

OPTIMAL CONTROL USING QUADRATIC-QUADRATIC REGULATOR (QQR) FOR MATHEMATICAL MODEL OF CATTLE FOOT AND MOUTH DISEASE (FMD)

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ABSTRACT

Foot and Mouth Disease (FMD), a prevalent disease among cattle in East Java, poses a serious threat to the livestock industry in the Province, Indonesia. Based on field observations, Revifir, the foot-and-mouth disease (FMD) virus, can disseminate via the air, direct contact, and carriers, resulting in decreased appetite and severe bleeding due to toenail loss from infected cattle. It is inevitable that losses will be incurred in the economic and food sectors due to the significant number of cattle that have perished as a result of this FMD infection outbreak. A mathematical model based on the SEIR (Susceptible, Exposed, Infected, and Recovered) model was developed to formulate an optimal strategy for mitigating the impact of FMD outbreaks. The analysis indicates that the model meets the well-posed criteria, thereby validating its use. The control design is presented as the vaccination and treatment of cattle using the Quadratic-Quadratic Regulator (QQR) method, a development of the Linear Quadratic Regulator (LQR). The results of the control design indicate that the optimal vaccination strategy should be administered to 45.93% of susceptible cattle, while treatment should be provided to 32.74% of infected cattle. The simulation results indicate that the QQR method is more optimal for managing FMD outbreaks in cattle. This is evident in its lower performance and cost, as well as its faster containment time when compared to the LQR method.



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1. INTRODUCTION

Foot and Mouth Disease (FMD) has a long history in Indonesia, beginning in 1887 when it was first discovered in Malang, East Java Province. Since then, it has spread to various regions across Indonesia's main islands. Indonesia was officially declared free of FMD in 1986, with various treatment measures, including vaccination. In 2013, the Indonesian government, in collaboration with the Ministry of Agriculture, designated FMD as a strategic infectious animal disease that necessitates vigilance and multiple preventive measures. This disease has a transmission rate of up to 95% [1]. Foot-and-mouth disease is a highly contagious viral infection that affects the mouth and hooves of cloven-hoofed animals, including both domestic and wild.

FMD poses a significant threat to animal health and economic stability in affected regions [2], [3]. In accordance with OIE Resolution XV of 2019, Indonesia revoked FMD vaccination, which reduces livestock immunity to the virus [4], [5]. The virus's virulence and transmissibility increased over time, leading to its resurgence in East Java, a region of Indonesia with a significant livestock industry, on May 5, 2022 [6]. The resurgence of FMD is believed to have originated from the illicit trade of meat and livestock without health screening between Indonesia, India, and Malaysia, where Malaysia continues to combat FMD [4]. The repercussions of the crisis include substantial losses across the livestock sector, the broader economy, and food production, particularly in the province of East Java [7]. The public's trepidation regarding the consumption of beef resulted in a precipitous decline in purchases, compounded by the swift demise of infected cattle due to severe hemorrhaging. Consequently, farmers and traders were compelled to sell or slaughter unsold cattle.

A surplus of meat, coupled with inadequate demand, has the potential to precipitate deflation [8]. Furthermore, the Foot-and-Mouth Disease (FMD) virus disseminates expeditiously through air, droplets, urine, and feces to hoofed animals [9], [10]. The clinical signs exhibited by infected livestock include elevated body temperature (41°C), ambulatory dysfunction, reduced milk output, hoof shedding with bleeding, oral inflammation, and excessive foam in the oral and nasal cavities [11], [12]. To mitigate the adverse consequences of FMD on communities, traders, and farmers, preventive measures must be implemented. These measures should be grounded in mathematical models that can effectively visualize the dynamics of spread in East Java. Research on mathematical models of FMD spread in cattle in Indonesia is scarce. Consequently, foreign case studies are referenced. For example, the SVUEIRP model [13] examines vaccine failure and environmental transmission, and the SEIAR model [14] is another example. This article will develop an original mathematical model based on the specific conditions of FMD in Indonesia [15]. The designed control will be analyzed as a mitigation recommendation to reduce the outbreak rate [16], answering the urgent need for an evidence-based approach.

The research will use the Quadratic-Quadratic Regulator (QQR) control method, which is commonly used to optimize mathematical model [17], [18]. QQR is a method derived from the Linear Quadratic Regulator (LQR). QQR is expected to improve the performance of LQR, which only solves problems in the linear scope, by approaching the solution of nonlinear (quadratic scope) problems. QQR and LQR can effectively mitigate significant disruptions to system stability while preserving work efficiency and can address any disturbances that may arise [19]. Furthermore, the numerical solution will be more accurate by using the 5th-order Runge-Kutta method, which is an advancement over the 5th-order Runge-Kutta method used in the simulation of the model system [20].

2. RESEARCH METHODS

The present study utilizes quantitative descriptive methodology to delineate the status of the FMD (Foot-and-Mouth Disease) outbreak. The data were obtained through field studies (observing outbreak behavior, symptoms, virus characteristics, and transmission mechanisms) and news sources, and supported by literature studies (scientific articles and books) for model development and data processing. The theoretical framework underpinning this study encompasses ordinary differential equations, model system analysis, optimal control theory, and simulation. Numerical data concerning the propagation of FMD in cattle were obtained from the Livestock Service Office of East Java Province. In light of the information and data gathered, as well as the assumptions pertinent to the prevailing circumstances, the subsequent phase entails

formulating a mathematical model to delineate the propagation of FMD infection. This model will be based on a system that prioritizes a single vector: the cattle population.

The model system is an epidemic model, with a basic approach that uses a dynamic system. The parameter values in the model will be obtained from previously collected numerical data, while others will be estimated using the Kalman Filter; accordingly, it is imperative to adhere to the following sequence when implementing [Algorithm 1](#). The subsequent step entails validating the existence of the solution to the system of differential equations that constitute the model, thereby ensuring adherence to the principles of biology [\[21\]](#), [\[22\]](#). The next step involves identifying the system's equilibrium point and conducting a local stability analysis around it [\[23\]](#), [\[24\]](#).

Algorithm 1. Kalman Filter Algorithm

Input : Matrix system (A);
 Measurement matrix (H);
 Error covariance matrix (P);
 System covariance matrix (Q);
 Measurement covariance matrix (R);
 Data as vector x .

Output : Estimation variables (\hat{x}_{i+1});
 Estimation Parameter (ω).

- 1: System Model and Measurement Model
 $x_{i+1} = A_i x_i + G w_i$
 $z_i = H_i x_i + v_i$
 $x_0 \sim N(\bar{x}_0, P_{x_0}); w_i \sim N(0, Q); v_i \sim N(0, R)$
- 2: Initialization (Initial Value)
 $\hat{x}_0 = \bar{x}_0$
 $P_0 = P_{x_0}$
- 3: Prediction Stage
 Estimation : $\hat{x}_{i+1}^- = A_i \hat{x}_i$
 Covariance Error : $P_i^- = A_i P_i A_i^T + G Q G^T$
- 4: Correction Stage
 Kalman Gain : $K_{i+1} = P_{i+1}^- H_{i+1}^T (H_{i+1} P_{i+1}^- H_{i+1}^T + R)^{-1}$
 Estimation : $\hat{x}_{i+1} = \hat{x}_{i+1}^- + K_{i+1} (z_{i+1} - H_{i+1} \hat{x}_{i+1}^-)$
 Covariance Error : $P_{i+1} = (I - K_{i+1} H_{i+1}) P_{i+1}^-$

Furthermore, the model system will be equipped with two mitigation actions as controls to optimally address the spread of FMD. At this stage, the objective function is formulated to identify a vaccination and treatment strategy that minimizes costs associated with the population within the system and the specified control [\[25\]](#). Prior to utilization, the objective function will undergo a test for existence to ascertain optimal control outcomes using convex analysis [\[26\]](#), [\[27\]](#). After determining the optimal control for the system, the optimal control amount to be applied to the system will be determined using the Quadratic-Quadratic Regulator (QQR). In the final step of the process, the system will be simulated using the 5th-order Runge-Kutta numerical method. The following is a general overview of the research, as depicted in the flow chart below:

