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Dynamical Analysis of Transmission Model of the Cattle Foot-and-Mouth Disease

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Abstract. The epidemic of foot-and-mouth disease (FMD) in cattle remains particular concern in many countries or areas. The epidemic can spread by direct contact with the carrier and symptomatic animals, as well as indirect contact with the contaminated environment. The outbreak of FMD indicates that the infection initially spreads through the farm before spreading between farms. In this paper, considering the cattle population, we establish a dynamical model of FMD with two patches: within-farm and outside-farm, and give the formulae of the basic reproduction number R_0. By constructing the Lyapunov function, we prove the disease-free equilibrium is globally asymptotically stable when $R_0<1$, and that of the unique endemic equilibrium when $R_0>1$. By numerical simulations, we confirm the global stability of equilibria. In addition, by carrying out the sensitivity analysis of the basic reproduction number on some parameters, we reach the conclusion that vaccination, quarantining or removing of the carrier and disinfection are the useful control measures for FMD at the large-scale cattle farm.

AMS subject classifications: 34D05,34D20

Key words: Foot and mouth disease, carriers, dynamical model, environment transmission, Lyapunov function.

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1 Introduction

Foot and mouth disease (FMD) was the first disease which the World Organization for Animal Health (OIE) established official status recognition. It is a highly contagious and economically devastating viral disease of cloven-hoofed animals, such as cattle, pigs, sheep, goats and deer. The typical clinical sign is the occurrence of blisters (or vesicles) on the muzzle, tongue, lips, mouth, between the toes, above the hooves, teats and potential pressure points on the skin. The earliest written records of FMD was in 1546, but the pathogenic agent was not discovered by two former pupils of Robert Koch until the late nineteenth century. FMD is notorious as a perennial threat to ruminants for centuries. FMD outbreaks have occurred in most countries containing the FMD virus (FMDV) susceptible animals. Australia, New Zealand and Indonesia, Central and North America and Western Europe are currently free of FMD. However, FMD is still prevalent in Africa, the Middle East, Asia, and South America. Depending on the epidemiological situation of the FMD, the control strategy is implemented varying from country to country. The FMD free countries or areas prefer to control epidemics by slaughtering infected animals, rather than using vaccination as the control strategy. In many FMD infected countries or areas, vaccination remains an alterative part of an effective control strategy, such as in China, Mongolia, Korea and India. But the decision on whether or not to use vaccination lies in national authorities [25].

FMD is transmitted by multiple routs. Susceptible animals may become infected by contact with infected animals or contaminated objects, and indirect contact with an infected environment [20, 29]. In addition, animals are considered to be carriers of FMDV if the virus or viral genome can still be isolated from the esophageal pharyngeal fluid more than 28 days after infection. The carrier state in the cattle usually does not persist for more than 6 months, although in a small proportion it may last up to 3 years. The carrier animals hold a high level of neutralizing antibody within their sera, but retain the live virus, meanwhile, excrete low-level of FMDV [16, 30]. A study quantifies the transmission rate of FMDV infection from carriers to susceptible animals [33]. The carrier animals are one of the possible sources, which may be occasional cause of new outbreaks [32, 34]. Therefore the model of FMD transmission should take into account the carriers, especially in many countries which use vaccination against FMD.

Dynamic models play the significant role in estimating transmission size and evaluating transmission intensity as well as the control measures. Numerous models studied the mechanisms of the disease transmission between farms, and the epidemiological unit of analysis was the individual farm. These models made predictions with different types of control measures that were taken prevent the epidemic from spreading [2, 5, 6, 8, 10, 11, 14, 21–23, 28]. These models were based on the unit of the farm, which considered that all the animals at the farm are infected when one case is found, as a consequence, many uninfected animals were culling. In addition, the infection will initially spread through the farm before spreading between farms [15, 26]. The within-farm transmission of FMD is module simulating a farm outbreak and modeled local control

measures, and parameter values are estimated for animals in literature and vaccination experiments [12, 23]. The qualitative analysis of dynamical model can give an insight into the mechanism of infection and highlight a 'threshold' effect which signals a radical change in behavior of the epidemic, and the quantitative analysis can estimate numbers of individuals likely to be affected by the disease. Therefore, in this paper we establish a dynamic model to describe propagation both on and off the farm and carry out dynamical analysis for the model. The model consists of two patches: within-farm and outside-farm. The model can provide the understanding of the spreading mechanism of FMD at a single farm as well as outside-farm, and give us threshold values and other constants which we use to describe the behavior of the disease and control of its spread.

The rest of the paper is organized as follows: In Section 2, we introduce the model in details, give the basic reproduction number of the model and carry out the dynamical analysis of the model. In Section 3, we take the large-scale cattle farm in China as a numerical example, and illustrate the effectiveness of the proposed results. We give a brief discussion about the main conclusions in Section 4.

2 Dynamics model and analysis

2.1 Model and basic reproduction number

We divide herds of cattle into two patches: within-farm and outside-farm. Cattle are homogeneously mixed in each patch. The within-farm is a scale cattle farm, which has its own staffs, feed mills and slaughterhouses. Farm staffs, visitors and vehicles visit the farm regularly. The outside-farm refers to the herds that are mainly composed of rural household's scatter breeding within a certain radius of the within-farm. Here, we ignore the migration of animals between the patches, since the artificial insemination (AI), in addition to captive breeding, have been extensively applied at the scale cattle farm. The transfer diagram of the model is depicted in Fig. 1.

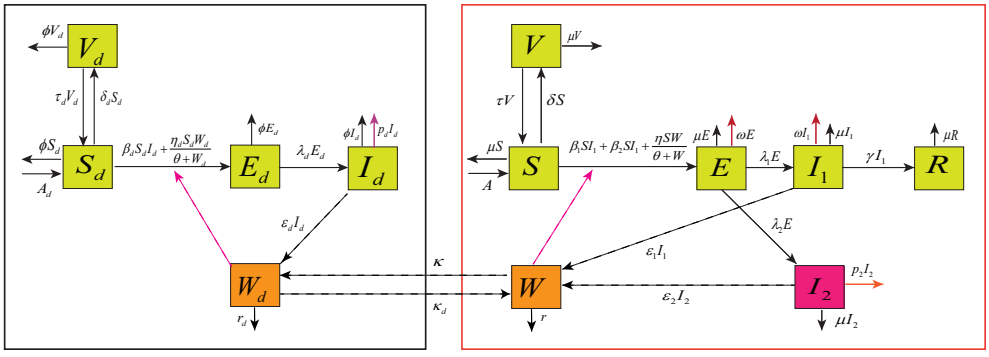


Figure 1: The general transfer diagram for the model.

