Design of Monkeypox Virus Spread Control in Humans Using Pontryagin Minimum Principle

Lukman Hanafi*, Mardlijah, Daryono Budi Utomo, Suhud Wahyudi and Alya Nur Sha-brina

***Abstract*—Monkeypox is a contagious disease caused by a virus. In Africa, monkeypox results in death in 1 out of 10 infected individuals. The Food and Drug Administration in the United States recommends vaccination as a preventive measure against monkeypox virus. If infected, the World Health Organization (WHO) advises quarantine to prevent further transmission to others. This research develops a mathematical model known as SIR (Susceptible-Infected-Recovered) for the spread of monkeypox virus, incorporating vaccination and quarantine as control measures. The SIR model utilized is based on an existing model and follows the conditions of monkeypox spread in Nigeria, represented as a system of nonlinear differential equations. Optimal control is determined using the Pontryagin Minimum Principle and simulated using the fourth-order forward-backward sweep Runge-Kutta method to assess the level of monkeypox infection before and after implementing control measures. Based on the simulation results, it is concluded that the application of control measures can reduce the population of infected monkeys by 70% and infected humans by 59%.**

I. INTRODUCTION

SINCE January 2022, 3413 laboratories from 50 countries have reported the emergence and fatalities associated with monkeypox, making it a matter of special concern [1]. Monkeypox is a contagious disease caused by a virus. The virus is typically transmitted to humans through contact with infected pets or primates, consumption of infected animal meat, direct contact, or animal scratches or bites. Human-to-human transmission mainly occurs through direct contact. In efforts to prevent the spread of monkeypox virus, the U.S. Food and Drug Administration recommends the use of the JYNNEOSTM vaccine, which has an effectiveness rate of 85%. For individuals already infected, quarantine is essential to break the chain of transmission. Additionally, maintaining personal hygiene, wearing masks, washing utensils with hot water, and disinfecting contaminated surfaces are advised [2].

This research optimizes the impact of vaccination and quarantine on the spread of monkeypox virus using the Pontryagin Maximum/Minimum Principle. The Pontryagin Maximum/Minimum Principle is a principle used to solve optimal control problems in the SIR model by finding controls that maximize or minimize the objective function. It has the advantage of stating the necessary conditions to obtain the most optimal control, thereby minimizing the objective function [3], [4]. The research also utilizes the Runge-Kutta method to solve the problem numerically. The Runge-Kutta method is an alternative method to Taylor series that does not require derivative calculations [5], [6]. Its advantages include higher accuracy compared to Euler's method, Heun's method, and Taylor series [7].

Theoretical studies on monkeypox are conducted by modeling them as systems of differential equations. Bhunu et al. conducted research by modeling the spread of diseases like monkeypox. The study concluded that the high transmission rate of monkeypox virus in Central and West Africa is attributed to poor nutrition and poverty, which forces people to hunt monkeys and wild animals that are infected with monkeypox. The study also suggests that further research should estimate the impact of vaccination in reducing monkeypox transmission [8]. Another study titled "The Transmission Potential of Monkeypox Virus in Human Populations" by Fine et al. concluded that without appropriate interventions, monkeypox has the potential to become a global health threat [9].

Considering the numerous reports from laboratories regarding monkeypox cases, it is crucial to control the spread of this disease. Based on the recommendations from Bhunu's research and the preventive measures suggested by the WHO, this study will apply the Pontryagin Minimum Principle to suppress the spread of monkeypox virus. It is hoped that by implementing vaccination and quarantine controls, the spread of monkeypox virus can be reduced, particularly among susceptible populations.

II. MODEL FORMULATION

A. Description of the Model

This research develops a model for the spread of monkeypox virus, which has been previously studied by Bhunu et al., as shown in the following equations:

$$\begin{aligned}
\frac{dS_n}{dt} &= \Lambda_n - (\mu_n + \lambda_n)S_n \\
\frac{dI_n}{dt} &= \lambda_n S_n - (\mu_n + d_n + \rho_n)I_n \\
\frac{dR_n}{dt} &= \rho_n I_n - \mu_n R_n \\
\frac{dS_h}{dt} &= \Lambda_h - (\mu_h + \lambda_h)S_h \\
\frac{dI_h}{dt} &= \lambda_h S_h - (\mu_h + d_h + \rho_h)I_h \\
\frac{dR_h}{dt} &= \rho_h I_h - \mu_h R_h
\end{aligned}$$

Furthermore, in this study, additional control variables are introduced, including the vaccination rate among susceptible

