Optimal control mathemathical SIR model of malaria spread in South Kalimantan

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Submission date: 18-Jun-2020 05:05PM (UTC+0700)
Submission ID: 1345885496
File name: 1.Affandi_2018_J._Phys.__Conf._Ser._1116_022001.pdf (565.79K)
Word count: 5755
Character count: 29602

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Abstract. South Kalimantan is one of the provinces vulnerable to malaria because their work is in the vicinity of forests such as miners, and seekers living on the edge of the forests based on a report from South Kalimantan Health Office (2013). Malaria eradication has always been carried out by the government through the South Kalimantan Health Office (2016) and its achievements have increased, but it is still a problem and needs tougher efforts to achieve malaria-free targets 2020. One way to eradicate the disease is to control it through mathematical modeling. This study discussed the formation of modified malaria distribution model. Analyze infection rates in South Kalimantan using the malaria distribution model. Conducting Optimal Control to complete Mathematical Model SIR of Malaria Spread in South Kalimantan.

1. Introduction

Malaria is a contagious disease caused by a female Anopheles mosquito bite that contains plasmodium. This disease was first discovered by Charles Alphonse Laveran in 1880 in Algeria, in the form of plasmodium falciparum gametocytes (banana form). Plasmodium will multiply in human blood cells. The cause of the disease is natural (natural), through the bite of anopheles female mosquito. This disease attacks all men and women. Symptoms that occur after infection include fever, chills, sweating, headache, nausea, and even vomiting based on reports from the Ministry of Health of the Republic of Indonesia in Data and Information Center in 2016.

Ministry of Health of the Republic of Indonesia in the Bulletin of Data and Health Information Data in 2011 states that malaria is one of the diseases that must be eradicated (total destruction of the affected part of the disease to the root to eradicate the disease). Most areas of Indonesia are still endemic areas of malaria. The rate of malaria transmission in a given region is determined, Reservoir, reflected by the prevalence of the case, the species suitability vector or anopheles mosquito strain as vector, breeding rate, flying distance, resting habits, eating habits and the amount. The new human Hospes, which is meant is the presence of non-immune human groups entering endemic areas, local climatic conditions, geographical and hydrographic conditions, coupled with human activities and activities, affecting their exposure and access to developing places and mosquito habitats anopheles. One of the areas suitable for the place is the area of South Kalimantan. In 2006 - 2009 there was an extraordinary incident (KLB) on

the island of Borneo and in 2009 occurred in South Kalimantan. This incident is said to be extraordinary because the number of deaths from malaria has doubled.

South Kalimantan is also vulnerable to malaria, due to the fact that the community's work is still in the vicinity of forests such as mining workers, gold miners, forest product seekers even living on the edge of the forests based on South Kalimantan Health Agency report in 2013. One of the local electronic media reported that there are two districts belonging to malaria endemic category namely Tanah Bumbu and Kotabaru. Throughout the year 2012, data from the Health Service of South Kalimantan recorded 9,385 cases of malaria or by 0.00248% of the population.

In a previous study "Optimal Control on Determination of Time Interval and Optimal Dosage of Malaria" Pardi Affandi et al. discussed the formation of malaria disease model then optimize the Determination of Time Interval and Optimal Dose of Malaria Disease, in the following study 'Optimal Control Mathematical Model of Malaria Spread in South Kalimantan' will be discussed modification of malaria spread model then model used to analyze the rate of invasion of malaria disease based on data obtained sourced from South Kalimantan Provincial Health Office will then be determined model solution by using control theory.

2. Theoretical basic

2.1 The set of convex and convex function

The concept of a convex function underlie some part in the discussion section. The following definitions and theorems related to the set and convex function.

Definition 1 (Mangasarian). The set $\Gamma \subset \mathbb{R}^n$ called convex set if for to any $x_1, x_2 \in \Gamma$ and for $\lambda \in \mathbb{R}$ such that $0 \leq \lambda \leq 1$ *will apply* $(1-\lambda)(x_1) + \lambda(x_2) \in \Gamma$.

2.2 Non homogen linear differential equation and solution

Definition 2 (Ross S L, 1984). Differential equations are equations containing derivatives of one or more dependent variables for one or more independent variables.

Definition 3 (Ross S L, 1984). Order linear differential equations-n, with the dependent variable, and the independent variablex, can be expressed as follows

$$a_0 x \frac{d^n y}{dx^n} + a_1 x \frac{d^{n-1} y}{dx^{n-1}} + \cdots + a_{n-1} x \frac{dy}{dx} + a_n(x) y = F(x)$$

With a_0 not equal to zero.If F is equal to zero then the equation reduces to

$$a_0 x \frac{d^n y}{dx^n} + a_1 x \frac{d^{n-1} y}{dx^{n-1}} + \cdots + a_{n-1} x \frac{dy}{dx} + a_n x y = 0$$

Called homogeneous differential equation. For F(x) ≠0, referred to as non homogeneous differential equation. Theorem 2.1.4 (Ross, S.L 1984) Provided y_p a solution to non homogeneous linear differential equation which does not contain any constants.

2.3 Basic reproduction numbers

The basic reproduction number serves to inform the spread of disease and can be a parameter in providing strategies for disease control. Biologically the reproduction number can mean the average number of secondary infection cases that occur when the infected individual enters the population that are all Susceptible.