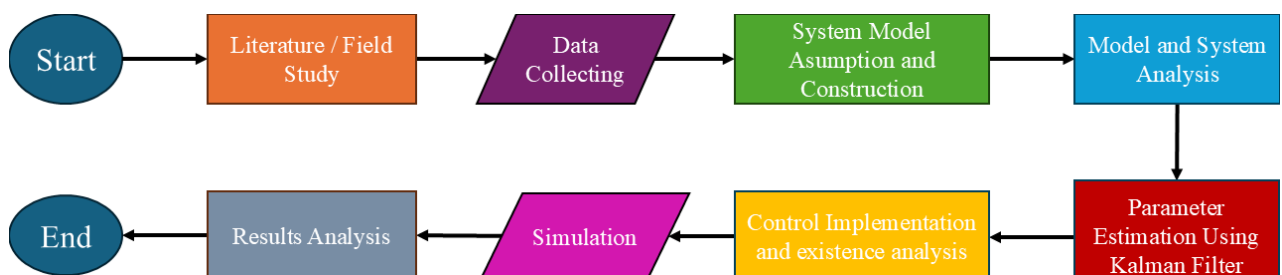


Figure 1. Research Flowchart

3. RESULTS AND DISCUSSION

The data used in this study can facilitate the research process. Specifically, the data set includes information on the total cattle population in East Java Province, the development of FMD outbreaks in livestock in East Java Province, and direct observation data from cattle farms in East Java Province. After acquiring all pertinent data, it is possible to formulate limitations and assumptions, which can then be compiled into a mathematical model of FMD.

3.1 Foot and Mouth Disease (FMD) Mathematical Modeling

Field studies in East Java have identified four common conditions in FMD outbreaks: (1) Healthy cattle that are susceptible to infection, (2) Cattle exposed to FMD virus (virus present but not yet fully active, mild symptoms), (3) Cattle infected with FMD (severe symptoms or illness), and (4) Cattle recovered from FMD. However, it should be noted that these recovered cattle may not be entirely free of the virus. The virus is passive, meaning that it can be transmitted to susceptible cattle. The model posits the following assumptions: first, that the entire cattle population is susceptible to the virus; second, that FMD can cause death (as opposed to natural death); and third, that the transmission rate is uniform. The infection is transmitted directly from infected to susceptible cattle. Exposed cattle that exhibit mild symptoms and do not progress to severe symptoms will return to the susceptible population.

In consideration of the aforementioned conditions, a compartmental dynamic model comprising four distinct groups was formulated. The following categories are used to describe the progression of the virus: *S* (susceptible), *E* (exposed, potential carrier), *I* (infected, severe symptoms), and *R* (recovered, remains a carrier due to passive virus carriage). Outbreak mitigation strategies are implemented through system control, including vaccination of susceptible cattle (u_1) and the treatment of infected cattle (u_2). The representation of these conditions and interactions can be facilitated by using a dynamic model diagram of the FMD outbreak.

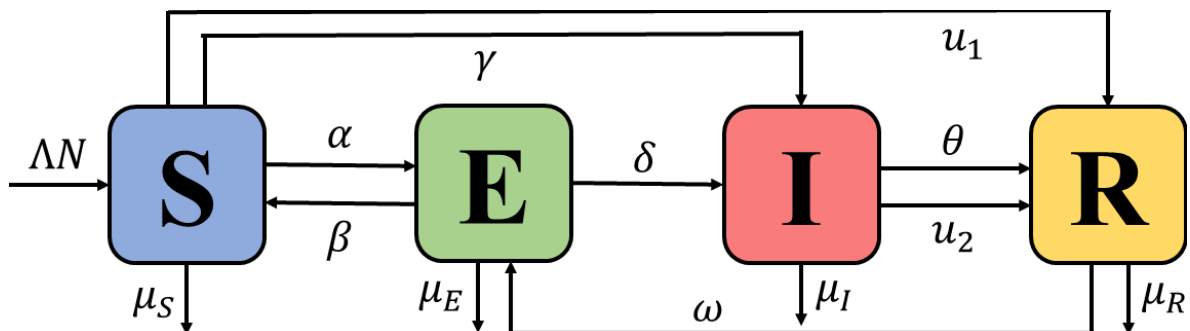


Figure 2. FMD Spread Diagram

The compartment diagram depicted in Fig. 2 is represented by the following system of differential equations when expressed in mathematical form:

$$\dot{S} = \Lambda N + \alpha E - \left(\frac{\beta E + \gamma I}{N} + \mu S + u_1 \right) S, \quad (1)$$

$$\dot{E} = \beta \frac{S}{N} E + \omega R - (\alpha + \delta + \mu_E) E, \quad (2)$$

$$\dot{I} = \delta E - \left(-\gamma \frac{S}{N} + \theta + \mu_I + u_2 \right) I, \quad (3)$$

$$\dot{R} = u_1 S + (\theta + u_2) I - (\omega + \mu_R) R. \quad (4)$$

The present system contains the following quantity of cattle:

$$N(t) = S + E + I + R. \quad (5)$$

Additionally, there are several model support parameters, namely:

Table 1. FMD Spread Model Parameters

Parameters	Value	Remarks	Status
Λ	0.0209	Cattle natural birth rate	Deterministic
α	0.0128	Individual rate of exposed cattle not becoming infected	Deterministic
β	0.0400	Individual rate of cattle exposed to FMD	Deterministic
γ	0.0085	Individual rate of cattle infected with FMD without incubation period	Deterministic
δ	0.2372	Individual rate of cattle being infected FMD through the incubation period	Deterministic
θ	0.7850	Individual rate of cattle cured from FMD	Deterministic
ω	[0, 1]	Rate of individual cattle that recover from FMD infection becoming carriers	To be estimate
μ_S	0.000877883	Natural mortality rate of cattle in the sub-population (S)	Deterministic
μ_E	0.021986190	Mortality rate of cattle indicated to be due to exposure to the virus that causes FMD	Deterministic
μ_I	0.166756674	Mortality rate of cattle due to FMD infection and forced slaughtering	Deterministic
μ_R	0.023073193	Natural mortality rate of cattle in the sub-population (R)	Deterministic
u_1	[0, 1]	Vaccination rate of susceptible cattle	To be calculate
u_2	[0, 1]	Treatment rate of infected cattle	To be calculate

3.2 Mathematical Model Analysis

3.2.1 Existence of Positive Solution in Model System

In this section, it is imperative to ascertain that the model system delineated in Eq. (1) to Eq. (4) is deemed both factually feasible. To that end, it is essential to ascertain that each solution remains positive for all values of $t > 0$. The solution region for the system Eq. (1) to Eq. (4) is designated as \mathbb{R}_+^4 , a designation that finds concurrence with the subsequent theorem concerning population dynamics.

