geq I_m(t_1)(1-\phi)^{m_2-m_1}e^{-\mu_m(t-t_1)} \geq \eta(1-\phi)^{m_2-m_1}e^{-\mu_m(m_2-m_1+1)T}.$$

Let $\eta_1 = \min\{\eta e^{-(\mu_h+d_h+\gamma)(m_2-m_1+1)T}, \eta(1-\phi)^{m_2-m_1}e^{-\mu_m(m_2-m_1+1)T}\}$, then $\eta_1 \geq 0$ cannot be infinitely small since $m_2 \geq m_1$ is finite. So, we have $I_i(t) \geq \eta_1 > 0$, $i = h,\ m$.

For $t > t_2$, the similar arguments can be continued and we similarly get non-infinitesimal positive η_2. Therefore, we can get the sequence $\{\eta_k\}$, where

$$\eta_k = \min\{\eta e^{-(\mu_h+d_h+\gamma)(m_{k+1}-m_k+1)T}, \eta(1-\phi)^{m_{k+1}-m_k}e^{-\mu_m(m_{k+1}-m_k+1)T}\}, \quad k = 1,2,\dots,$$

is non-infinitesimal since $m_{k+1} - m_k \geq 0$ is finite. So the solution of model (2.1) satisfies $I_i(t) \geq \eta_k > 0$, $i = h,\ m$ in the time interval $[t_k, t_{k+1}]$, where $t_k \in (m_k T, (m_k+1)T]$, $t_{k+1} \in (m_{k+1}T, (m_{k+1}+1)T]$. Let $\eta = \min_k\{\eta_k\} = \eta_l > 0, l \in N$ and $\eta_l \in \{\eta_k\}$. Hence from the above discuss, we get $I_i(t) \geq \eta > 0, i = h,\ m$ for all $t \geq t_1$. The proof is complete. □

5 Forward and backward bifurcation of endemic periodic solutions

In this section, we proceed to study bifurcation using the bifurcation theory (more details can be found in Lakmeche et al. [22]). Let the culling rate ϕ be the bifurcation parameter. We define the solution vector $X(t) := (S_h(t), S_m(t), R_h(t), S_m(t), I_m(t))$, the mapping $F(X(t)) = (F_1(X(t)), \ldots, F_5(X(t))) : \mathbb{R}^5 \to \mathbb{R}^5$ by the right hand side of the first to fifth equations of model (2.1), and the mapping

$$I(\phi, X(t)) = (I_1(\phi, X(t)), \ldots, I_5(\phi, X(t))) = (X_1(t), (1-\phi)X_2(t), X_3(t), X_4(t), (1-\phi)X_5(t)).$$

Furthermore, we define $\Phi(t, X_0)$, $0 < t \leq T$, to be the solution of model consisting of the first to fifth equations of model (2.1), where $X_0 = X(0)$. Then $X(T) = \Phi(T, X_0) := \Phi(X_0)$ and $X(T^+) = I(\phi, \Phi(X_0))$. We define the operator Ψ by $\Psi(\phi, X) := I(\phi, \Phi(X))$, where $\Psi(\phi, X) = (\Psi_1(\phi, X), \ldots, \Psi_5(\phi, X))$. Denote $D_X\Psi$ the derivative of Ψ with respect to X. Then X is a periodic solution of period T for model (2.1) if and only if its initial value X_0 is a fixed point for $\Psi(\phi, X)$. Namely, $\Psi(\phi, X_0) = X_0$. Consequently, to establish the existence of nontrivial periodic solutions of model (2.1), one needs to prove the existence of the nontrivial fixed point of Ψ.

Let us fix all parameters except the culling rate ϕ, and denote by ϕ_0 the critical culling rate, which corresponds to $\rho(P_1\Phi_{F-V}(T)) = 1$. We are interested in the bifurcation of nontrivial periodic solutions near the disease-free periodic solution $\widetilde{X} = (\widetilde{S}_h(t), \widetilde{S}_m(t), 0, 0, 0))$. Assuming that X_0 is the starting point for the disease-free periodic solution with the culling rate ϕ_0. It is obviously that $\Phi_3(X_0) = \Phi_4(X_0) = \Phi_5(X_0) = 0$. To find a nontrivial periodic solution with initial value X and culling rate ϕ, we need to solve the fixed point problem $\Psi(\phi, X) = X$. Denote $\phi = \phi_0 + \overline{\phi}$ and $X = X_0 + \widetilde{X}$, the fixed point problem reads as

$$N(\overline{\phi}, \widetilde{X}) = 0, \tag{5.1}$$

where $N(\overline{\phi}, \widetilde{X}) = (N_1(\overline{\phi}, \widetilde{X}), \ldots, N_5(\overline{\phi}, \widetilde{X})) = X_0 + \widetilde{X} - \Psi(\phi_0 + \overline{\phi}, X_0 + \widetilde{X})$. We have

$$D_{\widetilde{X}}N(\overline{\phi}, \widetilde{X}) = E_5 - D_{\widetilde{X}}I(\phi, \Phi(X))D_{\widetilde{X}}\Phi(X). \tag{5.2}$$

Since

$$\frac{\mathrm{d}}{\mathrm{dt}}(D_X\Phi(t, X_0)) = D_XF(\Phi(t, X_0))D_X\Phi(t, X_0) \tag{5.3}$$

with the initial condition $D_X\Phi(0, X_0) = E_5$ and $\Phi(t, X_0) = (\Phi_1(t, X_0), \Phi_2(t, X_0), 0, 0, 0)$, then (5.3) takes the form

$$\frac{\mathrm{d}}{\mathrm{dt}}(D_X\Phi(t, X_0))(t, X_0) = \mathcal{B}(t)D_X\Phi(t, X_0)(t, X_0),$$

where

$$\mathcal{B}(t) = \begin{pmatrix} M & -J \\ \mathbf{0} & F-V \end{pmatrix}.$$

It can be deduced that

$$D_XN(0, \mathcal{O}) = \begin{pmatrix} E_3 - P_2e^{MT} & P_2\Phi_{12}(T) \\ \mathbf{0} & E_2 - P_1\Phi_{F-V}(T) \end{pmatrix},$$

where $\mathcal{O} = (0, 0, 0, 0, 0)$. A necessary condition for the bifurcation for the nontrivial periodic solution near $\widetilde{X} = (\widetilde{S}_h(t), \widetilde{S}_m(t), 0, 0, 0))$ is $\det[D_XN(0, \mathcal{O})] = 0$. Obviously, $\det[E_3 - P_2e^{MT}] \neq 0$, then $\det[D_XN(0, \mathcal{O})] = 0$ is equal to $\det[E_2 - P_1\Phi_{F-V}(T)] = 0$. Therefore, $\det[E_2 - P_1\Phi_{F-V}(T)] = 0$

when $\rho(P_1\Phi_{F-V}(T)) = 1$. Assuming that $\rho(P_1\Phi_{F-V}(T)) = 1$ holds, we now investigate the sufficient conditions for the existence of bifurcation of nontrivial T-periodic solutions. From (5.2), it is convenient for the computations to denote

$$D_X N(0,\mathcal{O}) = \begin{pmatrix} e_0 & 0 & 0 & a_1 & b_1 \\ 0 & f_0 & 0 & c_1 & d_1 \\ 0 & 0 & a_2 & b_2 & c_2 \\ 0 & 0 & 0 & a_0 & b_0 \\ 0 & 0 & 0 & c_0 & d_0 \end{pmatrix}, \qquad A_1 = \begin{pmatrix} e_0 & 0 & 0 & a_1 \\ 0 & f_0 & 0 & c_1 \\ 0 & 0 & a_2 & b_2 \\ 0 & 0 & 0 & a_0 \end{pmatrix}.$$

See Appendix A for the expression of each element in the above matrices. Then $\det[E_2 - P_1\Phi_{F-V}(T)] = 0$ implies that there exists a constant k such that $c_0 = ka_0$ and $d_0 = kb_0$. Furthermore, we have $\dim \operatorname{Ker}(D_X(0,\mathcal{O})) = 1$, and a basis in $\operatorname{Ker}(D_X(0,\mathcal{O}))$ is

$$Y_1 = \left(\frac{a_1 b_0}{a_0 e_0} - \frac{b_1}{e_0}, \frac{c_1 b_0}{a_0 f_0} - \frac{d_1}{f_0}, \frac{b_0 b_2}{a_0} - c_2, -\frac{b_0}{a_0}, 1\right),$$

and we denote it as $Y_1 = (Y_{11}, Y_{12}, Y_{13}, Y_{14}, Y_{15})$. The basis in $\operatorname{Im}(D_X(0,\mathcal{O}))$ are $Y_2 = (1,0,0,0,0)$, $Y_3 = (0,1,0,0,0)$, $Y_4 = (0,0,1,0,0)$, $Y_5 = (0,0,0,1,0)$. From $\mathbb{R}^5 = \operatorname{Ker}(D_X(0,\mathcal{O})) \oplus \operatorname{Im}(D_X(0,\mathcal{O}))$, we have $\overline{X} = \alpha_1 Y_1 + \alpha_2 Y_2 + \alpha_3 Y_3 + \alpha_4 Y_4 + \alpha_5 Y_5$, where $\alpha_i \in \mathbb{R}$ $(i = 1,2,3,4,5)$ are unique. Then equation (5.1) is equivalent to

$$N_i(\overline{\phi}, \alpha_1, \alpha_2, \alpha_3, \alpha_4, \alpha_5) = N_i(\overline{\phi}, \alpha_1 Y_1 + \alpha_2 Y_2 + \alpha_3 Y_3 + \alpha_4 Y_4 + \alpha_5 Y_5) = 0, \quad i = 1,2,3,4,5. \tag{5.4}$$

From (5.1), we have

$$\frac{D(N_1, N_2, N_3, N_4)(0,\mathcal{O})}{D(\alpha_2, \alpha_3, \alpha_4, \alpha_5,)} = |A_1| \neq 0. \tag{5.5}$$