We interpret this model in three aspects: at the within-farm, the outside-farm and in the environment. At the within-farm, the total population (size of N) is divided into six states: susceptible (S), latent (E), carrier (asymptomatic, I_1), symptomatic (I_1), vaccinated (V) and recovered (R), with the total population $N = S+V+E+I_1+I_2+R$. The animal of the state E is infected but not infectious, has no symptoms and does not excrete virus. But the FMDV is replicating in its body, which can be detected by nonstructural protein antibody (e.g. 3A, 3B, 2B, 2C, 3ABC) tests (NSPS) [3, 7], and the positive animal would be quarantined or removed. The animal of the state I_1 is infectious and excretes virus but not shows symptoms, after which the animal recovers to the state R. The proportion of carrier animals are quarantined or removed by NSPS. The recovered animals is assumed to have the permanent immunity. The animal of the state I_2 shows signs of clinical or is tested in etiologic diagnose, which would be immediately culled. The animal of the state V cannot be infected and not transferred to the state I_1 but enter S when the immunity fades away. At the outside-farm, S_d, E_d, I_d and V_d denote the number of susceptible, latent, symptomatic and vaccinated animals, with the total population satisfying $N_d = S_d+V_d+E_d+I_d$. There is no the carrier state, as FMDV is exclusively localized to the nasopharyngeal mucosa for carriers [31] and not normally shed [24]. In the meanwhile, at the outside-farm, the cattle have few chance to contact with each other due to the low density of animals. In addition, given the limited economic sources, animals are not detected by NSPS. In the environment of the within-farm and outside-farm, the quantity of FMDV are denoted by W and W_d, respectively. In a word, the susceptible class has the input of new susceptible and removal (referred as natural death and out-migration in the paper), the remaining classes have removal.

We make the following hypotheses about the routes of infection of FMD. At the within-farm, the susceptible animals can be infected in two ways: the direct contact with the carrier and symptomatic animals, the indirect contact with the contaminated environment, which can be described by the incidence rates $\beta_1 S I_1$, $\beta_2 S I_2$, and $\eta S \frac{W}{\theta+W}$, respectively. At the outside-farm, the susceptible animals are infected by direct contact with the symptomatic animals and indirect contact with the contaminated environment, given by $\beta_d S_d I_d$ and $\eta_d S_d \frac{W_d}{\theta+W_d}$, respectively. Since the farm is confined in space in which animals uniformly mixed, an increase in population size will proportionally increase the population density, the direct contact number is proportional to the total population size. In this sense, the bilinear incidence $\beta_1 S I_1$, $\beta_2 S I_2$, and $\beta_d S_d I_d$ are suitable for the direct transmission. For FMDV in the environment, the higher the number of FMDV is, the greater the probability of an individual is infected. When the amount of FMDV increases to a certain degree, the probability of infection of an individual will tend to saturation and no longer increase. The bilinear and standard incidence are no longer valid, the saturation incidence is more appropriate, given by $\eta S \frac{W}{\theta+W}$ and $\eta_d S_d \frac{W_d}{\theta+W_d}$. In addition, since farm staffs, visitors and vehicles would carry FMDV in the infected environment when they enter and leave between the within-farm and outside-farm, which may induce the transmission of FMD across the farm.

Based on the transmission mechanisms and previous assumptions, we express the

time evolution of the population states in the following deterministic ordinary differential equations:

$$\begin{aligned}
\frac{\mathrm{d}S}{\mathrm{d}t} &= A-\beta_1 SI_1-\beta_2 SI_2-\eta S\frac{W}{\theta+W}-\delta S+\tau V-\mu S,\\
\frac{\mathrm{d}E}{\mathrm{d}t} &= \beta_1 SI_1+\beta_2 SI_2+\eta S\frac{W}{\theta+W}-\lambda_1 E-\lambda_2 E-\omega E-\mu E,\\
\frac{\mathrm{d}I_1}{\mathrm{d}t} &= \lambda_1 E-\gamma I_1-\omega I_1-\mu I_1,\\
\frac{\mathrm{d}I_2}{\mathrm{d}t} &= \lambda_2 E-p_2 I_2-\mu I_2,\\
\frac{\mathrm{d}V}{\mathrm{d}t} &= \delta S-\tau V-\mu V,\\
\frac{\mathrm{d}R}{\mathrm{d}t} &= \gamma I_1-\mu R,\\
\frac{\mathrm{d}S_d}{\mathrm{d}t} &= A_d-\beta_d S_d I_d-\eta_d S_d\frac{W_d}{\theta+W_d}-\delta_d S_d+\tau_d V_d-\phi S_d,\\
\frac{\mathrm{d}E_d}{\mathrm{d}t} &= \beta_d S_d I_d+\eta_d S_d\frac{W_d}{\theta+W_d}-\lambda_d E_d-\phi E_d,\\
\frac{\mathrm{d}I_d}{\mathrm{d}t} &= \lambda_d E_d-p_d I_d-\phi I_d,\\
\frac{\mathrm{d}V_d}{\mathrm{d}t} &= \delta_d S_d-\tau_d V_d-\phi V_d,\\
\frac{\mathrm{d}W}{\mathrm{d}t} &= \kappa_d W_d+\varepsilon_1 I_1+\varepsilon_2 I_2-rW-\kappa W,\\
\frac{\mathrm{d}W_d}{\mathrm{d}t} &= \kappa W+\varepsilon_d I_d-r_d W_d-\kappa_d W_d.
\end{aligned} \tag{2.1}$$

From system (2.1), all the parameters are described in Table 1, and assumed nonnegative, the total population $N=S+I_1+I_2+E+V+R$ satisfies

$$\frac{\mathrm{d}N}{\mathrm{d}t}=A-\mu N-p_2 I_2\le A-\mu N.$$

Similarly,

$$\frac{\mathrm{d}N_d}{\mathrm{d}t}=A_d-\phi N_d-p_d I_d\le A_d-\phi N_d,$$

which implies that the region Ω is positively invariant for system (2.1), that is

$$\begin{aligned}
\Omega=\Big\{&(S,E,I_1,I_2,V,R,S_d,I_d,E_d,V_d,W,W_d)\in R_+^{12},\\
&0\le S+E+I_1+I_2+V+R\le\frac{A}{\mu+\omega},\ 0\le S_d+I_d+E_d+V_d\le\frac{A_d}{\phi},\\
&0\le W+W_d\le\frac{(\varepsilon_1+\varepsilon_2)\frac{A}{\mu}+\varepsilon_d\frac{A_d}{\phi}}{\min\{r,r_d\}}\Big\},
\end{aligned}$$

Table 1: Notation for model parameters.

Parameter	Description
A, A_d	The birth and import number of animals
μ, ϕ	The removal rate
$\beta_1, \beta_2, \beta_d$	The transmission coefficient between the infected and susceptible animals
η, η_d	The transmission rate of FMDV in environment to the susceptible animals
γ	Rate of recovery of the carrier animals,
τ, τ_d	Rate of loss of vaccinal immunity
δ, δ_d	Rate of vaccination
$\lambda_1, \lambda_2, \lambda_d$	Rate of transfer from the latent to infected class
ω	The proportion of quarantining or removing in E and I_1 for NSPS
p_2, p_d	Disease induced death and slaughter rate
κ, κ_d	Transfer rate of FMDV in the environment for farm staffs, visitors and vehicles movements
r, r_d	The decaying and effective disinfection rate of FMDV in the environment
$\varepsilon_1, \varepsilon_2, \varepsilon_d$	FMDV shedding rate by infected individual
θ	A shape parameter that determines infectious dose

