Transmission Dynamics of Monkeypox Virus

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Abstract

A monkeypox disease transmission model of SVEIR type with two groups humans and reservoirs and delays in latent and temporary immune period is discussed. A general probability distrubution model is considered for accounting delays and used for proving the boundedness and positivity of solutions. A proof of existence and stability of desease free and endemic equilibrium is discussed for the specific probability distribution with the Reproduction Number. Later, the theoretical findings from stability analysis are verified with some numerical simulations of the specific probability distribution model.

Table of Contents

1 Introduction **1**

2 Model Description **3**

3 Analysis **7**

3.1 Positivity 7

3.2 Boundedness 7

3.3 Existence of DFE and EE 8

3.4 Stability Analysis 9

Chapter 1

Introduction

Monkeypox is a viral zoonosis (a virus that can be transmitted from animals to humans) with symptoms very similar to smallpox patients, but clinically less severe. It is caused by the monkeypox virus belonging to the Orthopoxvirus genus of the Poxviridae family. Monkeypox originates from the initial discovery of the virus in monkeys in Statens Serum Institute, Copenhagen Denmark, in 1958. The first human case was discovered in a child in the Democratic Republic of the Congo in 1970.

Monkeypox is usually observed in central and west Africa where there are tropical rainforests and where animals that may carry the virus. Following travel from regions where monkeypox is endemic, other countries outside of central and west Africa may also observe rare cases of monkeypox. Monkeypox virus can be spread from one person to another by close contact with lesions, respiratory droplets, body fluids, and contaminated materials such as bedding. The incubation period of monkeypox is usually from 6 to 13 days but can range from 5 to 21 days. Various animal species have been identified as susceptible to the monkeypox virus. Uncertainty remains on the natural history of the monkeypox virus and further studies are needed to identify the reservoir(s) and how virus circulation is maintained in nature. Eating inadequately cooked meat and other animal products of infected animals is a possible risk factor. Monkeypox is usually self-limiting but there is likely to be little immunity to monkeypox among people living in non-endemic countries since the virus has not previously been identified in those populations. There are two variants of the monkeypox virus: the West African variant and the Congo Basin (Central African) variant. The Congo Basin variant appears to cause severe disease more frequently with a case fatality ratio (CFR) previously reported of up to around 10%. Currently, the Democratic Republic of the Congo is reporting a CFR among suspected cases of around 3%. The West African clade has in the past been associated with an overall lower CFR of around 1% in a generally younger population in the African setting. Since 2017, the few deaths of persons with monkeypox in West Africa have been associated with young age or an untreated HIV infection.

Symptoms of monkeypox typically include a fever, intense headache, muscle aches, back pain, low energy, swollen lymph nodes, and a skin rash or lesions.

Since 13 May 2022, monkeypox has been appearing in 23 Member States that are not

endemic to the monkeypox virus, across four WHO regions. Epidemiological investigations are ongoing. The vast majority of reported cases so far have no established travel links to an endemic area and have presented through primary care or sexual health services. The identification of confirmed and suspected cases of monkeypox with no direct travel links to an endemic area is atypical. Early epidemiology of initial cases notified to WHO by countries shows that cases have been mainly reported amongst men who have sex with men (MSM). The sudden appearance of monkeypox simultaneously in several non-endemic countries suggests that there may have been undetected transmission for some time as well as recent amplifying events. As of 02 September, a cumulative total of 52000 cases have been confirmed and 18 deaths have been reported. The situation is evolving rapidly and WHO expects that there will be more cases identified as surveillance expands in non-endemic countries, as well as in countries known to be endemic who have not recently been reporting cases.

There are several vaccines available for prevention of smallpox that also provide some protection against monkeypox. A newer vaccine that was developed for smallpox (MVA-BN, also known as Imvamune, Imvanex or Jynneos) was approved in 2019 for use in preventing monkeypox and is not yet widely available. Vaccinia is also known to deliver long-lasting immunity against monkeypox, with 85% efficacy.