Therefore, by the implicit function theorem, one may solve (5.4) as $i = 1,2,3,4$ near $(0,\mathcal{O})$ with respect to α_i $(i = 1,2,3,4)$ as functions of $\overline{\phi}$ and α_1. That is, there exists $\widetilde{\alpha}_i = \widetilde{\alpha}_i(\overline{\phi}, \alpha_1)$ such that $\widetilde{\alpha}_i(0,0) = 0,\ i = 2,3,4,5$ and

$$N_i(\overline{\phi}, \alpha_1) = N_i(\overline{\phi}, \alpha_1 Y_1 + \widetilde{\alpha}_2 Y_2 + \widetilde{\alpha}_3 Y_3 + \widetilde{\alpha}_4 Y_4 + \widetilde{\alpha}_5 Y_5) = 0, \tag{5.6}$$

$i = 1,2,3,4$. Then $N(\overline{\phi}, \overline{X}) = 0$ if and only if

$$N_5(\overline{\phi}, \alpha_1) = N_5(\overline{\phi}, \overline{X}(\overline{\phi}, \alpha_1)) = 0 \tag{5.7}$$

with $\overline{X}(\overline{\phi}, \alpha_1) = (Y_{11}\alpha_1 + \widetilde{\alpha}_2, Y_{12}\alpha_1 + \widetilde{\alpha}_3, Y_{13}\alpha_1 + \widetilde{\alpha}_4, Y_{14}\alpha_1 + \widetilde{\alpha}_5, \alpha_1)$.

We proceed to solving (5.7) next. It is obvious that $N_5(\overline{\phi}, \alpha_1)$ vanishes at $(0,0)$. We determine the Taylor expansion of $N_5(\overline{\phi}, \alpha_1)$ around $(0,0)$. Now, we compute the first-order partial derivatives $\partial N_5(0,0)/\partial \alpha_1$ and $\partial N_5(0,0)/\partial \overline{\phi}$ and find that $\partial N_5(0,0)/\partial \alpha_1 = 0$ and $\partial N_5(0,0)/\partial \overline{\phi} = 0$. (See Appendix B for details). Then it is necessary for us to compute the second-order derivatives of $N_5(\overline{\phi}, \alpha_1)$. Denote

$$A = \frac{\partial^2 N_5(0,0)}{\partial \overline{\phi}^2}, \qquad B = \frac{\partial^2 N_5(0,0)}{\partial \overline{\phi} \partial \alpha_1}, \qquad C = \frac{\partial^2 N_5(0,0)}{\partial \alpha_1^2}.$$

It can be observed from Appendix C that $A = 0$, from Appendix D that

$$\begin{aligned} B &= \frac{\partial^2 N_5(0,0)}{\partial \overline{\phi} \partial \alpha_1} \\ &= \frac{\Phi_2(X_0)}{f_0} \left[\frac{\partial^2 \Phi_5(t, X_0)}{\partial S_m \partial I_h} Y_{14} + \frac{\partial^2 \Phi_5(t, X_0)}{\partial S_m \partial I_m} Y_{15} \right] - \frac{k\Phi_2(X_0))}{f_0} \left(\frac{\partial^2 \Phi_4(t, X_0)}{\partial S_m \partial I_h} Y_{14} + \frac{\partial^2 \Phi_4(t, X_0)}{\partial S_m \partial I_m} Y_{15} \right). \end{aligned}$$

and from Appendix E that

$$C = -\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2\Phi_5(0,0)}{\partial X_i \partial X_j}Y_{1i}Y_{1j} + k\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2\Phi_4(X_0)}{\partial X_i \partial X_j}Y_{1i}Y_{1j}.$$

Hence we have

$$N_5(\overline{\phi},\alpha_1) = B\alpha_1\overline{\phi} + C\frac{\alpha_1^2}{2} + o(\alpha_1,\overline{\phi})(\alpha_1^2+\overline{\phi}^2) = \alpha_1\left(B\overline{\phi} + C\frac{\alpha_1}{2} + \frac{1}{\alpha_1}o(\alpha_1,\overline{\phi})(\alpha_1^2+\overline{\phi}^2)\right).$$

Denoting

$$\widetilde{N}_5(\overline{\phi},\alpha_1) = B\overline{\phi} + C\frac{\alpha_1}{2} + \frac{1}{\alpha_1}o(\alpha_1,\overline{\phi})(\alpha_1^2+\overline{\phi}^2),$$

then $\partial\widetilde{N}_5(0,0)/\partial\alpha_1 = C/2$. So, for $C \neq 0$, we can use the implicit function theorem and solve the above equation near $(0,0)$ with respective to α_1 as a function of $\overline{\phi}$. Therefore, there exists $\alpha_1 = \alpha_1(\overline{\phi})$ such that $\alpha_1(0) = 0$ and $\widetilde{N}_5(\overline{\phi},\alpha_1(\overline{\phi})) = 0$. Meanwhile, by $\partial\widetilde{N}_5(0,0)/\partial\overline{\phi} = B$, we can also find $\overline{\phi} = \overline{\phi}(\alpha_1)$ such that $\widetilde{N}_5(\overline{\phi}(\alpha_1),\alpha_1) = 0$ for $B \neq 0$. Then, if $BC \neq 0$, we have $\alpha_1/\overline{\phi} \simeq -2B/C$.

According to above-mentioned discussion, we have the following theorem.

Theorem 5.1. *Considering the family of operators $\Psi(\phi, X)$ defined in $\Psi(\phi, X) := I(\phi, \Phi(X))$, as parameter ϕ passes through the critical value ϕ_0, a nontrivial fixed point appears near the fixed point X_0. The bifurcation is supercritical, if $BC < 0$, or else there will be a subcritical bifurcation as $BC > 0$.*

We know that the threshold value $\mathcal{R}_0$ decreases as ϕ increase. Then a supercritical bifurcation means a backward bifurcation in the model while the subcritical bifurcation equated to a forward bifurcation in the $\phi - \alpha_1$ plane. Thus we have the following theorem.

Theorem 5.2. *As the parameter ϕ passes through the critical value ϕ_0, a backward bifurcation occurs if $BC < 0$, or else there will be a forward bifurcation as $BC > 0$ at $\mathcal{R}_0 = 1$.*

6 Numerical simulation and discussion

In this paper, a mathematical model of dengue fever with impulsive culling of mosquitoes, saturation and bilinear incidence are considered. The main purpose is to investigate the effect of impulsive culling mosquitoes strategy, which govern whether the dengue fever dies out or not, and further to examine how the impulsive culling control strategy affects the prevention and control of dengue fever. By using the comparison principle, integral and differential inequalities, the way of spectral radius and analytical methods, some sufficient conditions for the existence and stability of disease-free periodic solution, and the uniform persistence of disease are obtained. Theoretical results show that dengue fever can be controlled via adjusting the control parameters of the model that depend on these conditions.

In this section, we give some numerical simulations to illustrate the main theoretical results and the feasibility of impulsive culling control strategy using the Runge–Kutta method in the software MATLAB. The values of parameters for model (2.1) are listed in Table 2.1, we fixed the values of model parameters as follows: $\Lambda_m = 28$, $b = 0.5$, $\rho_{hm} = 3 \times 10^{-4}$, $\rho_{mh} = 7 \times 10^{-4}$, $\mu_h = 4 \times 10^{-5}$, $d_h = 10^{-3}$, $\gamma_h = 0.153$, $\mu_m = 0.05$, $K = 9000$ and $\alpha = 0.4$.

We choose, firstly, culling period $T = 6$ (days) and culling rate $\phi = 0.72$. It is easy to calculate that $\mathcal{R}_0 \approx 0.9385 < 1$. So, from Theorem 3.2, we obtain that model (2.1) has a disease-free periodic solution which is globally asymptotically stable. The quantities of infectious human, infectious mosquitoes and uninfected mosquitoes in model (2.1) with or without impulsive culling are plotted against time in Figure 6.1 (a)–(c) with blue lines and red lines, respectively. Infected mosquitoes and infectious human in model (2.1) with impulsive culling control strategy and the stability of disease-free periodic solution of model (2.1) with or without impulsive culling are plotted in Figure 6.1 (d) with blue lines and red lines, respectively. Theoretical results and numerical simulations imply that we can eliminate dengue fever through vector-control strategy.

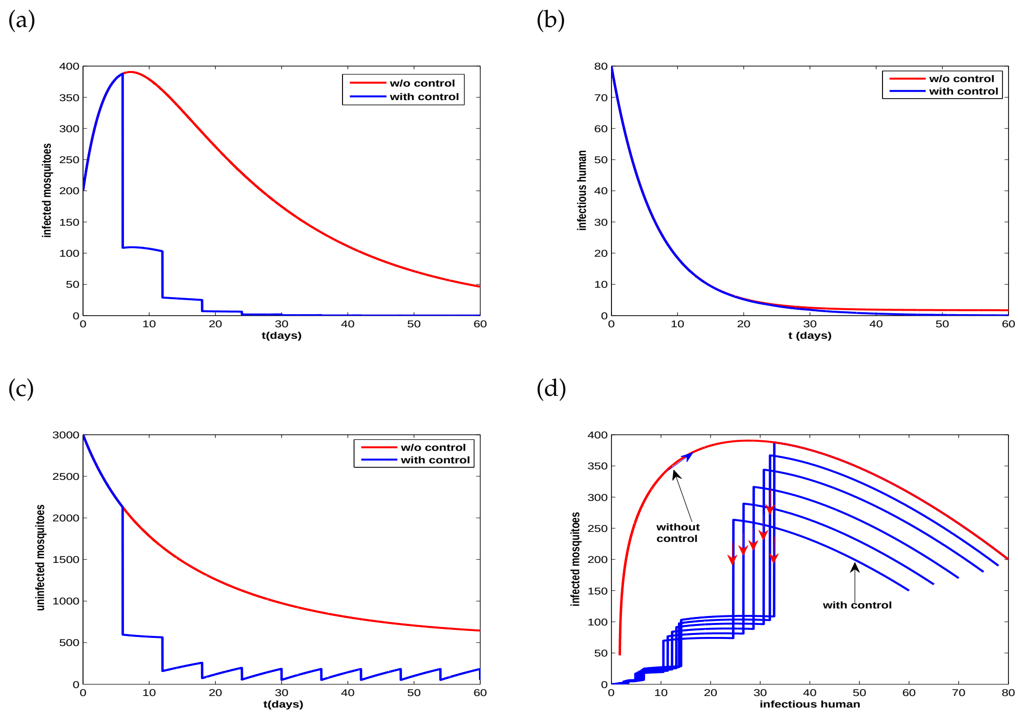

Figure 6.1: The stability of disease-free periodic solution of model (2.1) with control parameters $\phi = 0.72$ and $T = 6$ (days): (a) $(t, I_m(t))$; (b) $(t, I_h(t))$; (c) $(t, S_m(t))$; (d) $(I_m(t), I_h(t))$.