Theorem 1. *The solution to the epidemic model system's equations, given an initial value of positive, is guaranteed to remain positive for all time ($t > 0$) [28].*

Proof. It is posited that the mortality rate of the entire population is μN , where $\mu N = \mu S + \mu E + \mu I + \mu R$, and for the total population according to Eq. (5). The existence of a positive solution to the system can be proved by writing the system as follows:

$$\begin{aligned}\dot{S} + \dot{E} + \dot{I} + \dot{R} &= (\Lambda - \mu N)(S + E + I + R), \\ \dot{N} &= \Lambda N - \mu_N N.\end{aligned}$$

The general solution of the differential equation is obtained by employing variable separation and subsequently integrating the aforementioned equation as follows:

$$\begin{aligned}\dot{N} &= \Lambda N - \mu_N N \\ \frac{dN}{dt} &= (\Lambda - \mu_N)N \\ \int \frac{1}{N(t)} dN &= \int (\Lambda - \mu_N) dt \\ \ln N(t) &= (\Lambda - \mu_N)t + C \\ N(t) &= e^{(\Lambda - \mu_N)t + C} \\ &= e^C \cdot e^{(\Lambda - \mu_N)t} \\ &= C e^{(\Lambda - \mu_N)t}.\end{aligned}\tag{6}$$

To calculate the initial conditions of the general solution of the differential equation obtained, the value of $t = 0$ can be substituted. According to the sixth equation, the constant C is equivalent to 5,418,458. This calculation results in a particular solution to Eq. (6), which is expressed as follows:

$$N(t) = [5,418,458 \cdot e^{(\Lambda - \mu_N)t}] , N \geq 0.\tag{7}$$

According to the particular solution obtained from Eq. (7), for any value of $(\Lambda - \mu_N)$, the solution is always positive. It has been demonstrated that the solution to the system is always positive.

$$\Omega = \{(S, E, I, R \in \mathbb{R}_+^4 : N \leq [5,418,458 \cdot e^{(\Lambda - \mu_N)t}])\} \blacksquare$$

3.2.2 Existence of Unique Solution

The existence of a solution for the model can be ascertained by identifying the value of the Lipschitz constant $k(t)$ that satisfies the following equation:

$$\|f(x^1, t) - f(x^2, t)\| \leq k(t)\|x^1 - x^2\|.$$

It is assumed that

$$\|f(x^1, t) - f(x^2, t)\| = \left\| \begin{array}{l} f(S^1, t) - f(S^2, t) \\ f(E^1, t) - f(E^2, t) \\ f(I^1, t) - f(I^2, t) \\ f(R^1, t) - f(R^2, t) \end{array} \right\| = \left\| \begin{array}{l} a_1 \\ a_2 \\ a_3 \\ a_4 \end{array} \right\|,$$

$$\|f(x^1, t) - f(x^2, t)\| \leq k(t)\|f(x^1, t) - f(x^2, t)\|, \text{ with } \|a_i\| = \max \left\| \sum_{i=1}^4 |a_i| \right\|.$$

The results of the simplification process, which included model reduction, yielded the following findings:

$$\left\| \begin{array}{l} (\lambda_1 - \lambda_2 - \lambda_3 + \lambda_4 - \mu_S)(S_1 - S_2) \\ (\lambda_5 + \lambda_6 - \alpha - \delta - \mu_E)(E_1 - E_2) \\ (\lambda_7 + \lambda_8 - \theta - \mu_I)(I_1 - I_2) \\ (\lambda_9 - \omega - \mu_R)(R_1 - R_2) \end{array} \right\| \leq \max_i \{ |(\lambda_1 - \lambda_2 - \lambda_3 + \lambda_4 - \mu_S)|, |(\lambda_5 + \lambda_6 - \alpha - \delta - \mu_E)|, |(\lambda_7 + \lambda_8 - \theta - \mu_I)|, |(\lambda_9 - \omega - \mu_R)| \} \left\| \begin{array}{l} (S_1 - S_2) \\ (E_1 - E_2) \\ (I_1 - I_2) \\ (R_1 - R_2) \end{array} \right\|,$$

or

$$\left\| \begin{array}{l} (\lambda_1 - \lambda_2 - \lambda_3 + \lambda_4 - \mu_S)(S_1 - S_2) \\ (\lambda_5 + \lambda_6 - \alpha - \delta - \mu_E)(E_1 - E_2) \\ (\lambda_7 + \lambda_8 - \theta - \mu_I)(I_1 - I_2) \\ (\lambda_9 - \omega - \mu_R)(R_1 - R_2) \end{array} \right\| \leq k \left\| \begin{array}{l} (S_1 - S_2) \\ (E_1 - E_2) \\ (I_1 - I_2) \\ (R_1 - R_2) \end{array} \right\|.$$

It was determined that observations were exclusively conducted on the infection sub-population:

$$k = \{ |(\lambda_1 + \lambda_4)_{\max} - (\lambda_2 + \lambda_3 + \mu_S)_{\min}|, |(\lambda_5 + \lambda_6)_{\max} - (\alpha + \delta + \mu_E)_{\min}|, |(\lambda_7 + \lambda_8)_{\max} - (\theta + \mu_I)_{\min}|, |(\lambda_9)_{\max} - (\omega + \mu_R)_{\min}| \}.$$

The mathematical model of FMD infection outbreak in this study possesses a single and complete solution at time $k = |(\lambda_7 + \lambda_8)_{\max} - (\theta + \mu_I)_{\min}|$. Given that the model in this study possesses a unique solution, the mathematical model for the spread of FMD outbreaks is valid.

3.2.3 System Equilibrium Point

In order to ascertain the equilibrium point in the model system, Eq. (1) to Eq. (4) must be equalized to zero ($\dot{S} = \dot{E} = \dot{I} = \dot{R} = 0$). The objective of this study is to ascertain the conditions under which the system will remain static. The equilibrium point can be determined by substituting each equation into the other and setting the result equal to zero. The following steps should be taken to arrive at this solution:

$$S^* = \frac{\Lambda N^2 + \alpha EN}{\beta E + \gamma I + \mu_S N}, \quad (8)$$

$$E^* = \frac{\omega RN}{-\beta S + \alpha N + \mu_E N + \delta N}, \quad (9)$$

$$I^* = \frac{\delta EN}{-\gamma S + \mu_I N + \theta N}, \quad (10)$$

$$R^* = \frac{\theta I}{\omega + \mu_R}. \quad (11)$$

Within the framework of the epidemic model, two conditions can be adapted. These conditions are met when the disease free, signifying the absence of FMD virus propagation within the system ($E = I = 0$), and when the circumstances and conditions are analogous to those observed in the field. Substituting the number of sub-populations of E and I in the disease-free condition into Eqs. (8)-(10) yields the equilibrium point, which is given by:

$$\xi_0 = \{S_0^*, E_0^*, I_0^*, R_0^*\} = \{129065468, 0, 0, 0\} \quad (12)$$

Concurrently, within the FMD condition, an FMD virus is endemic to the system, and the equilibrium point is obtained, namely:

$$\xi_1 = \{S_1^*, E_1^*, I_1^*, R_1^*\} = \{14807341, 980859, 250568, 1598241\} \quad (13)$$

However, this value remains provisional due to the uncertainty surrounding the parameter ω , which is currently unknown. This uncertainty arises from the paucity of data elucidating the proportion of cattle that have recovered from FMD and subsequently become carriers. Consequently, the estimation of this parameter will be facilitated by employing the Kalman Filter in the next stage.