It is easy to see that system (2.1) has a unique disease-free equilibrium

$$P^0 = \left(S^0, 0, 0, 0, V^0, 0, S_d^0, 0, 0, V_d^0, 0, 0\right) \in R_+^{12},$$

where

$$S^0 = \frac{(\tau+\mu+\omega)A}{(\tau+\mu+\omega+\delta)(\mu+\omega)}, \quad V^0 = \frac{\delta A}{(\tau+\mu+\omega+\delta)(\mu+\omega)},$$
$$S_d^0 = \frac{(\tau_d+\phi)A_d}{(\tau_d+\phi+\delta_d)\phi}, \qquad V_d^0 = \frac{\delta_d A_d}{(\tau_d+\phi+\delta_d)\phi}.$$

The threshold condition known as the basic reproduction number R_0 which estimates the average number of secondary cases generated by one average primary case in an entirely susceptible population during the mean infectious period. Clearly, when $R_0 < 1$ each successive 'infection generation' is smaller than its predecessor, and the infection cannot persist with time. Conversely, when $R_0 > 1$ successive 'infection generations' are larger than their predecessors, an initial case will lead to an outbreak. Using the next generation matrix formulated in van den Driessche and Watmough [36], we will give the basic reproduction number of system (2.1). E, E_d, I_1, I_2, I_d, W and W_d are considered to be the disease compartments. Let $a = \lambda_1+\lambda_2+\omega+\mu$, $b = \gamma+\omega+\mu$, $c = p_2+\mu$, $e = \lambda_d+\phi$, $g = p_d+\phi$, $f = r+\kappa$, $h = r_d+\kappa_d$. $G = \frac{\varepsilon_1\lambda_1}{ab} + \frac{\varepsilon_2\lambda_2}{ac}$, $H = fh - \kappa\kappa_d$. We can obtain that the next

generation matrix is

$$FV^{-}=\begin{pmatrix} x_{11} & x_{12} & * \\ x_{21} & x_{22} & * \\ 0 & 0 & 0 \end{pmatrix},$$

where

$$x_{11}=\frac{\beta_1 S^0\lambda_1}{ab}+\frac{\beta_2 S^0\lambda_2}{ac}+\frac{\eta S^0 hG}{\theta H}, \quad x_{21}=\frac{\eta_d S_d^0 \kappa G}{\theta H},$$
$$x_{12}=\frac{\eta S^0\varepsilon_d\lambda_d\kappa_d}{\theta egH}, \quad x_{22}=\frac{\beta_d S_d^0\lambda_d}{eg}+\frac{\eta_d S_d^0\varepsilon_d\lambda_d f}{\theta egH}.$$

The basic reproduction number of system (2.1) is

$$R_0=\rho(\mathcal{F}\mathcal{V}^{-})=\frac{x_{11}+x_{22}+\sqrt{(x_{11}-x_{22})^2+4x_{12}x_{21}}}{2},$$
$$R_{01}=\frac{\beta_1 S^0\lambda_1}{ab}+\frac{\beta_2 S^0\lambda_2}{ac}+\frac{\eta S^0 G}{\theta f},$$
$$R_{02}=\frac{\beta_d S_d^0\lambda_d}{eg}+\frac{\eta_d S_d^0\lambda_d\varepsilon_d}{eg\theta h},$$

where R_{01}, R_{02} are the basic reproduction numbers which are induced by the within-farm and outside-farm transmission, respectively. Since $x_{11}=R_{01}+\frac{\eta S^0\kappa\kappa_d G}{\theta Hf}$, $x_{22}=R_{02}+\frac{\eta_d S_d^0\lambda_d\varepsilon_d\kappa\kappa_d}{\theta egHh}$, it can be given that $R_0=\max\{R_{01},R_{02}\}$, when $\kappa=0$ or $\kappa_d=0$, and others $R_0>\max\{R_{01},R_{02}\}$, especially,

$$R_0<1 \quad \text{when} \quad R_{01}<1-\frac{\eta S^0\kappa_d(f+\kappa)G}{\theta Hf} \quad \text{and} \quad R_{02}<1-\frac{\eta_d S_d^0\lambda_d\varepsilon_d\kappa(h+\kappa_d)}{\theta egHh}.$$

2.2 The global stability for the disease-free equilibrium

In this section, we will investigate global stability of the disease-free equilibrium. By van den Driessche and Watmough [36, Theorem 2], the disease-free equilibrium P^0 of system (2.1) is locally asymptotically stable when $R_0<1$. If $R_0>1$, the disease-free equilibrium P^0 of system (2.1) is unstable.

Theorem 2.1. *The disease-free equilibrium P^0 of the system (2.1) is globally asymptotically stable in Ω when $R_0<1$.*

Proof. We will prove global stability of the disease-free equilibrium by using a Lyapunov

function. For the disease-free equilibrium P^0, system (2.1) can be rewritten as follows:

$$\begin{aligned}
&\frac{\mathrm{d}S}{\mathrm{d}t}=S\left[A\left(\frac{1}{S}-\frac{1}{S^0}\right)+\tau\left(\frac{V}{S}-\frac{V^0}{S^0}\right)-\beta_1 I_1-\beta_2 I_2-\eta\frac{W}{\theta+W}\right],\\
&\frac{\mathrm{d}E}{\mathrm{d}t}=\left(\beta_1 I_1+\beta_2 I_2+\eta\frac{W}{\theta+W}\right)(S-S^0+S^0)-\lambda_1 E-\lambda_2 E-(\omega+\mu)E,\\
&\frac{\mathrm{d}I_1}{\mathrm{d}t}=\lambda_1 E-bI_1,\\
&\frac{\mathrm{d}I_2}{\mathrm{d}t}=\lambda_2 E-cI_2,\\
&\frac{\mathrm{d}V}{\mathrm{d}t}=\delta V\left(\frac{S}{V}-\frac{S^0}{V^0}\right),\\
&\frac{\mathrm{d}S_d}{\mathrm{d}t}=S_d\left[A_d\left(\frac{1}{S_d}-\frac{1}{S_d^0}\right)+\delta_d\left(\frac{V_d}{S_d}-\frac{V_d^0}{S_d^0}\right)-\beta_d I_d-\eta_d\frac{W_d}{\theta+W_d}\right],\\
&\frac{\mathrm{d}E_d}{\mathrm{d}t}=\left(\beta_d I_d+\eta_d\frac{W_d}{\theta+W_d}\right)(S_d-S_d^0+S_d^0)-\lambda_d E_d-\phi E_d,\\
&\frac{\mathrm{d}I_d}{\mathrm{d}t}=\lambda_d E_d-(p_d+\phi)I_d,\\
&\frac{\mathrm{d}V_d}{\mathrm{d}t}=\delta_d V_d\left(\frac{S_d}{V_d}-\frac{S_d^0}{V_d^0}\right),\\
&\frac{\mathrm{d}W}{\mathrm{d}t}=\kappa_d W_d+\varepsilon_1 I_1+\varepsilon_2 I_2-(r+\kappa)W,\\
&\frac{\mathrm{d}W_d}{\mathrm{d}t}=\kappa W+\varepsilon_d I_d-(r_d+\kappa_d)W_d.
\end{aligned}$$