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humans (u_1), the proportion of infected monkeys placed under quarantine (u_2), and the vaccination rate among susceptible monkeys (u_3). As a result, the model is formulated as follows:

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h - [\beta_h I_h + (1-u_2)\beta_{n2} I_n + u_1 + \mu_h] S_h \\
\frac{dI_h}{dt} &= [\beta_h I_h + (1-u_2)\beta_{n2} I_n] S_h - (\mu_h + d_h + \rho_h) I_h \\
\frac{dR_h}{dt} &= \rho_h I_h + u_1 S_h - \mu_h R_h \\
\frac{dS_n}{dt} &= \Lambda_n - [(1-u_2)\beta_{n1} I_n + u_3 + \mu_n] S_n \\
\frac{dI_n}{dt} &= [(1-u_2)\beta_{n1} I_n] S_n - (\mu_n + d_n + \rho_n) I_n \\
\frac{dR_n}{dt} &= u_3 S_n + \rho_n I_n - \mu_n R_n
\end{aligned}$$

Where:

- Λ_h: Birth rate of humans
- Λ_n: Birth rate of monkeys
- μ_h: Death rate of humans
- μ_n: Death rate of monkeys
- d_h: Death rate due to monkeypox in humans
- d_n: Death rate due to monkeypox in monkeys
- ρ_h: Natural recovery rate of humans
- ρ_n: Natural recovery rate of monkeys
- β_{n1}: Transmission rate of monkeypox in monkeys from contact with monkeys
- β_{n2}: Transmission rate of monkeypox in humans from contact with monkeys
- β_h: Transmission rate of monkeypox in humans from contact with humans
- S_h: Population of susceptible humans
- I_h: Population of infected humans
- R_h: Population of recovered humans
- S_n: Population of susceptible monkeys
- I_n: Population of infected monkeys
- R_n: Population of recovered monkeys

B. The Equilibrium Points

The equilibrium points of the system of equations are obtained when:

$$\begin{aligned}
\frac{dS_h}{dt} &= 0 \\
\frac{dI_h}{dt} &= 0 \\
\frac{dR_h}{dt} &= 0 \\
\frac{dS_n}{dt} &= 0 \\
\frac{dI_n}{dt} &= 0 \\
\frac{dR_n}{dt} &= 0
\end{aligned}$$

The disease-free equilibrium point is a condition where there is no spread of monkeypox virus in a population, resulting in no infected population ($I_h = 0$, $I_n = 0$). Thus, the disease-free equilibrium point can be obtained as follows:

$$E_0 = \left(\frac{\Lambda_h}{u_1\omega_v + \mu_h}, 0, \frac{u_1\gamma\omega_v\Lambda_h}{\mu_h(u_1\omega_v + \mu_h)}, \frac{\Lambda_n}{u_3\omega_k + \mu_n}, 0, \frac{u_3\omega_k\theta_n\Lambda_n}{(u_3\omega_k\theta_n + \mu_n)\mu_n} \right)$$

The endemic equilibrium points are used to indicate the potential occurrence of disease transmission. In essence, there are three possible endemic equilibrium states mathematically: the specific monkey endemic equilibrium, the specific human endemic equilibrium, and the equilibrium state where the disease coexists between humans and animals. Based on the fact that monkeypox infection is primarily transmitted from animals to humans, analyzing the endemic equilibrium solely in humans is not necessary since human-to-human transmission of monkeypox rarely causes outbreaks.

The specific animal endemic equilibrium point occurs when there is only infection from animal to animal, no infection from human to human, and no infection from animal to human ($\beta_{n2} = \beta_h = 0$). Therefore, the endemic equilibrium point specific to animal disease can be obtained as follows:

$$\begin{aligned}
E_1^* &= (S_h^*, 0, R_h^*, S_n^*, I_n^*, R_n^*) \\
S_h^* &= \frac{\Lambda_h}{u_1 + \mu_h} \\
R_h^* &= \frac{u_1 S_h^*}{\mu_h} \\
S_n^* &= \frac{\Lambda_n - (\rho_n + \mu_n + d_n) I_n^*}{u_3 + \mu_n} \\
I_n^* &= \frac{\Lambda_n - \mu_n}{d_n} \\
R_n^* &= \frac{u_3 S_n^* + \rho_n I_n^*}{\mu_n}
\end{aligned}$$