Secondly, we choose $T = 10$ (days), $\phi = 0.2$ and others parameters are fixed as above. By calculating, we get $\mathcal{R}_0 \approx 4.7336 > 1$. Therefore, model (2.1) has a positive periodic solution from Theorem 4.1. Figures 6.2 (a)–(c) show that the numerical solutions of infectious human, infectious mosquitoes and uninfected mosquitoes with different initial values. The plots in Figure 6.2 (d) show the uniform persistence of infected mosquitoes and infected humans. Theoretical results and numerical simulations show that dengue fever is uniformly persistent if the culling strength ϕ is low and the culling cycle period T is not too long.

Thirdly, we consider the frequencies of culling and culling rate how to impact on the uniform persistence and extinction of disease. We fixed $\phi = 0.1$ and other parameters are invariant, and chose different control period T for model (2.1). Figures 6.4 (a) and 6.4 (b) show the quantities of infectious human and infected mosquitoes with $T = 1, 7$ and 16 (days), respectively. Numerical simulations imply that disease is extinct when culling period T is short and disease is uniform persistent for long culling period T. Further, we fixed $T = 3$ (days), and chose culling rate $\phi = 0.1$, 0.4 and 0.8 for model (2.1), respectively. The plots in Figures 6.4 (c) and 6.4 (d) show the quantities of infectious human and infected mosquitoes, which imply that the disease is extinct

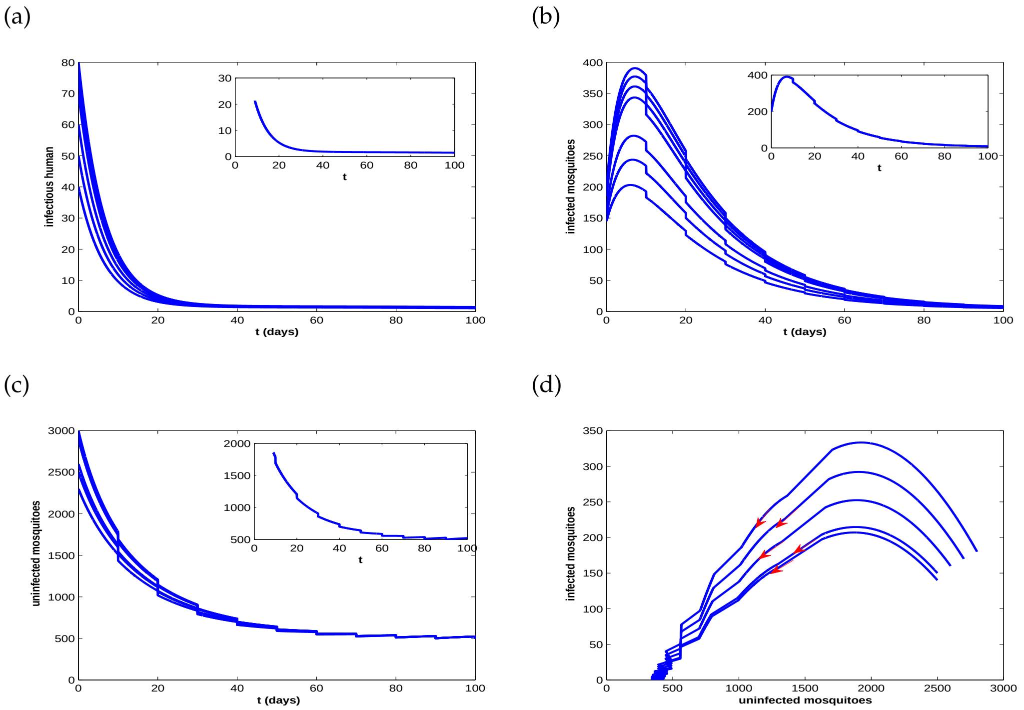

Figure 6.2: The uniform persistence of dengue fever in model (2.1) with $T = 10$ and $\phi = 0.2$, where $\mathcal{R}_0 = 4.7336$: (a) $(t, I_h(t))$; (b) $(t, I_m(t))$; (c) $(t, S_m(t))$; (d) $(I_m(t), S_m(t))$.

for high culling rate ϕ and is uniform persistent for low culling rate. All of these simulations indicate that the high frequency of culling and large culling rate are necessary for the goal of eliminating disease, The bifurcation diagram of infectious human and infected mosquitoes about culling rate ϕ in Figure 6.3 also accord with this result.

Finally, it is important to emphasize that the factors of seasonal variation in mosquito population size, the latent period of infected mosquitoes, the dispersion of both humans and mosquitoes, and vertical transmission of the virus in the mosquito population, affect the dynamical behaviors of both mosquitoes and humans and hence disease spread between mosquitoes and humans. We leave these topics for future work.

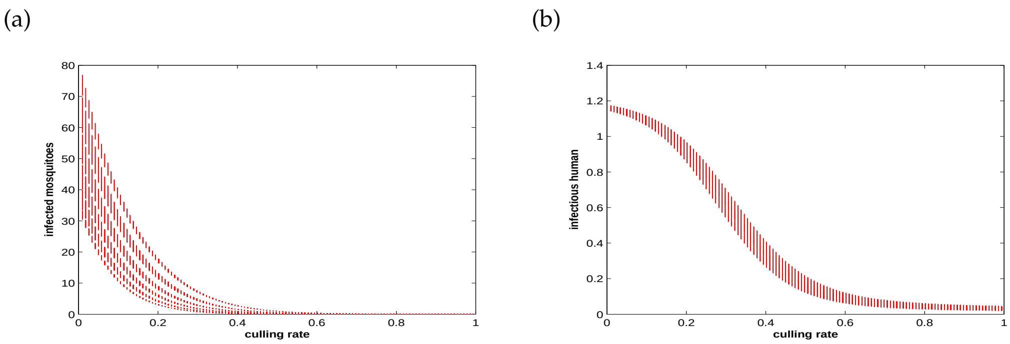

Figure 6.3: The bifurcation diagram of infected human and mosquitoes about culling rate ϕ in model (2.1), where $T = 2$ (days).

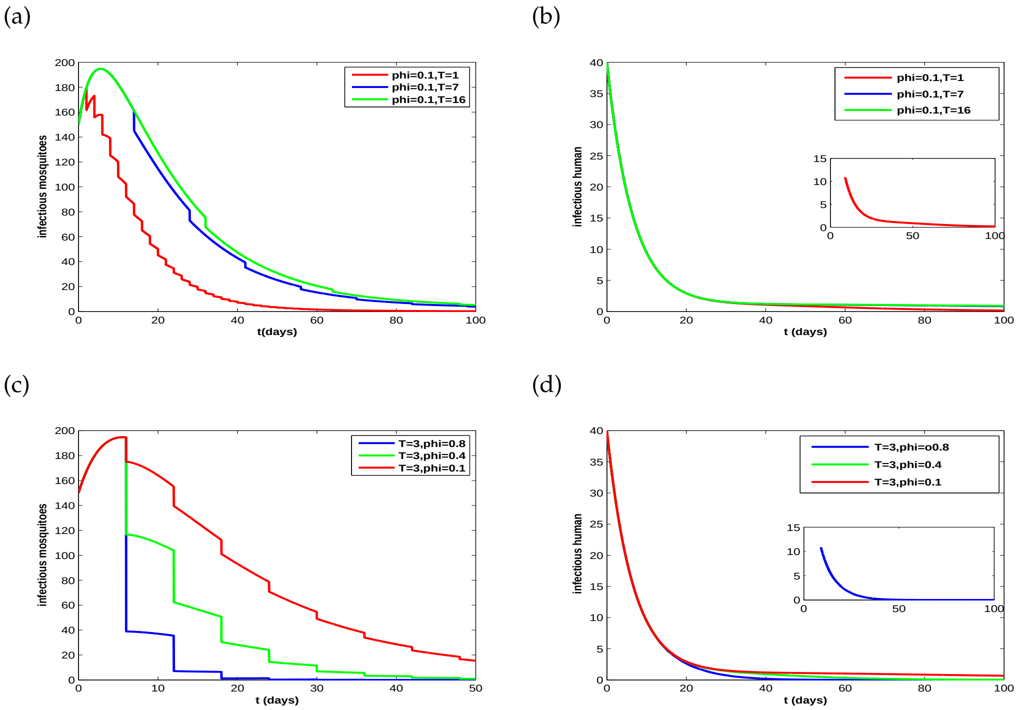

Figure 6.4: The quantities of infected mosquitoes and human in model (2.1): (a)–(b) infected mosquitoes $I_m(t)$ and human $I_h(t)$ with $\phi = 0.1$ and $T = 1, 7, 16$ (days), respectively; (c)–(d) infected mosquitoes $I_m(t)$ and infectious human $I_h(t)$ with $T = 3$ (days) and $\phi = 0.1, 0.4, 0.8$, respectively.

