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Optimal Control Solution for Rabies Disease Transmission within Free-ranging Dog

Eti D. Wiraningsih[1, a)], Z. Jamaludin[2)], A. P. Ramadhan[2)], M. Misbach[2)]

[1]*Department of Mathematics, Faculty of Mathematics and Natural Sciences, State University of Jakarta, DKI-Jakarta, Indonesia*
[2]*Department of Mathematics, Faculty of Mathematics and Natural Sciences, University of Padjadjaran, Bandung-West Java, Indonesia*

Email: [a)]eti_dwi@unj.ac.id

Abstract

This paper considers deterministic model for transmission dynamics of rabies virus in the free-ranging dog population. The stability of system near by Disease Free Equilibrium point is analized using Next Generation Matrix. The effect of vaccination in susceptible dog population is considered on the model. We then present the effective reproduction number in the present of the vaccination. Further we developed the formula to obtain the optimal vaccination to eliminate the endemic equilibrium, via the Pontryagin Maximum Principle. Numerical example are presented to show the properties of the optimal control solution.

Keywords: optimal control, rabies, free-ranging dog.

INTRODUCTION

Rabies is an acute and deadly disease caused by viral infection of the central nervous system. The rabies virus is most often spread by a bite and saliva from an infected (rabid) animal (e.g., bats, racoons, skunks, foxes, ferrets, cats and dogs). Virtually 100% of those infected with rabies who do not receive the vaccine will die. Rabies illness includes rapidly progressing central nervous system symptoms such as anxiety, different swallowing and seizures. The virus usually incubates from two to eight weeks before signs are noticed. However, transmission of the virus through saliva can happen as early as ten days before symptoms appear. Unvaccinated dogs who are allowed to roam outdoors without supervision are most at risk for infection. They're exposed to wild animals and have a greater chance of fighting with infected stray dogs or cats. There is no accurate test to diagnose rabies in live animals. The direct fluorescent antibody test is the most accurate test for diagnosis but because it requires brain tissue, it can only be performed after the death of the animal [2], [6], [10].

Rabies is a vaccine-preventable disease. Vaccinating dogs is the most cost-effective strategy for preventing rabies in people. Dog vaccination reduces deaths attributable to rabies and the need for PEP as a part of dog bite patient care [11], [14]. A lot of strategies have been applied to eradicate rabies infection. Related with some controls that applied to solve disease spread problem, many researcher developed optimal control methods to find the best strategy to distribute many controls that be applied. So far this technique has been used to study the dynamics of some diseases, such as vector-borne diseases, HIV and Tuberculosis and rabies. Rabies epidemiology studies have been carried out by researchers [4], [12], [13], [16]. Optimal control problems in the rabies model have also been discussed [8], [9].

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In this paper we analyze stability of the system and investigate the optimal control problem of rabies model in free-ranging dog population. We develop a compartmental model of rabies spread in free-ranging dogs. A free-ranging dog is a dog that is not confined to a yard or house.

METHOD

We develop a compartmental model of rabies spread in free-ranging dogs. A free-ranging dog is a dog that is not confined to a yard or house. Free-ranging dogs include street dogs, village dogs, stray dogs and feral dogs. In our model, the population of free-ranging dog is classified into four subclasses, namely susceptible class, exposed class, infectious class and vaccinated class with sizes denoted by S_d, E_d, I_d and R_d respectively. Then, we define some parameters i.e, δ_d denotes the birth rate, μ_d denotes the death rate, β_{dd} states the transmission coefficient, ε_d is the latency rate, m_d is the vaccination rate, and w_d is the waning immunity. All parameters in the model are non-negative, and the model will be analyzed in a biologically-feasible region defined as follows:

$$\mathcal{D} = \{(S_d, E_d, I_d, R_d) \in \mathbb{R}^4_+ : S_d \geq 0, E_d \geq 0, I_d \geq 0, R_d \geq 0\}.$$

A compartmental model diagram of this model is shown in the following figure.

