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# Modelling Avian Influenza In Bird-Human Systems

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## **Abstract**

In 1997, the first human case of avian influenza infection was reported in Hong Kong. Since then, avian influenza has become more and more hazardous for both animal and human health. Scientists believed that it would not take long until the virus mutates to become contagious from human to human.

In this thesis, we construct avian influenza with possible mutation situations in bird-human systems. Also, possible control measures for humans are introduced in the systems. We compare the analytical and numerical results and try to find the most efficient control measures to prevent the disease.



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# Chapter 1

## Introduction

Avian influenza (AI), commonly called the “bird flu”, is a bird adapted infectious disease caused by the Influenza A strain of virus. At present, there are 16 H subtypes and 9 N subtypes of avian influenza viruses that have been recognized, and only some viruses in two subtypes (H5 and H7) were found that could cause severe disease (death mostly) in poultry. They are known as high pathogenic avian influenza (HPAI). Other subtypes, usually called low pathogenic avian influenza (LPAI), cause symptoms such as ruffled feathers and reduced production of eggs that may be overlooked without testing [10].

Wild waterfowl are considered to be the natural carriers of the disease, mostly LPAI. Circumstantial evidence suggested that some LPAI viruses (in H5 and H7 subtypes) in domestic poultry (e.g. a chicken farm) that have been transmitted from migratory birds may mutate into HPAI form, which could cause an outbreak of avian influenza (in that farm). Other poultry farms,

could be infected by polluted vehicles, equipment or even shoes and clothing from humans. The avian influenza virus can live far more than 30 days at room temperature. The mortality rate due to HPAI can approach 100% within 48 hours [9].

Most recently, several deaths of chicken in a local farm have been reported in Hong Kong in December. It is confirmed to be due to H5 HPAI infection. Two farms have been shut down and around 80000 chickens killed and disposed off.

Other than infecting birds, avian influenza viruses are also infectious cross species, to humans for instance. Even though people do not get infected by eating properly cooked meat and eggs of birds, direct contact, e.g. with blood and faeces may infect. The HPAI also cause a high mortality rate in humans. The first human infections with HPAI were reported in Hong Kong in 1997, resulting in 6 deaths in 18 cases [11]. Since then, the number of cases of human infections has risen in many countries around the world. Fortunately, the virus is not transmitted from human to human, but scientists believe that it is just a matter of time for the virus to mutate so that it may be the case.

New Zealand is a country with a variety of birds. Therefore, biosecurity preventing avian influenza entering New Zealand is not only important for animal health, but also for human health. More over, in the case of an outbreak of avian influenza in birds or of the “reassorted” virus, with human from human transmission, what should we do?

In this thesis, we set up models for the HPAI infection in the bird and the human system in the case of human from human transmission, as well as for possible control measures. We compare the numerical and analytical results, and try to find the most efficient way to minimize the spreading of the disease based on our models.

## 1.1 Influenza pandemic history

An influenza pandemic is a worldwide epidemic of influenza viruses that infects a large number of the human population. Unlike seasonal influenza, with which it is often confused, pandemics often cause high mortality. The 1918 Spanish flu, which is considered to be the most serious pandemic in recent history, killed over 50 million people within two years. [13]

Since influenza pandemics are caused by the transmission of a new strain of virus to humans from other species, such as birds and pigs, they occur irregularly. Other than the Spanish flu, the most recent two in last century were the 1957 Asian flu and the 1968 Hong Kong flu. In April 2009, the WHO officially announced an outbreak of a new reassorted strain, commonly called “Swine flu”. It originated in Mexico and it is the first pandemic of the 21st century.

The 1957 Asian flu which originated in China lasted for two years. It was an outbreak of avian influenza H2N2 that mutated combining with a pre-existing human strain. The 1968 Hong Kong flu on the other hand, was

caused by a new virus strain H3N2, which was an antigenic shift from H2N2.

The 1918 Spanish flu and the 2009 Swine flu are both caused by the H1N1 strain of virus with different variants. The unusual feature of an H1N1 pandemic (the 1918 Spanish flu) is that most of the victims are healthy young adults whereas most pandemics only affect children, elderly and patients with immune systems. Research shows the H1N1 virus kills people with strong immune system that cause an overreaction of the body's immune system (cytokine storm). This explains why people with weaker immune system have fewer death.

The 2009 H1N1 pandemic took authorities by surprise, as they were preparing to an H5N1 bird flu pandemic. This is still a possibility. In this thesis we analyse models for bird-human and human-human transmission of H5N1.

## 1.2 The SIR endemic model

The “SIR” epidemic model is a special case of the Kermack-McKendrick model with constant rates [7]. The population is split into three compartments: susceptible ( $S(t)$ ), infected ( $I(t)$ ) and removed ( $R(t)$ ). A susceptible individual (susceptible stage) becomes infected (infectious stage) after infection, and then recovers to enter the removed stage. (Figure 1.1) In the removed stage, individuals are immune to further infection. The total population size  $N$  is the sum of the three:

$$N(t) = S(t) + I(t) + R(t). \quad (1.1)$$

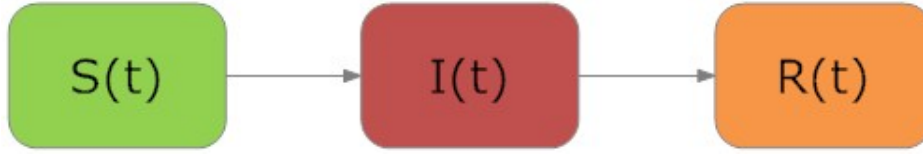


Figure 1.1: Relationships of the three compartments in the SIR model.

In some cases, an epidemic outbreak is much faster than the demographic time-scale. For example, seasonal influenza take place in a matter of months, whereas the time-scale of human population is measured in tens of years. In this model, we assume that the time-scale of the infection to be of the same order as the demographic time-scale and differential equations for the SIR endemic model are:

$$\frac{dS}{dt} = \Lambda - \mu S - \beta S \frac{I}{N}, \quad (1.2)$$

$$\frac{dI}{dt} = \beta S \frac{I}{N} - (\mu + \gamma)I, \quad (1.3)$$

$$\frac{dR}{dt} = \gamma I - \mu R, \quad (1.4)$$

where  $\Lambda$  ( $\text{people} \cdot \text{time}^{-1}$ ),  $\mu$  ( $\text{time}^{-1}$ ) and  $\gamma$  ( $\text{time}^{-1}$ ) are the birth, death and recovery rates of the host, respectively. Infected hosts contact and transmit the virus to susceptible hosts at rate  $\beta$  ( $\text{time}^{-1}$ ). The total population  $N$  is a constant number for all  $t$ .

We assume that the population represents the size in a given area. Hence, non-integer values are allowed.

This model has no deaths due to infection, where the models we constructed have an additional death rate due to HPAI.

### 1.3 The basic reproduction number

The basic reproduction number  $R_0$  is defined as “the expected number of secondary cases produced by a typical infected individual” when everyone is susceptible [3]. There is a threshold for infection: when  $R_0$  is less than 1, there is only a minor epidemic occur and when  $R_0$  is greater than 1, an major epidemic will occur. In the model Equation (1.2)-(1.4), the rate at which one infected host infects susceptible host is  $\beta S \frac{1}{N}$ , where  $S = N$  if there is no infection in the system. Since the mean time that an infected host remains infectious is  $\frac{1}{\mu+\gamma}$ , we have

$$R_0 = \frac{\beta}{\mu + \gamma}. \quad (1.5)$$

If the system includes multiple host types, then the value of  $R_0$  is the dominant eigenvalue of the next generation matrix ( $K$ ) [6]. The elements ( $K_{ij}$ ) in  $K$  are similar to  $R_0$  where  $i$  indicates the host type to be infected and  $j$  indicates the infected source host type. For example, in the models we are about to present, bird and human are the two hosts of the HPAI viruses. Let 1 stands for bird and 2 stands for human, then  $K$  is

$$K = \begin{pmatrix} K_{11} & K_{12} \\ K_{21} & K_{22} \end{pmatrix}, \quad (1.6)$$

where  $K_{12} = 0$  as there is no transmission from human to bird. Thus, the basic reproduction number of the bird-human system is equal to the maximum of  $K_{11}$  and  $K_{22}$ . An infection free steady state only exists when the values of  $K_{11}$  and  $K_{22}$  are both less than 1.

## 1.4 Control measures

In the situation where an endemic steady state exists in multiple host types (caused by the same virus strain or one mutate from the other), control measures should no longer applied to a single species. In bird-human models, in order to limit the spreading of HPAI in poultry, infected birds need to be killed in a humane way and disposed off safely (stamping out); or large groups of susceptible birds (e.g. in a farm) need to be vaccinated against the HPAI viruses. For humans, vaccination is also an option. The other widely used control measure is quarantine.

**Vaccination** The word “vaccination” was first used to describe the use of cowpox to protect humans against smallpox in the late 1700s [13]. It is perhaps the most commonly used, effective and cost-effective control measure to prevent contagious diseases. In New Zealand, children are recommended to have routine vaccination from age 6 weeks up to 11 years against tuberculosis, hepatitis B, measles, etc, in order to develop their full immune system [12].

However, vaccines do not ensure 100% immunity. For new diseases, such as SARS or avian influenza, developing the vaccine and producing sufficient quantities is a challenge. More over, for diseases like seasonal influenza, getting a vaccine shot last year may not help to prevent illness this year as the virus may mutate against the vaccine or to a different form.

**Quarantine** When the outbreak of a severe disease becomes out of control (no vaccine or effective treatment), the infected person is usually quarantined from other susceptible individuals. This is often established by a law or an act by the government rather than a recommendation for vaccination by doctors. Maybe it sounds like in a movie, but quarantine did actually happen not long ago while SARS emerged initially in mainland China. Not only infected individuals were quarantined, but also their recently contacted friends, families and even paramedics who looked after them.

Generally speaking, quarantine is an effective measure, but it may bring unnecessary tension and panic. People may doubt who needs to be quarantined and how long will it last.

## Chapter 2

### The Bird Model

There have been 385 confirmed human cases of HPAI since 2003 [11], but not a single case to show that HPAI can be transmitted from human to birds. As long as this stays true, the bird epidemic system is independent from the human system. Therefore, before analyzing the bird-human system, we can always look at the bird system separately.

As susceptible birds die quickly after being infected with HPAI in wild and domestic situations, we assume no bird survives or recovers from the disease. In other words, HPAI is fatal for all birds in the bird model. Without the “removed” class, the “SIR” model simply becomes the “SI” model. We use  $S_1$  to represent susceptible birds and  $I_1$  to represent infected birds. The relationship between susceptible and infected birds is shown in Figure 2.1 with parameters defined in Table 2.1. The ordinary differential equations

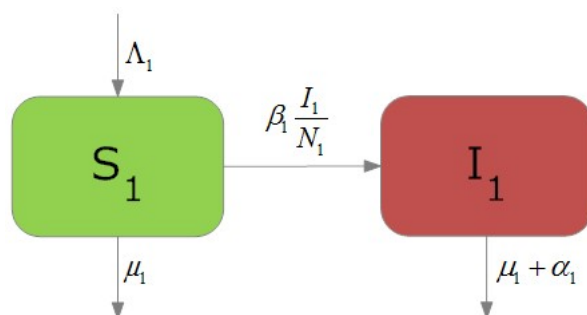


Figure 2.1: Relationship diagram for the bird system.