Basic reproduction numbers are generally written with R0, the form R0 can be one of three possible values:

$R_0 < 1$: The disease will disappear over time
$R_0 = 1$: The disease will become spread and remain on a large scale epidemic
$R_0 > 1$: There will be an epidemic with a very high degree of relevancewith death.

2.4 Epidemic model

Malaria is caused by parasites of the Plasmodium species. The parasite is transmitted to humans through the bite of Anopheles female mosquito. After biting the human parasite changes through a complex life cycle. Parasites multiply in the liver and bloodstream of humans. After 10 to 15 days mosquitoes carry parasites and can infect new people. Approximately 9 to 14 days after bitten, will show symptoms of malaria (Rollback, 2010). In Indonesia, the most commonly found species are 4, namely *Plasmodium falcifarum and Plasmodium vivax, Plasmodium malariae*, and *Plasmodium ovale*. According to Arsin (2012) ever found malaria caused by *Plasmodium ovale* reported from Flores.

The nature of the parasite varies with each species of malaria that affects its transmission. *Plasmodium falciparum* has the shortest period of infection, but it produces the highest parasitemia, the most severe symptoms and the shortest incubation period. *Plasmodium falciparum* gametocyte develops after 8-15 days after the entry of the parasite into the blood. *Plasmodium falciparum* gametocytes show the periodicity and infectivity associated with vector bite activity. *Plasmodium vivax* and *Plasmodium ovale* generally produce low parasitemia, milder symptoms but have a longer incubation period. Sporozoit *Plasmodium vivax* and *Plasmodium ovale* develop into primary and hypnozoit tissue scizons in the liver. This hypozoite results in relapse (Arsin, 2012).

2.5 Optimal control

In the following discussion, the problems given in the case of optimal control with state end and the end time is known. In other words, the target set S shaped $\{S = x_1(t_1)\}$ in the form (x_1, t_1) with x_1 specially elementin R^n and t_1 element at (T_1, T_2).Given the state system by the end and the end time unknown $\dot{x}(t) = f[x(t), u(t), t]$ with x(t) vector state sized $nx1$, u(t) input vector sized $mx1$, f a vector valued function. Initially given state is X_0 and initially time is t_0. Target set S form (x_1, t_1) with $t_1 \in (T_1, T_2)$ known value and $t_1 > t_0$. Optimal control problem is to find the admissible control u(t) with the initial value (x_0, t_0) and the final value (x_1, t_1) that maximizes the objective function

$$J(u) = \int_{t_0}^{t_1} L(x(t), u(t), t)\ dt.$$

Tosolve the problems mentioned above optimal control, first determined necessary condition for optimal control are met.

3. Discussion of problems

Patients with malaria with gametocytes become a source of transmission with an intermediary is a mosquito as a vector. Humans are an important reservoir, but the disease is transmitted through the bite of a female anopheles mosquito containing the plasmodium species parasite. Most occur naturally, through the bite of a female anopheles mosquito, rarely transmitted by blood transfusion and/or bone marrow transplantation. When female anopheles mosquitoes suck blood containing gametocytes, then in the body of the mosquito occurs fertilization that produces a zygote. The zygote develops into an ookinet then penetrates the gastric wall of the mosquito. On the outer wall of the ookinetic mosquito will become an oxista and then become sporozoit that is infective and ready to be transmitted to humans. When a mosquito sucks human blood, it will enter the bloodstream. Approximately 9 to 14 days after humans are bitten, the symptoms of malaria appear.

3.1. Mathematics modelling

Malaria is one of the epidemic diseases and can be modelled in mathematical models. The establishment of this malaria dispersion model follows a SIR model consisting of three compartments:

1. The susceptible (susceptible) group is further denoted by the number of individuals susceptible to malaria at the time.
2. Infected group (infected) further denoted by number of individuals infected with malaria at the time.
3. The recovered group is further denoted by the number of individuals who recover from malaria at the time.

The assumptions used in the malaria distribution model are as follows: Population is assumed to be open so that there is an increasing (incoming) or decreasing (out) population of the population, Natural birth and death are constant, There is only malaria disease in the population Disease spreads through contact between individuals with mosquitoes, Every individual born directly into a susceptible group, Malaria-infected individuals can recover from illness and can experience death only because of illness and the malaria-infected individuals can recover because of short cycles of malaria and the presence of natural immunity. Every individual in doing Immigration as well as Emigration.

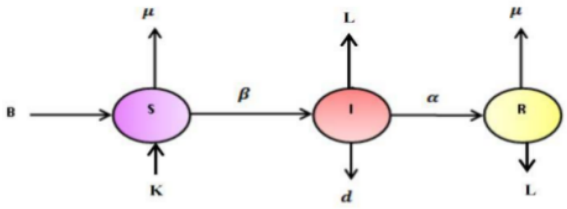

Figure 1. Diagram of malaria disease model

Based on the assumptions that have been determined, then formed the flow diagram of the spread of malaria as follows:

From the compartment above, the parameters used in the malaria dispersion model are defined as follows:

B: the number of individual births (constant)
K: the number of immigration individuals
L: the number of Emigration individuals
β : the rate of transmission of malaria
α : the rate of cure for malaria
μ: natural rate of death
d : the rate of death from malaria

The process of forming the model of malaria disease spread as follows obtained a system of nonlinear differential equations for the spread of malaria as follows is called the model of malaria transmission.

$$\frac{dS}{dt} = B + K - \beta SI - \mu S$$
$$\frac{dI}{dt} = \beta SI - (\alpha + d + L)I$$

$$\frac{dR}{dt} = \alpha I - (\mu + L)R$$

3.2 Stabilization analysis malaria spreading model

This malarial dispersion model has two equilibrium points, namely the disease-free equilibrium point and the endemic equilibrium point.