We define the Lyapunov function

$$\begin{aligned}
L=&X_0\left(S-S^0-S^0\ln\frac{S}{S^0}+V-V^0-V^0\ln\frac{V}{V^0}+E\right)\\
&+X_4\left(S_d-S_d^0-S_d^0\ln\frac{S_d}{S_d^0}+V_d-V_d^0-V_d^0\ln\frac{V_d}{V_d^0}+E_d\right)\\
&+X_1 I_1+X_2 I_2+X_3 W+X_5 I_d+X_3 W_d,
\end{aligned}$$

where $X_1>0$, $X_2>0$, $X_3>0$, $X_4>0$, $X_5>0$. Give

$$\begin{aligned}
&X_0=\frac{\eta_d S_d^0}{r_d}, && X_3=\frac{\eta S^0\eta_d S_d^0}{rr_d\theta},\\
&X_1=\frac{\eta_d S_d^0\beta_1 S^0}{r_d b}+\frac{\eta S^0\eta_d S_d^0\varepsilon_1}{rr_d b\theta}, && X_4=\frac{\eta S^0}{r},\\
&X_2=\frac{\eta_d S_d^0\beta_2 S^0}{r_d c}+\frac{\eta S^0\eta_d S_d^0\varepsilon_2}{rr_d c\theta}, && X_5=\frac{\eta S^0\beta_d S_d^0}{r(p_d+\phi)}+\frac{\eta S^0\eta_d S_d^0\varepsilon_d}{rr_d\theta(p_d+\phi)}.
\end{aligned}$$

The derivative of the Lyapunov function L is

$$\begin{aligned}
L' =& X_0\left((1-S^0)S'+(1-V^0)V'+E\right)+X_4\left((1-S_d^0)S'+(1-V_d^0)V'+E_d\right)\\
&+X_1I_1'+X_2I_2'+X_3W'+X_5I_d'+X_3W_d'\\
=&\frac{\eta_d S_d^0}{r_d}\left[A\left(2-\frac{S^0}{S}-\frac{S}{S^0}\right)+\tau V^0\left(1-\frac{S}{S^0}+\frac{V}{V^0}-\frac{S^0V}{SV^0}\right)+\delta S^0\left(1-\frac{V}{V^0}+\frac{S}{S^0}-\frac{SV^0}{S^0V}\right)\right]\\
&+\frac{\eta S^0}{r}\left[A_d\left(2-\frac{S_d^0}{S_d}-\frac{S_d}{S_d^0}\right)+\tau_d V_d^0\left(1-\frac{S_d}{S_d^0}+\frac{V_d}{V_d^0}-\frac{S_d^0V_d}{S_dV_d^0}\right)\right.\\
&\left.+\delta_d S_d^0\left(1-\frac{V_d}{V_d^0}+\frac{S_d}{S_d^0}-\frac{S_dV_d^0}{S_d^0V_d}\right)\right]+\frac{\eta S^0\eta_d S_d^0W}{r_d}\left(\frac{1}{\theta+W}-\frac{1}{\theta}\right)\\
&+\frac{\eta S^0\eta_d S_d^0W_d}{r}\left(\frac{1}{\theta+W_d}-\frac{1}{\theta}\right)+\frac{\eta S^0e}{r}\left(\frac{\beta_d S_d^0\lambda_d}{ep_d}+\frac{\eta_d S_d^0\lambda_d\varepsilon_d}{ep_d\theta r_d}-1\right)E_d\\
&+\frac{\eta_d S_d^0a}{r_d}\left(\frac{\beta_1 S^0\lambda_1}{ab}+\frac{\eta S^0\lambda_1\varepsilon_1}{ab\theta r}+\frac{\beta_2 S^0\lambda_2}{ac}+\frac{\eta S^0\lambda_2\varepsilon_2}{ac\theta r}-1\right)E.
\end{aligned}$$

For the function $v(x)=1-x+\ln x$, we know that $x>0$ leads to $v(x)\leq 0$. And if $x=1$, then $v(x)=0$. Note that

$$L'\leq\frac{\eta_d S_d^0a}{r_d}(R_{01}-1)E+\frac{\eta S^0e}{r}(R_{02}-1)E_d\leq 0.$$

Therefore, since $R_0<1$, it has $R_{01}<1$ and $R_{02}<1$, then $L'<0$, by using LaSalle'a Lyapunov's method, the disease-free equilibrium P^0 is globally asymptotically stable in Ω [17]. FMD can be eliminated from the herds if the basic reproduction number of the model is less than unity. □

2.3 Existence and stability for the endemic equilibrium of system

The system (2.1) is said to be uniform persistent [9,35] if there exists a constant $\varepsilon>0$ such that any solution $P(S,E,I_1,I_2,V,R,M,S_d,E_d,I_d,V_d,W,W_d)$ with P^0 belong to the interior of the Ω satisfies:

$$\begin{aligned}
\min\big\{&\liminf_{t\to\infty}S(t),\ \liminf_{t\to\infty}E(t),\ \liminf_{t\to\infty}I_1(t),\ \liminf_{t\to\infty}I_2(t),\\
&\liminf_{t\to\infty}V(t),\ \liminf_{t\to\infty}R(t),\ \liminf_{t\to\infty}S_d(t),\ \liminf_{t\to\infty}E_d(t),\\
&\liminf_{t\to\infty}I_d(t),\ \liminf_{t\to\infty}V_d(t),\ \liminf_{t\to\infty}W(t),\ \liminf_{t\to\infty}W_d(t)\big\}\geq\varepsilon.
\end{aligned}$$

By the using similar method of the proof of [19, Proposition 3.3] and [27, Theorem D.3], the positive endemic equilibrium $P^*=P(S^*,\ E^*,\ I_1^*,\ I_2^*,\ V^*,\ R^*,\ S_d^*,\ E_d^*,\ I_d^*,V_d^*,W^*,W_d^*)$ of system (2.1) is uniformly persistent if and only if $R_0>1$. Now we prove the global property of the endemic equilibrium of the system (2.1), which implies that the endemic equilibrium is unique. We establish the following result.

Theorem 2.2. *The unique endemic equilibrium P^* of system (2.1) is globally asymptotically stable when $R_0>1$.*

Proof. We define the following Lyapunov function L

$$\begin{aligned}L=&Y_1G_S+Y_2G_E+Y_3G_{I_1}+Y_4G_{I_2}+Y_5G_V+Y_6G_W\\&+Y_7G_{S_d}+Y_8G_{E_d}+Y_9G_{I_d}+Y_{10}G_{V_d}+Y_{11}G_{W_d},\end{aligned}$$

where

$$\begin{aligned}&G_X=X-X^*-X^*\frac{X}{X^*},\\&X=\{S,E,I_1,I_2,V,W,S_d,E_d,I_d,V_d,W_d\},\end{aligned}$$