The endemic equilibrium points in humans and monkeys occur when there is transmission from animal to animal, animal to human, and human to human. The endemic equilibrium points in this model can be obtained as follows:

$$\begin{aligned}
E_2^* &= (S_h^*, I_h^*, R_h^*, S_n^*, I_n^*, R_n^*) \\
S_h^* &= \frac{\Lambda_h - (\mu_h + d_h + \rho_h) I_h^*}{u_1 + \mu_h} \\
I_h^* &= \frac{\Lambda_h - \mu_h}{d_h} \\
R_h^* &= \frac{\rho_h I_h^* + u_1 S_h^*}{\mu_h} \\
S_n^* &= \frac{\Lambda_n - (\rho_n + \mu_n + d_n) I_n^*}{u_3 + \mu_n} \\
I_n^* &= \frac{\Lambda_n - \mu_n}{d_n} \\
R_n^* &= \frac{u_3 S_n^* + \rho_n I_n^*}{\mu_n}
\end{aligned}$$

C. The Basic Reproduction Number

The basic reproduction number, denoted as R_0, is the expected number of infections generated by a single infected individual in a susceptible population within a unit of time. In this research, the analysis of the reproduction number is conducted without implementing any control measures. The determination of the basic reproduction number is performed

using the Next Generation Matrix (NGM) method. The Next Generation Matrix is defined as follows:

$$K = FV^{-1} = \begin{pmatrix} \frac{\Lambda_h \beta_h}{\mu_h(d_h+\mu_h+\rho_h)} & \frac{\Lambda_h \beta_{n1}}{\mu_h(d_h+\mu_h+\rho_h)} \\ 0 & \frac{\Lambda_n \beta_{n1}}{\mu_n(d_n+\mu_n+\rho_n)} \end{pmatrix}$$

Therefore, the basic reproduction number of the monkeypox disease model is given by:

$$R_0 = \{R_{0,n}, R_{0,h}\}$$

where $R_{0,n}$ and $R_{0,h}$ are the basic reproduction numbers for monkeys and humans, respectively, with the following values:

$$R_{0,n} = \frac{\Lambda_n \beta_{n1}}{\mu_n(d_n+\mu_n+\rho_n)}$$
$$R_{0,h} = \frac{\Lambda_h \beta_h}{\mu_h(d_h+\mu_h+\rho_h)}$$

The disease-free equilibrium point will be asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$, where $R_0 = \max\{R_{0,n}, R_{0,h}\}$.

D. Local Stability

Local stability refers to the stability of a linear system or the stability of the linearization of a nonlinear system. The local stability at an equilibrium point is determined by the signs of the real parts of the characteristic roots of the system's Jacobian matrix computed around the equilibrium point. In the case of a nonlinear system, it needs to be linearized to obtain a linear system form. The following are the properties of local stability around an equilibrium point.

1) An equilibrium point is said to be asymptotically stable if and only if $\mathrm{Re}(\lambda_i) < 0$ for every $i = 1, 2, \ldots, n$.
2) An equilibrium point is said to be stable if and only if $\mathrm{Re}(\lambda_i) \leq 0$ for every $i = 1, 2, \ldots, n$.
3) An equilibrium point is said to be unstable if and only if $\mathrm{Re}(\lambda_i) > 0$ for every $i = 1, 2, \ldots, n$.

To analyze the stability, we will determine the equilibrium points of the dengue fever transmission model. The equilibrium points obtained are the disease-free equilibrium $E_0^* = (S_h^*, 0, R_h^*, S_n^*, 0, R_n^*)$, the endemic equilibrium specific to animals $E_1^* = (S_h^*, 0, 0, S_n^*, I_n^*, R_n^*)$, and the endemic equilibrium for both animals and humans $E_2^* = (S_h^*, I_h^*, R_h^*, S_n^*, I_n^*, R_n^*)$. Next, stability analysis is performed by finding the eigenvalues around the equilibrium points. It is found that the system is asymptotically stable towards the disease-free equilibrium and the endemic equilibrium if all eigenvalues have negative real parts ($\lambda < 0$).

E. Controllability Analysis

A system can be controlled if, based on control analysis, it is deemed controllable. The necessary and sufficient condition for a controllable system is as follows:

$$w(0, t_1) = \int_0^{t_1} e^{-AT} B B^T e^{-A^T T}\, dT \text{ is non-singular}$$

The matrix $M_c = (B \mid AB \mid A^2B \mid \cdots \mid A^{n-1}B)$ has the same rank as n.