Parameters	Units	Definition
$t$	time	Time (day)
$N_1$	bird	Total population
$S_1$	bird	Number susceptible
$I_1$	bird	Number infected
$\Lambda_1$	bird·day <sup>-1</sup>	Natural birth rate
$\mu_1$	day <sup>-1</sup>	Natural death rate
$\beta_1$	day <sup>-1</sup>	Transmission coefficient
$\alpha_1$	day <sup>-1</sup>	Additional death rate caused by HPAI
$R_0^{[1]}$	-	Basic reproduction number

Table 2.1: Definition of model parameters in the bird system

can then be written as follow:

$$\frac{dS_1}{dt} = \Lambda_1 - \mu_1 S_1 - \beta_1 S_1 \frac{I_1}{N_1}, \quad (2.1)$$

$$\frac{dI_1}{dt} = \beta_1 S_1 \frac{I_1}{N_1} - (\mu_1 + \alpha_1) I_1, \quad (2.2)$$

where the total population of birds  $N_1$  is

$$N_1 = S_1 + I_1. \quad (2.3)$$

In [4], there is a similar bird “SI” model for HPAI. It is an alternative version of the “SIR” epidemic model. However, it does not apply to the situation when the bird population is large.

**Remark.** If  $S_1(0) > 0$  and  $I_1(0) > 0$ , then the solution of Equation 2.1-2.2 is positive for all  $t$ .

**Proof.** Suppose the result is not true, then there exists a  $t^* > 0$  where  $S_1(t^*) = 0$  or  $I_1(t^*) = 0$ . Equation (2.2) can be rearranged to be:

$$I_1'(t) = \left( \beta_1 S_1(t) \frac{1}{N_1(t)} - (\mu_1 + \alpha_1) \right) I_1(t) \quad (2.4)$$

Thus, we obtain:

$$I_1(t) = I_1(0) e^{\int_0^t (\beta_1 S_1 \frac{1}{N_1} - (\mu_1 + \alpha_1)) ds} \quad (2.5)$$

which implies  $I_1(t) > 0$  for all  $t$ .

Assume  $S_1(t^*) = 0$ . As  $S_1(0) > 0$ , then  $S_1'(t^*) < 0$ . However, from Equation (2.1) we have  $S_1'(t^*) = \Lambda_1 > 0$ . Thus  $S_1 > 0$  for all  $t$ .  $\square$

## 2.1 Steady States

Let  $bs$  represents the steady state of the bird system. At the steady state,  $S_1$  can be rewritten in terms of  $I_1$ ,

$$S_1^{bs} = \frac{\Lambda_1}{\mu_1} - \frac{\mu_1 + \alpha_1}{\mu_1} I_1^{bs}. \quad (2.6)$$

Substitute Equation 2.6 into Equation 2.2 (or Equation 2.1 similarly) and simplify, we have a quadratic in the form of

$$f(I_1^{bs}) = a(I_1^{bs})^2 + bI_1^{bs} = 0, \quad (2.7)$$

where

$$a = (\mu_1 + \alpha_1)(-\beta_1 + \alpha_1), \quad (2.8)$$

$$b = \Lambda_1(\beta_1 - \mu_1 - \alpha_1). \quad (2.9)$$

Hence, Equation 2.7 has two roots:

$$I_1^{bs_1} = 0, \quad (2.10)$$

$$I_1^{bs_2} = \frac{\Lambda_1(\beta_1 - \mu_1 - \alpha_1)}{(\mu_1 + \alpha_1)(\beta_1 - \alpha_1)}. \quad (2.11)$$

Other variable values can be obtained from them and hence the system has two steady states:

$$bs_1 = \begin{pmatrix} S_1^{bs_1} \\ I_1^{bs_1} \end{pmatrix} = \begin{pmatrix} \frac{\Lambda_1}{\mu_1} \\ 0 \end{pmatrix}, \quad (2.12)$$

where  $N_1^{bs_1} = S_1^{bs_1} = \frac{\Lambda_1}{\mu_1}$ , represents the situation where HPAI is absent in the bird system. The second steady state

$$bs_2 = \begin{pmatrix} S_1^{bs_2} \\ I_1^{bs_2} \end{pmatrix} = \begin{pmatrix} \frac{\Lambda_1}{\beta_1 - \alpha_1} \\ \frac{\Lambda_1(\beta_1 - \mu_1 - \alpha_1)}{(\mu_1 + \alpha_1)(\beta_1 - \alpha_1)} \end{pmatrix}, \quad (2.13)$$

where  $N_1^{bs_2} = \frac{\Lambda_1\beta_1}{(\mu_1 + \alpha_1)(\beta_1 - \alpha_1)}$ , represents the situation where HPAI is present in birds. Note  $bs_2$  only exists for  $\beta_1 - \mu_1 - \alpha_1 > 0$ .

## 2.2 Basic reproduction number

The basic reproduction number for the bird system,  $R_0^{[1]}$ , is defined as the number of newly infected birds that are infected by a typical infected bird when all birds are susceptible. The rate at which one infected bird infects susceptible birds is  $\frac{\beta_1}{N_1} S_1$ , where  $S_1 = N_1$  when there is no infection of HPAI in birds. Since the life-time of an infected bird is  $\frac{1}{\mu_1 + \alpha_1}$ , we have

$$R_0^{[1]} = \frac{\beta_1}{\mu_1 + \alpha_1}. \quad (2.14)$$

Thus, the infection free steady state  $bs_1$  exists for all values of  $R_0^{[1]}$  and the infection steady state  $bs_2$  only exists when  $R_0^{[1]} > 1$  as it is equivalent to the condition  $\beta_1 - \mu_1 - \alpha_1 > 0$ . Note by exist we mean it is non-negative.

## 2.3 Local Stability

The total number of birds ( $N_1$ ) is not a constant as in the ‘‘SI’’ model. Therefore, by replacing  $N_1$  by  $S_1 + I_1$ , the Jacobian matrix for the bird system (Equation 2.1) and (2.2) is

$$J_b = \begin{pmatrix} -\mu_1 - \beta_1 i & -\beta_1 j \\ \beta_1 i & \beta_1 j - \mu_1 - \alpha_1 \end{pmatrix}, \quad (2.15)$$

where

$$\begin{aligned} i &= \left( \frac{I_1}{N_1} \right)^2, \\ j &= \left( \frac{S_1}{N_1} \right)^2. \end{aligned}$$

Note the Jacobian matrices evaluated at each steady state ( $J_{bs_1}$  and  $J_{bs_2}$ ) are in the same form, where only  $i$  and  $j$  are evaluated at different values. Terms  $i$  and  $j$  are non-negative.

### 2.3.1 Local stability of $bs_1$

At steady state  $bs_1$ ,

$$\begin{aligned}i &= 0, \\j &= 1.\end{aligned}$$

Hence,

$$J_{bs_1} = \begin{pmatrix} -\mu_1 & -\beta_1 \\ 0 & \beta_1 - \mu_1 - \alpha_1 \end{pmatrix}. \quad (2.16)$$

The eigenvalues for  $J_{bs_1}$  are all negative ( $-\mu_1$  and  $\beta_1 - \mu_1 - \alpha_1$ ), if the basic reproduction number  $R_0^{[1]}$  is less than 1. Thus, steady state  $bs_1$  is locally stable when  $R_0^{[1]}$  is less than 1.

### 2.3.2 Local stability of $bs_2$

At  $bs_2$ , the trace of  $J_{bs_2}$  is

$$\tau = -\mu_1 - \beta_1 i + \beta_1 j - \mu_1 - \alpha_1. \quad (2.17)$$

where  $i$  and  $j$  are evaluated at  $bs_2$ . Equation 2.2 can be developed into

$$\beta_1 S_1^{bs_2} \frac{1}{N_1^{bs_2}} = \mu_1 + \alpha_1, \quad (2.18)$$

as the number of infected birds is non-zero at  $bs_2$ . Hence, we have

$$\beta_1 j < \mu_1 + \alpha_1. \quad (2.19)$$

Thus,  $\tau < 1$  and steady state  $bs_2$  is locally stable when it exists.

## 2.4 Global Stability

### 2.4.1 Global stability of $bs_1$

At  $bs_1$ , we need to construct a trapping region ( $t_1$ ) which only includes  $bs_1$ . If  $t_1$  exists, then either  $bs_1$  is a globally stable steady state or there exists a periodic solution inside the region.

Nullclines (n1 and n2)

$$I_1 = 0, \quad (2.20)$$

$$I_1 = (R_0^{[1]} - 1)S_1 \quad (2.21)$$

are determined from Equation 2.2 at steady state. Note the intersection between the two nullclines  $(0, 0)$  is excluded. If  $R_0^{[1]} < 1$ , in the area under nullcline n2 (Equation 2.21),  $I_1'$  is positive and hence the flow is upwards. Also, in the area above nullcline n1 (Equation 2.20),  $I_1'$  is negative and hence the flow is downwards. Thus, the upper boundary of  $t_1$  could be a horizontal line above nullcline 2.20 and the lower boundary of the  $t_1$  could be another horizontal line below nullcline 2.21.

Nullcline (n3)

$$I_1 = \frac{\mu_1 S_1^2 - \Lambda_1 S_1}{\Lambda_1 - \mu_1 S_1 - \beta_1 S_1} \quad (2.22)$$

is determined from Equation 2.1 at steady state. It has an asymptote  $S_1 = \frac{\Lambda_1}{\mu_1 + \beta_1}$  which lies on the left hand side of  $bs_1$ . In the area above the curve (Equation (2.22)), let

$$I_1^* = \frac{\mu_1 S_1^2 - \Lambda_1 S_1}{\Lambda_1 - \mu_1 S_1 - \beta_1 S_1} + x \quad (2.23)$$

where  $x > 0$ . Substitute  $I_1^*$  into Equation 2.1, we have

$$\begin{aligned} \frac{dS_1}{dt}(I_1^*) &= \Lambda_1 - \mu_1 S_1 - \beta_1 S_1 \frac{\frac{\mu_1 S_1^2 - \Lambda_1 S_1}{\Lambda_1 - \mu_1 S_1 - \beta_1 S_1} + x}{S_1 + \frac{\mu_1 S_1^2 - \Lambda_1 S_1}{\Lambda_1 - \mu_1 S_1 - \beta_1 S_1} + x} \\ &= \Lambda_1 - \mu_1 S_1 + \frac{\mu_1 \beta_1 S_1^3 - \Lambda_1 \beta_1 S_1^2 + \beta_1 x S_1 (\Lambda_1 - (\mu_1 + \beta_1) S_1)}{\beta_1 S_1^2 - \Lambda_1 x + (\mu_1 + \beta_1) x S_1} \\ &= \frac{-x(-\Lambda_1 + (\mu_1 + \beta_1) S_1)^2}{\beta_1 S_1^2 - \Lambda_1 x + (\mu_1 + \beta_1) x S_1} \\ &= \frac{-x(-\Lambda_1 + (\mu_1 + \beta_1) S_1)^2}{\beta_1 S_1^2 + (\mu_1 + \beta_1) x S_1 - \Lambda_1 x}. \end{aligned}$$

Let

$$g(S_1) = \beta_1 S_1^2 + (\mu_1 + \beta_1) x S_1 - \Lambda_1 x, \quad (2.24)$$

hence  $g$  is a quadratic in  $S_1$  which open upwards. If  $S_1 > \frac{\Lambda_1}{\mu_1 + \beta_1}$ , then  $g(S_1) > 0$ . Hence  $S_1'$  is negative and the flow is going to the left. The right boundary of  $t1$  could be a vertical line that lies on the right hand side of  $bs_1$ .