and

$$\begin{aligned}&Y_1=Y_2=1+\frac{\varepsilon_1I_1^*}{\varepsilon_2I_2^*}+\frac{\varepsilon_2I_2^*}{\varepsilon_1I_1^*},\qquad Y_7=Y_8=\frac{\frac{\eta S^*W^*\kappa_dW_d^*}{\theta+W^*}\left(\frac{1}{\varepsilon_1I_1^*}+\frac{1}{\varepsilon_2I_2^*}\right)}{\frac{\eta_dS_d^*W_d^*\kappa W^*}{\varepsilon_dI_d^*(\theta+W_d^*)}},\\&Y_3=Y_1\frac{\beta_1S^*I_1^*}{\lambda_1E^*}+\frac{\eta S^*W^*(1+\frac{\varepsilon_1I_1^*}{\varepsilon_2I_2^*})}{(\theta+W^*)\lambda_1E^*},\qquad Y_9=Y_7\frac{\beta_dS_d^*I_d^*}{\lambda_dE_d^*}+\frac{\eta_dS_d^*W_d^*}{(\theta+W_d^*)\lambda_dE_d^*},\\&Y_4=Y_1\frac{\beta_2S^*I_2^*}{\lambda_2E^*}+\frac{\eta S^*W^*(1+\frac{\varepsilon_1I_1^*}{\varepsilon_2I_2^*})}{(\theta+W^*)\lambda_2E^*},\qquad Y_{10}=Y_7\frac{(\tau_d+\phi)(\delta_d+\phi)+\tau_d\delta_d}{\delta_d(\tau_d+\phi)},\\&Y_5=Y_1\frac{(\tau+\mu)(\delta+\mu)+\tau\delta}{\delta(\tau+\mu)},\qquad Y_{11}=Y_7\frac{\eta_dS_d^*W_d^*}{(\theta+W_d^*)\varepsilon_dI_d^*}.\\&Y_6=\frac{\eta S^*W^*}{\theta+W^*}\left(\frac{1}{\varepsilon_1I_1^*}+\frac{1}{\varepsilon_2I_2^*}\right),\end{aligned}$$

The derivative of the Lyapunov function L is

$$\begin{aligned}L'=&Y_1G_S'+Y_2G_E'+Y_3G_{I_1}'+Y_4G_{I_2}'+Y_5G_V'+Y_6G_W'\\&+Y_7G_{S_d}'+Y_8G_{E_d}'+Y_9G_{I_d}'+Y_{10}G_{V_d}'+Y_{11}G_{W_d}'.\end{aligned}$$

We have

$$\begin{aligned}G_S'=&\left(1-\frac{S^*}{S}\right)S'\\=&\beta_1S^*I_1^*\left(1-\frac{SI_1}{S^*I_1^*}-\frac{S^*}{S}+\frac{I_1}{I_1^*}\right)+\beta_2S^*I_2^*\left(1-\frac{SI_2}{S^*I_2^*}-\frac{S^*}{S}+\frac{I_2}{I_2^*}\right)\\&+\frac{(\tau+\mu)(\delta+\mu)+\tau\delta}{\delta}V^*\left(1+\frac{V}{V^*}-\frac{S}{S^*}-\frac{VS^*}{V^*S}\right)\\&+\eta S^*\frac{W^*}{\theta+W^*}\left(1-\frac{SW(\theta+W^*)}{S^*W^*(\theta+W)}-\frac{S^*}{S}+\frac{W(\theta+W^*)}{W^*(\theta+W)}\right),\end{aligned}$$

$$
\begin{aligned}
G'_E &= \left(1-\frac{E^*}{E}\right)E' \\
&= \beta_1 S^* I_1^* \left(\frac{SI_1}{S^*I_1^*} - \frac{E}{E^*} - \frac{SI_1E^*}{S^*I_1^*E} + 1\right) + \beta_2 S^* I_2^* \left(\frac{SI_2}{S^*I_2^*} - \frac{E}{E^*} - \frac{SI_2E^*}{S^*I_2^*E} + 1\right) \\
&\quad + \frac{\eta S^* W^*}{\theta + W^*}\left(\frac{SW(\theta+W^*)}{S^*W^*(\theta+W)} - \frac{E}{E^*} - \frac{SWE^*(\theta+W^*)}{S^*W^*E(\theta+W)} + 1\right), \\
G'_V &= \left(1-\frac{V^*}{V}\right)V' = (\tau+\mu+\omega)V^*\left(\frac{S}{S^*} - \frac{V}{V^*} - \frac{V^*S}{VS^*} + 1\right), \\
G'_{I_1} &= \left(1-\frac{I_1^*}{I_1}\right)I_1' = \lambda_1 E^*\left(\frac{E}{E^*} - \frac{I_1}{I_1^*} - \frac{I_1^*E}{I_1E^*} + 1\right), \\
G'_{I_2} &= \left(1-\frac{I_2^*}{I_2}\right)I_2' = \lambda_2 E^*\left(\frac{E}{E^*} - \frac{I_2}{I_2^*} - \frac{I_2^*E}{I_2E^*} + 1\right), \\
G'_W &= \left(1-\frac{W^*}{W}\right)W' \\
&= \kappa_d W_d^*\left(\frac{W_d}{W_d^*} - \frac{W}{W^*} - \frac{W^*W_d}{WW_d^*} + 1\right) + \varepsilon_1 I_1^*\left(\frac{I_1}{I_1^*} - \frac{W}{W^*} - \frac{W^*I_1}{WI_1^*} + 1\right) \\
&\quad + \varepsilon_2 I_2^*\left(\frac{I_2}{I_2^*} - \frac{W}{W^*} - \frac{W^*I_2}{WI_2^*} + 1\right), \\
G'_{S_d} &= \left(1-\frac{S_d^*}{S_d}\right)S_d' = \beta_d S_d^* I_d^*\left(1 - \frac{S_dI_d}{S_d^*I_d^*} - \frac{S_d^*}{S_d} + \frac{I_d}{I_d^*}\right) \\
&\qquad + \frac{\eta_d S_d^* W_d^*}{\theta + W_d^*}\left(1 - \frac{S_dW_d(\theta+W_d)}{S_d^*W_d^*(\theta+W_d^*)} - \frac{S_d^*}{S_d} + \frac{W_d(\theta+W_d)}{W_d^*(\theta+W_d^*)}\right) \\
&\qquad \frac{(\tau_d+\mu)(\delta_d+\mu)+\tau_d\delta_d}{\delta_d} V_d^*\left(1 + \frac{V_d}{V_d^*} - \frac{S_d}{S_d^*} - \frac{V_dS_d^*}{V_d^*S_d}\right), \\
G'_{E_d} &= \left(1-\frac{E_d^*}{E_d}\right)E_d' = \beta_d S_d^* I_d^*\left(\frac{S_dI_d}{S_d^*I_d^*} - \frac{E_d}{E_d^*} - \frac{S_dI_dE_d^*}{S_d^*I_d^*E_d} + 1\right) \\
&\quad + \frac{\eta_d S_d^* W_d^*}{\theta + W_d^*}\left(\frac{S_dW_d(\theta+W_d^*)}{S_d^*W_d^*(\theta+W_d)} - \frac{E_d}{E_d^*} - \frac{S_dW_dE_d^*(\theta+W_d^*)}{S_d^*W_d^*E_d(\theta+W_d)} + 1\right), \\
G'_{I_d} &= \left(1-\frac{I_d^*}{I_d}\right)I_d' = \lambda_d E_d^*\left(\frac{E_d}{E_d^*} - \frac{I_d}{I_d^*} - \frac{I_d^*E_d}{I_dE_d^*} + 1\right), \\
G'_{V_d} &= \left(1-\frac{V_d^*}{V_d}\right)V_d' = (\tau_d+\phi)V_d^*\left(\frac{S_d}{S_d^*} - \frac{V_d}{V_d^*} - \frac{V_d^*S_d}{V_dS_d^*} + 1\right), \\
G'_{W_d} &= \left(1-\frac{W_d^*}{W_d}\right)W_d' = \kappa W^*\left(\frac{W}{W^*} - \frac{W_d}{W_d^*} - \frac{WW_d^*}{W^*W_d} + 1\right) \\
&\qquad + \varepsilon_d I_d^*\left(\frac{I_d}{I_d^*} - \frac{W_d}{W_d^*} - \frac{W_d^*I_d}{W_dI_d^*} + 1\right).
\end{aligned}
$$