Appendix A The expression for each element of $D_X N(0, \mathcal{O})$

It is clear from equation (5.3) that

$$\frac{\mathrm{d}}{\mathrm{dt}}\begin{pmatrix} \frac{\partial \Phi_1}{\partial X_1} & \cdots & \frac{\partial \Phi_1}{\partial X_5} \\ \vdots & \ddots & \vdots \\ \frac{\partial \Phi_5}{\partial X_1} & \cdots & \frac{\partial \Phi_5}{\partial X_5} \end{pmatrix}(t, X_0) = \begin{pmatrix} \frac{\partial F_1}{\partial X_1} & \cdots & \frac{\partial F_1}{\partial X_5} \\ \vdots & \ddots & \vdots \\ \frac{\partial F_5}{\partial X_1} & \cdots & \frac{\partial F_5}{\partial X_5} \end{pmatrix}\begin{pmatrix} \frac{\partial \Phi_1}{\partial X_1} & \cdots & \frac{\partial \Phi_1}{\partial X_5} \\ \vdots & \ddots & \vdots \\ \frac{\partial \Phi_5}{\partial X_1} & \cdots & \frac{\partial \Phi_5}{\partial X_5} \end{pmatrix}(t, X_0)$$

So, from (5.2), we further get

$$\begin{aligned}
&\frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_4}{\partial X_1} = -(\mu_h + d_h + \gamma_h)\frac{\partial \Phi_4}{\partial X_1} + b\rho_{hm}\widetilde{S}_h\frac{\partial \Phi_5}{\partial X_1}, && \frac{\partial \Phi_4}{\partial X_1}(0, X_0) = 0,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_5}{\partial X_1} = -\mu_m\frac{\partial \Phi_5}{\partial X_1} + b\rho_{mh}\widetilde{S}_m\frac{\partial \Phi_4}{\partial X_1}, && \frac{\partial \Phi_5}{\partial X_1}(0, X_0) = 0,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_4}{\partial X_2} = -(\mu_h + d_h + \gamma_h)\frac{\partial \Phi_4}{\partial X_2} + b\rho_{hm}\widetilde{S}_h\frac{\partial \Phi_5}{\partial X_2}, && \frac{\partial \Phi_4}{\partial X_2}(0, X_0) = 0,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_5}{\partial X_2} = -\mu_m\frac{\partial \Phi_5}{\partial X_2} + b\rho_{mh}\widetilde{S}_m\frac{\partial \Phi_4}{\partial X_2}, && \frac{\partial \Phi_5}{\partial X_2}(0, X_0) = 0,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_4}{\partial X_3} = -(\mu_h + d_h + \gamma_h)\frac{\partial \Phi_4}{\partial X_3} + b\rho_{hm}\widetilde{S}_h\frac{\partial \Phi_5}{\partial X_3}, && \frac{\partial \Phi_4}{\partial X_3}(0, X_0) = 0,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_5}{\partial X_3} = -\mu_m\frac{\partial \Phi_5}{\partial X_3} + b\rho_{mh}\widetilde{S}_m\frac{\partial \Phi_4}{\partial X_3}, && \frac{\partial \Phi_5}{\partial X_3}(0, X_0) = 0.
\end{aligned}$$

Thus we obtain

$$\frac{\partial \Phi_i}{\partial X_j}(t, X_0) \equiv 0, \quad i = 4, 5, \quad j = 1, 2, 3,$$

for $0 \leq t < T$. Further, one has

$$\begin{aligned}
&\frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_1}{\partial X_1} = -\mu_h \frac{\partial \Phi_1}{\partial X_1}, \quad \frac{\partial \Phi_1}{\partial X_1}(0, X_0) = 1, \quad \frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_2}{\partial X_1} = -\mu_m \frac{\partial \Phi_2}{\partial X_1}, \quad \frac{\partial \Phi_2}{\partial X_1}(0, X_0) = 0,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_3}{\partial X_1} = -\mu_h \frac{\partial \Phi_3}{\partial X_1}, \quad \frac{\partial \Phi_3}{\partial X_1}(0, X_0) = 0, \quad \frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_1}{\partial X_2} = -\mu_h \frac{\partial \Phi_1}{\partial X_2}, \quad \frac{\partial \Phi_1}{\partial X_2}(0, X_0) = 0,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_2}{\partial X_2} = -\mu_m \frac{\partial \Phi_2}{\partial X_2}, \quad \frac{\partial \Phi_2}{\partial X_2}(0, X_0) = 1, \quad \frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_3}{\partial X_2} = -\mu_h \frac{\partial \Phi_3}{\partial X_2}, \quad \frac{\partial \Phi_3}{\partial X_2}(0, X_0) = 0,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_1}{\partial X_3} = -\mu_h \frac{\partial \Phi_1}{\partial X_3}, \quad \frac{\partial \Phi_1}{\partial X_3}(0, X_0) = 0, \quad \frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_2}{\partial X_3} = -\mu_m \frac{\partial \Phi_2}{\partial X_3}, \quad \frac{\partial \Phi_2}{\partial X_3}(0, X_0) = 0,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_3}{\partial X_3} = -\mu_h \frac{\partial \Phi_3}{\partial X_3}, \quad \frac{\partial \Phi_3}{\partial X_3}(0, X_0) = 1.
\end{aligned}$$

It is obvious that

$$\begin{aligned}
&\frac{\partial \Phi_1}{\partial X_1}(t, X_0) = e^{-\mu_h t}, && \frac{\partial \Phi_1}{\partial X_2}(t, X_0) = 0, && \frac{\partial \Phi_1}{\partial X_3}(t, X_0) = 0,\\
&\frac{\partial \Phi_2}{\partial X_1}(t, X_0) = 0, && \frac{\partial \Phi_2}{\partial X_2}(t, X_0) = e^{-\mu_m t}, && \frac{\partial \Phi_2}{\partial X_3}(t, X_0) = 0,\\
&\frac{\partial \Phi_3}{\partial X_1}(t, X_0) = 0, && \frac{\partial \Phi_3}{\partial X_2}(t, X_0) = 0, && \frac{\partial \Phi_3}{\partial X_3}(t, X_0) = e^{-\mu_h t}.
\end{aligned}$$

Consequently, we have

$$\begin{aligned}
&\frac{\mathrm{d}}{\mathrm{dt}}\left(\frac{\partial \Phi_4}{\partial X_4}\right) = -(\mu_h + d_h + \gamma_h)\frac{\partial \Phi_4}{\partial X_4} + b\rho_{hm}\widetilde{S}_h \frac{\partial \Phi_5}{\partial X_4}, && \frac{\partial \Phi_4}{\partial X_4}(0, X_0) = 1,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\left(\frac{\partial \Phi_5}{\partial X_4}\right) = -\mu_m \frac{\partial \Phi_5}{\partial X_4} + b\rho_{mh}\widetilde{S}_m \frac{\partial \Phi_4}{\partial X_4}, && \frac{\partial \Phi_5}{\partial X_4}(0, X_0) = 0,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\left(\frac{\partial \Phi_4}{\partial X_5}\right) = -(\mu_h + d_h + \gamma_h)\frac{\partial \Phi_4}{\partial X_5} + b\rho_{hm}\widetilde{S}_h \frac{\partial \Phi_5}{\partial X_5}, && \frac{\partial \Phi_4}{\partial X_5}(0, X_0) = 0,
\end{aligned}$$

$$\begin{aligned}
&\frac{\mathrm{d}}{\mathrm{dt}}\left(\frac{\partial \Phi_5}{\partial X_5}\right) = -\mu_m \frac{\partial \Phi_5}{\partial X_5} + b\rho_{mh}\widetilde{S}_m \frac{\partial \Phi_4}{\partial X_5}, && \frac{\partial \Phi_5}{\partial X_5}(0, X_0) = 1,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\left(\frac{\partial \Phi_1}{\partial X_4}\right) = -\mu_h \frac{\partial \Phi_1}{\partial X_4} - b\rho_{hm}\widetilde{S}_h \frac{\partial \Phi_5}{\partial X_4}, && \frac{\partial \Phi_1}{\partial X_4}(0, X_0) = 0,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\left(\frac{\partial \Phi_1}{\partial X_5}\right) = -\mu_m \frac{\partial \Phi_2}{\partial X_4} - b\rho_{mh}\widetilde{S}_m \frac{\partial \Phi_5}{\partial X_4}, && \frac{\partial \Phi_1}{\partial X_5}(0, X_0) = 0,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\left(\frac{\partial \Phi_2}{\partial X_4}\right) = -\mu_m \frac{\partial \Phi_2}{\partial X_4} - b\rho_{mh}\widetilde{S}_m \frac{\partial \Phi_4}{\partial X_4}, && \frac{\partial \Phi_2}{\partial X_4}(0, X_0) = 0,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\left(\frac{\partial \Phi_2}{\partial X_5}\right) = -\mu_m \frac{\partial \Phi_2}{\partial X_5} - b\rho_{mh}\widetilde{S}_m \frac{\partial \Phi_4}{\partial X_5}, && \frac{\partial \Phi_2}{\partial X_5}(0, X_0) = 0,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\left(\frac{\partial \Phi_3}{\partial X_4}\right) = -\mu_h \frac{\partial \Phi_3}{\partial X_4} + \gamma_h \frac{\partial \Phi_4}{\partial X_4}, && \frac{\partial \Phi_3}{\partial X_4}(0, X_0) = 0,\\
&\frac{\mathrm{d}}{\mathrm{dt}}\left(\frac{\partial \Phi_3}{\partial X_5}\right) = -\mu_h \frac{\partial \Phi_3}{\partial X_5} + \gamma_h \frac{\partial \Phi_4}{\partial X_5}, && \frac{\partial \Phi_3}{\partial X_5}(0, X_0) = 0.
\end{aligned}$$