Before conducting the control analysis, the model is constructed by adding the desired controls. In this study, controls u_1 and u_2 are given, which represent vaccination and quarantine controls, respectively. The controls are restricted to $0 \leq u \leq 1$. This leads to the state-space representation, and the matrices A and B are obtained as follows.

$$A = \begin{pmatrix} -a_1-a_2-a_3-\mu_h & -a_4 & 0 & 0 & 0 & 0 \\ a_1+a_2 & a_4-\mu_h-\rho_h-d_h & 0 & 0 & 0 & 0 \\ a_3 & \rho_h & -\mu_h & 0 & 0 & 0 \\ 0 & 0 & 0 & -a_5-\mu_n-a_8 & 0 & 0 \\ 0 & 0 & 0 & a_5 & -a_6 & 0 \\ 0 & 0 & 0 & 0 & a_6 & -\mu_n-\rho_n-d_n \end{pmatrix}$$

Where:

$$a_1 = \beta_h I_h$$
$$a_2 = (1-u_2)\beta_{n2} I_n$$
$$a_3 = u_1$$
$$a_4 = \beta_h S_h$$
$$a_5 = (1-u_2)\beta_{n1} I_n$$
$$a_6 = (1-u_2)\beta_{n2} S_h$$
$$a_7 = (1-u_2)\beta_{n1} S_n$$
$$a_8 = u_3$$

$$B = \begin{pmatrix} -S_h & I_n S_h \beta_{n2} & 0 \\ S_h & -I_n S_h \beta_{n2} & 0 \\ 0 & 0 & 0 \\ 0 & I_n S_n \beta_{n1} & 0 \\ 0 & -I_n S_n \beta_{n1} & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

Next, the rank of $M_c = [B \mid AB \mid A^2B \mid A^3B \mid A^4B \mid A^5B]$ is calculated to analyze controllability. If $\mathrm{rank}(M_c) = 6$, then the monkeypox spread model is a controllable system.

III. Research Method

The research was conducted using the following steps:

1) Literature review on mathematical modeling of monkeypox virus spread.
2) Modification of the mathematical model of monkeypox virus with vaccination and quarantine.
3) Determination of equilibrium points and analysis of their stability in the modified mathematical model of monkeypox virus spread.
4) Control solution using the Pontryagin's Minimum Principle (PMP) method.
5) Numerical simulation of the modified mathematical model of monkeypox virus spread.
6) Drawing conclusions and preparing the final report.

IV. Results and Discussions

A. Formulation and Solution of the Optimal Control Problem

The formulation of an optimal control problem consists of mathematically describing a system or model, determining an objective function, and specifying constraints or boundary conditions, with the aim of finding the value of $u(t)$ that can optimize the objective function.

In this study, the objective function to be minimized is:

$$J(u_1,u_2)=\int_0^{t_f}\left(I_h(t)+I_n(t)+\frac{1}{2}\left(C_1u_1^2(t)+C_2u_2^2(t)+C_3u_3^2(t)\right)\right)dt$$

where I_h represents the population of infected humans and I_n represents the population of infected monkeys, C_1 is the cost weight coefficient for human vaccination control, C_2 is the cost weight coefficient for infected monkey quarantine control, and C_3 is the cost weight coefficient for vulnerable monkey quarantine control. In other words, the infected population will be minimized by implementing vaccination and quarantine measures with minimum cost.

The Minimum Pontryagin's Principle is used to obtain the optimal control in a dynamic system from the initial state to the final state by minimizing the objective function with control $u(t)$ restricted to $u(t)\in U$. The steps to solve the optimal control problem using the Pontryagin's Minimum Principle are as follows.

Step 1: Formulate the Hamiltonian function

$$\begin{aligned}H=\;&I_h+I_n+\frac{1}{2}\left(C_1u_1^2+C_2u_2^2+C_3u_3^2\right)\\&+\lambda_{S_h}\left[\Lambda_h-\left(\beta_hI_h+(1-u_2)\beta_{n2}I_n+u_1+\mu_h\right)S_h\right]\\&+\lambda_{I_h}\left[\left(\beta_hI_h+(1-u_2)\beta_{n2}I_n\right)S_h-\left(\mu_h+d_h+\rho_h\right)I_h\right]\\&+\lambda_{R_h}\left[\rho_hI_h+u_1S_h-\mu_hR_h\right]\\&+\lambda_{S_n}\left[\Lambda_n-\left((1-u_2)\beta_{n1}I_n+u_3+\mu_n\right)S_n\right]\\&+\lambda_{I_n}\left[(1-u_2)\beta_{n1}I_nS_n-\left(\mu_n+d_n+\rho_n\right)I_n\right]\\&+\lambda_{R_n}\left[u_3S_n+\rho_nI_n-\mu_nR_n\right]\end{aligned}$$

Step 2: Minimize $\mathscr{H}$ to all control vectors $u(t)$ to determine the stationary conditions.