By definition, equilibrium point equations are derived from $\frac{dS}{dt} = 0.\ \frac{dI}{dt} = 0, \frac{dR}{dt} = 0$

To determine the equilibrium point, the equation is formed into $\beta SI - (\alpha + d + L)I = 0$ $I = 0$ or $\beta SI - (\alpha + d + L) = 0$. So obtained value $S = \frac{(\alpha+d+L)}{\beta}$

3.2.1 The disease-free equilibrium Point

The point of disease-free equilibrium is a condition in which no more illness attacks or no more infected individuals if $I = 0$ substituted to the previous equation then obtained: $S = \frac{B+K}{\mu}$.

Then if $I = 0$ substituted to the previous equation : $R = 0$

So that obtained point of equilibrium free of disease that is $E_0 = \left(\frac{B+K}{\mu}, 0, 0\right)$.

3.2.2 The endemic equilibrium point

The endemic equilibrium point is a condition in which the invading disease still exists and is still spreading if $I \neq 0$ then $\beta S - (\alpha + d + L) = 0$. So obtained equation value $= \frac{(\alpha+d+L)}{\beta}$.

Next we substituted to equation then obtained,

$$I = \frac{(B+K)\beta - \mu(\alpha + d + L)}{\beta(\alpha + d + L)}$$

and also we obtained,

$$\alpha\left[\frac{(B+K)\beta - \mu(\alpha + d + L)}{\beta(\alpha + d + L)}\right] - \grave{\imath}R = 0$$

So as to obtain the endemic equilibrium point that is :

$$E_1 = \left(\frac{(\alpha + d + L)}{\beta}, \frac{(B+K)\beta\text{-}\mu(\alpha + d + L)}{\beta(\alpha + d + L)}, \frac{(B+K)\beta\alpha\text{-}\mu\alpha(\alpha + d + L)}{\beta\mu(\alpha + d + L)}\right)$$

.3 Basic reproduction numbers

Basic reproduction number (R_0) is a certain parameter used to determine the dynamics of the spread of disease, R_0 is used as a quantity to express the extent of disease spread. To obtain R_0, so we have from equation $R_0 = \frac{\beta}{(\alpha+d+L)}$.

There are two states that occ from equation that is as follows.

- $\frac{dI}{dt} > 0$ there will be an increase in the number of infected populations, and

- $\frac{dI}{dt} < 0$ the disease will not spread so the number of infected population will not increase.Because the desired is when the disease does not spread meaninglessshould be obtained $R_0 < \frac{1}{S}$

Based on the statement of Driessche and Watmough (2005) the disease will disappear over time if $R_0 < 1$.

The following is obtained by Population (N) of South Kalimantan in 2012-2016, because to calculate the required R_0 value of total population data (N), infected population data (I) and vulnerable population data (S). The number of vulnerable populations (S) is obtained from the total population reduced by the infected population.

Table 1. Total population (n) of south Kalimantan year 2012-2016

	City	Population				
		2012	2013	2014	2015	2016
1.	Tanah Laut	308.510	313.725	319.098	324.283	329.286
2.	Kotabaru	302.982	308.730	314.492	320.208	325.827
3.	Banjar	527.195	536.328	545.397	554.443	563.062
4.	Barito Kuala	285.595	289.995	294.109	298.282	302.304
5.	Tapin	173.869	176.468	179.166	181.778	184.330
6.	Hulu Sungai Selatan	218.897	221.614	224.474	227.153	229.889
7.	Hulu Sungai Tengah	250.705	253.868	257.107	260.292	263.376
8.	Hulu Sungai Utara	215.980	219.210	222.314	225.386	228.528
9.	Tabalong	227.714	231.718	235.777	239.593	243.477
10.	Tanah Bumbu	295.032	306.185	315.815	325.115	334.314
11.	Balangan	117.088	119.171	121.318	123.449	125.534
12.	Banjarmasin	647.403	656.778	666.223	675.440	684.183
13.	Banjarbaru	214.011	220.695	227.500	234.371	241.369
	Kalimantan Selatan	3.784.981	3.854.485	3.922.790	3.989.793	4.055.479

Source: Central Bureau of Statistics of South Kalimantan Province

The infection rate will decrease when $R_0 < 1$. In the equation obtained value $R_0 = \frac{1}{S}$. So conditions $R_0 < 1$so let it be

$$R_0 = \frac{K}{S} \text{ with } 0 < K \leq 1.$$

After the calculation obtained value R_0 can be seen from the table as follows.