We solve the above equations and denote

$$
\begin{aligned}
&a_0 = 1 - \frac{\partial \Phi_4}{\partial X_4}(T, X_0), \qquad b_0 = -\frac{\partial \Phi_4}{\partial X_5}(T, X_0), \qquad c_0 = -(1-\phi)\frac{\partial \Phi_5}{\partial X_4}(T, X_0),\\
&e_0 = 1 - \frac{\partial \Phi_1}{\partial X_1}(T, X_0) = 1 - e^{-\mu_h T}, \qquad f_0 = 1 - (1-\phi)\frac{\partial \Phi_2}{\partial X_2}(T, X_0) = 1 - (1-\phi)e^{-\mu_m T},\\
&a_1 = -\frac{\partial \Phi_1}{\partial X_4}(T, X_0), \qquad b_1 = -\frac{\partial \Phi_1}{\partial X_5}(T, X_0), \qquad c_1 = -(1-\phi)\frac{\partial \Phi_2}{\partial X_4}(T, X_0),\\
&a_2 = 1 - \frac{\partial \Phi_3}{\partial X_3}(T, X_0) = 1 - e^{-\mu_h T}, \qquad b_2 = 1 - \frac{\partial \Phi_3}{\partial X_4}(T, X_0), \qquad c_2 = 1 - \frac{\partial \Phi_3}{\partial X_5}(T, X_0),\\
&d_0 = 1 - (1-\phi)\frac{\partial \Phi_5}{\partial X_5}(T, X_0).
\end{aligned}
$$

Appendix B The first-order partial derivatives of $N_5(\overline{\phi}, \alpha_1)$

We can easily get

$$
\begin{aligned}
\frac{\partial N_5(0,0)}{\partial \alpha_1} &= \frac{\partial N_5(0,0)}{\partial S_h}\left(Y_{11} + \frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \alpha_1}\right) + \frac{\partial N_5(0,0)}{\partial S_m}\left(Y_{12} + \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \alpha_1}\right)\\
&\quad + \frac{\partial N_5(0,0)}{\partial R_h}\left(Y_{13} + \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \alpha_1}\right)\\
&\quad + \frac{\partial N_5(0,0)}{\partial I_h}\left(Y_{14} + \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \alpha_1}\right) + \frac{\partial N_5(0,0)}{\partial I_m}Y_{15},\\
\frac{\partial N_5(0,0)}{\partial \overline{\phi}} &= (1-\phi)\left[-\frac{\partial \Phi_5(X_0)}{\partial S_h}\frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \overline{\phi}} - \frac{\partial \Phi_5(X_0)}{\partial S_m}\frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \overline{\phi}}\right.\\
&\quad \left. - \frac{\partial \Phi_5(X_0)}{\partial R_h}\frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \overline{\phi}} - \frac{\partial \Phi_5(X_0)}{\partial I_h}\frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \overline{\phi}}\right].
\end{aligned} \tag{B.1}
$$

From the equation of (5.6) as $i = 1$, we have

$$
\begin{aligned}
0 &= \frac{\partial N_1(0,0)}{\partial \alpha_1}\\
&= \frac{\partial N_1(0,0)}{\partial S_h}Y_{11} + \frac{\partial N_1(0,0)}{\partial S_m}Y_{12} + \frac{\partial N_1(0,0)}{\partial R_h}Y_{13} + \frac{\partial N_1(0,0)}{\partial I_h}Y_{14} + \frac{\partial N_1(0,0)}{\partial I_m}Y_{15}\\
&\quad + \frac{\partial N_1(0,0)}{\partial S_h}\frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \alpha_1} + \frac{\partial N_1(0,0)}{\partial S_m}\frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \alpha_1}\\
&\quad + \frac{\partial N_1(0,0)}{\partial R_h}\frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \alpha_1} + \frac{\partial N_1(0,0)}{\partial I_h}\frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \alpha_1}.
\end{aligned} \tag{B.2}
$$

Since Y_1 is a basis in $\mathrm{Ker}(D_X N(0,0))$, then we have

$$
\frac{\partial N_i(0,0)}{\partial S_h}Y_{11} + \frac{\partial N_i(0,0)}{\partial S_m}Y_{12} + \frac{\partial N_i(0,0)}{\partial R_h}Y_{13} + \frac{\partial N_i(0,0)}{\partial I_h}Y_{14} + \frac{\partial N_i(0,0)}{\partial I_m}Y_{15} = 0, \quad i = 1, \ldots, 5. \tag{B.3}
$$

Thus we can deduce from (B.2) and (B.3) that

$$
e_0\frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \alpha_1} + 0 \times \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \alpha_1} + 0 \times \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \alpha_1} + a_1\frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \alpha_1} = 0. \tag{B.4}
$$

Similarly, from the equation of (5.6) as $i = 2, 3, 4$, we can obtain that

$$
\begin{aligned}
0 \times \frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \alpha_1} + f_0 \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \alpha_1} + 0 \times \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \alpha_1} + c_1 \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \alpha_1} &= 0, \\
0 \times \frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \alpha_1} + 0 \times \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \alpha_1} + a_2 \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \alpha_1} + b_2 \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \alpha_1} &= 0, \\
0 \times \frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \alpha_1} + 0 \times \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \alpha_1} + 0 \times \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \alpha_1} + a_0 \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \alpha_1} &= 0.
\end{aligned} \tag{B.5}
$$

It is obvious from (B.4) and (B.5) that

$$
\frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \alpha_1} = \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \alpha_1} = \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \alpha_1} = \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \alpha_1} = 0. \tag{B.6}
$$

Considering equation (5.1) as $i = 1$, we have

$$
N_1(\overline{\phi}, \alpha_1) = X_{01} + Y_{11}\alpha_1 + \widetilde{\alpha}_2 - \Phi_1(t, X_0 + \overline{X}(\overline{\phi}, \alpha_1)) \tag{B.7}
$$

with $X_0 = (X_{01}, X_{02}, X_{03}, X_{04}, X_{05})$, and $\overline{X} = (\overline{X}_1, \overline{X}_2, \overline{X}_3, \overline{X}_4, \overline{X}_5)$. Thus one obtains

$$
\begin{aligned}
0 = \frac{\partial N_1(0,0)}{\partial \overline{\phi}} &= \frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \overline{\phi}} - \sum_{i=1}^{4} \frac{\partial \Phi_1(\phi_0, X_0)}{\partial X_i} \frac{\partial \widetilde{\alpha}_{i+1}(0,0)}{\partial \overline{\phi}} \\
&= e_0 \frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \overline{\phi}} + 0 \times \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \overline{\phi}} + 0 \times \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \overline{\phi}} + a_1 \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \overline{\phi}}.
\end{aligned} \tag{B.8}
$$

We can similarly obtain from (5.1) as $i = 2, 3, 4$ that

$$
\begin{aligned}
0 = \frac{\partial N_2(0,0)}{\partial \overline{\phi}} &= \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \overline{\phi}} + \Phi_2(\phi_0, X_0) - (1-\phi_0) \sum_{i=1}^{4} \frac{\partial \Phi_2(\phi_0, X_0)}{\partial X_i} \frac{\partial \widetilde{\alpha}_{i+1}(0,0)}{\partial \overline{\phi}} \\
&= 0 \times \frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \overline{\phi}} + f_0 \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \overline{\phi}} + 0 \times \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \overline{\phi}} + c_1 \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \overline{\phi}} + \Phi_2(\phi_0, X_0), \\
0 = \frac{\partial N_3(0,0)}{\partial \overline{\phi}} &= \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \overline{\phi}} - \sum_{i=1}^{4} \frac{\partial \Phi_3(\phi_0, X_0)}{\partial X_i} \frac{\partial \widetilde{\alpha}_{i+1}(0,0)}{\partial \overline{\phi}} \\
&= 0 \times \frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \overline{\phi}} + \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \overline{\phi}} + a_2 \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \overline{\phi}} + b_2 \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \overline{\phi}}, \\
0 = \frac{\partial N_4(0,0)}{\partial \overline{\phi}} &= \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \overline{\phi}} - \sum_{i=1}^{4} \frac{\partial \Phi_4(\phi_0, X_0)}{\partial X_i} \frac{\partial \widetilde{\alpha}_{i+1}(0,0)}{\partial \overline{\phi}} \\
&= 0 \times \frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \overline{\phi}} + 0 \times \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \overline{\phi}} + 0 \times \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \overline{\phi}} + a_0 \times \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \overline{\phi}}.
\end{aligned} \tag{B.9}
$$

From equations (B.8) and (B.9), we get

$$
\frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \overline{\phi}} = \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \overline{\phi}} = \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \overline{\phi}} = 0, \qquad \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \overline{\phi}} = -\frac{\Phi_2(X_0)}{f_0}. \tag{B.10}
$$

Since

$$
\frac{\partial N_5(0,0)}{\partial S_h} = \frac{\partial N_5(0,0)}{\partial S_m} = \frac{\partial N_5(0,0)}{\partial R_h} = 0,
$$

we can thus observe from (B.1), (B.3), (B.6) and (B.10) that

$$
\frac{\partial N_5(0,0)}{\partial \alpha_1} = \frac{\partial N_5(0,0)}{\partial \overline{\phi}} = 0.
$$

Appendix C The second-order partial derivatives of $N_5(\overline{\phi}, \alpha_1)$ with respect to ϕ