Chapter 2

Model Description

The model is composed of human population given by N_h and reservoir population given by N_r. We divide the human population (N_h) in 5 categories namely, Susceptibles (S_h), Vaccinated (V_h), Exposed (E_h), Infected (I_h) and Recovered (R_h) whereas the reservoir population (N_r) is divided among Susceptibles (S_r), Infected(I_r) and Recovered (R_r), such that

$$N_h = S_h + V_h + E_h + I_h + R_h$$

$$N_r = S_r + I_r + R_r$$

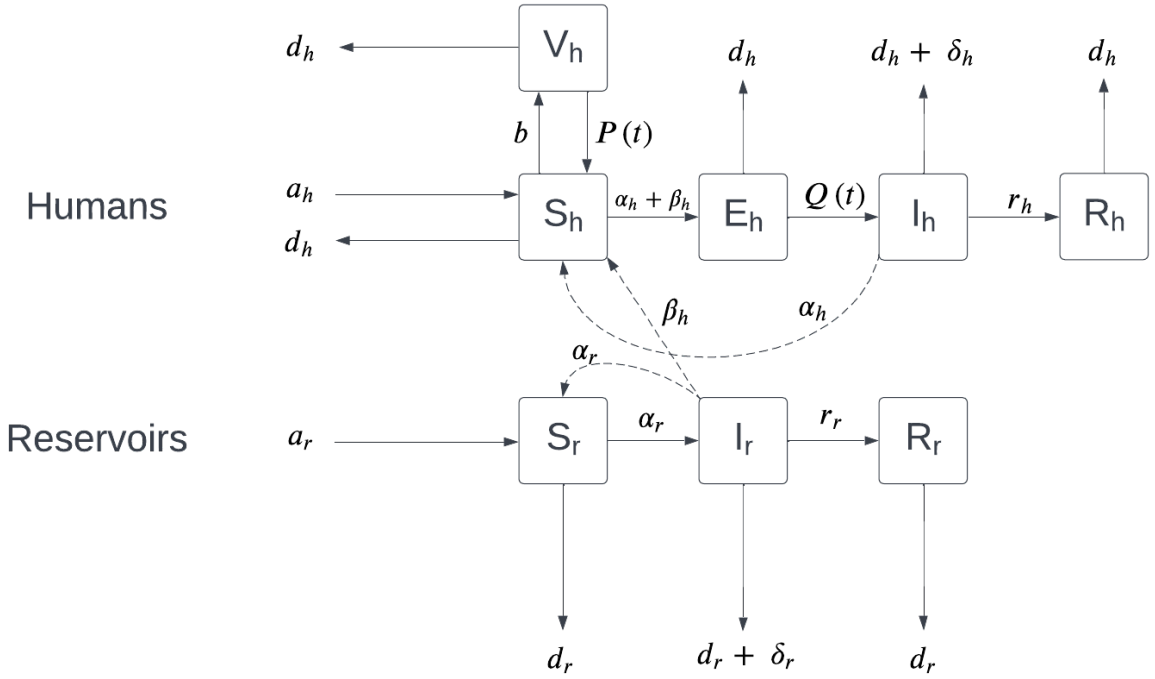

Figure 2.1: Model Flow Diagram

Parameters	Meaning	Values (year $^{-1}$)	Source
a_h	import in susceptible humans	0.029	[1]
a_r	import in susceptible reservoirs	2	[1]
b	vaccination rate	0.1 - 1	[2]
α_h	human to human infection rate	0.000063	[1]
β_h	reservoir to human infection rate	000252	[1]
α_r	reservoir to reservoir infection rate	0.0027	[1]
r_h	recovery rate for humans	0.83 - 0.9	[1]
r_r	recovery rate for reservoirs	0.6	[1]
d_h	natural death rate for humans	0.02	[1]
d_r	natural death rate for reservoirs	1.5	[1]
δ_h	disease related death rate for humans	0.1 - 0.17	[1]
δ_r	disease related death rate for reservoirs	0.4	[1]

Figure 2.2: Parameters Table

To allow for a general latent period, we further assume that $P(t)$ is the probability of individuals remaining in the vaccinated class t units after being vaccinated and $Q(t)$ is the probability of individuals remaining in the exposed class t units after being exposed to the monkeypox virus. According to the natural progression of the disease, we assume $P(t)$ and $Q(t)$ non-negative, non-increasing and piecewise continuous with

$$P(0^+) = Q(0^+) = 1 \text{ and } P(\infty) = Q(\infty) = 0$$

The number of individuals who become exposed at some time $\mu \in (0, t)$ and are still in the exposed class at time t is given by

$$E_h(t) = \int_0^t (\alpha_h S_h(\mu) I_h(\mu) + \beta_h S_h(\mu) I_r(\mu)) e^{-d_h(t-\mu)} Q(t-\mu)\, d\mu \tag{2.1}$$

and the number of individuals who get vaccinated at some time $\mu \in (0, t)$ and are still in the vaccinated class at time t is given by