Suppose two roots of  $g(S_1)$  are  $s_1$  and  $s_2$  ( $s_1 < s_2 < \frac{\Lambda_1}{\mu_1 + \beta_1}$ ). Since  $g(0) < 0$ , then  $s_1 < 0$  and  $s_2 > 0$ .  $g(S_1)$  is negative when  $S_1$  is inside the interval  $[s_1, s_2]$ . Thus, the left boundary of  $t1$  could be another vertical line that lies in the interval  $[s_1, s_2]$  where  $S_1'$  is positive and the flow is going to the right. Hence, we have a trapping region which only include  $bs_1$ . Figure 2.2 (A) shows the trapping region  $t1$  when  $R_0^{[1]} < 1$ .

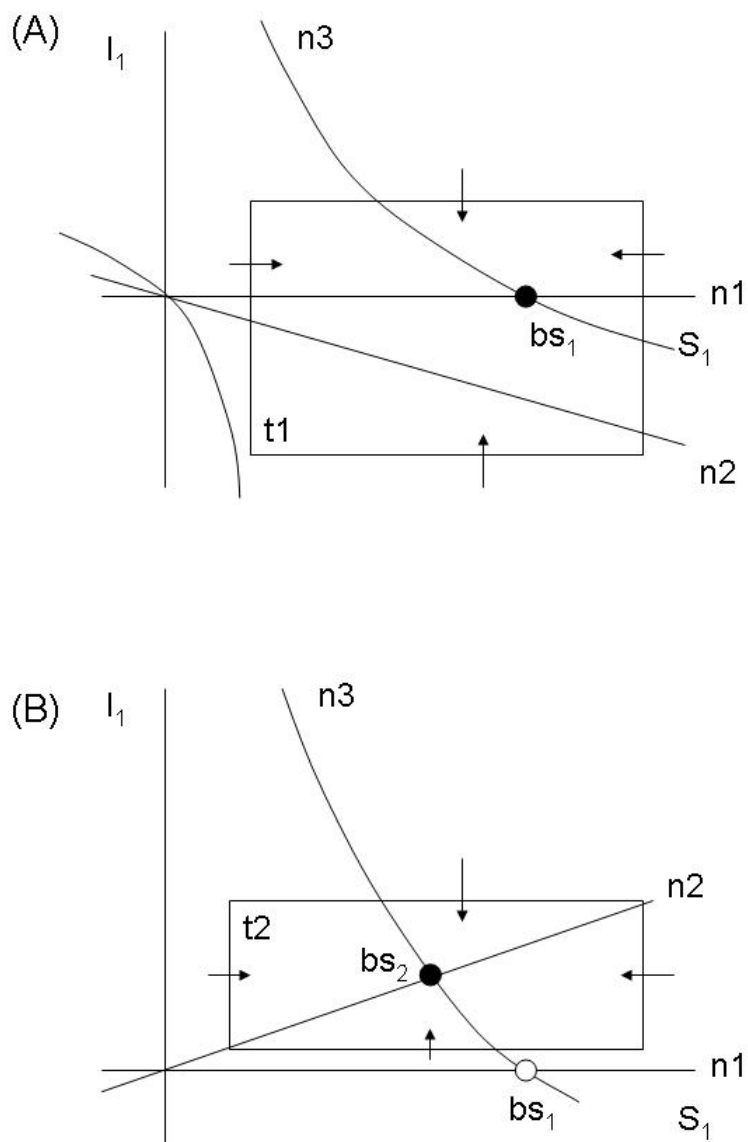


Figure 2.2: Trapping regions for steady state in the bird system. Figure (A): steady state  $bs_1$  ( $R_0^{[1]} < 1$ ). Figure (B): steady state  $bs_2$  ( $R_0^{[1]} > 1$ ).

Then choose a positive function  $\rho = \frac{1}{S_1 I_1}$  and denote the right hand side of the bird system as  $f(S_1, I_1)$ , we have

$$\nabla(\rho f) = -\frac{\Lambda_1}{S_1^2 I_1} < 0 \quad (2.25)$$

Dulac's criterion implies that there is no periodic solution. Thus, we can conclude that  $bs_1$  is a globally stable steady state when  $R_0^{[1]} < 1$ .

### 2.4.2 Global stability of $bs_2$

At  $bs_2$ , we need to construct another trapping region ( $t2$ ) which only includes  $bs_2$ . If such a trapping region exists, then either  $bs_2$  is a globally stable steady state or there exists a periodic solution inside the region. Note  $bs_2$  only exists when  $R_0^{[1]} > 1$ .

Nullclines  $n1$  (Equation 2.20) and  $n2$  (Equation 2.21) cut the  $\mathbb{R}_+^2$  plane into two parts:  $I_1' > 0$  when  $0 < I_1 < (R_0^{[1]} - 1)S_1$  (lower triangle) and  $I_1' < 0$  when  $I_1 > (R_0^{[1]} - 1)S_1$  (upper triangle). Thus, the lower boundary of  $t2$  could be a horizontal line in the lower triangle and the upper boundary could be another horizontal line in the upper triangle. The left and right boundary of the trapping region are the same as in  $t1$ . Hence, we have a trapping  $t2$  region which only include  $bs_2$ . Figure 2.2 (B) shows the trapping region  $t2$  when  $R_0^{[1]} > 1$ .

Refer to section 2.4.1 Equation 2.25, Dulac's criterion implies that there is no periodic solution in  $\mathbb{R}_+^2$ . Thus, we can conclude that  $bs_2$  is a globally stable steady state when it exists.

## 2.5 Summary

There are two steady states in the bird HPAI system:

Steady state  $bs_1$  represents the situation where there is no infection of HPAI in the bird system.  $bs_1$  exists for all values of  $R_0^{[1]}$  and it is stable when  $R_0^{[1]}$  is less than the threshold 1. Steady state  $bs_2$  represents the state where infection of HPAI is present in the bird system.  $bs_2$  exists when  $R_0^{[1]}$  is greater than 1 and it is stable when it exists.

## 2.6 Numerical results

For numerical results, we choose two different values of  $\beta_1$  (9.6/10.6 day<sup>-1</sup>) in order to adjust  $R_0^{[1]}$  to be greater or less than 1. Other parameters value and analytic steady state computed from which are shown in Table 2.2.

Parameters	Value		$\beta_1 = 9.6$	$\beta_1 = 10.6$
$\Lambda_1$	26.5 birds · day <sup>-1</sup>	$S_1$	5.3	4.7321
$\mu_1$	5 day <sup>-1</sup>	$I_1$	0	0.2839
$\alpha_1$	5 day <sup>-1</sup>	$N_1$	5.3	5.0161
$\beta_1$	9.6/10.6 day <sup>-1</sup>	$R_0^{[1]}$	0.96	1.06

Table 2.2: Parameter values and analytic steady state values in the bird systems. Parameter values referenced to [4].

We use MATLAB “ode15s” to solve the differential equations to have more exact results (than “ode45”). The results are shown in Figure 2.3.

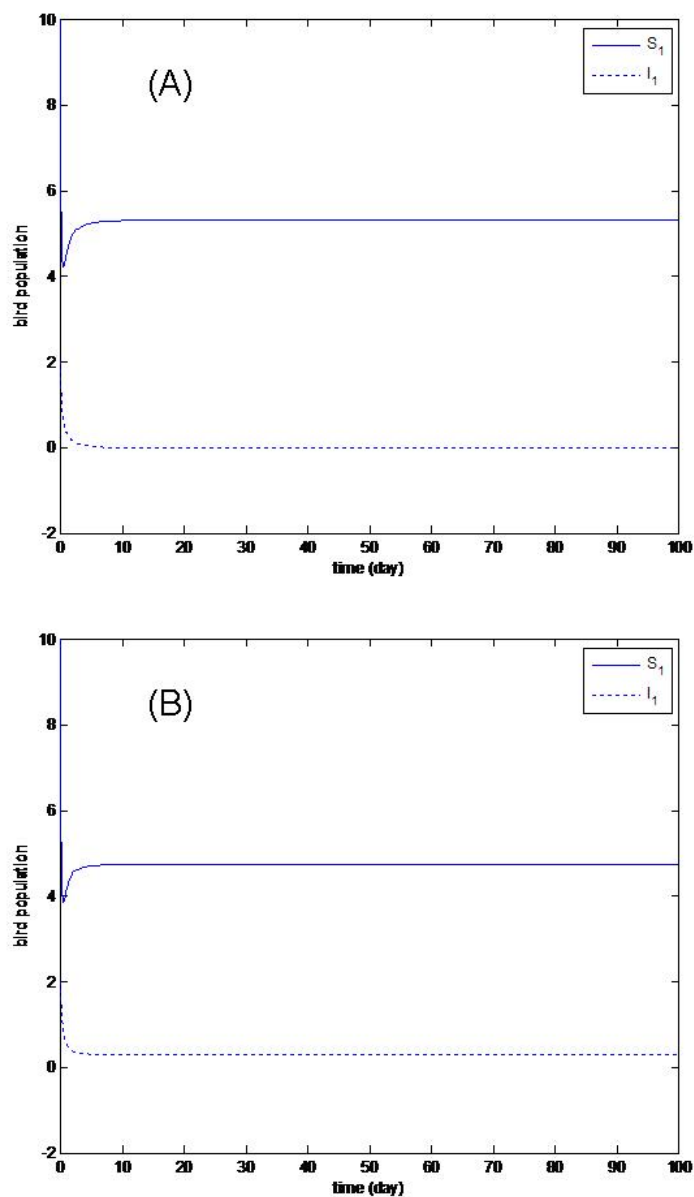


Figure 2.3: Numerical results for the bird HPAI system with initial values  $(S_1, I_1) = (10, 2)$ . Figure (A):  $\beta_1 = 9.6$  where  $R_0^{[1]} = 0.96 < 1$ . Figure (B):  $\beta_1 = 10.6$  where  $R_0^{[1]} = 1.06 > 1$ .