3.3 Linearization of Differential Equation System Model

The system model described in Eqs. (1)-(4) exhibits non-linear behavior, making it more amenable to analysis, estimation, and control. The process of linearization around the equilibrium point involves using the Jacobi matrix to create the system matrix A and control matrix B :

$$J_A = \begin{bmatrix} \frac{\partial \dot{S}(t)}{\partial S} & \frac{\partial \dot{S}(t)}{\partial E} & \frac{\partial \dot{S}(t)}{\partial I} & \frac{\partial \dot{S}(t)}{\partial R} \\ \frac{\partial \dot{E}(t)}{\partial S} & \frac{\partial \dot{E}(t)}{\partial E} & \frac{\partial \dot{E}(t)}{\partial I} & \frac{\partial \dot{E}(t)}{\partial R} \\ \frac{\partial \dot{I}(t)}{\partial S} & \frac{\partial \dot{I}(t)}{\partial E} & \frac{\partial \dot{I}(t)}{\partial I} & \frac{\partial \dot{I}(t)}{\partial R} \\ \frac{\partial \dot{R}(t)}{\partial S} & \frac{\partial \dot{R}(t)}{\partial E} & \frac{\partial \dot{R}(t)}{\partial I} & \frac{\partial \dot{R}(t)}{\partial R} \end{bmatrix}_{\xi_i}.$$

The matrix A is obtained as follows:

$$A = \begin{bmatrix} -a & b & -c & 0 \\ d & e & 0 & f \\ g & h & -i & 0 \\ 0 & 0 & j & k \end{bmatrix}_{\xi_i}, \quad (14)$$

where:

$$\begin{aligned} a &= \frac{\beta E + \gamma I}{N} + \mu_S & c &= \gamma \frac{S}{N} & e &= \beta \frac{S}{N} - (\alpha + \delta + \mu_E) & g &= \gamma \frac{I}{N} \\ b &= \alpha - \beta \frac{S}{N} & d &= \beta \frac{E}{N} & f &= \omega & h &= \delta \\ i &= -\gamma \frac{S}{N} + \theta + \mu_I & j &= \theta & k &= \omega + \mu_R \end{aligned}$$

After obtaining the matrix A as the matrix of the analyzed system, the next step is to find the matrix as the control matrix of the model system.

$$J_B = \begin{bmatrix} \frac{\partial \dot{S}}{\partial u_1} & \frac{\partial \dot{S}}{\partial u_2} \\ \frac{\partial \dot{E}}{\partial u_1} & \frac{\partial \dot{E}}{\partial u_2} \\ \frac{\partial \dot{I}}{\partial u_1} & \frac{\partial \dot{I}}{\partial u_2} \\ \frac{\partial \dot{R}}{\partial u_1} & \frac{\partial \dot{R}}{\partial u_2} \end{bmatrix}_{\xi_1}.$$

The matrix B is obtained as follows:

$$B = \begin{bmatrix} -S & 0 \\ 0 & 0 \\ 0 & -I \\ S & I \end{bmatrix}_{\xi_1}.$$

3.4 Parameter Estimation

Within the modeled system, an unknown parameter exists: the rate at which cattle recover into carriers, denoted as ω . This value will be estimated utilizing a Kalman filter observer. However, prior to estimation, the model system's observability will be tested.

3.4.1 System Observability

Generally, the form of a model system is

$$\begin{aligned} \dot{\mathbf{x}} &= A\mathbf{x} + B\mathbf{u}, \\ \mathbf{y} &= C\mathbf{x}, \end{aligned} \quad (15)$$

Where \mathbf{x} represents the state vector, \mathbf{y} represents the output, \mathbf{u} represents the control input, and C denotes the output matrix, which typically includes the identity matrix. The next step involves assessing the system's observability using Eq. (16) according to the following procedure:

$$M_O = \begin{bmatrix} C \\ CA \\ CA^2 \\ CA^3 \end{bmatrix}. \quad (16)$$

Where a model system can be considered fully observed when its $\text{rank}(M_O)$ equals the dimension of the state vector \mathbf{x} , denoted as n . It has been determined that the $\text{rank}(M_O)$ is 4, and the dimension of matrix A is also 4 ($n = 4$), thus indicating that the model system that has been formed is fully observed.

3.4.2 Kalman Filter

The parameter ω is a newly added state variable with the assumption that its value changes by ($\dot{\omega} = 0.1$). Consider $x_1 = S$, $x_2 = E$, $x_3 = I$, $x_4 = R$, and $x_5 = \omega$ [29]. We can derive an augmented system as follows:

$$\begin{aligned} \dot{\mathbf{x}} &= A\mathbf{x} \\ \begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \dot{x}_3 \\ \dot{x}_4 \\ \dot{x}_5 \end{bmatrix} &= \begin{bmatrix} -a & b & -c & 0 & 0 \\ d & e & 0 & f & R_0 \\ g & h & -i & 0 & 0 \\ 0 & 0 & j & k & -R_0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \end{bmatrix}. \end{aligned} \quad (17)$$

The Kalman filter requires a discrete linear system. Therefore, before implementing the Kalman Filter method, the obtained linear model must first be discretized using the forward difference method ($\dot{x} \rightarrow \frac{x_{i+1} - x_i}{\Delta t}$) to obtain a linear equation in discrete time.

$$x_{i+1} = (A\Delta t + I)x_i \quad (18)$$

Eq. (18) represents the discrete system form utilized in the foot and mouth spread model prior to implementation of the Kalman Filter method. A denotes the augmented system matrix [30], [31]. The model discretization outcomes can then be obtained as follows.

$$\begin{aligned} \dot{x}_{i+1} &= A_i x_i, \\ \begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \dot{x}_3 \\ \dot{x}_4 \\ \dot{x}_5 \end{bmatrix}_{i+1} &= \begin{bmatrix} a\Delta t + 1 & b\Delta t & c\Delta t & d\Delta t & 0 \\ d\Delta t & e\Delta t + 1 & 0 & f\Delta t & R_0 \\ g\Delta t & h\Delta t & i\Delta t + 1 & 0 & 0 \\ 0 & 0 & j\Delta t & k\Delta t + 1 & -R_0 \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \end{bmatrix}_i. \end{aligned} \quad (19)$$

After discretizing the FMD spread model, parameter estimation is performed using the Kalman Filter, a method that minimizes estimation errors in stochastic linear systems. The Kalman Filter algorithm estimates a value. Even though the FMD spread model in Eq. (19) remains in a deterministic form, the system of equations in actual conditions ought to include random variables. Therefore, it is necessary to introduce stochastic factors through system noise. The Kalman Filter algorithm is presented in Algorithm 1.

Simulations utilized endemic equilibrium points, specifically $x_1, x_2, x_3,$ and x_4 as outlined in Eqs. (9)-(11). The variables x_1, x_2, x_3, x_4 are subject to measurement based on data. Therefore, the measurement matrix implemented is:

$$H = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \end{bmatrix},$$

while the matrices P_0, Q_0 and R_0 utilized by tuning process based on Bryson's rule are as follows:

$$P_0 = \begin{bmatrix} 58 & 0 & 0 & 0 & 0 \\ 0 & 0.375 & 0 & 0 & 0 \\ 0 & 0 & 0.375 & 0 & 0 \\ 0 & 0 & 0 & 65 & 0 \\ 0 & 0 & 0 & 0 & 10^{-2} \end{bmatrix}, \quad Q_0 = \begin{bmatrix} 58 & 0 & 0 & 0 & 0 \\ 0 & 0.375 & 0 & 0 & 0 \\ 0 & 0 & 0.375 & 0 & 0 \\ 0 & 0 & 0 & 65 & 0 \\ 0 & 0 & 0 & 0 & 10^{-2} \end{bmatrix},$$

$$R_0 = [10^{-6}],$$

with the initial error covariance matrix P_0 , system covariance matrix Q_0 , and measurement covariance matrix R_0 , the Kalman Filter Algorithm in Algorithm 1 was used to obtain a parameter estimate of $x_5 = 0.0969$. The Root Mean Square Error (RMSE) value for each variable $x_1, x_2, x_3,$ and x_4 is 0.0431.

Based on Fig. 3, it seems that the estimates for each variable are precise as the estimate matches the actual data closely. After obtaining the parameter value for ω , the value of the equilibrium point for the temporary system in (8)-(11) changes to a new equilibrium point with the following values $s_1^* = 14934523,$ $E_1^* = 970373, I_1^* = 247942,$ dan $R_1^* = 1622359$.