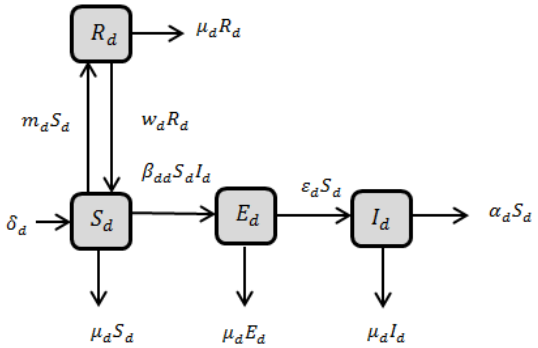

FIGURE 1. Transfer diagram the spread of rabies in free-ranging dog

Based on the transfer diagram above, the transmission model of rabies in free-ranging dog with the effect of Pre-Exposure Prophylaxis vaccine (Pr-EP) can be formulated as a continuous deterministic model of a differential equation system, which consists of eight differential equations, as follows:

$$\begin{aligned}
\frac{dS_d(t)}{dt} &= \partial_d - \mu_d S_d(t) - \beta_{dd} S_d(t) I_d(t) - m_d S_d(t) + w_d R_d(t) \qquad (1)\\
\frac{dE_d(t)}{dt} &= \beta_{dd} S_d(t) I_d(t) - (\varepsilon_d + \mu_d) E_d(t)\\
\frac{dI_d(t)}{dt} &= \varepsilon_d E_d(t) - (\alpha_d + \mu_d) I_d(t)\\
\frac{dR_d(t)}{dt} &= m_d S_d(t) - (w_d + \mu_d) R_d(t),
\end{aligned}$$

All of the parameters in the model are not negative. Given in domain $\mathcal{D}$ as follows $\mathcal{D} = \left\{(S_d, E_d, I_d, R_d) \in \mathbb{R}^4_+ : \ S_d \geq 0, \ E_d \geq 0, \ I_d \geq 0, \ R_d \geq 0; \quad N_d = S_d + E_d + I_d + R_d \leq \frac{\partial_d}{\mu_d} \right\}$.

RESULT AND DISCUSSION

Stability analysis of Disease Free Equilibrium (DFE) point

Theorem 1. The DFE of model (1) is given by

$$DFE\ (E_d^*, I_d^*, S_d^*, R_d^*) = \left(0,0,\frac{(w_d+\mu_d)\partial_d}{\mu_d(w_d+\mu_d+m_d)}, \frac{\partial_d m_d}{\mu_d(w_d+\mu_d+m_d)}\right).$$

Then, the basic reproduction number $\mathcal{R}_0$ is given by

$$\mathcal{R}_0 = \frac{\beta_{dd}(\omega_d + \mu_d)\partial_d \varepsilon_d}{\mu_p(\omega_d + \mu_d + m_d)(\alpha_d + \mu_d)(\varepsilon_d + \mu_d)}.$$

If $\mathcal{R}_0 < 1$, then DFE is local asymptotic stable, and if $\mathcal{R}_0 > 1$, then DFE is not stable.

Proof: In the next generation matrix technique, we have two 'infectious' classes E_d, I_d and

$$F = \begin{pmatrix} 0 & \frac{\beta_{dd}(w_d + \mu_d)\partial_d}{\mu_d(w_d + \mu_d + m_d)} \\ 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} \varepsilon_d + \mu_d & 0 \\ -\varepsilon_d & \alpha_d + \mu_d \end{pmatrix}.$$

Then, using $\mathcal{R}_0 = \rho(FV^{-1})$ with ρ being the spectral radius, we obtain

$$\mathcal{R}_0 = \frac{\beta_{dd}(\omega_d + \mu_d)\partial_d \varepsilon_d}{\mu_d(\omega_d + \mu_d + m_d)(\alpha_d + \mu_d)(\varepsilon_d + \mu_d)}.$$

By Theorem 2 of Driessche-Watmough[3], we have the DFE of basic model (1) is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable, if $\mathcal{R}_0 > 1$.■

Furthermore, consider the domain $\mathcal{D}_1 = \{(S_D, E_D, I_D, R_D) \in \mathcal{D}: S_D^* \geq S_D\}$.

Theorem 2 The DFE of model (1), *is global asymptotic stable in* $\mathcal{D}_1$ *whenever* $\mathcal{R}_0 < 1$.

Proof. The proof is based on using a comparison theorem. The equation of the infected components can be written in terms of

$$\begin{pmatrix} \frac{dE_d}{dt} \\ \frac{dI_d}{dt} \end{pmatrix} = (F - V)\begin{pmatrix} E_d \\ I_d \end{pmatrix} - M_1 Q_1 \begin{pmatrix} E_d \\ I_d \end{pmatrix},$$

where $M_1 = \frac{(w_d+\mu_d)\partial_d}{\mu_d(w_d+\mu_d+m_d)} - S_d$, and $Q_1 = \begin{pmatrix} 0 & 0 \\ 0 & \beta_{dd} \end{pmatrix}$, is non negative matrix.