In Figure 2.3 (A) when  $\beta_1 = 9.6$  and  $R_0^{[1]} < 1$ , the system approaches  $(S_1, I_1) = (5.3, 0)$  which is infection free as the number of infected birds goes to zero. In Figure 2.3 (B) when  $\beta_1 = 10.6$  and  $R_0^{[1]} > 1$ , the system approaches  $(S_1, I_1) = (4.732, 0.283)$  where infections of HPAI are present in the bird system. Thus, the numerical results are consistent with the analytic results.

## 2.7 Phase portrait

Taking the same parameter values as in last section, the diagrams of phase portrait of the bird HPAI system are shown in Figure 2.4.

In Figure 2.4 (A) where  $R_0^{[1]} < 1$ , the solid circle point indicates the stable infection free steady state of the bird system since the flows from all directions are going into the point. In Figure 2.4 (B) where  $R_0^{[1]} > 1$ , there is one stable infected steady state indicated by a solid circle and one unstable infection free steady state indicated by a circle. Notice that the flows between the two (circle) points are going into the infected steady state (solid circle).

The phase portrait is also evidence supporting the analytic and numerical results.

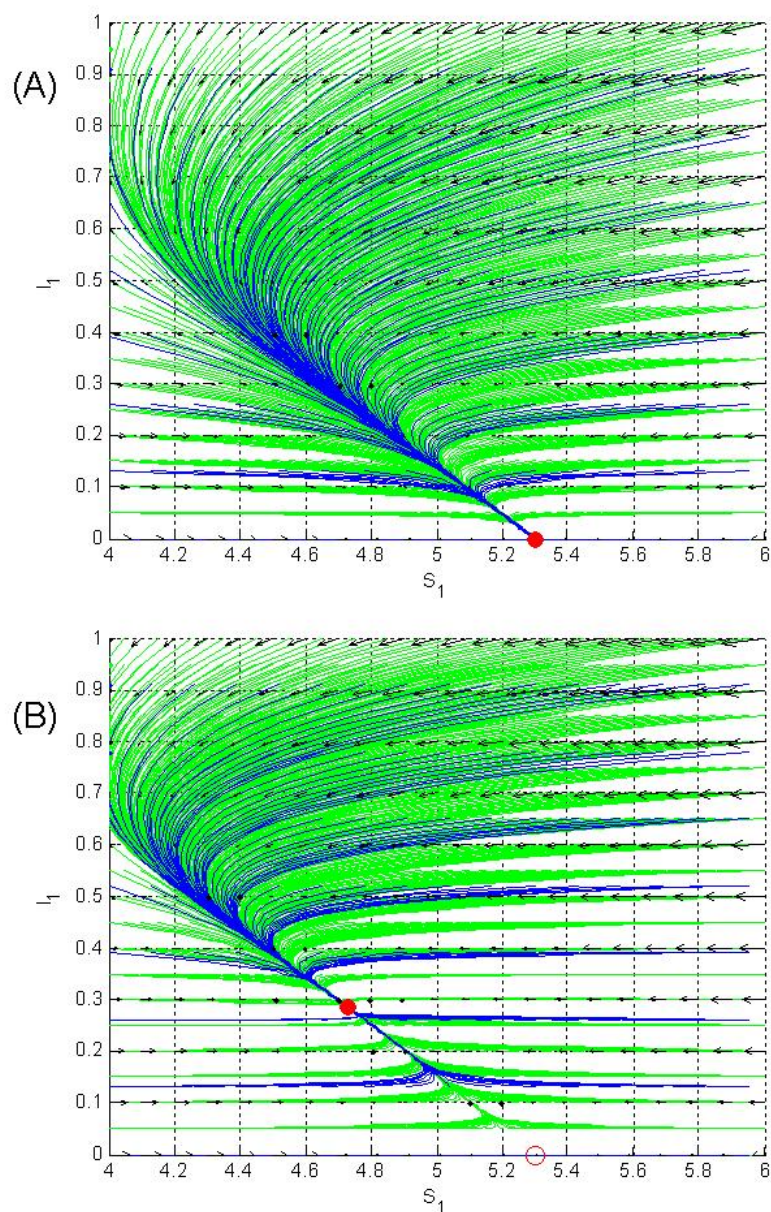


Figure 2.4: The phase portrait of the bird system. Figure (A):  $\beta_1 = 9.6$  where  $R_0^{[1]} = 0.96 < 1$ . Figure (B):  $\beta_1 = 10.6$  where  $R_0^{[1]} = 1.06 > 1$ . The arrows show the direction of the flow.

## 2.8 Bifurcation

There is a transcritical bifurcation from the infection free to the infected steady state when  $R_0^{[1]}$  increases through the threshold 1. When  $R_0^{[1]}$  is less than 1, only the infection free steady state exists and it is stable. When  $R_0^{[1]}$  becomes greater than 1, the infection free steady state becomes unstable and the stable infected steady state exists. The bifurcation diagram is shown in Figure 2.5.

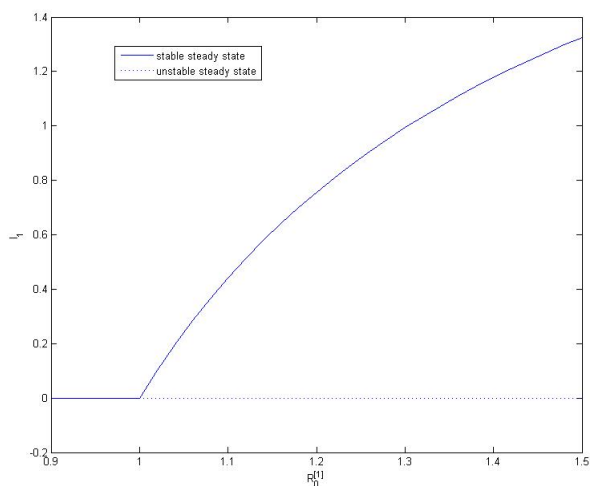


Figure 2.5: Bifurcation diagram of the bird system.



## Chapter 3

# Bird-Human Systems

For humans, we present two models for HPAI, one derived from the other. We assume that the viruses inside the human system mutate at a constant rate  $\epsilon$  ( $\text{time}^{-1}$ ) to become infectious to another susceptible human. That means, susceptible humans are getting infected from both infected birds with HPAI and infected humans with mutated HPAI. Thus, the “SIR” model needs to be extended into a “SIMR” model, where “M” stands for human infected by mutated HPAI. This is a four dimensional human model. The other simpler model, represents the situation where  $\epsilon$  goes to infinity. Hence, class “I” and “M” are combined so that we just use the “SIR” model (three dimensional). Both the SIR and the SIMR human (mutated) HPAI model are parts of the bird-human HPAI system, hence we have one 5-D and one 6-D bird-human mutated HPAI system. The steady states of the bird-human systems are also combinations of steady states from both the bird and the human systems.

### 3.1 The SIR human model

In this simpler model when  $\epsilon \Rightarrow \infty$ , we use  $S_2$ ,  $I_2$  and  $R_2$  to represent human susceptible, human infected with (mutated) HPAI, and human removed, respectively. Consider the relationship diagram of the human SIR system in Figure 3.1 with parameters defined in Table (3.1).

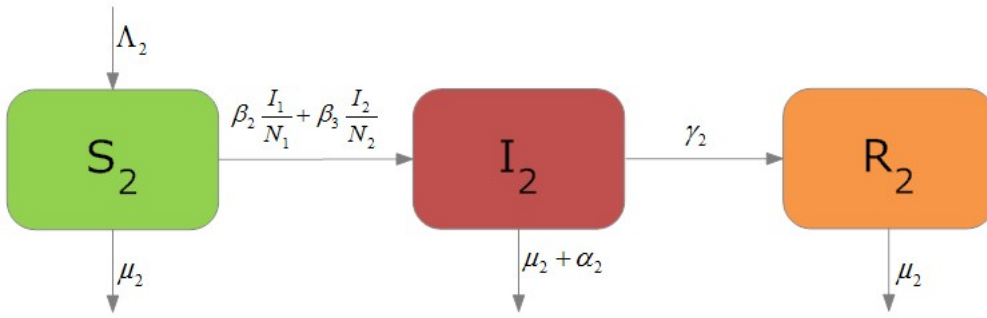


Figure 3.1: Relationship diagram of the human system.

The model equations of the human SIR system are:

$$\frac{dS_2}{dt} = \Lambda_2 - \mu_2 S_2 - \beta_2 S_2 \frac{I_1}{N_1} - \beta_3 S_2 \frac{I_2}{N_2} \quad (3.1)$$

$$\frac{dI_2}{dt} = \beta_2 S_2 \frac{I_1}{N_1} + \beta_3 S_2 \frac{I_2}{N_2} - (\mu_2 + \alpha_2 + \gamma_2) I_2 \quad (3.2)$$

$$\frac{dR_2}{dt} = \gamma_2 I_2 - \mu_2 R_2. \quad (3.3)$$

The total population of humans ( $N_2$ ) is

$$N_2 = S_2 + I_2 + R_2. \quad (3.4)$$

Each human has infectious contact with birds at the rate  $\beta_2$ , and a proportion  $\frac{I_1}{N_1}$  of birds is infectious. Similarly, each human has infectious contact with other humans at rate  $\beta_3$ , and a proportion  $\frac{I_2}{N_2}$  of human is infectious. Hence the transmission terms in (3.1) and (3.2) are  $\beta_2 S_2 \frac{I_1}{N_1}$  and  $\beta_3 S_2 \frac{I_2}{N_2}$ .