From equation (5.3), we have

$$\frac{\mathrm{d}}{\mathrm{dt}}\frac{\partial \Phi_4(t,X_0)}{\partial X_1} = \frac{\partial F_4(\widetilde{X}(t))}{\partial X_1}\frac{\partial \Phi_1(t,X_0)}{\partial X_1} + \frac{\partial F_4(\widetilde{X}(t))}{\partial X_2}\frac{\partial \Phi_2(t,X_0)}{\partial X_1} + \frac{\partial F_4(\widetilde{X}(t))}{\partial X_3}\frac{\partial \Phi_3(t,X_0)}{\partial X_1} + \frac{\partial F_4(\widetilde{X}(t))}{\partial X_4}\frac{\partial \Phi_4(t,X_0)}{\partial X_1} + \frac{\partial F_4(\widetilde{X}(t))}{\partial X_5}\frac{\partial \Phi_5(t,X_0)}{\partial X_1}.$$

Then

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{dt}}\left(\frac{\partial^2 \Phi_4(t,X_0)}{\partial X_1^2}\right) = {}& \frac{\partial^2 F_4(\widetilde{X}(t))}{\partial X_1^2}\frac{\partial \Phi_1(t,X_0)}{\partial X_1} + \frac{\partial F_4(\widetilde{X}(t))}{\partial X_1}\frac{\partial^2 \Phi_1(t,X_0)}{\partial X_1^2} + \frac{\partial^2 F_4(\widetilde{X}(t))}{\partial X_1 \partial X_2}\frac{\partial \Phi_2(t,X_0)}{\partial X_1} \\ &+ \frac{\partial F_4(\widetilde{X}(t))}{\partial X_2}\frac{\partial^2 \Phi_2(t,X_0)}{\partial X_1^2} + \frac{\partial^2 F_4(\widetilde{X}(t))}{\partial X_1 \partial X_3}\frac{\partial \Phi_3(t,X_0)}{\partial X_1} + \frac{\partial F_4(\widetilde{X}(t))}{\partial X_3}\frac{\partial^2 \Phi_3(t,X_0)}{\partial X_1^2} \\ &+ \frac{\partial^2 F_4(\widetilde{X}(t))}{\partial X_1 \partial X_4}\frac{\partial \Phi_4(t,X_0)}{\partial X_1} + \frac{\partial F_4(\widetilde{X}(t))}{\partial X_4}\frac{\partial^2 \Phi_4(t,X_0)}{\partial X_1^2} + \frac{\partial^2 F_4(\widetilde{X}(t))}{\partial X_1 \partial X_5}\frac{\partial \Phi_5(t,X_0)}{\partial X_1} \\ &+ \frac{\partial F_4(\widetilde{X}(t))}{\partial X_5}\frac{\partial^2 \Phi_5(t,X_0)}{\partial X_1^2}.\end{aligned}$$

It is obvious that

$$\begin{aligned}\frac{\partial^2 F_4(\widetilde{X}(t))}{\partial X_1^2} = \frac{\partial F_4(\widetilde{X}(t))}{\partial X_1} = \frac{\partial^2 F_4(\widetilde{X}(t))}{\partial X_1 \partial X_2} = \frac{\partial^2 F_4(\widetilde{X}(t))}{\partial X_1 \partial X_3} = 0, \\ \frac{\partial F_4(\widetilde{X}(t))}{\partial X_2} = \frac{\partial F_4(\widetilde{X}(t))}{\partial X_3} = \frac{\partial \Phi_4(t,X_0)}{\partial X_1} = \frac{\partial \Phi_5(t,X_0)}{\partial X_1} = 0.\end{aligned}$$

Thus

$$\frac{\mathrm{d}}{\mathrm{dt}}\left(\frac{\partial^2 \Phi_4(t,X_0)}{\partial X_1^2}\right) = \frac{\partial F_4(\widetilde{X}(t))}{\partial X_4}\frac{\partial^2 \Phi_4(t,X_0)}{\partial X_1^2} + \frac{\partial F_4(\widetilde{X}(t))}{\partial X_5}\frac{\partial^2 \Phi_5(t,X_0)}{\partial X_1^2}. \tag{C.1}$$

We can similarly obtain that

$$\frac{\mathrm{d}}{\mathrm{dt}}\left(\frac{\partial^2 \Phi_5(t,X_0)}{\partial X_1^2}\right) = \frac{\partial F_5(\widetilde{X}(t))}{\partial X_4}\frac{\partial^2 \Phi_4(t,X_0)}{\partial X_1^2} + \frac{\partial F_5(\widetilde{X}(t))}{\partial X_5}\frac{\partial^2 \Phi_5(t,X_0)}{\partial X_1^2}. \tag{C.2}$$

Consider the initial conditions

$$\frac{\partial^2 \Phi_4(0,X_0)}{\partial X_1^2} = \frac{\partial^2 \Phi_5(0,X_0)}{\partial X_1^2} = 0,$$

it can be deduced from (C.1) and (C.2) that

$$\frac{\partial^2 \Phi_4(t,X_0)}{\partial X_1^2} = \frac{\partial^2 \Phi_5(t,X_0)}{\partial X_1^2} = 0.$$

The same method can be adopted to get that

$$\frac{\partial^2 \Phi_4(t,X_0)}{\partial X_2^2} = \frac{\partial^2 \Phi_5(t,X_0)}{\partial X_2^2} = 0 \tag{C.3}$$

and

$$\begin{aligned}\frac{\partial^2\Phi_4(t,X_0)}{\partial X_1\partial X_2}=\frac{\partial^2\Phi_4(t,X_0)}{\partial X_2\partial X_1}=\frac{\partial^2\Phi_5(t,X_0)}{\partial X_1\partial X_2}=\frac{\partial^2\Phi_5(t,X_0)}{\partial X_2\partial X_1}=0,\\ \frac{\partial^2\Phi_4(t,X_0)}{\partial X_2\partial X_3}=\frac{\partial^2\Phi_4(t,X_0)}{\partial X_3\partial X_2}=\frac{\partial^2\Phi_5(t,X_0)}{\partial X_2\partial X_3}=\frac{\partial^2\Phi_5(t,X_0)}{\partial X_3\partial X_2}=0.\end{aligned}\tag{C.4}$$

Based on the third equation of (B.9), we have

$$\begin{aligned}0&=\frac{\partial^2 N_4(0,0)}{\partial\overline{\phi}^2}=\frac{\partial}{\partial\overline{\phi}}\frac{\partial N_4(0,0)}{\partial\overline{\phi}}=\frac{\partial}{\partial\overline{\phi}}\left(\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\overline{\phi}}-\sum_{i=1}^{4}\frac{\partial\Phi_4(t,X_0)}{\partial X_i}\frac{\partial\widetilde{\alpha}_{i+1}(0,0)}{\partial\overline{\phi}}\right)\\
&=\frac{\partial^2\widetilde{\alpha}_5(0,0)}{\partial\overline{\phi}^2}-\left(\frac{\partial\Phi_4(t,X_0)}{\partial X_1}\frac{\partial^2\widetilde{\alpha}_2(0,0)}{\partial\overline{\phi}^2}+\frac{\partial\Phi_4(t,X_0)}{\partial X_2}\frac{\partial^2\widetilde{\alpha}_3(0,0)}{\partial\overline{\phi}^2}+\frac{\partial\Phi_4(t,X_0)}{\partial X_3}\frac{\partial^2\widetilde{\alpha}_4(0,0)}{\partial\overline{\phi}^2}\right.\\
&\quad\left.+\frac{\partial\Phi_4(t,X_0)}{\partial X_4}\frac{\partial^2\widetilde{\alpha}_5(0,0)}{\partial\overline{\phi}^2}\right)-\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\overline{\phi}}\left[\frac{\partial^2\Phi_4(t,X_0)}{\partial X_1^2}\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\overline{\phi}}+\frac{\partial^2\Phi_4(t,X_0)}{\partial X_1\partial X_2}\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\overline{\phi}}\right.\\
&\quad\left.+\frac{\partial^2\Phi_4(t,X_0)}{\partial X_1\partial X_3}\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\overline{\phi}}+\frac{\partial^2\Phi_4(t,X_0)}{\partial X_1\partial X_4}\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\overline{\phi}}\right]-\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\overline{\phi}}\left[\frac{\partial^2\Phi_4(t,X_0)}{\partial X_1\partial X_2}\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\overline{\phi}}\right.\\
&\quad\left.+\frac{\partial^2\Phi_4(t,X_0)}{\partial X_2^2}\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\overline{\phi}}+\frac{\partial^2\Phi_4(t,X_0)}{\partial X_2\partial X_3}\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\overline{\phi}}+\frac{\partial^2\Phi_4(t,X_0)}{\partial X_2\partial X_4}\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\overline{\phi}}\right]\\
&\quad-\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\overline{\phi}}\left[\frac{\partial^2\Phi_4(t,X_0)}{\partial X_1\partial X_3}\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\overline{\phi}}+\frac{\partial^2\Phi_4(t,X_0)}{\partial X_2\partial X_3}\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\overline{\phi}}+\frac{\partial^2\Phi_4(t,X_0)}{\partial X_3^2}\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\overline{\phi}}\right.\\
&\quad\left.+\frac{\partial^2\Phi_4(t,X_0)}{\partial X_3\partial X_4}\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\overline{\phi}}\right]-\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\overline{\phi}}\left[\frac{\partial^2\Phi_4(t,X_0)}{\partial X_1\partial X_4}\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\overline{\phi}}\right.\\
&\quad\left.+\frac{\partial^2\Phi_4(t,X_0)}{\partial X_2\partial X_4}\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\overline{\phi}}+\frac{\partial^2\Phi_4(t,X_0)}{\partial X_3\partial X_4}\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\overline{\phi}}+\frac{\partial^2\Phi_4(t,X_0)}{\partial X_4^2}\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\overline{\phi}}\right].\end{aligned}$$

Substituting (B.10) and (C.3) into the above equation, we have

$$\frac{\partial^2\widetilde{\alpha}_5(0,0)}{\partial\overline{\phi}^2}=0.\tag{C.5}$$