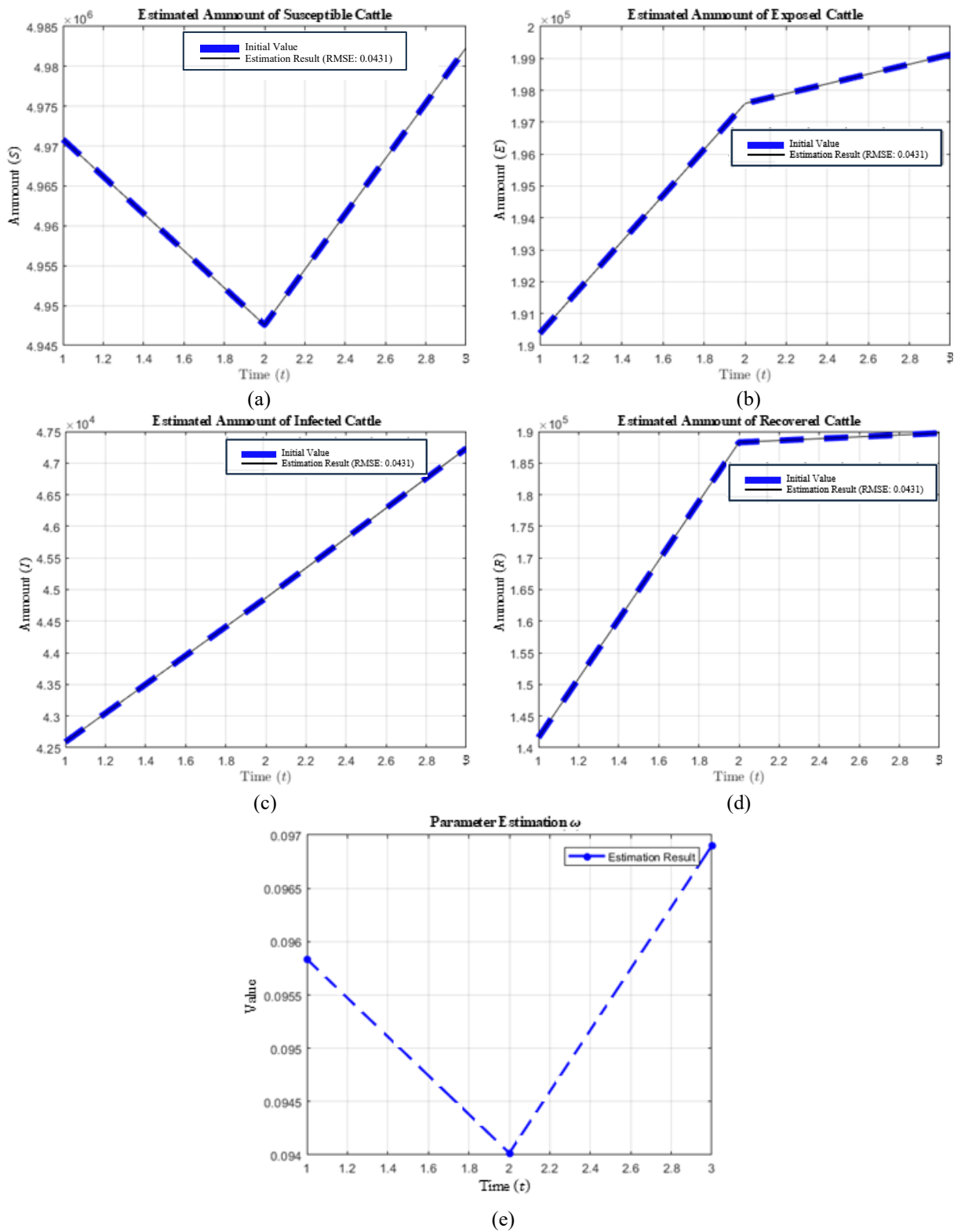


Figure 3. Estimation Results with Kalman Filter (a) Susceptible Cattle, (b) Exposed Cattle, (c) Infected Cattle, (d) Recovered Cattle, and (e) Parameter ω

3.5 Basic Reproduction Number

In this section, we will examine the basic reproduction number denoted by \mathcal{R}_0 , which represents the level of FMD transmission in the system [32]. The basic reproduction number indicates the transmission level of FMD within the system. In other words, it quantifies how many individuals an infected cattle can spread the disease to in the system. To obtain it, we will utilize Eq. (2) and Eq. (3), specifically \dot{E} and \dot{I} . The equation will be divided into two matrices, with one containing the numbers of incoming populations of the FMD-causing virus (F).

$$\varphi = \begin{bmatrix} \beta \frac{S}{N} E + \omega R \\ \gamma \frac{S}{N} I \end{bmatrix} \rightarrow J_{\varphi} = \begin{bmatrix} \frac{\partial \varphi_1}{\partial E} & \frac{\partial \varphi_1}{\partial I} \\ \frac{\partial \varphi_2}{\partial E} & \frac{\partial \varphi_2}{\partial I} \end{bmatrix}_{\xi_0},$$

$$F = \begin{bmatrix} \beta \frac{S^*}{N} & 0 \\ 0 & \gamma \frac{S^*}{N} \end{bmatrix}. \quad (20)$$

The matrix of the number of outgoing populations containing the virus that causes FMD (V) is as follows:

$$\psi = \begin{bmatrix} (\alpha + \mu_E + \delta)E \\ -\delta E + (\mu_I + \theta)I \end{bmatrix} \rightarrow J_{\psi} = \begin{bmatrix} \frac{\partial \psi_1}{\partial E} & \frac{\partial \psi_1}{\partial I} \\ \frac{\partial \psi_2}{\partial E} & \frac{\partial \psi_2}{\partial I} \end{bmatrix}_{\xi_0}.$$

$$V = \begin{bmatrix} \alpha + \mu_E + \delta & 0 \\ -\delta & \mu_I + \theta \end{bmatrix}. \quad (21)$$

Next, create the next-generation matrix by multiplying FV^{-1} . The largest eigenvalue of the FV^{-1} matrix can determine the value of the basic reproduction number.

$$\mathcal{R}_0 = \max(|FV^{-1} - \lambda I| = 0)$$

$$\mathcal{R}_0 = 3.4892.$$

This suggests a high level of FMD spread within the system, with a single infected animal infecting 3-4 others.

3.6 System Stability Analysis

Next, the system's stability will be analyzed through an overview of the numerical simulation results. Two types of stability are present in the system: one when the system is disease-free and another when it is endemic. These conditions are reliant on the system's equilibrium point, which has two conditions. Hence, two analyses for the system's stability are required. The system's stability can be determined using the eigenvalues of matrix A . In matrix A , we substituting S_0^* , E_0^* , I_0^* , and R_0^* . This enables us to determine the eigenvalues of matrix A as follows:

$$|A_{\xi_0} - \lambda I| = 0.$$

The eigenvalues are $\lambda_1 = -0.0009$, $\lambda_2 = 1.1497$, $\lambda_3 = 0.5542$, and $\lambda_4 = -0.2776$. This indicates that when the condition is disease-free, the system is unstable, as it has two positive eigenvalues. This is consistent with the system's inherent instability, as the cattle population is expected to increase over time. The subsequent step is to calculate the eigenvalue of matrix A by substituting S_1^* , E_1^* , I_1^* , and R_1^* as follow:

$$|A_{\xi_1} - \lambda I| = 0.$$

The eigenvalues are $\lambda_1 = 0.1963 + 0.0000i$, $\lambda_2 = -0.0030 + 0.0000i$, $\lambda_3 = -0.4377 + 0.3060i$, and $\lambda_4 = -0.4377 - 0.3060i$. This indicates that the system becomes unstable when the condition is endemic, as one of the eigenvalues is positive. This is consistent with contemporary circumstances, in which the spread of the disease has led to an increase in the number of infected cattle.

3.7 Designing Optimal Control for Model System

3.7.1 System Controllability

When designing control for a model system, it is essential to test whether the system is under control. To do this, create a controllability matrix (M_0) according to the following method [33]:

$$M_C = [B \quad AB \quad A^2B \quad A^3B]. \quad (22)$$

Where a model system can be considered controllable when its $\text{rank}(M_C)$ equals the dimension of the state vector \mathbf{x} , denoted as n . It has been determined that the $\text{rank}(M_C)$ is 4, and the dimension of matrix A is also 4 ($n = 4$), thus indicating that the model system that has been formed is controllable.