Table 2. The calculation results value R_0 for $K = 0{,}75$

	Regencies/ Cities	R_0 Value				
		2012	2013	2014	2015	2016
1.	Tanah Laut	0,00000325	0,00000319	0,00000314	0,00000308	0,00000304
2.	Kotabaru	0,00000249	0,00000244	0,00000239	0,00000234	0,00000230
3.	Banjar	0,00000142	0,00000140	0,00000138	0,00000135	0,00000133
5.	Tapin	0,00000432	0,00000426	0,00000419	0,00000413	0,00000407
4.	Barito Kuala	0,00000263	0,00000259	0,00000255	0,00000251	0,00000248
6.	Hulu Sungai Selatan	0,00000343	0,00000339	0,00000334	0,00000330	0,00000326
7.	Hulu Sungai Tengah	0,00000299	0,00000296	0,00000292	0,00000288	0,00000285
8.	Hulu Sungai Utara	0,00000348	0,00000342	0,00000337	0,00000333	0,00000328
9.	Tabalong	0,00000331	0,00000325	0,00000320	0,00000315	0,00000309
10.	Tanah Bumbu	0,00000257	0,00000246	0,00000238	0,00000231	0,00000224
11.	Balangan	0,00000641	0,00000630	0,00000619	0,00000609	0,00000599
12.	Banjarmasin	0,00000116	0,00000114	0,00000113	0,00000111	0,00000110
13.	Banjarbaru	0,00000351	0,00000340	0,00000330	0,00000320	0,00000311

Based on table 2 with the value of K given the smaller the value of R_0 obtained is also smaller from year to year every Regency/City. This is due to the fact that when the large total population, with small infected populations, has a large vulnerable population, so the value of R_0obtained is small. Whereas if the total population is small, with a large infected population then the small vulnerable population so that the value of R_0 obtained is also large.

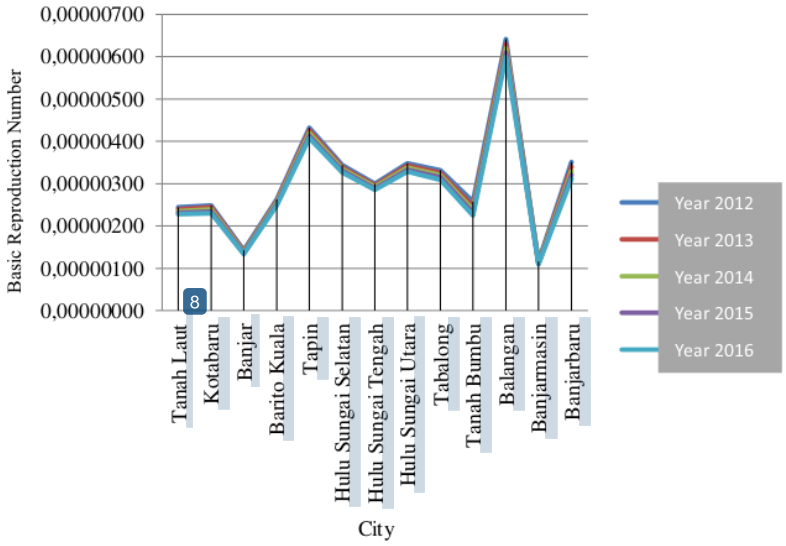

Figure 2. The spread of malaria infection rate for K = 0.75

Furthermore, we can see the spread of malaria infection rate in South Kalimantan from the figure below based on R_0 value.

In Figure 3 given the value of K = 0.75 from 2012 to 2016 can be seen the spread of malaria infection rate in South Kalimantan based on R_0 value. The lowest rate of malaria infections occurred in Banjarmasin, while the highest malaria infection rate occurred in Balangan Regency.

Based on the figure 3 with the value of K is getting smaller then the value of R_0 in each Regency/City is also getting smaller every year. Based on the value R_0 obtained gives information that the lowest level of malaria infection occurred in Banjarmasin City because the lowest R_0 value while the highest malaria infection rate occurred in Balangan regency because the value of R_0 is the greatest.

3.3 Linearization of the System at the Point of Equilibrium Free of Illness

The stability of an equilibrium point can be determined based on the eigenvalues. Since the system of this model is a system of nonlinear differential equations it can be determined by linearizing using a Jacobian matrix.Furthermore, the above equation is exemplified :

$$\mathrm{f_1} = \mathrm{B} + \mathrm{K} - \beta \mathrm{SI} - \mu \mathrm{S}$$
$$\mathrm{f_2} = \beta \mathrm{SI} - (\alpha + \mathrm{d} + \mathrm{L})\mathrm{I}$$
$$\mathrm{f_3} = \alpha \mathrm{I} - (\mu + \mathrm{L})\mathrm{R}$$

Function $\mathrm{f_1}$,$\mathrm{f_2}$, dan $\mathrm{f_3}$derived to S obtained :

$$\frac{\partial \mathrm{f_1}}{\partial \mathrm{S}} = -\beta \mathrm{I} - \mu$$
$$\frac{\partial f_2}{\partial S} = \beta I$$
$$\frac{\partial f_3}{\partial S} = 0$$