Let

$$\begin{aligned}
M_1 &= \left(1+\frac{\varepsilon_1 I_1^*}{\varepsilon_2 I_2^*}+\frac{\varepsilon_2 I_2^*}{\varepsilon_1 I_1^*}\right)\left(G_S'+G_E'+\frac{\beta_1 S^* I_1^*}{\lambda_1 E^*}G_{I_1}'+\frac{\beta_2 S^* I_2^*}{\lambda_2 E^*}G_{I_2}'+\frac{(\tau+\mu)(\delta+\mu)+\tau\delta}{\delta(\tau+\mu)}G_V'\right)\\
&\quad+\frac{\eta S^* W^*}{\theta+W^*}\left(\frac{1+\frac{\varepsilon_1 I_1^*}{\varepsilon_2 I_2^*}}{\lambda_1 E^*}G_{I_1}'+\frac{1+\frac{\varepsilon_2 I_2^*}{\varepsilon_1 I_1^*}}{\lambda_2 E^*}G_{I_2}'+\left(\frac{1}{\varepsilon_1 I_1^*}+\frac{1}{\varepsilon_2 I_2^*}\right)G_W'\right)\\
&\le \frac{\eta S^* W^* \kappa_d W_d^*}{\theta+W^*}\left(\frac{1}{\varepsilon_1 I_1^*}+\frac{1}{\varepsilon_2 I_2^*}\right)\left(\frac{W_d}{W_d^*}-\frac{W}{W^*}-\frac{W^* W_d}{W W_d^*}+1\right),\\
M_2 &= G_{S_d}'+G_{E_d}'+\frac{\beta_d S_d^* I_d^*}{\lambda_d E_d^*}G_{I_d}'+\frac{(\tau_d+\phi)(\delta_d+\phi)+\tau_d\delta_d}{\delta_d(\tau_d+\phi)}G_{V_d}'\\
&\quad+\frac{\eta_d S_d^* W_d^*}{\theta+W_d^*}\left(\frac{1}{\lambda_d E_d^*}G_{I_d}'+\frac{1}{\varepsilon_d I_d^*}G_{W_d}'\right)\\
&\le \frac{\eta_d S_d^* W_d^* \kappa W^*}{\varepsilon_d I_d^*(\theta+W_d^*)}\left(\frac{W}{W^*}-\frac{W_d}{W_d^*}-\frac{W W_d^*}{W^* W_d}+1\right).
\end{aligned}$$

In order to prove the global stability of P^* for system (2.1), we consider the derivative of the Lyapunov function L is

$$\begin{aligned}
L' &= M_1+\frac{\frac{\eta S^* W^* \kappa_d W_d^*}{\theta+W^*}\left(\frac{1}{\varepsilon_1 I_1^*}+\frac{1}{\varepsilon_2 I_2^*}\right)}{\frac{\eta_d S_d^* W_d^* \kappa W^*}{\varepsilon_d I_d^*(\theta+W_d^*)}}M_2\\
&\le \frac{\eta S^* W^* \kappa_d W_d^*}{\theta+W^*}\left(\frac{1}{\varepsilon_1 I_1^*}+\frac{1}{\varepsilon_2 I_2^*}\right)\left(2-\frac{W^* W_d}{W W_d^*}-\frac{W W_d^*}{W^* W_d}\right)\le 0.
\end{aligned}$$

Since L is a Lyapunov function on the interior of Ω, there is the largest compact invariant subset of the set where $L'=0$ is the singleton P^*. We know that $L'=0$ if and only if

$$\begin{aligned}
&S=S^*,\quad E=E^*,\quad I_1=I_1^*,\quad I_2=I_2^*,\quad V=V^*,\quad W=W^*,\\
&S_d=S_d^*,\quad E_d=E_d^*,\quad I_d=I_d^*,\quad V_d=V_d^*,\quad W_d=W_d^*.
\end{aligned}$$

By LaSalle's Invariance Principle, the endemic equilibrium P^* is unique. The positive endemic equilibrium state P^* is globally asymptotically stable on Ω when $R_0>1$ by Lyapunov LaSalle asymptotic stability theorem [4, 17, 18]. This completes the proof. □

Here based on the dynamic model with two patches, and under the size of the basic reproduction number R_0, we take advantage of Lyapunov functions to prove the globally asymptotically stability of the disease-free equilibrium and endemic equilibrium.

3 Numerical simulations

In the epidemic model, the basic reproduction number is calculated and shown to be a threshold for the dynamics of the disease. In this section, we consider the large-scale

cattle farm in China as a numerical example, and FMD outbreaks due to FMD type O at the farm. Then we give sensitivity analysis of the basic reproduction number on the model parameters, and show that the basic reproduction number is a global threshold parameter for the extinction and persistence of the FMD.

3.1 Parameter evaluation

On the basis of the field investigation and data collection, the expert's information consultation feedback, consulting official publication and literatures, and estimation method, we acquire the value of parameters of the model (2.1). Since the number of outbreak points of FMD in China was reported monthly, the time unit of the model in the manuscript is adopted as month.

The approximation of parameters $A=0.5\times N/12, A_d=0.5\times N_d/12$, $\mu=\phi=0.41$ are estimated by fitting the production data of the cattle in China Statistical Yearbook. The latent period may vary from 2-14 days in a cattle, with a mean of 5 days, giving $\lambda_1=\lambda_2=\lambda_d=6$ [37]. The recovery rate is $\gamma=0.1076$ [33]. In China, the number of the household's scatter breeding is on the decrease, the scale farm is increasing rapidly at present. The number of cattle ranging from 1 thousands to 10 thousands at the large-scale cattle farm, thus the average number of cattle about 10^4 is adopted at the farm. Therefore, we assume $N=10^4$. For simplicity, we set the transmission coefficients $\beta_1=\beta_2=\eta=\frac{\zeta C(N)}{N}$ are equal, in which $\zeta=0.026$ is the probability that a contact with an infections beef produces an infection [33], the effective contact number $C(N)=20$ is the number of cattle living in a byre. Farm staffs, visitors and vehicles visit the farm over twice a month, which may carry the virus from the environment about 10% at a time, so $\kappa=\kappa_d=2\times 0.1$. The random sample of 3 per cent of cattle at the farm every 6 months is detected by NSPS, in which the part of positive cattle is quarantined or removed, assume $\omega=0.03/6$. We take one month as the average survival time of FMDV in environment, so the natural decay rate of FMDV is 1. The average peak amounts of expelling of virus discharged by a heifer per day can reach $10^{4.3}$ TCID50 (the tissue culture 50% infective doses), and the median duration of shedding is 3 days, so the shedding rate is $\varepsilon_1=\varepsilon_2=\varepsilon_d=3\times 10^{4.3}$ [1,24].