3.7.2 Construct an Objective Function for Quadratic-Quadratic Regulator (QQR)

The objective of this research is to ascertain the optimal control $\mathbf{u}(t)$ in the form of optimal strategies for vaccination (u_1) and treatment (u_2) that can minimize the costs associated with the population in the system and the costs associated with the given control. The state vector is to be formed by assuming the following $x_1 = S$, $x_2 = E$, $x_3 = I$, and $x_4 = R$. The objective function in the quadratic regulator method is formed as follows:

$$\begin{aligned} \min_{\mathbf{u}} J(\mathbf{x}, \mathbf{u}, t) &= \int_{t_0}^{t_f} (\mathbf{x}Q_c\mathbf{x}^T + \mathbf{u}R_c\mathbf{u}^T) dt \\ &= \int_{t_0}^{t_f} \left([x_1(t) \ x_2(t) \ x_3(t) \ x_4(t)]Q_c \begin{bmatrix} x_1(t) \\ x_2(t) \\ x_3(t) \\ x_4(t) \end{bmatrix} + [u_1 \ u_2]R_c \begin{bmatrix} u_1 \\ u_2 \end{bmatrix} \right) dt \\ &= \int_{t_0}^{t_f} (q_1x_1^2(t) + q_2x_2^2(t) + q_3x_3^2(t) + q_4x_4^2(t) + r_1u_1^2 + r_2u_2^2) dt. \end{aligned}$$

It can be demonstrated that matrices Q_c and R_c are both symmetric and positive definite. Therefore, $Q_c = Q_c^T$ and $R_c = R_c^T$, where q_1, q_2, q_3 , and q_4 are elements of the matrix Q_c and r_1, r_2 are elements of the matrix R_c . The objective function in the aforementioned form is a commonly used objective for quadratic regulators. In order to employ QQR, it is necessary to modify the form of the objective function by squaring the state vector and control vector using Kronecker multiplication.

The objective function in the second-order quadratic regulator method for QQR can be expressed as follows:

$$\begin{aligned} \min_{\mathbf{u}} J(\mathbf{x}, \mathbf{u}, t) &= \int_{t_0}^{t_f} v(\mathbf{x}, \mathbf{u}, t) dt \\ &= \int_{t_0}^{t_f} (\mathbf{q}(\mathbf{x}^T \otimes \mathbf{x}^T) + \mathbf{r}(\mathbf{u}^T \otimes \mathbf{u}^T)) dt. \end{aligned} \quad (23)$$

with the constraint of this objective function is:

$$\dot{\mathbf{x}} = A\mathbf{x}(t) + B\mathbf{u}(t) + N^T(\mathbf{x}^T(t) \otimes \mathbf{x}^T(t)) \quad (24)$$

For each $\mathbf{x}(0) = \mathbf{x}_0 \in \mathbb{R}^n$, In this form, the matrices above remain bounded in time, as well as in dimension

$$\begin{aligned} A \in \mathbb{R}^{n \times n}, \quad B \in \mathbb{R}^{n \times n}, \quad N \in \mathbb{R}^{n \times n^2}, \\ \mathbf{q} \in \mathbb{R}^{n \times n}, \quad \text{and} \quad \mathbf{r} \in \mathbb{R}^{n \times n}, \end{aligned}$$

where

\mathbf{q} : vector of state cost;

\mathbf{r} : vector of control input cost weights;

N_c : matrix interpretation of the cross interaction between the state and input;

$u_1, u_2 : [0, 1]$.

According to Eq. (23), the calculation of the Kronecker product of the state vector and the control vector is as follows:

$$\begin{aligned} \mathbf{x}^T \otimes \mathbf{x}^T &= [x_1 \ x_2 \ x_3 \ x_4] \otimes [x_1 \ x_2 \ x_3 \ x_4] \\ &= [A. \ B. \ C. \ D.] \end{aligned} \quad (25)$$

with

$$A_o = [x_1^2 \quad x_1x_2 \quad x_1x_3 \quad x_1x_4],$$

$$B_o = [x_1x_2 \quad x_2^2 \quad x_2x_3 \quad x_2x_4],$$

$$C_o = [x_1x_3 \quad x_2x_3 \quad x_3^2 \quad x_3x_4],$$

$$D_o = [x_1x_4 \quad x_2x_4 \quad x_3x_4 \quad x_4^2],$$

and

$$\begin{aligned} \mathbf{u}^T \otimes \mathbf{u}^T &= [u_1 \quad u_2] \otimes [u_1 \quad u_2] \\ &= [u_1[u_1 \quad u_2] \quad u_2[u_1 \quad u_2]] \\ &= [[u_1^2 \quad u_1u_2] \quad [u_1u_2 \quad u_2^2]]. \end{aligned} \quad (26)$$

3.7.3 Existence of Optimal Control on Objective Function

The analysis is conducted to ascertain the existence of the optimal control \mathbf{u} , i.e., the number of cattle vaccinated (u_1) and treated (u_2) that minimizes the objective function J . As per the literature review, this existence is proven by convex analysis of Eq. (23). The initial step in substantiating Eq. (23) as upwardly dominant entails demonstrating that the state cost weight matrix (Q_c) and the control cost weight matrix (R_c) are positive definite. Given that both matrices represent costs that cannot be negative, it follows that their elements are positive real numbers (\mathbb{R}^+). Therefore, it can be concluded that Q_c and R_c must be positive definite. The subsequent step involves verifying that the second derivative of the objective function with respect to the control variable \mathbf{u} is not zero ($\mathbf{u} > 0$). Given that \mathbf{u} consists of two variables (u_1 and u_2), there are three possible derivative scenarios: two-time derivative of u_1 , two-time derivative of u_2 , and mixed derivative. In convex analysis, the emphasis is placed on the segment of Eq. (23) that encompasses the control variables. This approach enables the simplification of the cost function for the purpose of proof, as follows:

$$v(x, \mathbf{u}, t) = (q_1x_1^2 + q_2x_2^2q_3x_3^2q_4x_4^2 + r_1u_1^2 + r_2u_2^2). \quad (27)$$

The subsequent step involves deriving Eq. (27) on the control variable u_1 and u_2 twice, as outlined below:

$$\frac{\partial v(x, \mathbf{u}, t)}{\partial u_1} = 2r_1u_1 \rightarrow \frac{\partial^2 v(x, \mathbf{u}, t)}{\partial u_1^2} = 2r_1, \quad (28)$$

$$\frac{\partial v(x, \mathbf{u}, t)}{\partial u_2} = 2r_2u_2 \rightarrow \frac{\partial^2 v(x, \mathbf{u}, t)}{\partial u_2^2} = 2r_2. \quad (29)$$

The first derivative of the function $v(x, \mathbf{u}, t)$ is positive, indicating that the gradient points toward the positive (predominantly upward) axis and forms a parabolic curve. The second derivative, which is also positive, confirms the existence of a minimum point, as the parabola opens upwards. This result substantiates the assertion that the cost function delineated in Eq. (23) is convex, thereby guaranteeing the existence of an optimal control \mathbf{u} (u_1 and u_2) that minimizes the objective function J in the system design.