Thus, since by the definition of $\mathcal{D}_1$, $M_1 \geq 0$ for all $t \geq 0$ and all parameters are positive, it follows that

$$\begin{pmatrix} \frac{dE_d}{dt} \\ \frac{dI_d}{dt} \end{pmatrix} \leq (F - V)\begin{pmatrix} E_d \\ I_d \end{pmatrix} \quad (2)$$

Using the fact that the eigenvalues of the matrix $F - V$ all have negative real parts, it follows that the linearized differential inequality system (2) is stable whenever $\mathcal{R}_0 < 1$. $(E_d(t), I_d(t)) \to (0,0)$ for $t \to \infty$. By standard comparison results, substituting $E_d = I_d = 0$ in the first and the forth of model (1), it is obtained $S_d(t) \to \frac{(\omega_d+\mu_d)\partial_d}{\mu_p(\omega_d+\mu_d+m_d)}$, and $R_d(t) \to \frac{\partial_d m_d}{\mu_d(\omega_d+\mu_d+m_d)}$ as $t \to \infty$.

Thus $E_d(t), I_d(t), S_d(t), I_d(t) \to \left(0,0, \frac{(w_d+\mu_d)\partial_d}{\mu_d(w_d+\mu_d+m_d)}, \frac{\partial_d m_d}{\mu_d(w_d+\mu_d+m_d)}\right)$ as $t \to \infty$ for $\mathcal{R}_0 < 1$.

Hence, the DFE is global asymptotically stable if $\mathcal{R}_0 < 1$. ■

Model simulation

The numerical solution of the system is obtained using the application of MAPLE with parameters as stated in this following table:

TABLE 1. Parameter Value (Source: Zhang et al)

Definition	Parameter	Value	Unit
Birth rate	∂_d	3x10^6	Year^{-1}
Death rate	μ_d	0.08	Year^{-1}
Death rate cause by rabies infection	α_p	1	Year^{-1}
Transmission coefficient	β_{dd}	2.7x10^{-8}	Year^{-1}
Average latency / incubation period	ε_d	6	Year^{-1}
Average vaccine delivery	m_d	0.09	Year^{-1}
Average loss of vaccine immunity	w_d	1	Year^{-1}

From the analysis of rabies case in China, during five-year period, it is obtained DFE disease free equilibrium point: $S_d^* = 3.461538462 \times 10^7$, $E_d^* = 0$, $I_d^* = 0, R_d^* = 2.884615385 \times 10^6$ and value $\mathcal{R}_0 = 0.8539979757$. With initial value that satisfied $\mathcal{D}_1$ which is: $S_d(0)$ = 3x10^7, $E_d(0)$ = 1, $I_d(0)$ = 1, $R_d(0)$ = 2x10^6 It is obtained the simulation result illustrated in Figure 2.

Based on the value of $\mathcal{R}_0$ and the figure, it can be seen for any initial value given, the curve going to the DFE disease free equilibrium point. This means the equilibrium of DFE is locally asymptotically stable, if $\mathcal{R}_0 < 1$. Furthermore, for randomany selection of initial value, which is far, enough from the DFE point, located in the domain $\mathcal{D}_1$, then the DFE point is globally asymptotically stable. I_d, E_d tends to go to zero point, this means in long period of time, not more than 20 years, The infected dog population will be gone, in other words, the disease will extinct. S_d, R_d tends to go up. This means that in a long period of time, those who will remail are healthy dog population.