We apply the least-square estimation method to obtain the values of β_d, η_d, τ_d, δ_d and p_d, and fit the model with the cattle cases of FMD type O from 2010 to 2016, which is reported in monthly or yearly units in China Yearbook of animal husbandry and veterinary medicine. These parameters are estimated by fitting the patch of outside-farm in model (2.1) with actual monthly accumulative number of the cases. The data fitting result is shown in Fig. 2.

3.2 Sensitivity analysis on the basic reproduction number R_0

Based on the model (2.1), and the parameter values in Table 2, we give the phase diagram of $S(t)$ and $E(t)$ with different initial conditions of the model (2.1), when $R_0<1$ and $R_0>1$, respectively (see Fig. 3), which shows that the disease-free equilibrium is

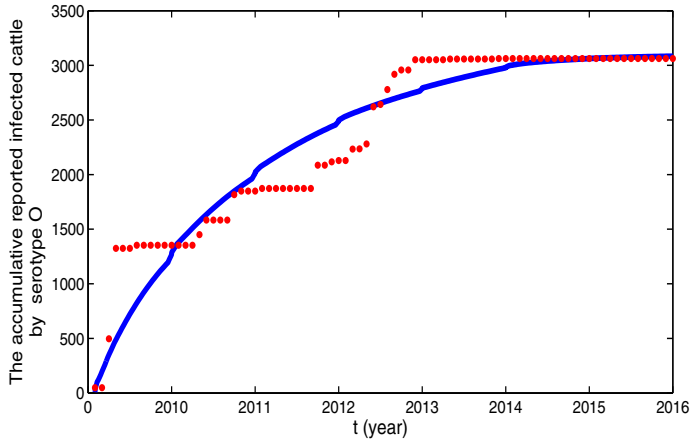


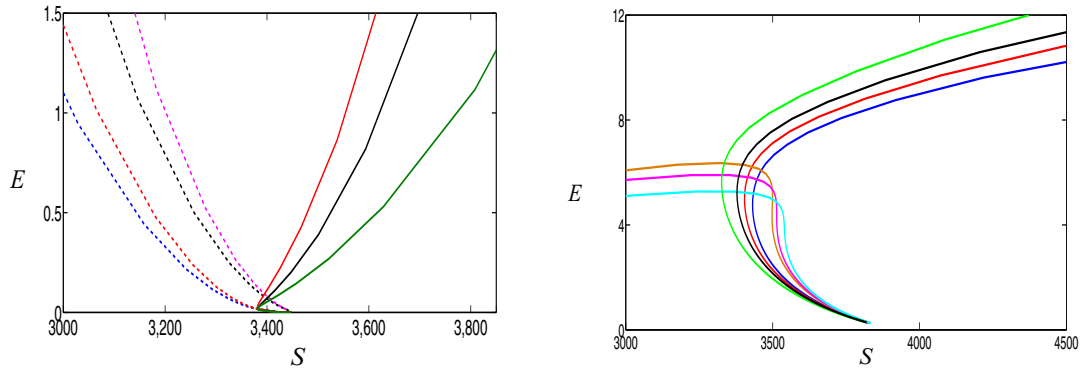
Figure 2: The fitting result of the outside-farm patch in the model (2.1) with the accumulative reported infected cattle of FMD type O in China from 2010 to 2016. Where the smooth curve is the solution to the model; the circles represent monthly accumulative reported number of the infected cattle.

Table 2: The values of parameters in the model (unit: month^{-1}).

Parameter	Value	Source	Parameter	Value	Source
N	10^4	Assumption	N_d	$10^4/20$	Assumption
A	$0.5*N/12$	Estimated	A_d	$0.5*N_d/12$	Estimated
μ	0.41	Estimated	ϕ	0.41	Estimated
β_1	$\zeta\times 20/10^4$	Assumption	β_d	1.045×10^{-8}	Estimated
β_2	$\zeta\times 20/10^4$	Assumption	η_d	1.045×10^{-8}	Estimated
η	$\zeta\times 20/10^4$	Assumption	γ	0.1076	[33]
τ	0.3/2	Assumption	τ_d	0.3/2	Estimated
δ	0.8/2	Assumption	δ_d	0.8/2	Estimated
ω	0.03/6	Assumption	λ_d	6	[37]
λ_1	6	[37]	λ_2	6	[37]
κ	0.2	Assumption	κ_d	0.2	Assumption
r	1	Assumption	r_d	1	Assumption
$\varepsilon_{1,2}$	$3\times 10^{4.3}$	[1,24]	p_d	0.7	Estimated
ε_d	$3\times 10^{4.3}$	[1,24]	p_2	0.7	Assumption
ζ	0.026	[33]	θ	10^5	Estimated

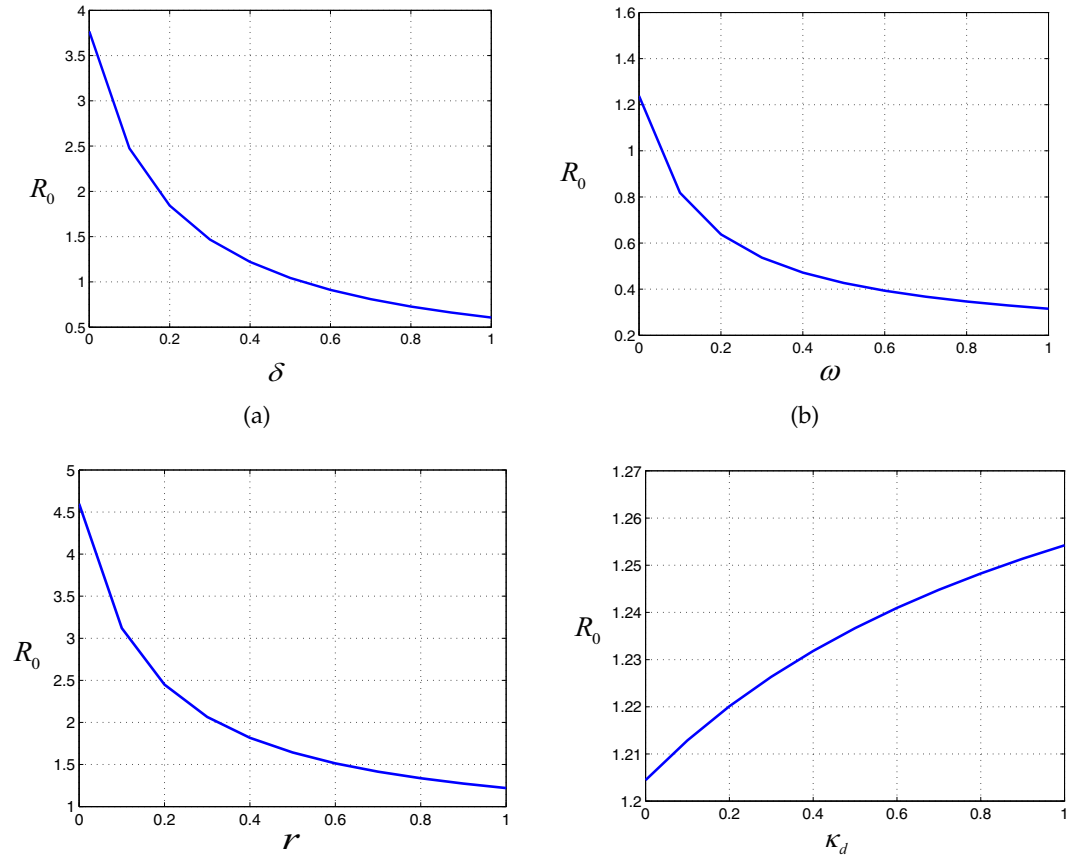
globally asymptotically stable when $R_0<1$, then an epidemic will not occur, the endemic equilibrium exists uniquely and is globally asymptotically stable when $R_0>1$, it means that an initial case will lead to an outbreak.