3.7.4 Optimal Control of Model System with QQR

At this stage, the Quadratic-Quadratic Regulator process is used to determine the values of the control variables added to the system. The initial step in this process is to determine the Q_c and R_c matrices through a process of tuned based on Bryson's rule, with the objective of obtaining the appropriate Q_c and R_c matrices.

$$Q_c = \begin{bmatrix} 2 \cdot 10^{-12} & 0 & 0 & 0 \\ 0 & 2 \cdot 10^{-10} & 0 & 0 \\ 0 & 0 & 10^{-8} & 0 \\ 0 & 0 & 0 & 10^{-10} \end{bmatrix}, \quad R_c = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}. \quad (30)$$

Subsequent to acquiring the Q_c and R_c matrices, the N_c matrix is to be formed. This N_c matrix is an interpretation of the cross interaction between the state and input. The formation of this matrix is predicated on the nonlinearity of the model system, as delineated by the Matrix system Eq. (14). The N_c matrix is thus obtained as follows:

$$N_c = \begin{bmatrix} 0 & -1 & -1 & 0 & -1 & 0 & 0 & 0 & -1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}. \quad (31)$$

Following the execution of the QQR process, the P_c matrix is derived from the solution to the Riccati algebraic equation, which is expressed as follows:

$$P_c = \begin{bmatrix} 0.0406 & 0.0410 & 0.0397 & 0.0406 \\ 0.0410 & 0.0753 & 0.0434 & 0.0412 \\ 0.0397 & 0.0434 & 0.1522 & 0.0397 \\ 0.0406 & 0.0412 & 0.0397 & 0.0407 \end{bmatrix}, \quad (32)$$

and the optimal gain obtained is:

$$K_1 = \begin{bmatrix} 0.0406 & 0.0410 & 0.0397 & 0.0406 \\ 0.0410 & 0.0753 & 0.0434 & 0.0412 \end{bmatrix}, \quad (33)$$

$$K_2 = \begin{bmatrix} -0.0267 & 0.0183 & 0.0279 & \dots & -0.267 \\ -0.0368 & -0.0502 & -0.0350 & \dots & 0.0368 \end{bmatrix}. \quad (34)$$

The feedback law that applies to QQR, as delineated in Eq. (35), must be implemented. QQR is part of a quadratic regulator with order 2, and the calculation of the feedback law is as follows:

$$\begin{aligned} \mathbf{u} &= \mathcal{K}(\mathbf{x}(t)) \\ &= K_1^T(\mathbf{x}_0^T) + K_2^T(\mathbf{x}_0^T \otimes \mathbf{x}_0^T), \\ \begin{bmatrix} u_1 \\ u_2 \end{bmatrix} &= \begin{bmatrix} 0.4593 \\ 0.3274 \end{bmatrix}. \end{aligned} \quad (35)$$

This indicates that the vaccination rate among susceptible cattle was 45.93%, while treatment was administered to 32.74% of infected cattle.

3.8 Numerical Simulations

In this section, the 5th Order Runge-Kutta numerical method is employed to obtain the solution and visualization of the model system that has been formed as follows [20], [34]:

$$y_{i+1} = y_i + \frac{h}{6}(k_1 + 4k_4 + k_5), \quad i = 0, 1, 2, \dots, n, \quad (36)$$

with

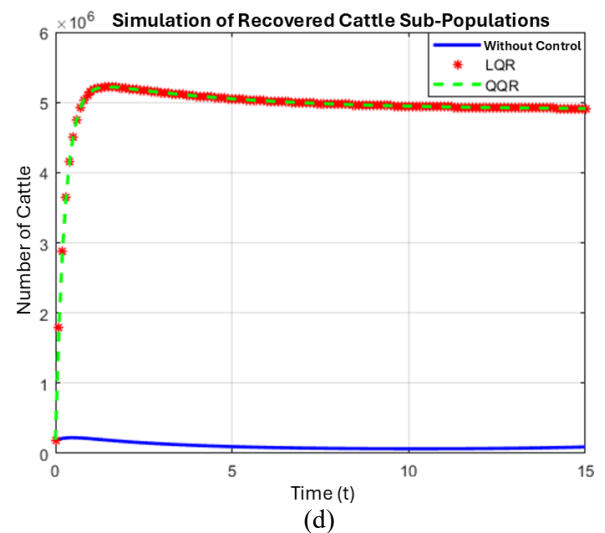
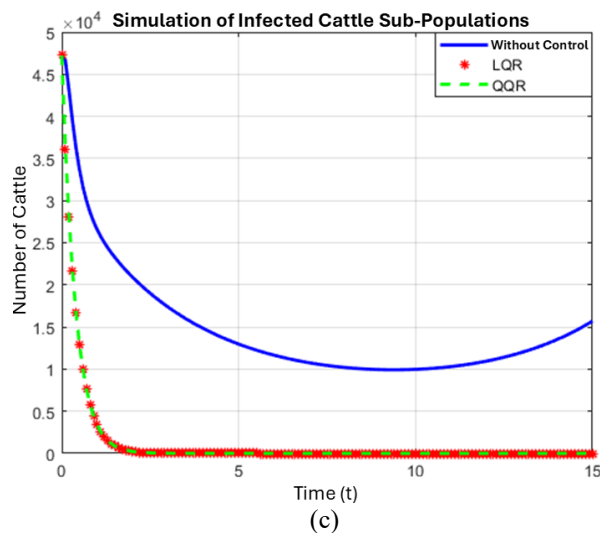
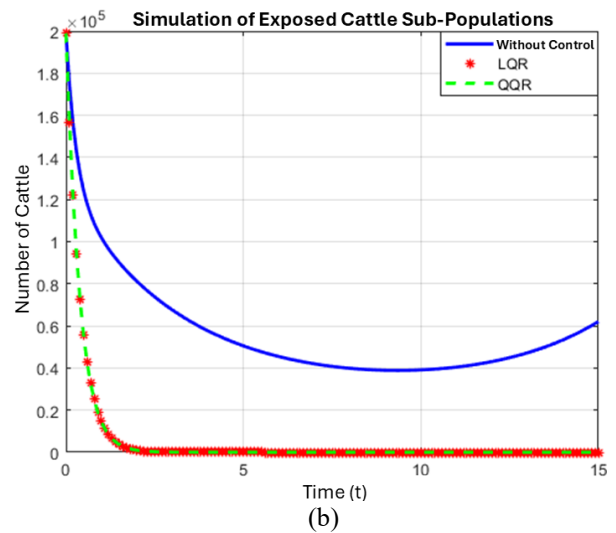
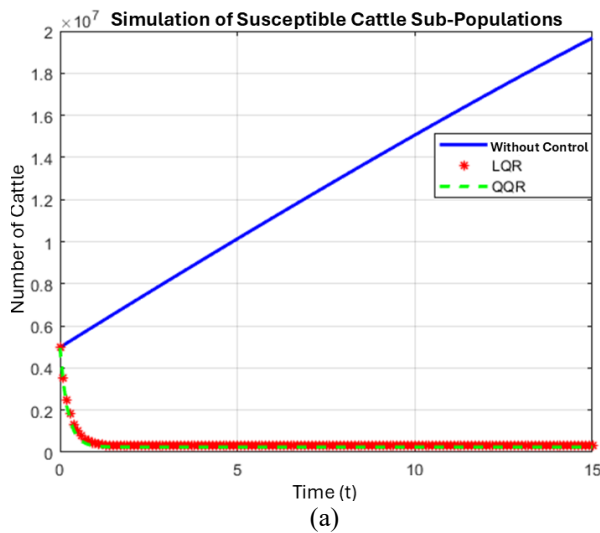
$$\begin{aligned} k_1 &= f(t_i, y_i), \\ k_2 &= f\left(t_i + \frac{h}{3}, y_i + \frac{h}{3}k_1\right), \\ k_3 &= f\left(t_i + \frac{h}{3}, y_i + h\left(\frac{1}{6}k_1 + \frac{1}{6}k_2\right)\right), \\ k_4 &= f\left(t_i + \frac{h}{2}, y_i + h\left(\frac{1}{8}k_1 + \frac{3}{8}k_3\right)\right), \\ k_5 &= f\left(t_i + \frac{h}{2}, y_i + h\left(\frac{1}{2}k_1 - \frac{3}{2}k_3 + 2k_4\right)\right). \end{aligned} \quad (37)$$

The following section presents the monthly ($\Delta t =$ per-month) population simulation results, using 5th-Order Runge-Kutta.