Function f_1,f_2, dan $f_3$derived to$I$ obtained:

$$\frac{\partial f_1}{\partial I} = -S$$
$$\frac{\partial f_2}{\partial I} = \beta S - (\alpha + d + L)$$
$$\frac{\partial f_3}{\partial I} = \acute{a}$$

Function f_1,f_2, dan $f_3$derived toR obtained:

$$\frac{\partial \mathrm{f_1}}{\partial \mathrm{R}} = 0$$
$$\frac{\partial \mathrm{f_2}}{\partial \mathrm{R}} = 0$$
$$\frac{\partial \mathrm{f_3}}{\partial \mathrm{R}} = -(\mu + \mathrm{L})$$

based on the above scaling process, a Jacobian matrix of the following equation system is formed :

$$\Leftrightarrow \boldsymbol{J} = \begin{bmatrix} -\beta I - \mu & -\beta S & 0 \\ \beta I & \beta S - (\alpha + d + L) & 0 \\ 0 & \alpha & -(\mu + L) \end{bmatrix}$$

Characteristikequations :

$$|\boldsymbol{J}-\boldsymbol{\lambda I}|=0$$

$$\Leftrightarrow \begin{vmatrix} -\beta I-\mu-\lambda & -\beta S & 0 \\ \beta I & \beta S-(\alpha+d+L)-\lambda & 0 \\ 0 & \alpha & -(\mu+L)-\lambda \end{vmatrix} (\frac{B}{\mu},0,0)=0$$

$\Leftrightarrow (-\beta I-\mu-\lambda)[\beta S-(\alpha+d+L)-\lambda](-(\mu+L)-\lambda)-(\mu+L)\beta^2 IS-\lambda\beta^2 IS=0$...(4.15)
to determine the eigenvalues of the malaria dispersion model at the point of disease-free equilibrium, then substitution$E_0=\left(\frac{B}{\mu},0,0\right)$.So we have

$$\Leftrightarrow (-\mu-\lambda)\left[\beta\frac{B}{\mu}-(\alpha+d)+L-\lambda\right](-(\mu+L)-\lambda)=0$$

$(-\mu-\lambda)=0$or$(-(\mu+L)-\lambda)=0$ or $\beta\frac{B}{\mu}-(\alpha+d)-\lambda=0$

$\lambda_1=-\mu,\lambda_2=-\mu-L,\lambda_3=\beta\frac{B}{\mu}-(\alpha+d)$

The equation is called the characteristic equation and the eigenvalues obtained from the malaria dispersion model are$\lambda_{1,}=-\mu,\lambda_2=-\mu-$ Land$\lambda_3=\beta\frac{B}{\mu}-(\alpha+d)$. $\lambda_{1,2}$ negative value because natural death and big emigration always positive so negative eigen value, whereas λ3 will be negative if $\beta\frac{B}{\mu}<(\alpha+d)$. Where $\beta\frac{B}{\mu}$is the number of infected populations that means when the number of infected populations is smaller than the number of recovered individuals plus the individual who has suffered good death from the disease then the eigenvalue is negative. So in time the system will stabilize toward the point of disease-free equilibrium.

3.4 Optimal Control for Malaria Distribution Model.

Optimal control of the Malaria distribution model aims to maximize the number of healthy pink (reticulocyte) blood cells by controlling malarial drugs that inhibit reticulocyte invasion in the human body. The action of this drug can be controlled optimally by applying the maximum principle of Pontryagin. The maximum principle of Pontryagin is a condition such that it can be obtained by completion of optimal control in accordance with the objective of maximizing performance index.
The state equation is:

$\dot{x}=f(x(t),u(t),t)$danx$=\begin{bmatrix}S\\I\\R\end{bmatrix}$so the state equation becomes$\dot{x}=\begin{bmatrix}\dot{S}\\\dot{I}\\\dot{R}\end{bmatrix}$ atau $\dot{x}=\begin{bmatrix}B+K-\dot{\beta SI}-\mu\dot{S}\\\beta S\dot{I}-(\alpha+d+L)\dot{I}\\\alpha I-(\mu+L)\dot{R}\end{bmatrix}$

becouse$\frac{dS}{dt}=B+K-\beta SI-\mu S$ $\frac{dI}{dt}=\beta SI-(\alpha+d+L)\frac{dR}{dt}=\alpha I-(\mu+L)R$

Equations *performance index* is:

$$J(u)-\int_{t_1}^{t_1}L(x(t),u(t),t)dt$$

With $t_0$adalah first time, t_f is finishing time, x(t) is state variable and u(t) is control variable. Equations performance index expressed as the system from the initial state to the final state is:

$$J(T,u)=\int_{t_0}^{t_f}(T-A(u(t))^2)dt$$

With T s the initial state of healthy reticulocyte cells, Aweighting parameters used in controls andu (t)is a drug control. Then, the maximum valueJ(u) $=\frac{1}{2}$for u(t)-1which indicates that the

administration of the drug works optimally so that the weight parameter can be assumed $A = \frac{1}{2}\gamma$ with γ is a controlling weight in the form of malaria drugs. Furthermore, u is squared to become a quadratic function u^2 to maximize the action of the drug by doubled administration so that the performance index for the malaria dispersion model is as follows:

$$J(T,u) = \int_{t_0}^{t_f} (T - \frac{1}{2}\gamma(u(t))^2)dt$$

Model of malaria spread before being given control $(u(t))$ that:

$$\frac{dS}{dt} = B + K - \beta SI - \mu S$$

$$\frac{dI}{dt} = \beta SI - (\alpha + d + L)I$$

$$\frac{dR}{dt} = \alpha I - (\mu + L)R$$

In the equation above there are two equations that are influenced by the virus is the equation $\dot{S}$ and $\dot{I}$. In the equation $\dot{S}$ and $\dot{I}$ the mosquito-infected reticulocyte cell is symbolized by βSI. Control variable $(u(t))$n the form of malaria drugs given when the human body is attacked by mosquitoes and reticulocyte cells begin to become infected. In this case, drug efficiency $u \equiv 1$ which means the reticulocyte cell is not infected again. While, $u \equiv 0$ is a case where the drug does not provide changes to the disease. Then, to know the value of u (t) is optimal then the value of the controller is $(1 - u(t))$ so the model changes after being given the controller as follows:

$$\frac{dS}{dt} = B + K - \mu S - \beta SI$$
$$\frac{dI}{dt} = \beta SI - (\alpha + d + L)D$$
$$\frac{dR}{dt} = \alpha I - (\mu + L)R$$

with boundary conditions $t_0 < t < t_f$ dan $0 \leq u(t) \leq 1$. With t_0 is the initial time when malaria-infected reticulocyte cells were administered malaria and drugs t_f is the final time when reticulocyte cells infected with the malaria virus are given the drug.

Then, based on the principle of maximum Pontryagin the first step is to determine the Hamiltonian function is as follows:

$$H(x(t), u(t), \lambda(t), t) = L(x(t), u(t), t) + \lambda(t), f(x(t), u(t), t)$$

$$= \left(T - \frac{1}{2}\gamma\left(u(t)\right)^2\right) + (\lambda_1\lambda_2\lambda_3)\begin{bmatrix} B + K - \mu S - \beta SI(1 - u[(t)]) \\ \beta SI - (\alpha + d + L)I(1 - u[(t)]) \\ \alpha I - (\mu_L)R \end{bmatrix}$$

$$= \left(T - \frac{1}{2}\gamma\left(u(t)\right)^2\right) + (\lambda_1\left(B + K - \mu S - \beta SI(1 - u[(t)])\right) + \lambda_2(\beta SI - (\alpha + d + L)I(1 - u[(t)])) + \lambda_3\,(\alpha I - (\mu + L)R)$$

The second step is assumed that at the optimum time, the control variables and state variables are respectively

$u^*(t)$ dan $x^*(t)$ must : $\frac{\partial H}{\partial u} = 0$

$-\gamma u[(t)] + \lambda_1 \beta SI - \lambda_2 \beta SI = 0$

$$u[(t)] = \frac{\lambda_1 \beta SI - \lambda_2 \beta SI}{\gamma}$$

$u(t)$optimally expressed as$u^*(t)$so $u^*[(t)] = \frac{(\lambda_1 - \lambda_2)\beta SI}{\gamma}$.

Because value$u(t)$ is$0 \leq u(t) \leq 1$so can$u^*(t)$ is $0 \leq u^*(t) \leq 1$so as to obtain the following possibilities:

$$u^*[(t)] = \begin{cases} \frac{(\lambda_1 - \lambda_2)\beta SI}{\gamma}, & \text{jika } 0 < \frac{(\lambda_1 - \lambda_2)\beta SI}{\gamma} < 1 \\ 0, & \text{jika } 0 < \frac{(\lambda_1 - \lambda_2)\beta SI}{\gamma} \leq 0 \\ 1, & \text{jika } 0 < \frac{(\lambda_1 - \lambda_2)\beta SI}{\gamma} \geq 1 \end{cases}$$

Based on the above three possibilities, the first possibility in the calculation of the mathematical value obtained

$u^*(t)$ is$0 < \frac{(\lambda_1 - \lambda_2)\beta SI}{\gamma} < 1$and in this case meet the limits

$0 \leq u^*(t) \leq 1$so the value

$$u^*[(t)] = \frac{(\lambda_1 - \lambda_2)\beta SI}{\gamma}$$

The second possibility on the calculation values$u^*(t)$ is $\frac{(\lambda_1 - \lambda_2)\beta SI}{\gamma} \leq 0$and in this case the drug work is not optimal with limitation$0 \leq u^*(t) \leq 1$so the value $u^*(t) = 0$. Then, the third possibility on the calculation obtained value$u^*(t)$ is $\frac{(\lambda_1 - \lambda_2)\beta SI}{\gamma} \geq 1$ and in this case the calculation passes the threshold of drug delivery $0 \leq u^*(t) \leq 1$so the value$u^*(t) = 1$.