Parameters	Units	Definition
$t$	time	Time (day)
$N_2$	people	Total population
$S_2$	people	Number of susceptible
$I_2$	people	Number of infected by avian influenza
$R_2$	people	Number of removed
$\Lambda_2$	day <sup>-1</sup>	Natural birth rate
$\mu_2$	day <sup>-1</sup>	Natural death rate
$\beta_2$	day <sup>-1</sup>	Transmission coefficient from bird to human
$\beta_3$	day <sup>-1</sup>	Transmission coefficient from human to human
$\alpha_2$	day <sup>-1</sup>	Additional death rate caused by the avian influenza
$\gamma_2$	day <sup>-1</sup>	Recovery rate from avian influenza
$R_0^{[2]}$		Basic reproduction number

Table 3.1: Definition of model parameters in the human system

### 3.1.1 Steady States

Let  $hs$  and  $fs$  represent the steady state of the ‘‘SIR’’ human and the full bird-human 5-D systems, respectively. The steady states of the SIR human system are derived from Equation (3.1)-(3.3) fixed by the steady state values of the bird system ( $bs_1$  and  $bs_2$ ). At  $hs$ ,  $S_2^{hs}$  and  $R_2^{hs}$  can be rewritten in terms of  $I_2^{hs}$  and hence  $fs$  can be expressed as

$$fs = \begin{pmatrix} S_1^{bs} \\ I_1^{bs} \\ S_2^{hs} \\ I_2^{hs} \\ R_2^{hs} \end{pmatrix} = \begin{pmatrix} S_1^{bs} \\ I_1^{bs} \\ \frac{\Lambda_2 - (\mu_2 + \alpha_2 + \gamma_2)I_2^{hs}}{\mu_2} \\ I_2^{hs} \\ \frac{\gamma_2 I_2^{hs}}{\mu_2} \end{pmatrix}, \quad (3.5)$$

where  $N_2^{hs} = \frac{\Lambda_2 - \alpha_2 I_2^{hs}}{\mu_2}$ . Substitute the steady state values in Equation 3.5 into Equation (3.2) and simplify it to be a quadratic equation in  $I_2^{hs}$  (or into Equation (3.1) to get a similar quadratic):

$$f(I_2^{hs}) = a(I_2^{hs})^2 + bI_2^{hs} + c = 0, \quad (3.6)$$

where

$$\begin{aligned} a &= \frac{\mu_2 + \alpha_2 + \gamma_2}{\mu_2} \left( \beta_2 \frac{\alpha_2}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} + \alpha_2 - \beta_3 \right), \\ b &= \frac{\Lambda_2}{\mu_2} \left( \beta_3 - \mu_2 - \alpha_2 - \gamma_2 - \beta_2 \frac{\mu_2 + 2\alpha_2 + \gamma_2}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} \right), \\ c &= \beta_2 \left( \frac{\Lambda_2}{\mu_2} \right)^2 \frac{I_1^{bs}}{N_1^{bs}}. \end{aligned}$$

Notice  $c$  is always positive and the signs of  $a$  and  $b$  are determined by the value of the parameters. Also,

$$\begin{aligned} b^2 - 4ac &= \left( \frac{\Lambda_2}{\mu_2} \left( \beta_3 - \mu_2 - \alpha_2 - \gamma_2 - \beta_2 \frac{\mu_2 + 2\alpha_2 + \gamma_2}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} \right) \right)^2 \\ &\quad - 4 \left( \frac{\mu_2 + \alpha_2 + \gamma_2}{\mu_2} \left( \beta_2 \frac{\alpha_2}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} + \alpha_2 - \beta_3 \right) \right) \left( \beta_2 \left( \frac{\Lambda_2}{\mu_2} \right)^2 \frac{I_1^{bs}}{N_1^{bs}} \right) \\ &= \left( \frac{\Lambda_2}{\mu_2} \right)^2 \left( (\beta_3 - \mu_2 - \alpha_2 - \gamma_2)^2 + \left( \beta_2 \frac{\mu_2 + \gamma_2}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} \right)^2 \right. \\ &\quad \left. + 2\beta_2 \frac{\mu_2 + \gamma_2}{\mu_2} (\beta_3 + \mu_2 + \alpha_2 + \gamma_2) \frac{I_1^{bs}}{N_1^{bs}} \right) > 0, \end{aligned} \quad (3.7)$$

which shows that the roots of Equation 3.6 are real for all parameter values.

The roots of Equation 3.6 have to be non-negative to be valid steady state values of  $I_2$ , and so have the  $S_2$  and  $R_2$  derived from it.

**Steady States  $f_{s_1}$  and  $f_{s_2}$** 

The steady states of the full system  $f_{s_1}$  and  $f_{s_2}$  are combinations of the steady state of the bird system ( $b_{s_1}$ ) and the human system ( $h_{s_1}$  and  $h_{s_2}$ ) fixed by the value of  $b_{s_1}$ . At  $b_{s_1}$ , where  $I_1 = 0$ , the coefficients of Equation 3.6 can be simplified as

$$\begin{aligned} a &= \frac{\mu_2 + \alpha_2 + \gamma_2}{\mu_2}(\alpha_2 - \beta_3), \\ b &= \frac{\Lambda_2}{\mu_2}(\beta_3 - \mu_2 - \alpha_2 - \gamma_2), \\ c &= 0, \end{aligned}$$

which gives

$$\begin{aligned} I_2^{hs_1} &= 0, \\ I_2^{hs_2} &= \frac{\Lambda_2(\beta_3 - \mu_2 - \alpha_2 - \gamma_2)}{(\beta_3 - \alpha_2)(\mu_2 + \alpha_2 + \gamma_2)}. \end{aligned}$$

Hence, steady state values of  $S_2$  and  $R_2$  can be derived from them. The first steady state of the full system is

$$f_{s_1} = \begin{pmatrix} S_1^{bs_1} \\ I_1^{bs_1} \\ S_2^{hs_1} \\ I_2^{hs_1} \\ R_2^{hs_1} \end{pmatrix} = \begin{pmatrix} \frac{\Lambda_1}{\mu_1} \\ 0 \\ \frac{\Lambda_2}{\mu_2} \\ 0 \\ 0 \end{pmatrix}, \quad (3.8)$$

where  $N_2^{hs_1} = \frac{\Lambda_2}{\mu_2}$ . It represents the state with an absence of (mutated) HPAI infection in both the bird and the human system.

The second steady state,

$$f s_2 = \begin{pmatrix} S_1^{bs_1} \\ I_1^{bs_1} \\ S_2^{hs_2} \\ I_2^{hs_2} \\ R_2^{hs_2} \end{pmatrix} = \begin{pmatrix} \frac{\Lambda_1}{\mu_1} \\ 0 \\ \frac{\Lambda_2(\mu_2 + \gamma_2)}{\mu_2(\beta_3 - \alpha_2)} \\ \frac{\Lambda_2(\beta_3 - \mu_2 - \alpha_2 - \gamma_2)}{(\beta_3 - \alpha_2)(\mu_2 + \alpha_2 + \gamma_2)} \\ \frac{\gamma_2 \Lambda_2(\beta_3 - \mu_2 - \alpha_2 - \gamma_2)}{\mu_2(\beta_3 - \alpha_2)(\mu_2 + \alpha_2 + \gamma_2)} \end{pmatrix}, \quad (3.9)$$

where  $N_2^{hs_2} = \frac{\beta_3 \Lambda_2 (\mu_2 + \gamma_2)}{\mu_2 (\beta_3 - \alpha_2) (\mu_2 + \alpha_2 + \gamma_2)}$ . It represents the situation where there is no infection of HPAI in birds but infection of mutated HPAI is present in humans.  $f s_2$  exists for all  $R_0^{[1]}$  values and for  $\beta_3 - \mu_2 - \alpha_2 - \gamma_2 > 0$ .

### Steady States $f s_3$

The steady state of the full system  $f s_3$  is a combination of steady state of the bird system  $bs_2$  ( $I_1^{bs_2} > 0$ ) and the steady state of the human system derived with fixed value of  $bs_2$ . The roots of Equation 3.6 have two cases depending on the value of parameters:

Case (1):

$$\beta_2 \frac{\alpha_2}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} + \alpha_2 - \beta_3 < 0 \quad (3.10)$$

Case (2):

$$\beta_2 \frac{\alpha_2}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} + \alpha_2 - \beta_3 > 0 \quad (3.11)$$

Under the condition of Case (1),  $a < 0$ . Because

$$f(0) = \beta_2 \left( \frac{\Lambda_2}{\mu_2} \right)^2 \frac{I_1^{bs}}{N_1^{bs}} > 0, \quad (3.12)$$

Equation 3.6 has one positive root and one negative root (which we ignore).

Under the condition of Case (2),  $a > 0$  and  $b < 0$ . As  $\sqrt{b^2 - 4ac} < |b|$  and  $b^2 > 4ac$  (Equation 3.7), it implies both roots of Equation 3.6 are positive.

$R_2^{fs_3}$  has the same sign as  $I_2^{fs_3}$ . However, this is not necessarily true for  $S_2^{fs_3}$ .

Rewrite  $I_2^{fs}$  as

$$I_2^{fs} = \frac{\Lambda_2}{\mu_2 + \alpha_2 + \gamma_2} - \frac{\mu_2}{\mu_2 + \alpha_2 + \gamma_2} S_2^{fs}, \quad (3.13)$$

and substitute it into Equation 3.6, we have another quadratic equation in  $S_2^{fs}$ :

$$g(S_2^{hs}) = a^*(S_2^{hs})^2 + b^*S_2^{hs} + c^* = 0, \quad (3.14)$$

where

$$\begin{aligned} a^* &= \frac{\mu_2}{\mu_2 + \alpha_2 + \gamma_2} \left( \beta_2 \frac{\alpha_2}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} + \alpha_2 - \beta_3 \right), \\ b^* &= \frac{\Lambda_2}{\mu_2 + \alpha_2 + \gamma_2} \left( \beta_3 - \alpha_2 + \mu_2 + \gamma_2 + \beta_2 \frac{\mu_2 + \gamma_2}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} \right), \\ c^* &= -\frac{\Lambda_2^2(\mu_2 + \gamma_2)}{\mu_2(\mu_2 + \alpha_2 + \gamma_2)}. \end{aligned}$$

The roots of Equation 3.14 also have two cases depending on the value of parameters:

Under the condition of Case (1),  $a^* < 0$  and  $b^* > 0$ . As  $\sqrt{(b^*)^2 - 4a^*c^*} < |b^*|$  and  $b^2 > 4ac$  (Equation ), this implies both roots of Equation 3.14 are positive.

Under the condition of Case (2),  $a^* > 0$ . Because

$$g(0) = -\frac{\Lambda_2^2(\mu_2 + \gamma_2)}{\mu_2(\mu_2 + \alpha_2 + \gamma_2)} < 0, \quad (3.15)$$

Equation 3.14 has one positive root and one negative root (which we ignore).

To sum up, there is only one steady state  $f s_3$  that exists in either case and it is unique.  $f s_3$  represents the situation where infection of (mutated) HPAI is present in both the bird and the human system. It exists only when  $R_0^{[1]} > 1$ .

### 3.1.2 Basic reproduction number

The basic reproduction number for the SIR human system,  $R_0^{[2]}$ , is defined as the expected number of newly infected humans that are infected by a typical infectious human when all humans are susceptible. The rate at which one infected human infects susceptible humans is  $\frac{\beta_2}{N_2} S_2$ , where  $S_2 = N_2$  if there is no infection in the system. Since the infectious life-time of an infected human is  $\frac{1}{\mu_2 + \alpha_2 + \gamma_2}$ , we have

$$R_0^{[2]} = \frac{\beta_3}{\mu_2 + \alpha_2 + \gamma_2}. \quad (3.16)$$

Hence,  $f s_1$  exists for all values of  $R_0^{[1]}$  and  $R_0^{[2]}$ . Recall one of the conditions for the existence of  $f s_2$  is  $\beta_3 - \mu_2 - \alpha_2 - \gamma_2 > 0$ , which is equivalent to  $R_0^{[2]} > 1$ . Thus, we can conclude that  $f s_2$  exist for all  $R_0^{[1]}$  values and for  $R_0^{[2]} > 1$ .  $f s_3$  exists only when  $R_0^{[1]} > 1$  and for all values of  $R_0^{[2]}$ .