Table 2. Comparison of Number of Cattle Sub-Populations

Variables	Scenario	$t = 1$	$t = 2$	$t = 3$	$t = 4$	$t = 5$
S	Without Control	6027166	7067626	8099293	9122305	10136652
	LQR	410739	303898	301348	301285	301283
	QQR	294058	246619	246100	246091	246091
E	Without Control	101886	99597	67539	57665	50518
	LQR	14674	991	67	5	0
	QQR	14403	967	65	4	0
I	Without Control	26565	20914	17378	14822	26280
	LQR	3408	231	16	1	0
	QQR	3386	228	15	1	0
R	Without Control	208993	167552	135995	113136	96567
	LQR	5151056	5199996	5140430	5090311	5050418
	QQR	5218699	5203808	5142166	5092075	5052250

The detailed data in the table is represented in the graph as follows:



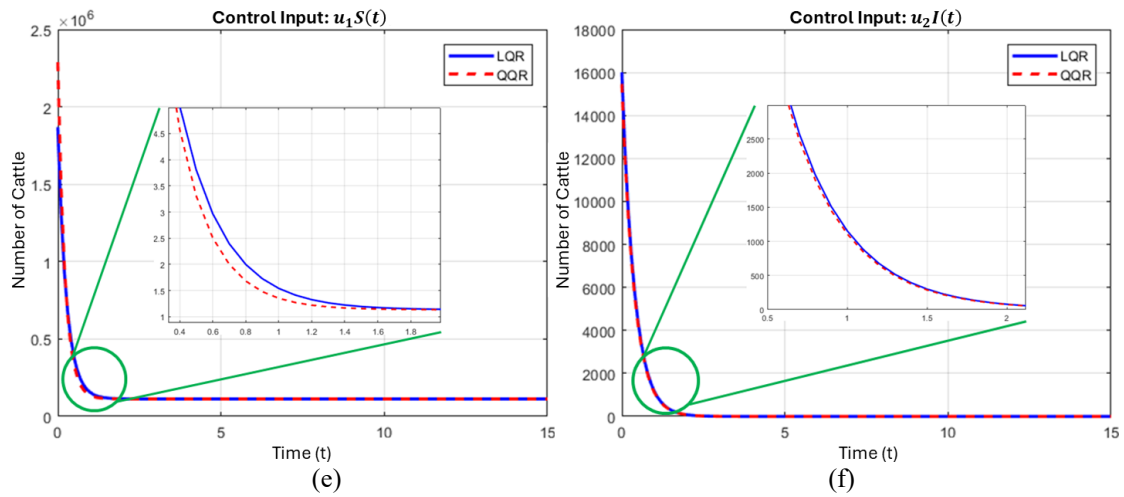


Figure 4. System Simulation of the Spread of Cattle FMD in East Java for (a) Susceptible, (b) Exposed, (c) Infected, (d) Recovered, (e) Vaccination Performance, (f) Treatment Performance

The simulation results in Table 3 and Fig. 4 demonstrate that implementing control measures significantly reduces the susceptible population through vaccination. This decrease can be attributed to the boost in immunity that results from vaccination, which consequently moves individuals to the recovered group. The exposed population also experiences a precipitous decline due to the reduction in susceptible animals, thereby limiting transmission to the infected group. The infected group exhibited a precipitous decline, attributable to diminished exposure sources and the availability of treatment that expedited recovery, thereby accelerating the transition to the recovered group. Concurrently, the recovered population experienced rapid increases through two mechanisms: direct vaccination and treatment that accelerated recovery. A comparison of the vaccination (u_1S) and treatment (u_2I) controls reveals that QQR is more effective, although the difference with LQR is not too significant. The primary benefit of QQR lies in its ability to minimize operational expenditures while enhancing system performance, thereby delivering efficient, competitive control outcome. A comparison of operational costs between the Quadratic-Quadratic Regulator (QQR) and Linear Quadratic Regulator (LQR) methods is presented in Fig. 5.

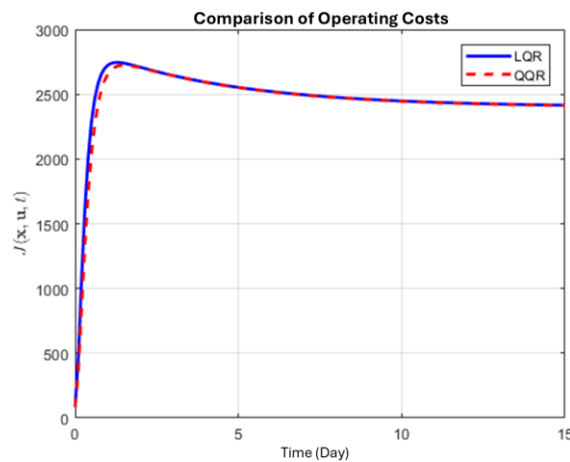


Figure 5. Comparison of Control Operating Costs

The QQR method requires a smaller financial investment than the LQR method. Therefore, in the context of optimal control methods, it can be posited that QQR demonstrates superior performance in comparison to LQR. The comparison of operational costs between QQR and LQR is measured using Integral Times Absolute Error (ITAE) as follows:

$$\begin{aligned}
 ITAE &= \int_{t_0}^{t_f} |e(t)| \cdot t \, dt \\
 &= \int_0^{15} |J_{LQR} - J_{QQR}| \cdot t \, dt = 3312.30.
 \end{aligned}
 \tag{38}$$

The findings, derived from calculations using ITAE metrics, reveal a substantial discrepancy in operating costs. Therefore, it is evident that the cost results obtained from QQR are more optimal.

4. CONCLUSION

The present study developed a mathematical model of SEIR-based FMD spread, with the primary variables defined as follows: Susceptible (S), Exposed (E), Infected (I), and Recovered (R). The model meets the well-posed criteria, ensuring its validity. The analysis indicates that the system exhibits instability under both disease-free and endemic conditions. However, after incorporating controls, the system exhibits asymptotic stability, as evidenced by simulation results. Two control strategies are applied: vaccination of susceptible cattle and treatment of infected cattle. The analysis demonstrated that the system attained full controllability following the incorporation of control variables. The existence of an optimal control that minimizes the objective function is guaranteed by convex analysis. The optimal strategy employing the Quadratic-Quadratic Regulator (QQR) method suggests that 45.93% of the susceptible cattle population in East Java should be vaccinated, and that 32.74% of infected cattle should be treated. The optimal control of QQR yielded results that were not significantly different from LQR; however, its performance and operational costs were lower than those of LQR. Future research is recommended to optimize the QQR algorithm to reduce computation time. It is imperative to optimize the determination of the state cost weight matrix (Q_c) and the control cost weight matrix (R_c). The current QQR processing time is relatively prolonged, necessitating the development of an efficient algorithm. Optimizing speed is imperative for the successful implementation of QQR in autonomous systems that require rapid decision-making. In addition, the parameters in our model could be analyzed for sensitivity in future research. The objective is to further develop the model to make it more generalizable and applicable to other situations and conditions, thereby ensuring the sustainability of our research endeavors.

Author Contributions

Fadilah Akbar: Data Curation, Formal Analysis, Investigation, Methodology, Resources, Software, Visualization, Writing - Original Draft. Mardijah: Supervision, Validation, Project Administration, Funding Acquisition. Mahmud Yunus: Supervision, Validation. All authors have read and agreed to the published version of the manuscript.

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Declarations

The authors declare no competing interest on this research work/article.

Declaration of Generative AI and AI-assisted technologies

Generative AI tools (e.g., DeepL Write) were used solely for academic language refinement (grammar, spelling, and clarity). The scientific content, analysis, interpretation, and conclusions were developed entirely by the authors. The authors reviewed and approved all final text.

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