Furthermore, of the three possible values of $u^*(t)$ obtained then a value can be determine$u^*(t)$ which is optimal in step three. Because

$$u(t) \in U = \{u(t) | 0 \leq u(t) \leq 1, t_0 < t < t_f\}$$

so as to obtain the value of the smallest limit (supremum) as follows:

$$\max\left(0, \frac{(\lambda_1 - \lambda_2)(\beta SI)}{\gamma}\right)$$

and obtained the value of the largest lower limit (infimum) as follows:

$$\min\left(\max\left(0, \frac{(\lambda_1 - \lambda_2)(\beta SI)}{\gamma}\right), 1\right)$$

so the value$u^*(t)$is :

$$u^*[(t)] = \min\left(\max\left(0, \frac{(\lambda_1 - \lambda_2)(\beta SI)}{\gamma}\right), 1\right)$$

Based on this case$u^*(t)$in equation$u^*(t)$ optimally declare the maximum of drug work with minimal medication.Then, the fourth step is to solve the state equation because of the controller form$u^*(t)$contains state variables(S, I, R)that is

$$\dot{x} = \frac{\partial H}{\partial \lambda}$$

so as to obtain the optimal state equation as follows:

$$\dot{S} = \frac{\partial H}{\partial \lambda_1} = B + K - \mu S - \beta SI(1 - u^*[(t)])$$

$$\dot{I} = \frac{\partial H}{\partial \lambda_2} = \beta SI - (\alpha + d + L)I(1 - u^*[(t)])$$

$$\dot{R} = \frac{\partial H}{\partial \lambda_3} = \alpha I - u^* R$$

In addition to state variables there are also variable costate $\lambda_1, \lambda_2$and $\lambda_3$on the form of the controller $u^*(t)$it is necessary to solve the costate equation to obtain the optimal costate equation in the fifth step is as follows:

$$\dot{\lambda^*} = \frac{\partial H}{\partial \lambda}$$

So that

$$\dot{\lambda_1} = \frac{\partial H}{\partial S} = -(1 - \lambda_1 k - \lambda_1 \beta I + \lambda_1 \beta I - \lambda_2 \beta I u([t])$$

$$\dot{\lambda_2} = \frac{\partial H}{\partial I} = -(-\lambda_2 \beta - \lambda_3 \gamma$$

$$\dot{\lambda_3} = \frac{\partial H}{\partial R} = -(\lambda_1 \alpha S - \lambda_1 \alpha S u + \lambda_2 \alpha S - \lambda_2 \alpha S u([t]) - \lambda_3 k$$

Then the sixth step substitutes the equation$u^*(t)$which has been obtained into the state equation to obtain the optimal form of the solution. Here are the results of the optimal equation system obtained:

$$\dot{S} = B - \mu S - \beta SI\left[\min\left(\max\left(0, \frac{(\lambda_1 - \lambda_2)(\hat{a}SI)}{\gamma}\right), 1\right)\right]$$

$$\dot{I} = \beta SI - (\alpha + d)I\left[\min\left(\max\left(0, \frac{(\lambda_1 - \lambda_2)(\beta SI)}{\gamma}\right), 1\right)\right]$$

$$\dot{R} = \alpha I - u^* R$$

Based on the above description, to obtain S, I and R from the optimal form $u^*(t)$ then it is necessary to solve the non-linear state and costate equations. Because the system of nonlinear equations is difficult to resolve analytically, it can be resolved and numerically illustrated.

3.5 Simulation results

The optimal control of the malaria distribution model obtained in the previous section can be illustrated in graphical form. The result of the optimal equation system that has been obtained is simulated using MATLAB application. In the simulation model of malaria distribution by defining with S = y_1, I = y_2 and R = y_3 as well as some parameters. **Table 1**. Parameter model of malaria distribution and its value

Table 5. Parameter model of malaria distribution and its value

Parameter Symbols	B	μ	β	d	α	α	m
Value Parameter	6 /day	0.0256 / day	0.00000042163 / day	0.09 / day	0.009 / day	90.67 / day	0.2 / day

Table 6. Begin and end values

Symbols	t_0	t_f	a	b	S1(0)	$I_1(0)$	R1(0)	S2(0)	$I_2(0)$	R2(0)
Value	0	1000 Hari	0	1	1000 Cell	0 Cell	7000 Virus	363 Cell	57 Cell	28860 Virus

Then, the above parameters are used in the simulation process to find out the results of the optimum equation system. Here is a picture of the simulation results obtained:

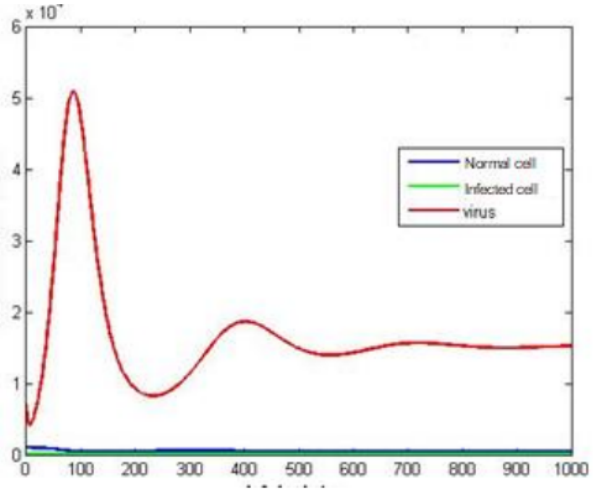

Figure 3. Simulation model of malaria distribution before being given control

In Figure 3 is a simulation result of the system of equation model of malaria spread before given control in the form of drugs.