$$V_h(t) = \int_0^t b S_h(\mu) e^{-d_h(t-\mu)} P(t-\mu)\, d\mu \tag{2.2}$$

The general model is represented as follows

$$S_h'(t) = a_h - d_h S_h(t) - bS_h(t) - (\alpha_h S_h(t) I_h(t) + \beta_h S_h(t) I_r(t)) - \int_0^t bS_h(\mu) e^{-d_h(t-\mu)} P'(t-\mu)\, d\mu \tag{2.3}$$

$$V_h'(t) = bS_h(t) - d_h V_h(t) + \int_0^t bS_h(\mu) e^{-d_h(t-\mu)} P'(t-\mu)\, d\mu \tag{2.4}$$

$$E_h'(t) = \alpha_h S_h(t) I_h(t) + \beta_h S_h(t) I_r(t)) - d_h E_h(t) + \int_0^t (\alpha_h S_h(\mu) I_h(\mu) + \beta_h S_h(\mu) I_r(\mu)) e^{-d_h(t-\mu)} Q'(t-\mu)\, d\mu \tag{2.5}$$

$$I_h'(t) = -\int_0^t (\alpha_h S_h(\mu) I_h(\mu) + \beta_h S_h(\mu) I_r(\mu)) e^{-d_h(t-\mu)} Q'(t-\mu)\, d\mu - d_h I_h(t) - \delta_h I_h(t) - r_h I_h(t) \tag{2.6}$$

$$R_h'(t) = r_h I_h(t) - d_h R_h(t) \tag{2.7}$$

$$S_r'(t) = a_r - d_r S_r(t) - \alpha_r S_r(t) I_r(t) \tag{2.8}$$

$$I_r'(t) = \alpha_r S_r(t) I_r(t) - d_r I_r(t) - \delta_r I_r(t) - r_r I_r(t) \tag{2.9}$$

$$R_r'(t) = r_r I_r(t) - d_r R_r(t) \tag{2.10}$$

To obtain more specific models, we have discussed four cases with different values for the functions $P(t)$ and $Q(t)$.

Case I $[P(t) = e^{-\omega_1 t}, Q(t) = e^{-\omega_2 t}]$

Equation 2.1 becomes

$$E_h(t) = \int_0^t (\alpha_h S_h(\mu) I_h(\mu) + \beta_h S_h(\mu) I_r(\mu)) e^{(d_h+\omega_2)\mu - (d_h+\omega_2)t}\, d\mu$$

$$\Rightarrow E_h(t) = e^{-(d_h+\omega_2)t} \int_0^t (\alpha_h S_h(\mu) I_h(\mu) + \beta_h S_h(\mu) I_r(\mu)) e^{(d_h+\omega_2)\mu}\, d\mu$$

$$\Rightarrow E_h'(t) = -(d_h+\omega_2) E_h(t) + e^{-(d_h+\omega_2)t} (\alpha_h S_h(t) I_h(t) + \beta_h S_h(t) I_r(t)) e^{(d_h+\omega_2)t}$$

$$\Rightarrow E_h'(t) = \alpha_h S_h(t) I_h(t) + \beta_h S_h(t) I_r(t) - (d_h+\omega_2) E_h(t)$$

Again, equation 2.2 becomes

$$V_h(t) = \int_0^t bS_h(\mu) e^{(d_h+\omega_1)\mu - (d_h+\omega_1)t}\, d\mu$$

$$\Rightarrow V_h(t) = e^{-(d_h+\omega_1)t} \int_0^t bS_h(\mu) e^{(d_h+\omega_1)\mu}\, d\mu$$

$$\Rightarrow V_h'(t) = -(d_h+\omega_1) V_h(t) + e^{-(d_h+\omega_1)t} bS_h(t) e^{(d_h+\omega_1)t}$$

$$\Rightarrow V_h'(t) = bS_h(t) - (d_h+\omega_1) V_h(t)$$

The model for case I is represented as follows

$$S_h'(t) = a_h + \omega_1 V_h(t) - d_h S_h(t) - bS_h(t) - (\alpha_h S_h(t) I_h(t) + \beta_h S_h(t) I_r(t)) \tag{2.11}$$
$$V_h'(t) = bS_h(t) - (d_h + \omega_1) V_h(t) \tag{2.12}$$
$$E_h'(t) = \alpha_h S_h(t) I_h(t) + \beta_h S_h(t) I_r(t) - (d_h + \omega_2) E_h(t) \tag{2.13}$$
$$I_h'(t) = \omega_2 E_h(t) - d_h I_h(t) - \delta_h I_h(t) - r_h I_h(t) \tag{2.14}$$
$$R_h'(t) = r_h I_h(t) - d_h R_h(t) \tag{2.15}$$
$$S_r'(t) = a_r - d_r S_r(t) - \alpha_r S_r(t) I_r(t) \tag{2.16}$$
$$I_r'(t) = \alpha_r S_r(t) I_r(t) - d_r I_r(t) - \delta_r I_r(t) - r_r I_r(t) \tag{2.17}$$
$$R_r'(t) = r_r I_r(t) - d_r R_r(t) \tag{2.18}$$

Chapter 3

Analysis

3.1 Positivity

In equations 2.1 and 2.2, we can clearly see that the integrand is positive, and thus, the integral i.e $E_h(t)$ and $V_h(t)$ will also be positive.

