Transmission Dynamics of Monkeypox Virus

by

Shivam Grover
Yuan Yuan

Paper submitted to the
Department of Mathematics
for the Summer Undergraduate Research Apprenticeship (SURA)

Departement of Mathematics
Memorial University of Newfoundland (MUN)

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

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.

1.1 Background

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.

1.2 Symptoms

Symptoms of monkeypox typically include a fever, intense headache, muscle aches, back pain, low energy, swollen lymph nodes, and a skin rash or lesions. The rash usually begins within one to three days of the start of a fever. Lesions can be flat or slightly raised, filled with clear or yellowish fluid, and can then crust, dry up and fall off. The number of lesions on one person can range from a few to several thousand. Symptoms typically last between 2 to 4 weeks and go away on their own without treatment.

1.3 OutBreak in Endemic and Non-Endemic Countries

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). One case of monkeypox in a non-endemic country is considered an outbreak. 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 26 May, a cumulative total of 257 laboratory-confirmed cases and around 120 suspected cases have been reported to WHO. No 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.

1.4 Vaccinations

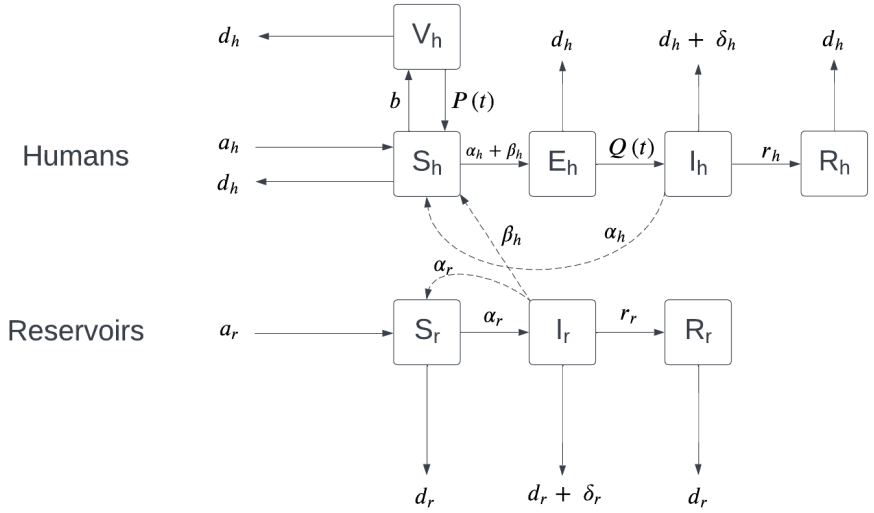
There are several vaccines available for prevention of smallpox that also provide some protection against monkeypox. A newer vaccine that was developed for smallpox (MVA-BN, also known as Imvamune, Imvanex or Jynneos) was approved in 2019 for use in preventing monkeypox and is not yet widely available.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

$$N_h = S_h + V_h + E_h + I_h + R_h$$
$$N_r = S_r + I_r + R_r$$



a	birth rate
b	vaccination rate
β_h	contact rate between infected reservoirs and susceptible humans
α_h	contact rate between infected and susceptible humans
α_r	contact rate between infected reservoirs and susceptible reservoirs
$P(t)$	probability of individuals remaining in the vaccinated class t units after being vaccinated
$Q(t)$	probability of individuals remaining in the exposed class t units after being exposed to the monkeypox virus
r	recovery rate
d	natural death rate
δ	disease related death rate

Figure 2.1: Model Flow Diagram

We assume that a_h and a_r is the constant birth rate of susceptible humans and reservoirs respectively and susceptibles are vaccinated at a constant rate b. α_r, α_h and β_h are the infection rates from reservoir to reservoir, reservoir to human and from human to human

respectively. 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. r_h and r_r are the recovery rates of the humans and the reservoirs respectively from the infection. Lastly, we consider that d_h and δ_h is the natural and infection related death rate of humans whereas d_r and δ_r is the natural and infection-related death rate of reservoirs. 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

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

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

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

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

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

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

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

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

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

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

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

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

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

3.4 Stability Analysis

Here, you need to check the type of equilibrium point and identify whether it is stable, unstable or semi-stable.