1)

$$\begin{aligned}\frac{\partial H}{\partial u_1}&=0\\C_1u_1^c+(\lambda_{R_h}-\lambda_{S_h})\omega_vS_h&=0\\u_1^c&=\frac{(\lambda_{S_h}-\lambda_{R_h})S_h}{C_1}\end{aligned}$$

2)

$$\begin{aligned}\frac{\partial H}{\partial u_2}&=0\\C_2u_2^c+(\lambda_{S_h}-\lambda_{I_h})(\beta_{n2}I_nS_h)&\\+(\lambda_{S_n}-\lambda_{I_n})(\beta_{n1}I_nS_n)&=0\\u_2^c&=\frac{(\lambda_{I_n}-\lambda_{S_n})\beta_{n1}I_nS_n+(\lambda_{S_h}-\lambda_{I_h})\beta_{n2}I_nS_h}{C_2}\end{aligned}$$

3)

$$\begin{aligned}\frac{\partial H}{\partial u_3}&=0\\C_3u_3^c+(\lambda_{R_n}-\lambda_{S_n})S_n&=0\\u_3^c&=\frac{(\lambda_{S_n}-\lambda_{R_n})S_n}{C_3}\end{aligned}$$

Step 3: Use the result from Step 2 by substituting it into Step 1 and determine the optimal $\mathscr{H}$.

$$\begin{aligned}H^*=\;&I_h+I_n+\frac{1}{2}\left(C_1u_1^{*2}+C_2u_2^{*2}+C_3u_3^{*2}\right)\\&+\lambda_{S_h}\left[\Lambda_h-\left(\beta_hI_h+(1-u_2^*)\beta_{n2}I_n+u_1^*+\mu_h\right)S_h\right]\\&+\lambda_{I_h}\left[\left(\beta_hI_h+(1-u_2^*)\beta_{n2}I_n\right)S_h-\left(\mu_h+d_h+\rho_h\right)I_h\right]\\&+\lambda_{R_h}\left[\rho_hI_h+u_1^*S_h-\mu_hR_h\right]\\&+\lambda_{S_n}\left[\Lambda_n-\left((1-u_2^*)\beta_{n1}I_n+u_3^*+\mu_n\right)S_n\right]\\&+\lambda_{I_n}\left[(1-u_2^*)\beta_{n1}I_nS_n-\left(\mu_n+d_n+\rho_n\right)I_n\right]\\&+\lambda_{R_n}\left[u_3^*S_n+\rho_nI_n-\mu_nR_n\right]\end{aligned}$$

Step 4: Solve the state equations

$$\begin{aligned}\dot{S_h}^*&=\frac{\partial H}{\partial\lambda_{S_h}}=\Lambda_h-\left(\beta_hI_h+(1-u_2)\beta_{n2}I_n+u_1+\mu_h\right)S_h,\\\dot{I_h}^*&=\frac{\partial H}{\partial\lambda_{I_h}}=\left(\beta_hI_h+(1-u_2)\beta_{n2}I_n\right)S_h-\left(\mu_h+d_h+\rho_h\right)I_h,\\\dot{R_h}^*&=\frac{\partial H}{\partial\lambda_{R_h}}=\rho_hI_h+u_1\omega_vS_h-\mu_hR_h,\\\dot{S_n}^*&=\frac{\partial H}{\partial\lambda_{S_n}}=\Lambda_n-\left((1-u_2)\beta_{n1}I_n+u_3+\mu_n\right)S_n,\\\dot{I_n}^*&=\frac{\partial H}{\partial\lambda_{I_n}}=(1-u_2)\beta_{n1}I_nS_n-\left(\mu_n+d_n+\rho_n\right)I_n,\\\dot{R_n}^*&=\frac{\partial H}{\partial\lambda_{R_n}}=\rho_nI_n+u_3S_n-\mu_nR_n.\end{aligned}$$