Therefore, we can easily get that

$$\begin{aligned}\frac{\partial^2 N_5(0,0)}{\partial\overline{\phi}^2}=&-(1-\phi)\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\overline{\phi}}\left(\frac{\partial^2\Phi_5(X_0)}{\partial S_h\partial S_m}\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\overline{\phi}}+\frac{\partial^2\Phi_5(X_0)}{\partial S_m^2}\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\overline{\phi}}\right.\\
&\left.+\frac{\partial^2\Phi_5(X_0)}{\partial S_m\partial R_h}\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\overline{\phi}}+\frac{\partial^2\Phi_5(X_0)}{\partial S_m\partial I_h}\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\overline{\phi}}\right)-\frac{\partial\Phi_5(X_0)}{\partial I_h}\frac{\partial^2\widetilde{\alpha}_5(0,0)}{\partial\overline{\phi}^2}.\end{aligned}\tag{C.6}$$

Substituting (B.10), (C.3) and (C.5) into (C.6), we have

$$A=\frac{\partial^2 N_5(0,0)}{\partial\overline{\phi}^2}=0.$$

Appendix D The second-order partial derivatives of $N_5(\overline{\phi},\alpha_1)$ with respect to ϕ and α_1

We will first calculate the value of $\partial^2\widetilde{\alpha}_5(0,0)/\partial\overline{\phi}\partial\alpha_1$

$$0=\frac{\partial^2 N_4(0,0)}{\partial\overline{\phi}\partial\alpha_1}=\frac{\partial}{\partial\alpha_1}\frac{\partial N_4(0,0)}{\partial\overline{\phi}}=\frac{\partial^2\widetilde{\alpha}_5(0,0)}{\partial\overline{\phi}\partial\alpha_1}-\frac{\partial}{\partial\alpha_1}\left(\sum_{i=1}^{4}\frac{\partial\Phi_4(t,X_0)}{\partial X_i}\frac{\partial\widetilde{\alpha}_{i+1}(0,0)}{\partial\overline{\phi}}\right)$$

$$
\begin{aligned}
=& \frac{\partial^2 \widetilde{\alpha}_5(0,0)}{\partial \overline{\phi} \partial \alpha_1} - \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \overline{\phi}} \left[\frac{\partial^2 \Phi_4(t,X_0)}{\partial X_1 \partial X_2} \left(Y_{11} + \frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \widetilde{\alpha}_1} \right) + \frac{\partial^2 \Phi_4(t,X_0)}{\partial X_2^2} \left(Y_{12} + \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \widetilde{\alpha}_1} \right) \right. \\
&+ \left. \frac{\partial^2 \Phi_4(t,X_0)}{\partial X_2 \partial X_3} \left(Y_{13} + \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \widetilde{\alpha}_1} \right) + \frac{\partial^2 \Phi_4(t,X_0)}{\partial X_2 \partial X_4} \left(Y_{14} + \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \widetilde{\alpha}_1} \right) + \frac{\partial^2 \Phi_4(t,X_0)}{\partial X_2 \partial X_5} Y_{15} \right] \\
&- \frac{\partial \Phi_4(t,X_0)}{\partial X_1} \frac{\partial^2 \widetilde{\alpha}_2(0,0)}{\partial \alpha_1 \partial \overline{\phi}} - \frac{\partial \Phi_4(t,X_0)}{\partial X_2} \frac{\partial^2 \widetilde{\alpha}_3(0,0)}{\partial \alpha_1 \partial \overline{\phi}} - \frac{\partial \Phi_4(t,X_0)}{\partial X_3} \frac{\partial^2 \widetilde{\alpha}_4(0,0)}{\partial \alpha_1 \partial \overline{\phi}} \\
&- \frac{\partial \Phi_4(t,X_0)}{\partial X_4} \frac{\partial^2 \widetilde{\alpha}_5(0,0)}{\partial \alpha_1 \partial \overline{\phi}} - \frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \alpha_1} \frac{\partial}{\partial \alpha_1} \left(\frac{\partial \Phi_4(t,X_0)}{\partial X_1} \right) \\
&- \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \alpha_1} \frac{\partial}{\partial \alpha_1} \left(\frac{\partial \Phi_4(t,X_0)}{\partial X_3} \right) - \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \alpha_1} \frac{\partial}{\partial \alpha_1} \left(\frac{\partial \Phi_4(t,X_0)}{\partial X_4} \right).
\end{aligned}
$$

Once again, by substituting (B.10), (C.2) and (C.4) into the above equation, we can thus deduce that

$$
\frac{\partial^2 \widetilde{\alpha}_5(0,0)}{\partial \overline{\phi} \partial \alpha_1} = -\frac{\Phi_2(X_0))}{a_0 f_0} \left(\frac{\partial^2 \Phi_4(t,X_0)}{\partial S_m \partial I_h} Y_{14} + \frac{\partial^2 \Phi_4(t,X_0)}{\partial S_m \partial I_m} Y_{15} \right). \tag{D.1}
$$

It can be calculated that

$$
\begin{aligned}
0 =& \frac{\partial^2 N_5(0,0)}{\partial \overline{\phi} \partial \alpha_1} = \frac{\partial}{\partial \alpha_1} \left[(1-\phi) \left(-\frac{\partial \Phi_5(X_0)}{\partial S_h} \frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \overline{\phi}} - \frac{\partial \Phi_5(X_0)}{\partial S_m} \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \overline{\phi}} \right. \right. \\
&- \left. \left. \frac{\partial \Phi_5(X_0)}{\partial R_h} \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \overline{\phi}} - \frac{\partial \Phi_5(X_0)}{\partial I_h} \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \overline{\phi}} \right) \right] \\
=& -(1-\phi) \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \overline{\phi}} \left[\frac{\partial^2 \Phi_5(t,X_0)}{\partial S_h \partial S_m} \left(Y_{11} + \frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \widetilde{\alpha}_1} \right) + \frac{\partial^2 \Phi_5(t,X_0)}{\partial S_m^2} \left(Y_{12} + \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \widetilde{\alpha}_1} \right) \right. \\
&+ \left. \frac{\partial^2 \Phi_5(t,X_0)}{\partial S_m \partial R_h} \left(Y_{13} + \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \widetilde{\alpha}_1} \right) + \frac{\partial^2 \Phi_5(t,X_0)}{\partial S_m \partial I_h} \left(Y_{14} + \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \widetilde{\alpha}_1} \right) + \frac{\partial^2 \Phi_5(t,X_0)}{\partial S_m \partial I_m} Y_{15} \right] \\
&- \frac{\partial \Phi_5(X_0)}{\partial I_h} \frac{\partial^2 \widetilde{\alpha}_5(0,0)}{\partial \overline{\phi} \partial \alpha_1} \\
=& -(1-\phi) \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \overline{\phi}} \left[\frac{\partial^2 \Phi_5(t,X_0)}{\partial S_m \partial I_h} Y_{14} + \frac{\partial^2 \Phi_5(t,X_0)}{\partial S_m \partial I_m} Y_{15} \right] + k a_0 \frac{\partial^2 \widetilde{\alpha}_5(0,0)}{\partial \overline{\phi} \partial \alpha_1}.
\end{aligned} \tag{D.2}
$$

Substituting (D.1) and (B.9) into (D.2), we can easily get

$$
\begin{aligned}
\frac{\partial^2 N_5(0,0)}{\partial \overline{\phi} \partial \alpha_1} =& \frac{\Phi_2(X_0)}{f_0} \left[\frac{\partial^2 \Phi_5(t,X_0)}{\partial S_m \partial I_h} Y_{14} + \frac{\partial^2 \Phi_5(t,X_0)}{\partial S_m \partial I_m} Y_{15} \right] \\
&- \frac{k \Phi_2(X_0))}{f_0} \left(\frac{\partial^2 \Phi_4(t,X_0)}{\partial S_m \partial I_h} Y_{14} + \frac{\partial^2 \Phi_4(t,X_0)}{\partial S_m \partial I_m} Y_{15} \right).
\end{aligned}
$$

Appendix E The second-order partial derivatives of $N_5(\overline{\phi}, \alpha_1)$ with respect to α_1

By calculating we have

$$
\begin{aligned}
0 =& \frac{\partial^2 N_5(0,0)}{\partial \alpha_1^2} = \frac{\partial}{\partial \alpha_1} \left[\frac{\partial N_5(0,0)}{\partial S_h} \left(Y_{11} + \frac{\partial \widetilde{\alpha}_2(0,0)}{\partial \alpha_1} \right) + \frac{\partial N_5(0,0)}{\partial S_m} \left(Y_{12} + \frac{\partial \widetilde{\alpha}_3(0,0)}{\partial \alpha_1} \right) \right. \\
&+ \left. \frac{\partial N_5(0,0)}{\partial R_h} \left(Y_{13} + \frac{\partial \widetilde{\alpha}_4(0,0)}{\partial \alpha_1} \right) + \frac{\partial N_5(0,0)}{\partial I_h} \left(Y_{14} + \frac{\partial \widetilde{\alpha}_5(0,0)}{\partial \alpha_1} \right) + \frac{\partial N_5(0,0)}{\partial I_m} Y_{15} \right]
\end{aligned}
$$