### 3.1.3 Local Stability

The Jacobian matrix of the full bird-human system is given as

$$J_f = \begin{pmatrix} J_b & 0 \\ j & J_h \end{pmatrix}, \quad (3.17)$$

where  $J_b$  is the Jacobian matrix of the bird system shown in section 2.3 (Equation 2.15) and  $J_h$  is the Jacobian matrix of the human system. The value of  $j$  does not effect the stability of the full system so we may ignore it.

The steady states of the full system are combinations of the steady states in birds and humans, therefore, they are only stable if the steady states of both the bird and the human systems are stable as determined by  $J_b$  and  $J_h$ , respectively. The stability of  $bs_1$  and  $bs_2$  are already determined in section 2.3. Thus, we need to check the steady state stability of the human system.

The Jacobian matrix of the human system  $J_h$  is

$$J_h = \begin{pmatrix} -\mu_2 - \beta_2 \frac{I_1}{N_1} - \beta_3 i & -\beta_3 j & \beta_3 k \\ \beta_2 \frac{I_1}{N_1} + \beta_3 i & \beta_3 j - \mu_2 - \alpha_2 - \gamma_2 & -\beta_3 k \\ 0 & \gamma_2 & -\mu_2 \end{pmatrix}, \quad (3.18)$$

where

$$\begin{aligned} i &= \frac{I_2(I_2 + R_2)}{N_2^2}, \\ j &= \frac{S_2(S_2 + R_2)}{N_2^2}, \\ k &= \frac{S_2 I_2}{N_2^2}. \end{aligned}$$

Terms  $i$ ,  $j$  and  $k$  are non-negative.

**Stability of  $hs_1$** 

At  $hs_1$ , where  $I_2 = 0$ ,

$$\begin{aligned} i &= 0, \\ j &= 1, \\ k &= 0, \end{aligned}$$

and hence

$$J_{hs_1} = \begin{pmatrix} -\mu_2 & -\beta_3 & 0 \\ 0 & \beta_3 - \mu_2 - \alpha_2 - \gamma_2 & 0 \\ 0 & \gamma_2 & -\mu_2 \end{pmatrix}. \quad (3.19)$$

The eigenvalues of  $J_{hs_1}$  are  $-\mu_2$ ,  $\beta_3 - \mu_2 - \alpha_2 - \gamma_2$  and  $-\mu_2$ . They are all negative if  $R_0^{[2]} < 1$ . Hence, we can conclude that  $hs_1$  is locally stable when  $R_0^{[2]} < 1$ .

**Stability of  $hs_2$** 

The Jacobian matrix evaluated at  $hs_2$  ( $I_1^{bs_1} = 0$  and  $I_2^{hs_2} \neq 0$ ) is

$$J_{hs_2} = \begin{pmatrix} -\mu_2 - \beta_3 i & -\beta_3 j & \beta_3 k \\ \beta_3 i & \beta_3 j - \mu_2 - \alpha_2 - \gamma_2 & -\beta_3 k \\ 0 & \gamma_2 & -\mu_2 \end{pmatrix}, \quad (3.20)$$

with  $i$ ,  $j$  and  $k$  evaluated at  $hs_2$ . The characteristic equation of  $J_{hs_2}$  is

$$\lambda^3 + a_0 \lambda^2 + a_1 \lambda + a_2 = 0 \quad (3.21)$$

where

$$a_0 = 2\mu_2 + \beta_3 i + \mu_2 + \alpha_2 + \gamma_2 - \beta_3 j,$$

$$\begin{aligned}
a_1 &= (2\mu_2 + \beta_3 i)(\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) + (\mu_2 + \beta_3 i)\mu_2 + \beta_3 k \gamma_2 + \beta_3 j \beta_3 i, \\
a_2 &= (\mu_2 + \beta_3 i)(\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j)\mu_2 + \beta_3 j \beta_3 i \mu_2 + \mu_2 \beta_3 k \gamma_2.
\end{aligned}$$

Also,

$$\begin{aligned}
a_0 a_1 - a_2 &= (2\mu_2 + \beta_3 i + \mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) ((2\mu_2 + \beta_3 i)(\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) \\
&\quad + (\mu_2 + \beta_3 i)\mu_2 + \beta_3 k \gamma_2 + \beta_3 j \beta_3 i) - ((\mu_2 + \beta_3 i)(\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j)\mu_2 \\
&\quad + \beta_3 j \beta_3 i \mu_2 + \mu_2 \beta_3 k \gamma_2) \\
&= (\mu_2 + \beta_3 i) ((2\mu_2 + \beta_3 i)(\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) + (\mu_2 + \beta_3 i)\mu_2 \\
&\quad + \beta_3 k \gamma_2 + \beta_3 j \beta_3 i) + (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) ((2\mu_2 + \beta_3 i)(\mu_2 + \alpha_2 \\
&\quad + \gamma_2 - \beta_3 j) + \beta_3 k \gamma_2 + \beta_3 j \beta_3 i) + \mu_2 ((2\mu_2 + \beta_3 i)(\mu_2 + \alpha_2 + \gamma_2 \\
&\quad - \beta_3 j) + (\mu_2 + \beta_3 i)\mu_2)
\end{aligned}$$

Equation 3.2 can be rearranged at  $hs_2$  where  $I_1^{bs_1} = 0$  and  $I_2^{hs_2} \neq 0$  into

$$\mu_2 + \alpha_2 + \gamma_2 = \beta_3 \frac{S_2}{N_2}. \quad (3.22)$$

Hence, we can conclude that

$$\beta_3 j - \mu_2 - \alpha_2 - \gamma_2 < 0 \quad (3.23)$$

at steady state  $hs_2$ . Hence,  $a_0$ ,  $a_1$ ,  $a_2$  and  $a_0 a_1 - a_2$  are all positive. Refer to Routh-Hurwitz criteria [8], steady state  $hs_2$  is locally stable when it exists.

### Stability of $hs_3$

The characteristic equation of  $J_{hs_3}$  is similar to that of  $J_h^{hs_2}$ , only  $I_1^{bs_2}$  is non-zero at  $hs_3$  and  $i$ ,  $j$  and  $k$  evaluated at different steady states. Hence,

$$\lambda^3 + b_0 \lambda^2 + b_1 \lambda + b_2 = 0 \quad (3.24)$$

where

$$\begin{aligned}
b_0 &= 2\mu_2 + \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i + \mu_2 + \alpha_2 + \gamma_2 - \beta_3 j, \\
b_1 &= \left( 2\mu_2 + \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) + \left( \mu_2 + \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) \mu_2 \\
&\quad + \beta_3 k \gamma_2 + \beta_3 j \left( \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right), \\
b_2 &= \left( \mu_2 + \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) \mu_2 + \beta_3 j \left( \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) \mu_2 \\
&\quad + \mu_2 \beta_3 k \gamma_2.
\end{aligned}$$

Also,

$$\begin{aligned}
b_0 b_1 - b_2 &= \left( 2\mu_2 + \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i + \mu_2 + \alpha_2 + \gamma_2 - \beta_3 j \right) \left( \left( 2\mu_2 + \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) \right. \\
&\quad \left. (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) + \left( \mu_2 + \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) \mu_2 + \beta_3 k \gamma_2 + \beta_3 j \right. \\
&\quad \left. \left( \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) \right) - \left( \left( \mu_2 + \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) \mu_2 \right. \\
&\quad \left. + \beta_3 j \left( \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) \mu_2 + \mu_2 \beta_3 k \gamma_2 \right) \\
&= \left( \mu_2 + \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) \left( \left( 2\mu_2 + \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) \right. \\
&\quad \left. + \left( \mu_2 + \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) \mu_2 + \beta_3 k \gamma_2 + \beta_3 j \left( \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) \right) \\
&\quad + (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) \left( \left( 2\mu_2 + \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) \right. \\
&\quad \left. + \beta_3 k \gamma_2 + \beta_3 j \left( \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) \right) + \mu_2 \left( \left( 2\mu_2 + \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) \right. \\
&\quad \left. (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) + \left( \mu_2 + \beta_2 \frac{I_1^{bs_2}}{N_1^{bs_2}} + \beta_3 i \right) \mu_2 \right)
\end{aligned}$$

At  $hs_3$ , where  $I_1^{bs_2} \neq 0$  and  $I_2^{hs_3} \neq 0$ , Equation 3.2 can be developed into

$$\mu_2 + \alpha_2 + \gamma_2 > \beta_3 \frac{S_2}{N_2}, \quad (3.25)$$

hence

$$\beta_3 j - \mu_2 - \alpha_2 - \gamma_2 < 0. \quad (3.26)$$

Thus,  $b_0$ ,  $b_1$ ,  $b_2$  and  $b_0 b_1 - b_2$  are all positive. According to Routh-Hurwitz criteria [8], steady state  $hs_3$  is locally stable.

### 3.1.4 Summary

Over all, there are three steady states in the bird-human 5-D mutated HPAI system:

Steady state  $hs_1$  represents the situation where there is no infection of (mutated) HPAI in the human system. It exists for all values of  $R_0^{[1]}$  and  $R_0^{[2]}$ , but it is stable only when  $R_0^{[2]}$  is less than the threshold 1. Hence, combining this with the stability of  $bs_1$ , we can conclude that the steady state of the full bird-human system  $fs_1$  represents the situation where there is no infection of (mutated) HPAI in both the bird and the human system. It exists for all values of  $R_0^{[1]}$  and  $R_0^{[2]}$ , but it is stable only when both  $R_0^{[1]}$  and  $R_0^{[2]}$  are less than the threshold 1.

Steady state  $hs_2$  represents the situation where infection of mutated HPAI is present in humans. It exists for all  $R_0^{[1]}$  values and when  $R_0^{[2]}$  is greater than 1. It is stable when it exists. Hence, combining this with the stability of  $bs_1$ , we can conclude that the steady state of the full bird-human system  $fs_2$  represents the situation where there is no infection of HPAI in birds, but infection of mutated HPAI is present in humans. It exists for all  $R_0^{[1]}$  values and  $R_0^{[2]} > 1$ .  $fs_2$  is stable when  $R_0^{[1]}$  is less than 1 and  $R_0^{[2]}$  is greater than

zero.

Steady state  $hs_3$  represents the situation where infection of mutated HPAI is present in humans. It exists when  $R_0^{[1]} > 1$  and all values of  $R_0^{[2]}$ . It is stable when it exists. Hence, combining this with the stability of  $bs_2$ , we can conclude that the steady state of the full bird-human system  $fs_3$  represents the situation where infection of (mutated) HPAI is present in both birds and humans. It exists when  $R_0^{[1]} > 1$  and all values of  $R_0^{[2]}$  and it is stable when it exists.