And the costate

$$\begin{aligned}\lambda_{S_h}'&=-\frac{\partial H}{\partial S_h}=(\lambda_{S_h}-\lambda_{I_h})\left[\beta_hI_h+(1-u_2)\beta_{n2}I_n\right]+(\lambda_{S_h}-\lambda_{R_h})u_1+\mu_h\lambda_{S_h},\\\lambda_{I_h}'&=-\frac{\partial H}{\partial I_h}=-1+(\lambda_{S_h}-\lambda_{I_h})\left[\beta_hS_h\right]+(\mu_h+d_h+\rho_h)\lambda_{I_h}-\rho_h\lambda_{R_h},\\\lambda_{R_h}'&=-\frac{\partial H}{\partial R_h}=\mu_h\lambda_{R_h},\\\lambda_{S_n}'&=-\frac{\partial H}{\partial S_n}=(\lambda_{S_n}-\lambda_{I_n})\left[(1-u_2)\beta_{n1}I_n\right]+(\lambda_{S_n}-\lambda_{R_n})u_3+\lambda_{S_n}\mu_n,\\\lambda_{I_n}'&=-\frac{\partial H}{\partial I_n}=-1+(\lambda_{S_h}-\lambda_{I_h})\left[(1-u_2)\beta_{n2}S_h\right]+(\lambda_{S_n}-\lambda_{I_n})\left[(1-u_2)\beta_{n1}S_n\right]\\&\quad+(\mu_n+d_n+\rho_n)\lambda_{I_n}-\rho_n\lambda_{R_n},\\\lambda_{R_n}'&=-\frac{\partial H}{\partial R_n}=\mu_n\lambda_{R_n}.\end{aligned}$$

B. Numerical Solution

The Runge-Kutta method is a numerical method used to solve initial value problems in differential equations. The Runge-Kutta method provides smaller errors compared to other numerical methods such as the Euler method and the Heun method. The fourth-order Runge-Kutta method is widely used because it offers higher accuracy. Let's consider the following differential equation as an example:

$$\frac{dy}{dx}=f(x,y)$$

In the fourth-order Runge-Kutta method, it is formulated as follows:

$$y_{n+1}=y_n+\frac{h}{6}\left(k_1+2k_2+2k_3+k_4\right)$$

with,

$$\begin{aligned}k_1&=f(x_n,y_n),\\k_2&=f\left(x_n+\frac{h}{2},y_n+\frac{k_1}{2}\right),\\k_3&=f\left(x_n+\frac{h}{2},y_n+\frac{k_2}{2}\right),\end{aligned}$$

$$k_4 = f(x_n + h, y_n + k_3).$$

To obtain the optimal control, a numerical solution using the fourth-order forward-backward sweep Runge-Kutta method is required. This is done because the state equation is given by $S_h(0) = S_{h0}, S_n(0) = S_{n0}, I_h(0) = I_{h0}, I_n(0) = I_{n0}, R_h(0) = R_{h0}, R_n(0) = R_{n0}$, while the costate equation is given by the final values

$$\lambda_1(T) = \lambda_2(T) = \lambda_3(T) = \lambda_4(T) = \lambda_5(T) = \lambda_6(T) = 0.$$

C. Analysis of Simulation Results

In this discussion, the initial conditions for each population are given as follows:

$$S_h(0) = 0.6, \quad I_h(0) = 0.4, \quad R_h(0) = 0,$$
$$S_n(0) = 0.6, \quad I_n(0) = 0.4, \quad R_n(0) = 0.$$

According to the development of monkeypox cases in Nigeria, the parameters of this study are obtained from the research conducted by Bhunu et al. [5] with the following values.

TABLE I: Model Parameter Values

Parameter	Value	Description
Λ_n	$0.2\,\mathrm{yr}^{-1}$	birth rate of monkeys
Λ_h	$0.029\,\mathrm{yr}^{-1}$	birth rate of humans
μ_n	$0.15\,\mathrm{yr}^{-1}$	death rate of monkeys
μ_h	$0.02\,\mathrm{yr}^{-1}$	death rate of humans
ρ_n	$0.3\,\mathrm{yr}^{-1}$	natural recovery rate of mo
ρ_h	$0.33\,\mathrm{yr}^{-1}$	natural recovery rate of hur
d_n	$0.2\,\mathrm{yr}^{-1}$	death rate due to monkeypo
d_h	$0.1\,\mathrm{yr}^{-1}$	death rate due to monkeypo
β_{n1} monkeys from contact with monkeys	$0.87\,\mathrm{yr}^{-1}$	[I]transmission rate of mon
β_{n2} humans from contact with monkeys	$0.62\,\mathrm{yr}^{-1}$	[I]transmission rate of mon
β_h humans from contact with humans	$0.73\,\mathrm{yr}^{-1}$	[I]transmission rate of mon

With the simulation results as follows:

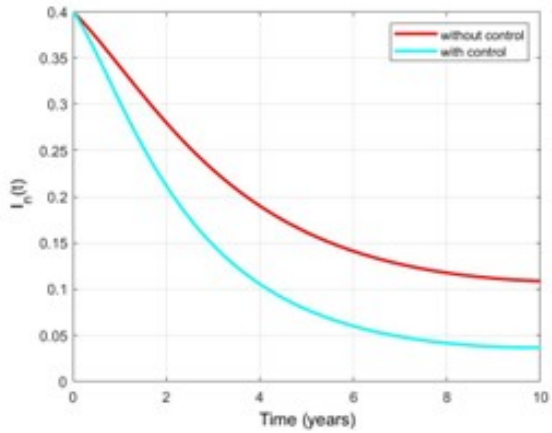

Fig. 1: Graph of Infected Monkey Population

Figure 1 and 2 show a decrease in the population of infected humans and monkeys. The simulation results indicate that implementing control measures reduces the population by 40%. This decrease occurs because the control measures inhibit the spread of the virus.

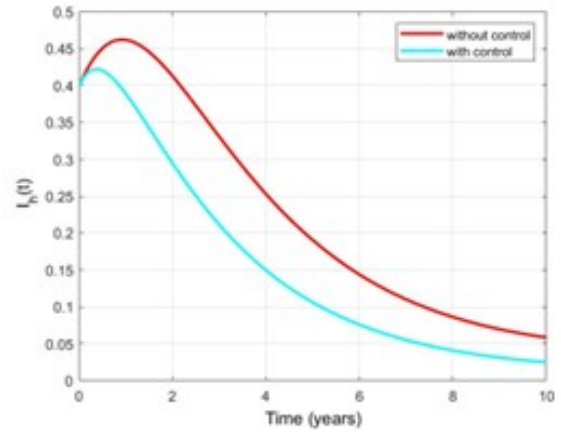

Fig. 2: Graph of Infected Human Population

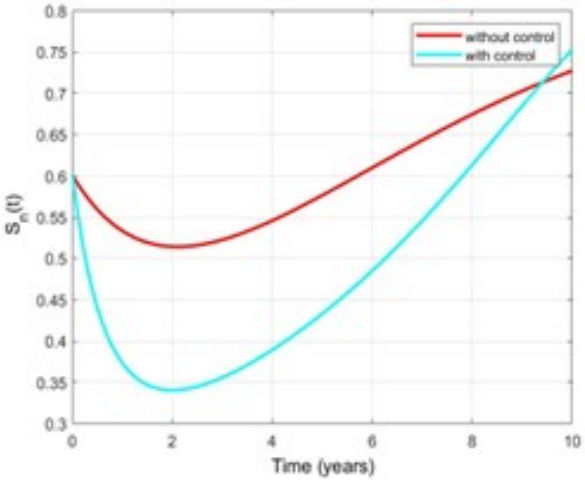

Fig. 3: Graph of Susceptible Monkey Population

From Figure 3, the monkey population experiences a decline in the first two years due to the movement of vulnerable monkey population towards the recovered monkey population through quarantine measures. However, the population starts to increase as the control over quarantine measures decreases.

From Figure 4, there is a decrease in the susceptible human population from the first year to the fourth year. This decline in population in the simulation is due to the movement of susceptible humans towards the recovered human population through vaccination. However, after the fourth year, the susceptible population starts to increase as the vaccination control in humans decreases.

From Figure 5, it can be observed that there is an increase in the population of recovered monkeys. The simulation shows a 20% increase in the population, which is attributed to the influence of the movement from the vulnerable monkey population towards the recovered monkey population through quarantine measures.