Now, assume that $S_h(0) > 0$. From equation 2.3, we get

$$S_h'(t) = -kS_h(t) + a_h - \int_0^t bS_h(\mu)e^{-d_h(t-\mu)}P'(t-\mu)\,d\mu \tag{3.1}$$

where $k = d_h + b + \beta_h I_r + \alpha_h I_h$ In equation 3.1, we see that $a_h - \int_0^t bS_h(\mu)e^{-d_h(t-\mu)}P'(t-\mu)\,d\mu$ is positive. Hence, we get

$$S_h'(t) \geq -kS_h(t)$$

By using Gronwall Inequality, we get

$$S_h(t) \geq S_h(0)e^{-\int k\,dt}$$

$$\Rightarrow S_h(t) \geq 0 \qquad \forall\, t \geq 0$$

Similarly by assuming that $I_h(0) \geq 0$, $R_h(0) \geq 0$, $S_r(0) \geq 0$, $I_r(0) \geq 0$ and $R_r(0) \geq 0$, we can show that I_h, R_h, S_r, I_r and R_r are all positive respectively $\forall\, t \geq 0$.

3.2 Boundedness

Let $R = \{(S_h(t), V_h(t), E_h(t), I_h(t), R_h(t), S_r(t), I_r(t), R_r(t)) \in \Re^8+\}$ represent the region. By adding the equations 2.3 - 2.7, we get

$$N_h'(t) = a_h - d_h N_h(t) - \delta_h I_h(t)$$

$$\Rightarrow N_h'(t) \leq a_h - d_h N_h(t)$$

By using Gronwall Inequality, we get

$$N_h(t) \leq \frac{a_h}{d_h} + (N_h(0) - \frac{a_h}{d_h})e^{-d_h t}$$

now if $N_h(0) \leq \frac{a_h}{d_h}$, then

$$N_h(t) \leq \frac{a_h}{d_h}$$

and if $N_h(0) \geq \frac{a_h}{d_h}$, then

$$N_h(t) \leq N_h(0)$$

and similarly, we can show that
if $N_r(0) \leq \frac{a_r}{d_r}$, then

$$N_r(t) \leq \frac{a_r}{d_r}$$

and if $N_h(0) \geq \frac{a_r}{d_r}$, then

$$N_r(t) \leq N_r(0)$$

Now since both $N_h(t)$ and $N_r(t)$ are bounded, all the solutions are also bounded.

3.3 Existence of DFE and EE

Disease free equilibrium exists at $(S_h(t), V_h(t), 0, 0, 0, S_r(t), 0, 0)$. Equation 2.8 at the disease free equilibrium point becomes

$$a_r - d_r S_r(t) = 0$$

$$\Rightarrow S_r(t) = \frac{a_r}{d_r}$$

Now, consider equation 2.3. At the disease free equilibrium point, equation 2.3 becomes

$$a_h - d_h S_h(t) - bS_h(t) - \int_0^t bS_h(\mu)e^{-d_h(t-\mu)}P'(t-\mu)\,d\mu = 0$$

At $t \to \infty$, by assuming that $S_h(t) \to S_h^*(t)$, we get

$$a_h - d_h S_h^*(t) - bS_h^*(t) - bS_h^*(t)\int_0^t e^{-d_h(t-\mu)}P'(t-\mu)\,d\mu = 0$$

By substituting $v = t - \mu$, we get

$$a_h - d_h S_h^*(t) - bS_h^*(t) - bS_h^*(t)\int_0^t e^{-d_h(v)}P'(v)\,d\mu = 0$$

$$\Rightarrow a_h - d_h S_h^*(t) - bS_h^*(t)\left(\left[e^{-d_h v}P(v)\right]_0^t - \int_0^t (-d_h)P(v)e^{-d_h v}\,dv\right) = 0$$

$$\Rightarrow d_h(1 - bP^*)S_h^*(t) = a_h$$

where $P^* = -\int_0^\infty e^{-d_h v}\, dP(v)$ is the average time an individual spends in the vaccinated class

$$\Rightarrow S_h^*(t) = \frac{a_h}{d_h(1-bP^*)}$$

Similarly, we can find that

$$V_h^*(t) = \frac{-ba_hP^*}{d_h(1-bP^*)}$$

Hence, disease free equilibrium exists at $\left(\frac{a_h}{d_h(1-bP^*)}, \frac{-ba_hP^*}{d_h(1-bP^*)}, 0, 0, 0, \frac{a_r}{d_r}, 0, 0\right)$