### 3.1.5 Numerical results

Choose different values of  $\beta_1$  (9.6/10.6 day<sup>-1</sup>) and  $\beta_3$  (0.1/1.2 day<sup>-1</sup>) in order to adjust  $R_0^{[1]}$  and  $R_0^{[2]}$  to be less and greater than the threshold 1. Parameter values of the bird system are in Table 2.2. Parameters values and analytic steady states of the human system are shown in Table 3.2.

	Value		$\beta_1 = 9.6$		$\beta_1 = 10.6$	
			$\beta_3 = 0.1$	$\beta_3 = 1.2$	$\beta_3 = 0.1$	$\beta_3 = 1.2$
$\Lambda_2$	3 people · day <sup>-1</sup>					
$\mu_2$	0.015 day <sup>-1</sup>	$S_2$	200	5	30.6711	4.4621
$\alpha_2$	0.2 day <sup>-1</sup>	$I_2$	0	13	11.2886	13.0359
$\beta_2$	1.06 day <sup>-1</sup>	$R_2$	0	8.6667	7.5257	8.6906
$\gamma_2$	0.01 day <sup>-1</sup>	$N_2$	200	26.6667	49.4854	26.1886
$\beta_3$	0.1/1.2 day <sup>-1</sup>	$R_0^{[2]}$	0.4444	5.3333	0.4444	5.3333

Table 3.2: Parameter values and analytic steady states of the SIR human systems. Values referenced to [4].

We use Matlab “ode15s” to solve for steady states. The results are shown in Figure 3.2 and 3.3.

In Figure 3.2 (A) when  $\beta_1 = 9.6$  and  $\beta_3 = 0.1$  ( $R_0^{[1]} < 1$  and  $R_0^{[2]} < 1$ ), the system approaches  $(S_2, I_2, R_2) = (200, 0, 0)$  which is the infection free steady state for the human system ( $I_2 = 0$ ). In Figure 3.2 (B) where  $\beta_1 = 9.6$  and  $\beta_3 = 1.2$  ( $R_0^{[1]} < 1$  and  $R_0^{[2]} > 1$ ), the system approaches  $(S_2, I_2, R_2) = (4.997, 13, 8.664)$  where infection is present in the human system ( $I_2 \neq 0$ ).

In Figure 3.3 (A) where  $\beta_1 = 10.6$  ( $R_0^{[1]} > 1$ ) and  $\beta_3 = 0.1$  ( $R_0^{[2]} < 1$ ), the system approaches  $(S_2, I_2, R_2) = (30.67, 11.29, 7.523)$ . In Figure 3.3 (B) where  $\beta_1 = 10.6$  ( $R_0^{[1]} > 1$ ) and  $\beta_3 = 1.2$  ( $R_0^{[2]} > 1$ ), the system approaches  $(S_2, I_2, R_2) = (4.463, 8.688, 13.04)$ . Hence, a stable steady state is always present when  $R_0^{[1]}$  is greater than 1 whatever  $R_0^{[2]}$  is. It represents the state where infection of mutated HPAI is present in humans. We can conclude that the numerical results are consistent with the analytic results.

### 3.1.6 Bifurcation

There is a transcritical bifurcation in the human system when  $R_0^{[2]}$  increases through the threshold 1 while  $R_0^{[1]}$  is less than 1. When  $R_0^{[1]} < 1$  and  $R_0^{[2]} < 1$ , there is only one stable steady state (infection free) and when  $R_0^{[1]} < 1$  and  $R_0^{[2]} > 1$ , another stable steady state (infected) appears and the infection free steady state become unstable. The bifurcation diagram is shown in Figure 3.4.

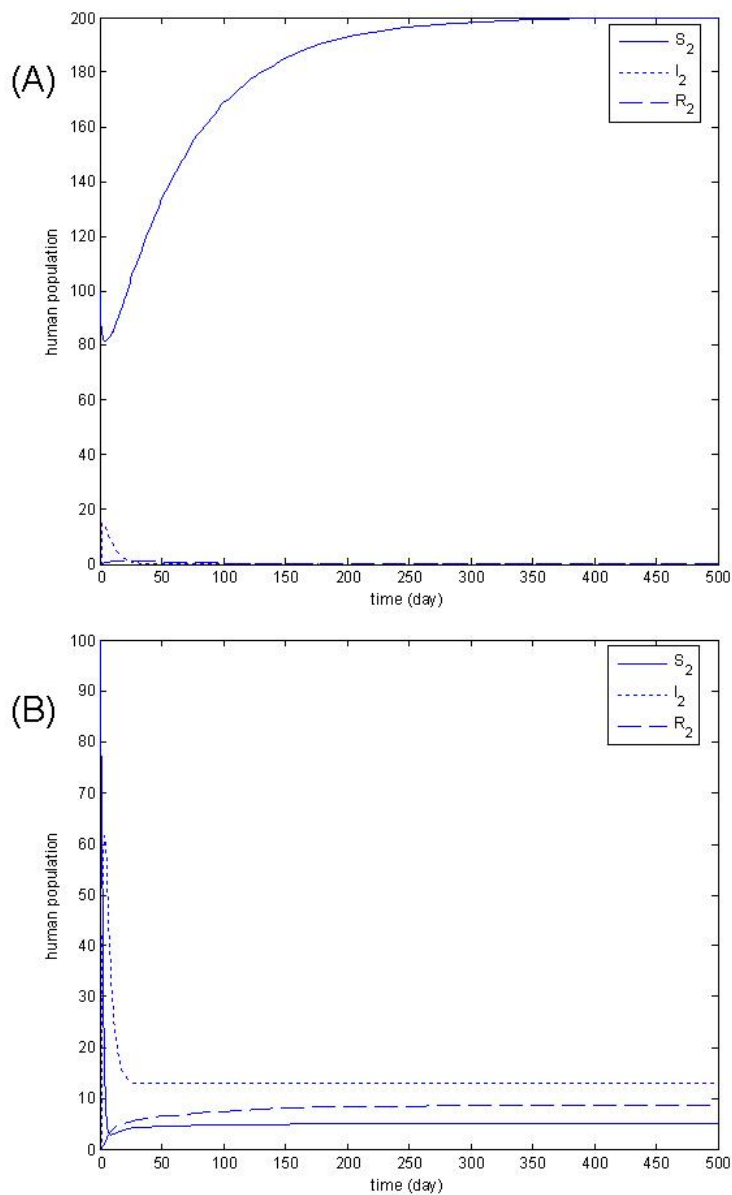


Figure 3.2: Numerical results for the human SIR system with initial values of  $(S_2, I_2, R_2) = (100, 0, 0)$  when  $\beta_1 = 9.6$  ( $R_0^{[1]} = 0.96 < 1$ ) up to day 500. Figure (A):  $\beta_3 = 0.1$  ( $R_0^{[2]} = 0.4444 < 1$ ). Figure (B):  $\beta_3 = 1.2$  ( $R_0^{[2]} = 5.3333 > 1$ ).

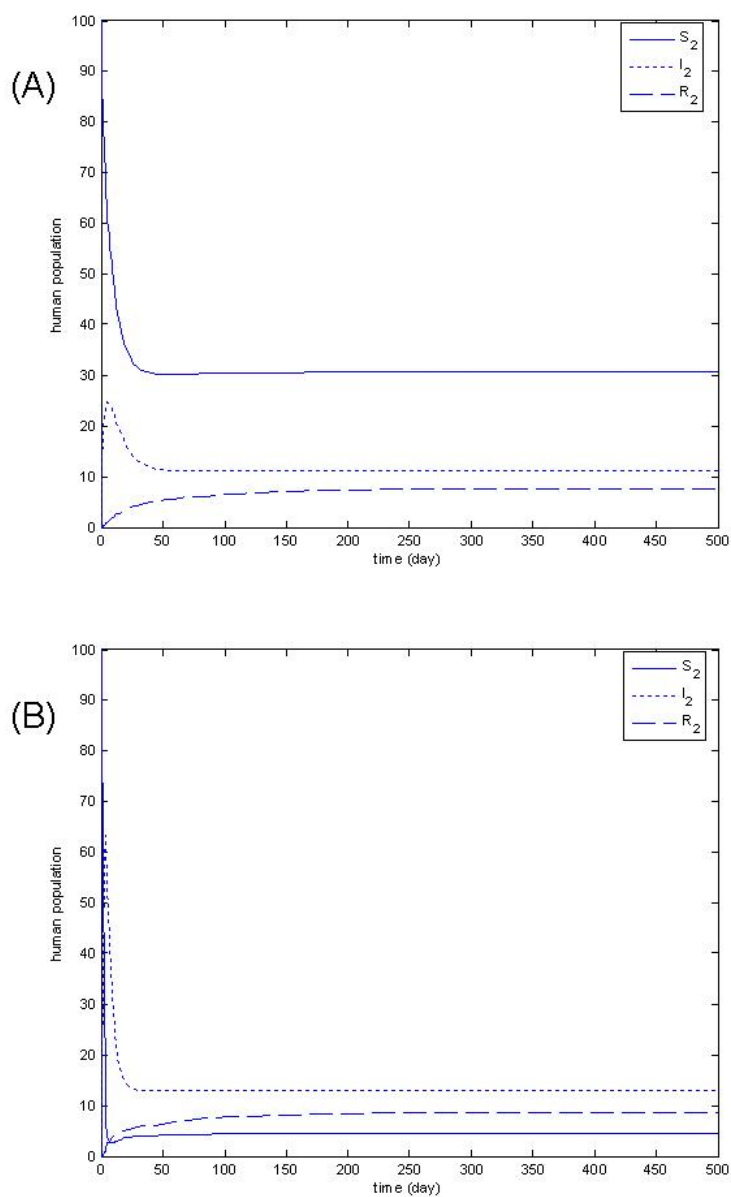


Figure 3.3: Numerical results for the human SIR system with initial values of  $(S_2, I_2, R_2) = (100, 0, 0)$  for  $\beta_1 = 10.6$  ( $R_0^{[1]} = 10.6 > 1$ ) up to day 500. In Figure (A):  $\beta_3 = 0.1$  ( $R_0^{[2]} = 0.4444 < 1$ ). Figure (B):  $\beta_3 = 1.2$  ( $R_0^{[2]} = 5.3333 > 1$ ).

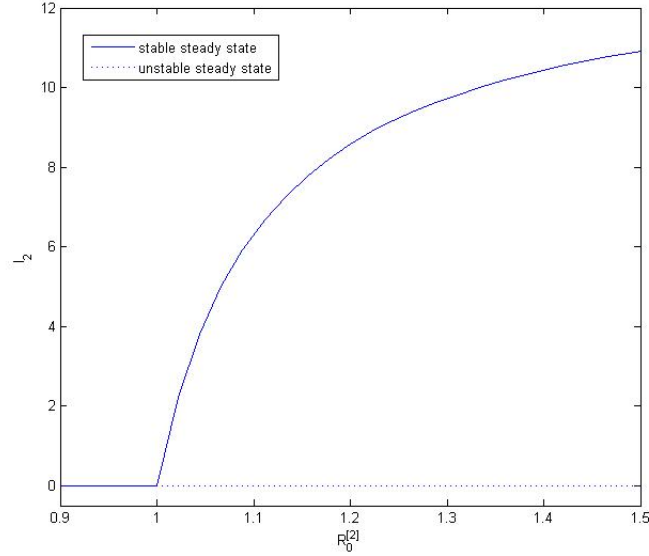


Figure 3.4: Bifurcation diagram of the bird system.