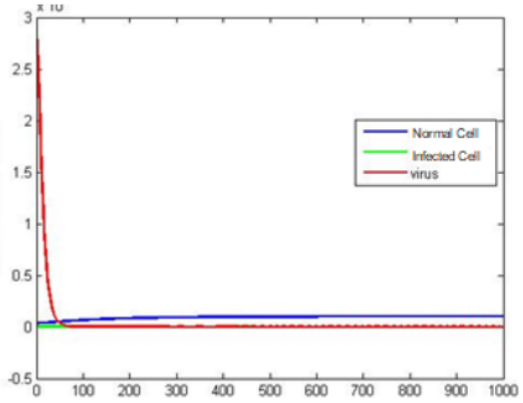

Figure 4. Simulation model of malaria distribution after being given control

Figure 4 is a simulation result of the equation system of malarial distribution model after given control in the form of drug. Based on the simulation model of malaria distribution before and after being given controller there is a difference in the two pictures above.

3.5.1 Simulation for a healthy reticulocyte cell population (T)
The graphic results obtained after the simulation are as follows:

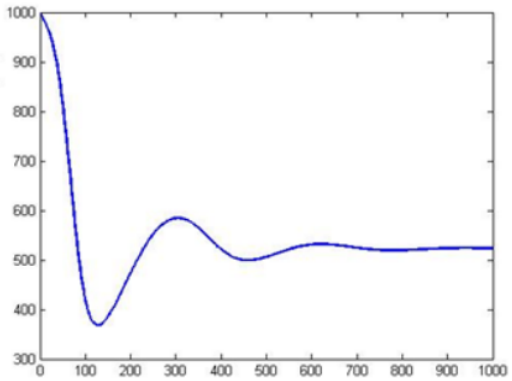

Figure 5. The number of healthy reticulocyte cells before being given control

Figure 5 shows that the population of reticulocyte cells continues to decline every day so that the immune system decreases.

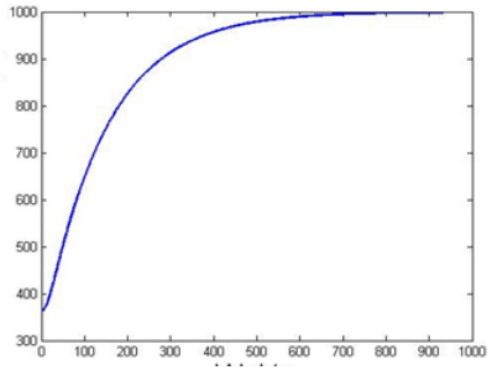

Figure 6. The number of healthy reticulocyte cells after being given control.

Whereas, in Figure 6 it is seen that after administration of the control of drugs the population of reticulocyte cells continues to increase every day. This suggests that the drug works to maximize the number of healthy reticulocyte cells for better immunity.

3.5.2 Simulation for population of infected cells reticulocytes

The second simulation is a simulation for infected cell populations of reticulocytes before being given a control of the formate. Then the next simulation is a simulation for the population of infected cells of the reticulocytes after being given a controlled drug. The graphic results obtained after the simulation are as follows:

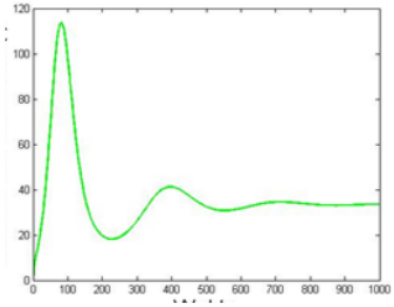

Figure 7. The number of infected cells of the reticulocytes before being given control

Figure 7 shows that the population of infected cells of the reticulocytes before being given control. The number of infected cell reticulocyte populations has increased and then decreases and moves constantly indicating that this population will remain unlimited.

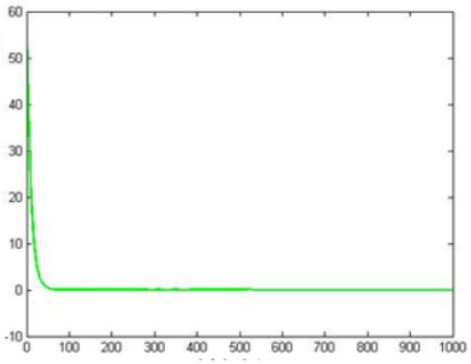

Figure 8. The number of infected cells of reticulocytes after being given control

Whereas, in Figure 8 it appears that after administration of a drug-controlled population the infected reticulocyte cell continues to decline every day. From the graph can be determined the optimum time interval for malaria treatment, and the optimal dose of treatment for malaria disease

4. Conclusions and Suggestions

From the discussion obtained some conclusions:

Model of malaria distribution in South Kalimantan as follows:

$$\frac{dS}{dt} = B + K - \beta SI - \mu S$$
$$\frac{dI}{dt} = \beta SI - (\alpha + d + L)I$$
$$\frac{dR}{dt} = \alpha I - (\mu + L)R$$

The lowest level of malaria infection occurs in Banjarmasin City because the value of reproduction numbers is essentially the smallest. While the highest malaria infection rate occurred in Balangan Regency because the value of reproduction is essentially the largest number.

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