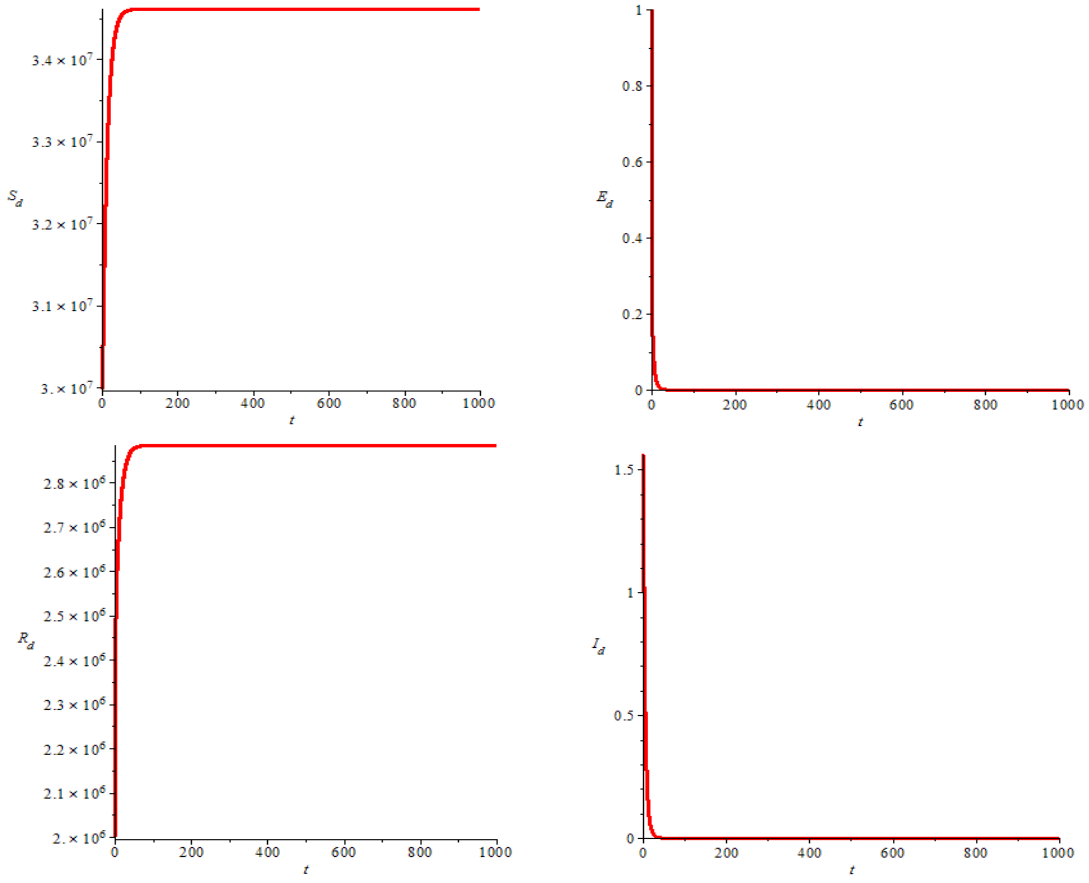

FIGURE 2. Rabies in China

Next, the projection plot of phase portrait of I_d towards S_d is given as follows:

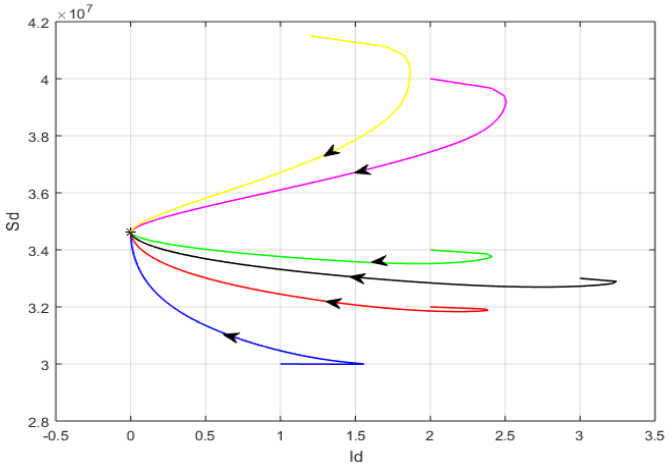

FIGURE 3. Phase Portrait I_d toward S_d

From the above figure, it can be shown that for any initial values all curves will go up and then the value goes to the point of $(I_d^*, S_d^*) = (0, 3.461538462 \times 10^7)$, which is part of the disease-free equilibrium point. This means the point (I_d^*, S_d^*) is asymptotic stable.

Optimal control problem

Next taking m_d, the vaccination rate of dogs, as a function of time, we formulate an optimal control problem. Taking $m_d(t)$ as the control, our objective functional is

$$J(m_d) = \int_0^T (A_1 I_d - A_2 S_d + A_3 m_d + A_4 m_d^2) dt$$

We seek to minimize infected class, I_d, and the cost of the control and maximize the susceptible class, S_d. We seek to find the optimal control m_d^*, i.e., $J(m_d^*) = \min_U J(m_d)$, where the control set is $U = \{m_d : [0,T] \to [0,M] |\ m_d \text{ lebesgue measurable}\}$.