Then, we give the sensitivity analysis of R_0 for the control parameters δ, r and ω, respectively, in Fig. 4(a), (b), (c). And the effect of δ, r and ω on R_0 are studied by global



(a) (b)

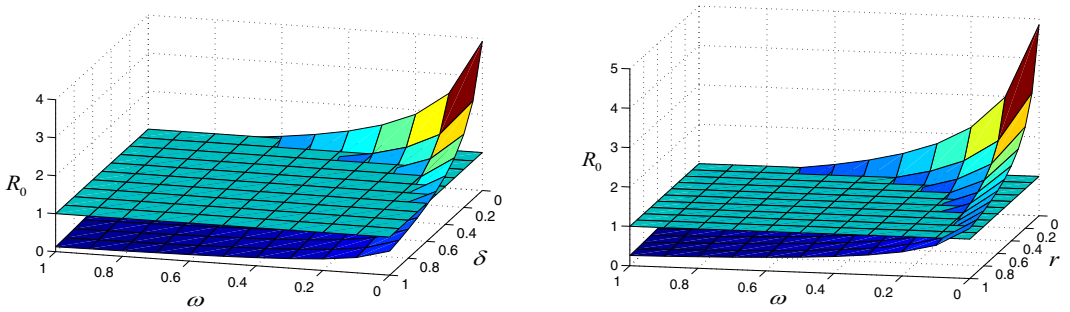
Figure 3: The phase diagram of $S(t)$ and $E(t)$ with different initial conditions. (a) $r=1$, $\omega=0.03\times 1/6$. This gives $R_0=0.99<1$, (b) $r=0$, $\omega=0$. This gives $R_0=1.28>1$.



(a) (b)

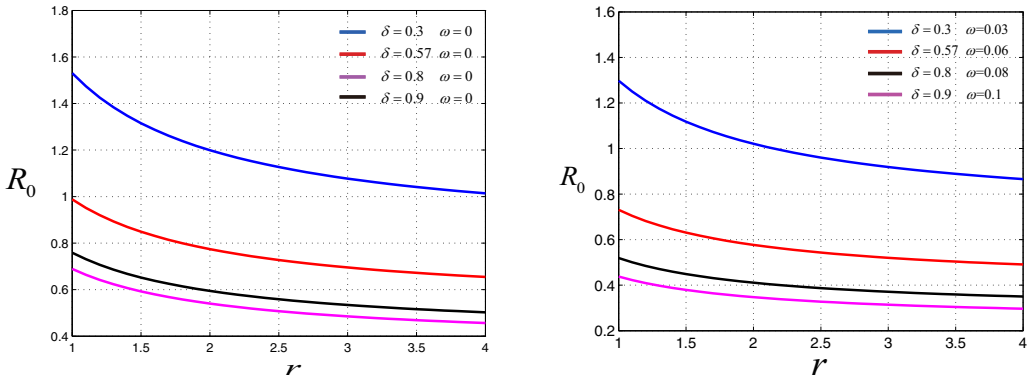
(c) (d)

Figure 4: Sensitivity analysis of R_0 on δ, ω, r and κ_d of the model (2.1).



(a) (b)

Figure 5: Sensitivity analysis of R_0 on δ and ω, r and ω of the model (2.1).



(a) (b)

Figure 6: Sensitivity analysis of R_0 on variable δ, ω and r of the model (2.1).

sensitivity analysis, respectively: $\frac{\partial R_0}{\partial \delta}\cdot\frac{\delta}{R_0}=-0.39$, $\frac{\partial R_0}{\partial \omega}\cdot\frac{\omega}{R_0}=-0.07$, $\frac{\partial R_0}{\partial r}\cdot\frac{r}{R_0}=-0.04$. We can see that vaccination is the most effective measure to decrease R_0. Vaccination remain the main strategies to control the spread of FMD type O at the lager-scale cattle farm. in Fig. 4(d) shows R_0 increases at higher κ_d it is easy to see that work staffs, visitors and vehicles must be stringently disinfected before they enter and leave the farm. From Fig. 5, we can see that the effect of δ and ω, r and ω seem rather obvious on R_0, comparing Fig. 5 with Fig. 6. It argues that $R_0<1$ when $\delta=0.57$, $\omega=0$, $r=1$, and $R_0<0.8$ when $\delta=0.57$, $\omega=0.06$, $r=4$, thus the more vaccination, quarantining or removing of the positive cattle by NSPS and disinfection, the less infection will be caused.

4 Conclusion

Foot and mouse disease (FMD) is a highly contagious viral disease of cloven-hooved animals with significant the economic impact. Of the OIE Member Countries and Territories,

65 are recognized as free from FMD without vaccination, 1 country is recognized as free with vaccination. Several other countries are recognized as zones that are free with or without vaccination. Over 100 countries are still not considered to be FMD free regions. FMD is endemic in Asia, Africa, Australia, New Zealand and the Middle East, in which some countries take the vaccination.

Considering the transmission mechanism of cattle FMD both on and off the farm, and the existence of the carrier, we have constructed a dynamic model to study the transmission dynamics of cattle FMD. The model consists of two patches: within-farm and outside-farm. Firstly, we have given the formula of the basic reproduction number R_0, which determines whether the disease dies out or persist in the population. By constructing the Lyapunov function, we prove the disease-free equilibrium is globally asymptotically stable if $R_0 < 1$, while the endemic equilibrium exists uniquely and is globally asymptotically stable if $R_0 > 1$.

As a numerical example, we apply the dynamical model to assess the spread of FMD type O at the large-scale cattle farm in China. The globally asymptotically stability of the equilibria was confirmed by numerical simulation. By the sensitivity analysis of the basic reproduction number R_0 on parameters, we find that the vaccination is the most effective measure to decrease R_0. In order to control the spread of FMD type O at the large-scale cattle farm, the condition of $R_0 < 1$ must be sufficient, we suggest that success rate of the vaccination is higher than 0.57 of the cattle, work staffs, visitors and vehicles must be stringently disinfected before they enter and leave the farm, quarantining or removing of the positive cattle by NSPS and disinfection four times a month, FMD will become disappeared at the large-scale cattle farm by doing so.

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