$$
\begin{aligned}
&= Y_{11}\left[\frac{\partial^2 N_5(0,0)}{\partial S_h^2}\left(Y_{11}+\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_5(0,0)}{\partial S_h\partial S_m}\left(Y_{12}+\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\alpha_1}\right)\right.\\
&\quad\left.+\frac{\partial^2 N_5(0,0)}{\partial S_h\partial R_h}\left(Y_{13}+\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_5(0,0)}{\partial S_h\partial I_h}\left(Y_{14}+\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_5(0,0)}{\partial S_h\partial I_m}Y_{15}\right]\\
&\quad+Y_{12}\left[\frac{\partial^2 N_5(0,0)}{\partial S_h\partial S_m}\left(Y_{11}+\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_5(0,0)}{\partial S_m^2}\left(Y_{12}+\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\alpha_1}\right)\right.\\
&\quad\left.+\frac{\partial^2 N_5(0,0)}{\partial S_m\partial R_h}\left(Y_{13}+\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_5(0,0)}{\partial S_m\partial I_h}\left(Y_{14}+\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_5(0,0)}{\partial S_m\partial I_m}Y_{15}\right]\\
&\quad+Y_{13}\left[\frac{\partial^2 N_5(0,0)}{\partial S_h\partial R_h}\left(Y_{11}+\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_5(0,0)}{\partial S_m\partial R_h}\left(Y_{12}+\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\alpha_1}\right)\right.\\
&\quad\left.+\frac{\partial^2 N_5(0,0)}{\partial R_h^2}\left(Y_{13}+\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_5(0,0)}{\partial R_h\partial I_h}\left(Y_{14}+\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_5(0,0)}{\partial R_h\partial I_m}Y_{15}\right]\\
&\quad+Y_{14}\left[\frac{\partial^2 N_5(0,0)}{\partial S_h\partial I_h}\left(Y_{11}+\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_5(0,0)}{\partial S_m\partial I_h}\left(Y_{12}+\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\alpha_1}\right)\right.\\
&\quad\left.+\frac{\partial^2 N_5(0,0)}{\partial R_h\partial I_h}\left(Y_{13}+\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_5(0,0)}{\partial I_h^2}\left(Y_{14}+\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_5(0,0)}{\partial I_h\partial I_m}Y_{15}\right]\\
&\quad+Y_{15}\left[\frac{\partial^2 N_5(0,0)}{\partial S_h\partial I_m}\left(Y_{11}+\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_5(0,0)}{\partial S_m\partial I_m}\left(Y_{12}+\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\alpha_1}\right)\right.\\
&\quad\left.+\frac{\partial^2 N_5(0,0)}{\partial R_h\partial I_m}\left(Y_{13}+\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_5(0,0)}{\partial I_h\partial I_m}\left(Y_{14}+\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_5(0,0)}{\partial I_m^2}Y_{15}\right]\\
&\quad+\frac{\partial N_5(0,0)}{\partial I_h}\frac{\partial^2\widetilde{\alpha}_5(0,0)}{\partial\alpha_1^2}=\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2 N_5(0,0)}{\partial X_i\partial X_j}Y_{1i}Y_{1j}+c_0\frac{\partial^2\widetilde{\alpha}_5(0,0)}{\partial\alpha_1^2}.
\end{aligned}
$$

Consider the equation (B.7) as $i=1$, we have

$$
\begin{aligned}
0 &= \frac{\partial^2 N_1(0,0)}{\partial\alpha_1^2}=\frac{\partial}{\partial\alpha_1}\left(\frac{\partial N_1(0,0)}{\partial\alpha_1}\right)\\
&= \left(Y_{11}+\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\alpha_1}\right)\left[\frac{\partial^2 N_1(0,0)}{\partial X_1^2}\left(Y_{11}+\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_1(0,0)}{\partial X_1\partial X_2}\left(Y_{12}+\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\alpha_1}\right)\right.\\
&\quad\left.+\frac{\partial^2 N_1(0,0)}{\partial X_1\partial X_3}\left(Y_{13}+\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_1(0,0)}{\partial X_1\partial X_4}\left(Y_{14}+\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_1(0,0)}{\partial X_1\partial X_5}Y_{15}\right]\\
&\quad+\left(Y_{12}+\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\alpha_1}\right)\left[\frac{\partial^2 N_1(0,0)}{\partial X_1\partial X_2}\left(Y_{11}+\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_1(0,0)}{\partial X_2^2}\left(Y_{12}+\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\alpha_1}\right)\right.\\
&\quad\left.+\frac{\partial^2 N_1(0,0)}{\partial X_2\partial X_3}\left(Y_{13}+\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_1(0,0)}{\partial X_2\partial X_4}\left(Y_{14}+\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_1(0,0)}{\partial X_2\partial X_5}Y_{15}\right]\\
&\quad+\left(Y_{13}+\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\alpha_1}\right)\left[\frac{\partial^2 N_1(0,0)}{\partial X_1\partial X_3}\left(Y_{11}+\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_1(0,0)}{\partial X_2\partial X_3}\left(Y_{12}+\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\alpha_1}\right)\right.\\
&\quad\left.+\frac{\partial^2 N_1(0,0)}{\partial X_3^2}\left(Y_{13}+\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_1(0,0)}{\partial X_3\partial X_4}\left(Y_{14}+\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_1(0,0)}{\partial X_3\partial X_5}Y_{15}\right]\\
&\quad+\left(Y_{14}+\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\alpha_1}\right)\left[\frac{\partial^2 N_1(0,0)}{\partial X_1\partial X_4}\left(Y_{11}+\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_1(0,0)}{\partial X_2\partial X_4}\left(Y_{12}+\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\alpha_1}\right)\right.\\
&\quad\left.+\frac{\partial^2 N_1(0,0)}{\partial X_3\partial X_4}\left(Y_{13}+\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_1(0,0)}{\partial X_4^2}\left(Y_{14}+\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_1(0,0)}{\partial X_4\partial X_5}Y_{15}\right]
\end{aligned}
$$

$$+ Y_{15}\left[\frac{\partial^2 N_1(0,0)}{\partial X_1 \partial X_5}\left(Y_{11}+\frac{\partial\widetilde{\alpha}_2(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_1(0,0)}{\partial X_2 \partial X_5}\left(Y_{12}+\frac{\partial\widetilde{\alpha}_3(0,0)}{\partial\alpha_1}\right)\right.$$
$$\left.+\frac{\partial^2 N_1(0,0)}{\partial X_3 \partial X_5}\left(Y_{13}+\frac{\partial\widetilde{\alpha}_4(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_1(0,0)}{\partial X_4 \partial X_5}\left(Y_{14}+\frac{\partial\widetilde{\alpha}_5(0,0)}{\partial\alpha_1}\right)+\frac{\partial^2 N_1(0,0)}{\partial X_5^2}Y_{15}\right]$$
$$+\frac{\partial N_1(0,0)}{\partial X_1}\frac{\partial^2\widetilde{\alpha}_2(0,0)}{\partial\alpha_1^2}+\frac{\partial N_1(0,0)}{\partial X_2}\frac{\partial^2\widetilde{\alpha}_3(0,0)}{\partial\alpha_1^2}+\frac{\partial N_1(0,0)}{\partial X_3}\frac{\partial^2\widetilde{\alpha}_4(0,0)}{\partial\alpha_1^2}+\frac{\partial N_1(0,0)}{\partial X_4}\frac{\partial^2\widetilde{\alpha}_5(0,0)}{\partial\alpha_1^2}.$$

Substituting (B.10) into the above equation, we have

$$\frac{\partial N_1(0,0)}{\partial X_1}\frac{\partial^2\widetilde{\alpha}_2(0,0)}{\partial\alpha_1^2}+\frac{\partial N_1(0,0)}{\partial X_4}\frac{\partial^2\widetilde{\alpha}_5(0,0)}{\partial\alpha_1^2}=-\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2 N_1(0,0)}{\partial X_i\partial X_j}Y_{1i}Y_{1j}$$
$$=\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2\Phi_1(X_0)}{\partial X_i\partial X_j}Y_{1i}Y_{1j}. \tag{E.1}$$

We can similarly get from (B.7) as $i=2,3,4$ that

$$\frac{\partial N_2(0,0)}{\partial X_2}\frac{\partial^2\widetilde{\alpha}_3(0,0)}{\partial\alpha_1^2}+\frac{\partial N_2(0,0)}{\partial X_4}\frac{\partial^2\widetilde{\alpha}_5(0,0)}{\partial\alpha_1^2}=-\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2 N_2(0,0)}{\partial X_i\partial X_j}Y_{1i}Y_{1j}$$
$$=(1-\phi_0)\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2\Phi_2(X_0)}{\partial X_i\partial X_j}Y_{1i}Y_{1j}, \tag{E.2}$$

$$\frac{\partial N_3(0,0)}{\partial X_3}\frac{\partial^2\widetilde{\alpha}_4(0,0)}{\partial\alpha_1^2}+\frac{\partial N_3(0,0)}{\partial X_4}\frac{\partial^2\widetilde{\alpha}_5(0,0)}{\partial\alpha_1^2}=-\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2 N_2(0,0)}{\partial X_i\partial X_j}Y_{1i}Y_{1j}$$
$$=\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2\Phi_3(X_0)}{\partial X_i\partial X_j}Y_{1i}Y_{1j}, \tag{E.3}$$

$$\frac{\partial N_4(0,0)}{\partial X_4}\frac{\partial^2\widetilde{\alpha}_5(0,0)}{\partial\alpha_1^2}=-\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2 N_4(0,0)}{\partial X_i\partial X_j}Y_{1i}Y_{1j}=\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2\Phi_4(X_0)}{\partial X_i\partial X_j}Y_{1i}Y_{1j}. \tag{E.4}$$

From equations (E.1)–(E.4), we get

$$\frac{\partial^2\widetilde{\alpha}_5(0,0)}{\partial\alpha_1^2}=\frac{1}{a_0}\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2\Phi_4(X_0)}{\partial X_i\partial X_j}Y_{1i}Y_{1j}.$$

Therefore,

$$\frac{\partial^2 N_5(0,0)}{\partial\alpha_1^2}=\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2 N_5(0,0)}{\partial X_i\partial X_j}Y_{1i}Y_{1j}+k\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2\Phi_4(X_0)}{\partial X_i\partial X_j}Y_{1i}Y_{1j}$$
$$=-\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2\Phi_5(0,0)}{\partial X_i\partial X_j}Y_{1i}Y_{1j}+k\sum_{i=1}^{5}\sum_{j=1}^{5}\frac{\partial^2\Phi_4(X_0)}{\partial X_i\partial X_j}Y_{1i}Y_{1j}.$$

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