The structure of this problem would give the existence of a bounded state solution with non-negative components and the existence of an optimal control. Applying the Pontryagin's Maximum Principle [8], we form the Hamiltonian and derive the optimality system:

$$H = A_1 I_d - A_2 S_d + A_3 m_d + A_4 m_d^2 + \lambda_1(\delta_d - \beta_{dd} S_d I_d - m_d S_d + w_d R_d) + \lambda_2(\beta_{dd} S_d I_d - (\varepsilon_d + \mu_d) E_d) + \lambda_3(\varepsilon_d E_d - (\alpha_d + \mu_d) I_d) + \lambda_4(m_d S_d - (w_d + \mu_d) R_d).$$

There exists adjoint functions, $\lambda_i(t) = 1, \ldots, 4$, satisfying

$$\lambda_1' = -\frac{dH}{dS_d} = A_2 + \lambda_1 \mu_d + \lambda_1 \beta_{dd} I_d + \lambda_1 m_d - \lambda_2 \beta_{dd} I_d - \lambda_4 m_d$$

$$\lambda_2' = -\frac{dH}{dE_d} = \lambda_2(\varepsilon_d + \mu_d) - \lambda_3 \varepsilon_d$$

$$\lambda_3' = -\frac{dH}{dI_d} = -A_1 + \lambda_1 \beta_{dd} S_d - \lambda_2 \beta_{dd} S_d + \lambda_3(\alpha_d + \mu_d)$$

$$\lambda_4' = -\frac{dH}{dR_d} = -\lambda_1 w_d + \lambda_4(w_d + \mu_d)$$

We have tranversality conditions, $\lambda_i(t) = 1, \ldots, 4$.

On the interior of the control set U, we have

$$\frac{dH}{dm_d} = A_3 + 2A_4 m_d - \lambda_1 S_d + \lambda_4 S_d$$

$$\left.\frac{dH}{dm_d}\right|_{m_d=m_d^*} = A_3 + 2A_4 m_d - \lambda_1 S_d + \lambda_4 S_d = 0$$

This gives

$$m_d^* = \frac{\lambda_1 S_d - \lambda_4 S_d - A_3}{2A_4}$$

Using an appropriate variation argument and take the bounds intoaccount, we obtain

$$m_d^* = \min\left\{M, max\left\{0, \frac{\lambda_1 S_d - \lambda_4 S_d - A_3}{2A_4}\right\}\right\}$$

Using a Runge-Kutta four algorithm for differential equations with the forward-backward sweep method, we solve the state and adjoint equations with the optimal control characterization. With the same data we get

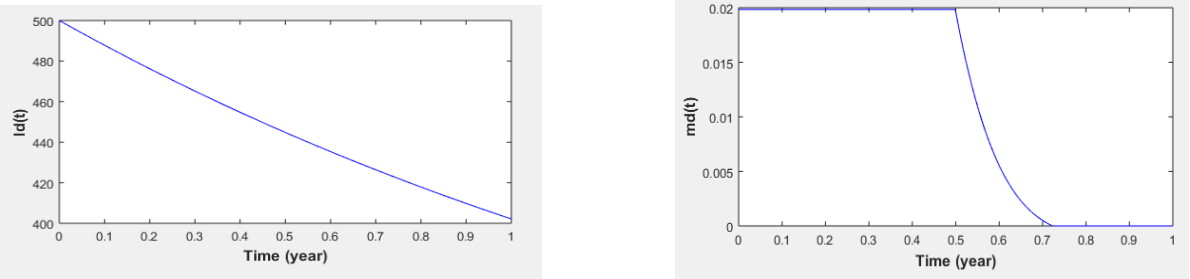

FIGURE 4. Optimal control of Rabies with weight coefficient $A_1 = A_2 = A_3 = A_4 = 1$

CONCLUSION

The basic reproductive number R_0 of rabies model in free-ranging dogs with the effect of pre exposure prophylaxis vaccine is defined and the behavior of the model is studied. It is proved that the disease free equlibrium is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$. Furthermore the diseases free equilibrium is globally asymptotically stable if $R_0 < 1$. It has a biologycal meaning that if $R_0 < 1$, the disease cannot invade the population. Than for an initial population, the rabies epidemic will be extinct and would extinct forever the healthy dogs as time goes on. Based on the solution to the problem of optimal control, procurement of vaccines is needed to reduce the spread of the disease.

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