Endemic Equilibrium point

3.4 Stability Analysis

The basics reproduction number of the model represented in Case I is calculated using the next generation matrix method as follows

From the equations 2.13, 2.14 and 2.17, we get

$$f = \begin{pmatrix} \alpha_h S_h(t) I_h(t) + \beta_h S_h(t) I_r(t) \\ 0 \\ \alpha_r S_r(t) I_r(t) \end{pmatrix} \text{ and } v = -\begin{pmatrix} -(d_h+\omega_2)E_h(t) \\ \omega_2 E_h(t) - (d_h+\delta_h+r_h)I_h(t) \\ -(d_h+\delta_h+r_h)I_r(t) \end{pmatrix}$$

$$\Rightarrow F = \begin{bmatrix} 0 & \alpha_h S_h & \beta_h S_h \\ 0 & 0 & 0 \\ 0 & 0 & \alpha_r S_r \end{bmatrix} \text{ and } V = \begin{bmatrix} d_h+\omega_2 & 0 & 0 \\ -\omega_2 & d_h+\delta_h+r_h & 0 \\ 0 & 0 & d_r+\delta_r+r_r \end{bmatrix}$$

Now,

$$K = FV^{-1}$$

$$= c \begin{bmatrix} 0 & \alpha_h S_h & \beta_h S_h \\ 0 & 0 & 0 \\ 0 & 0 & \alpha_r S_r \end{bmatrix} \begin{bmatrix} (d_h+\delta_h+r_h)(d_r+\delta_r+r_r) & 0 & 0 \\ \omega_2(d_r+\delta_r+r_r) & (d_h+\omega_2)(d_r+\delta_r+r_r) & 0 \\ 0 & 0 & (d_h+\omega_2)(d_h+\delta_h+r_h) \end{bmatrix}$$

where $c = \frac{1}{(d_h+\omega_2)(d_h+\delta_h+r_h)(d_r+\delta_r+r_r)}$

$$= c \begin{bmatrix} \omega_2\alpha_h S_h(d_r+\delta_r+r_r) & \alpha_h S_h(d_h+\omega_2)(d_r+\delta_r+r_r) & \beta_h S_h(d_h+\omega_2)(d_h+\delta_h+r_h) \\ 0 & 0 & 0 \\ 0 & 0 & \alpha_r S_r(d_h+\omega_2)(d_h+\delta_h+r_h) \end{bmatrix}$$

Eigen Values of K are as follows

$$\left|K - \lambda I\right| = 0$$

$$\Rightarrow \begin{vmatrix} c\omega_2\alpha_h S_h(d_r+\delta_r+r_r) - \lambda & \alpha_h S_h(d_h+\omega_2)(d_r+\delta_r+r_r) & \beta_h S_h(d_h+\omega_2)(d_h+\delta_h+r_h) \\ 0 & -\lambda & 0 \\ 0 & 0 & c\alpha_r S_r(d_h+\omega_2)(d_h+\delta_h+r_h) - \lambda \end{vmatrix} = 0$$

$$\Rightarrow -\lambda\left[c\omega_2\alpha_h S_h(d_r+\delta_r+r_r) - \lambda\right]\left[c\alpha_r S_r(d_h+\omega_2)(d_h+\delta_h+r_h) - \lambda\right] = 0$$

$$\Rightarrow \lambda = 0,\, c\omega_2\alpha_h S_h(d_r+\delta_r+r_r),\, c\alpha_r S_r(d_h+\omega_2)(d_h+\delta_h+r_h)$$

where, 0 is not a dominant eigen value. After substituting back the value of c, we get

$$\lambda = \frac{\omega_2 \alpha_h S_h}{(d_h + \omega_2)(d_h + \delta_h + r_h)}, \frac{\alpha_r S_r}{(d_r + \delta_r + r_r)}$$

using the values of S_h and S_r at the disease free equilibrium, we get

$$\lambda_1 = \frac{\omega_2 \alpha_h a_h (d_h + \omega_1)}{d_h (d_h + \omega_2)(d_h + \delta_h + r_h)(d_h + \omega_1 + b)}, \lambda_2 = \frac{a_r \alpha_r}{d_r (d_r + \delta_r + r_r)}$$