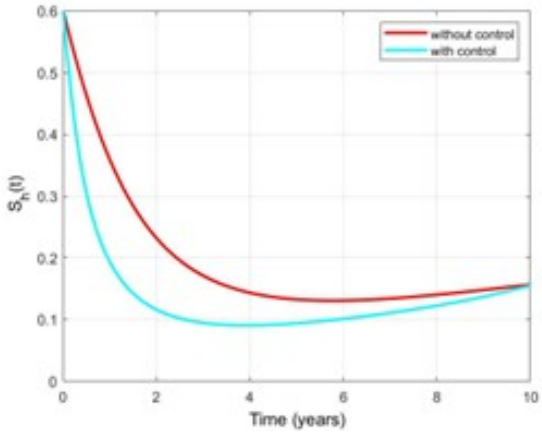

Fig. 4: Graph of Susceptible Human Population

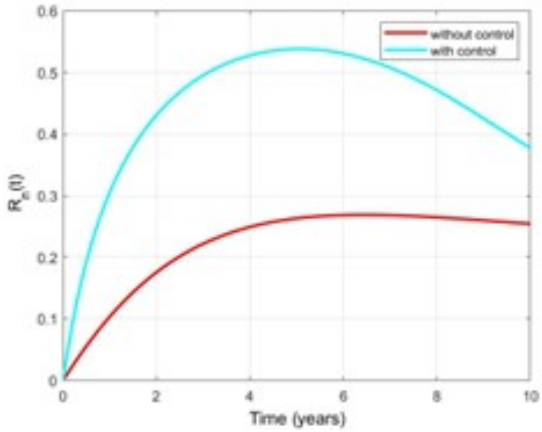

Fig. 5: Graph of Recovered Monkey Population

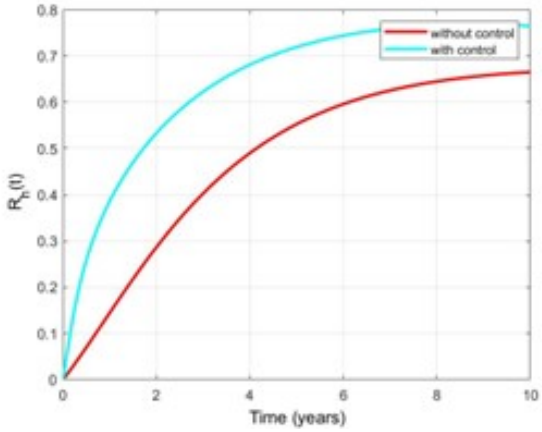

Fig. 6: Graph of Recovered Human Population

In Figure 6, there is a 5% increase in the population in the simulation. This increase is due to the movement from the susceptible human population towards the recovered human population through vaccination.

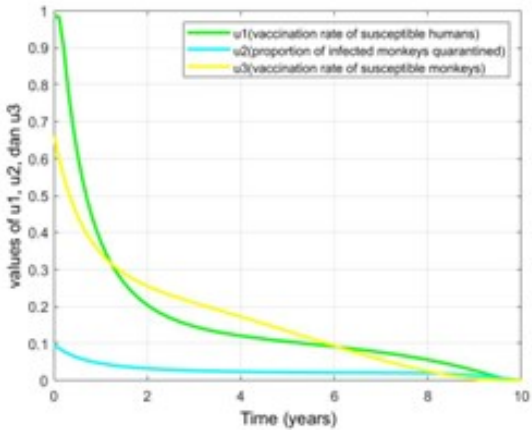

Fig. 7: Graph of Recovered Monkey Population

Figure 7 shows that the green line represents the vaccination rate (u_1), the blue line represents the quarantine control on infected monkeys (u_2), and the yellow line represents the quarantine control on vulnerable monkeys (u_3). In the year when vaccination and quarantine control measures are implemented, the required vaccination rate for the susceptible human population is 1 per year, the proportion of infected monkeys to be quarantined is 0.1, and the required quarantine rate for the vulnerable monkey population is 0.66 per year.

V. Conclusions

Based on the previous analysis and discussion, several conclusions can be drawn as follows:

1) The mathematical model developed for the simulation is as follows:

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h - [\beta_h I_h + (1-u_2)\beta_{n2} I_n + u_1 + \mu_h] S_h, \\
\frac{dI_h}{dt} &= [\beta_h I_h + (1-u_2)\beta_{n2} I_n] S_h - (\mu_h + d_h + \rho_h) I_h, \\
\frac{dR_h}{dt} &= \rho_h I_h + u_1 S_h - \mu_h R_h, \\
\frac{dS_n}{dt} &= \Lambda_n - [(1-u_2)\beta_{n1} I_n + u_3 + \mu_n] S_n, \\
\frac{dI_n}{dt} &= [(1-u_2)\beta_{n1} I_n] S_n - (\mu_n + d_n + \rho_n) I_n, \\
\frac{dR_n}{dt} &= u_3 S_n + \rho_n I_n - \mu_n R_n.
\end{aligned}$$

2) By using the Maximum Pontryagin's Principle, the optimal control u obtained from the mathematical model of monkeypox spread is as follows:

$$\begin{aligned}
u_1^c &= \frac{(\lambda_{S_h} - \lambda_{R_h}) S_h}{C_1}, \\
u_2^c &= \frac{(\lambda_{I_n} - \lambda_{S_n})(\beta_{n1} I_n S_n) + (\lambda_{I_h} - \lambda_{S_h})(\beta_{n2} I_n S_h)}{C_2},
\end{aligned}$$

$$u_3^c = \frac{(\lambda_{S_n} - \lambda_{R_n})S_n}{C_3}.$$

3) The simulation results after implementing the control measures indicate that the population of infected monkeys and humans can be reduced by 40

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