## 3.2 The SIMR human model

In this SIMR human model where  $\epsilon$  does not go to infinity, we use  $S_2$ ,  $I_2$ ,  $M_2$  and  $R_2$  to represent human susceptible, human infected with HPAI, human infected with mutated HPAI and human removed, respectively. Consider the relationship diagram for humans (Figure 3.5) with the definition of variables in Table 3.3.

The model equations of the human 4-D system are:

$$\frac{dS_2}{dt} = \Lambda_2 - \mu_2 S_2 - \beta_2 S_2 \frac{I_1}{N_1} - \beta_3 S_2 \frac{M_2}{N_2} \quad (3.27)$$

$$\frac{dI_2}{dt} = \beta_2 S_2 \frac{I_1}{N_1} - (\mu_2 + \alpha_2 + \gamma_2 + \epsilon) I_2 \quad (3.28)$$

$$\frac{dM_2}{dt} = \beta_3 S_2 \frac{M_2}{N_2} + \epsilon I_2 - (\mu_2 + \alpha_3 + \gamma_3) M_2 \quad (3.29)$$

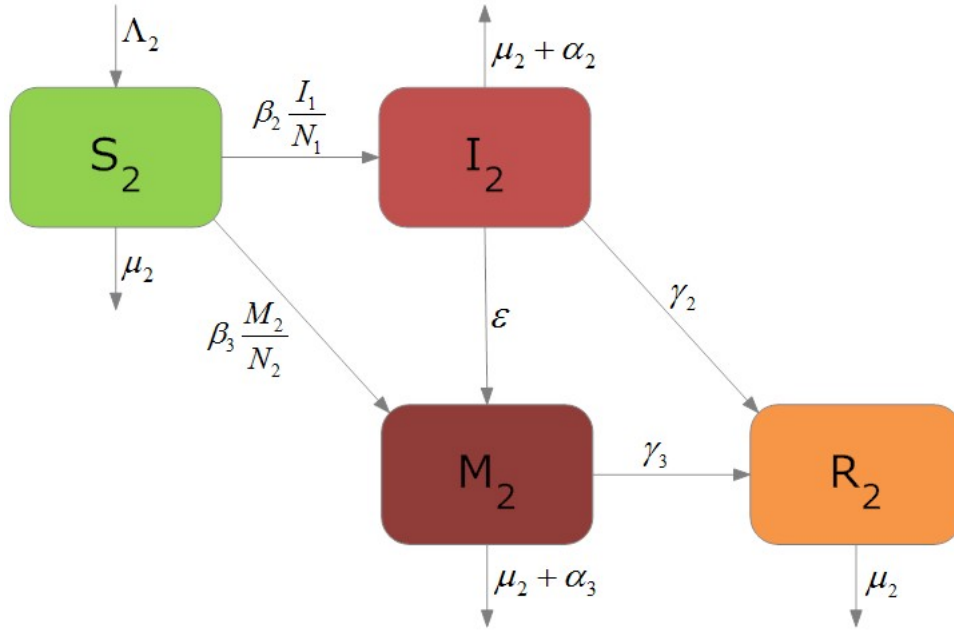


Figure 3.5: At each time step, avian influenza inside the human body mutate, become the mutated avian influenza at a constant rate  $\epsilon$ .

$$\frac{dR_2}{dt} = \gamma_2 I_2 + \gamma_3 M_2 - \mu_2 R_2. \quad (3.30)$$

The total population of humans ( $N_2$ ) is

$$N_2 = S_2 + I_2 + M_2 + R_2. \quad (3.31)$$

There is a bird-human model with the presence of (mutated) HPAI in [4]. Similar to the bird model in that paper, the human to human model is also an alternative version of the “SIR” epidemic. However, it does not reflect the situation when the human population is large as the transmission term depends on the number infected rather than the proportion infected. For example, in a crowded population, even if the population size doubles, an individual human will always contact other individuals at a constant number. Hence, our model is more suited when the human population is big.

Parameters	Units	Definition
$t$	day	Time
$N_2$	people	Total population
$S_2$	people	Number of susceptible
$I_2$	people	Number of infected by avian influenza
$M_2$	people	Number of infected by mutated avian influenza
$R_2$	people	Number of removed
$\Lambda_2$	$\text{day}^{-1}$	Natural birth rate
$\mu_2$	$\text{day}^{-1}$	Natural death rate
$\beta_2$	$\text{day}^{-1}$	Transmission coefficient from bird to human
$\beta_3$	$\text{day}^{-1}$	Transmission coefficient from human to human
$\alpha_2$	$\text{day}^{-1}$	Additional death rate caused by the avian influenza
$\alpha_3$	$\text{day}^{-1}$	Additional death rate caused by the mutated avian influenza
$\gamma_2$	$\text{day}^{-1}$	Recovery rate from avian influenza
$\gamma_3$	$\text{day}^{-1}$	Recovery rate from mutated avian influenza
$\epsilon$	$\text{day}^{-1}$	Mutation rate
$R_0^{[2]}$		Basic reproduction number

Table 3.3: Definition of model parameters in the 4-D human system

Also, in [4], there is no recovery rate for infected humans of HPAI. In contrast, our model has two recovery rates for humans infected with HPAI and mutated HPAI ( $\gamma_2$  and  $\gamma_3$ ).

### 3.2.1 Steady States

Let  $hms$  and  $fms$  represent the steady states of the SIMR human and the full bird-human 6-D systems, respectively. The steady states of the SIMR human system ( $hms$ ) are derived from Equation (3.1)-(3.3) fixed by the steady state values in the bird system ( $bs_1$  and  $bs_2$ ).

#### Steady States $fms_1$ and $fms_2$

Steady States  $fms_1$  and  $fms_2$  are combinations of the steady state of the bird system  $bs_1$  and the steady states of the human system  $hms_1$  and  $hms_2$  derived with fixed value of  $bs_1$ . At  $bs_1$ , where  $I_1^{bs_1} = 0$ , from Equation 3.28, we have

$$I_2^{fms_1} = I_2^{fms_2} = 0. \quad (3.32)$$

Hence,  $S_2$  and  $R_2$  can be rewritten in terms of  $M_2$  and the steady state of the full system is:

$$fms = \begin{pmatrix} S_1^{bs} \\ I_1^{bs} \\ S_2^{hms} \\ I_2^{hms} \\ M_2^{hms} \\ R_2^{hms} \end{pmatrix} = \begin{pmatrix} S_1^{bs} \\ I_1^{bs} \\ \frac{\Lambda_2 - (\mu_2 + \alpha_3 + \gamma_3)M_2^{hms}}{\mu_2} \\ 0 \\ M_2^{hms} \\ \frac{\gamma_3 M_2^{hms}}{\mu_2} \end{pmatrix}, \quad (3.33)$$

where  $N_2^{hms} = \frac{\Lambda_2 - \alpha_3 M_2^{hms}}{\mu_2}$ . Substitute the steady state values into Equation (3.28) and simplify it to be a quadratic equation in  $M_2^{hms}$  (or substitute into

Equation (3.27) to get a similar quadratic):

$$f(M_2^{hms}) = a(M_2^{hms})^2 + bM_2^{hms} = 0, \quad (3.34)$$

where

$$\begin{aligned} a &= \frac{\mu_2 + \alpha_3 + \gamma_3}{\mu_2} (\alpha_3 - \beta_3), \\ b &= \frac{\Lambda_2}{\mu_2} (\beta_3 - \mu_2 - \alpha_3 - \gamma_3). \end{aligned}$$

Hence, Equation 3.34 has two roots

$$\begin{aligned} M_2^{hms_1} &= 0, \\ M_2^{hms_2} &= \frac{\Lambda_2(\beta_3 - \mu_2 - \alpha_3 - \gamma_3)}{(\mu_2 + \alpha_3 + \gamma_2)(\beta_3 - \alpha_3)}. \end{aligned}$$

Hence, steady state values of  $S_2$  and  $R_2$  can be derived from them. The first steady state of the full system is

$$fms_1 = \begin{pmatrix} S_1^{bs_1} \\ I_1^{bs_1} \\ S_2^{hms_1} \\ I_2^{hms_1} \\ M_2^{hms_1} \\ R_2^{hms_1} \end{pmatrix} = \begin{pmatrix} \frac{\Lambda_1}{\mu_1} \\ 0 \\ \frac{\Lambda_2}{\mu_2} \\ 0 \\ 0 \\ 0 \end{pmatrix} \quad (3.35)$$

where  $N_2 = \frac{\Lambda_2}{\mu_2}$ . It represents the state where there is no infection of HPAI in both birds and humans.

The second steady state is

$$fms_2 = \begin{pmatrix} S_1^{bs_1} \\ I_1^{bs_1} \\ S_2^{hms_2} \\ I_2^{hms_2} \\ M_2^{hms_2} \\ R_2^{hms_2} \end{pmatrix} = \begin{pmatrix} \frac{\Lambda_1}{\mu_1} \\ 0 \\ \frac{\Lambda_2(\mu_2 + \gamma_3)}{\mu_2(\beta_3 - \alpha_3)} \\ 0 \\ \frac{\Lambda_2(\beta_3 - \mu_2 - \alpha_3 - \gamma_3)}{(\beta_3 - \alpha_3)(\mu_2 + \alpha_3 + \gamma_3)} \\ \frac{\gamma_3 \Lambda_2(\beta_3 - \mu_2 - \alpha_3 - \gamma_3)}{\mu_2(\beta_3 - \alpha_3)(\mu_2 + \alpha_3 + \gamma_3)} \end{pmatrix} \quad (3.36)$$

where  $N_2 = \frac{\beta_3 \Lambda_2 (\mu_2 + \gamma_3)}{\mu_2 (\beta_3 - \alpha_3) (\mu_2 + \alpha_3 + \gamma_3)}$ . It represents the state where there is no infection of HPAI in birds but infections of mutated HPAI exist in humans.

Steady state  $fms_1$  exists for all  $R_0^{[1]}$  and  $R_0^{[3]}$  values and steady state  $fms_2$  exists for all  $R_0^{[1]}$  values and  $\beta_3 - \mu_2 - \alpha_3 - \gamma_3 > 0$ .

### Steady State $fms_3$

Steady State  $fms_3$  is a combination of steady states of the bird system ( $bs_2$ ) and the human system ( $hms_3$ ) derived with fixed value of  $bs_2$ . As  $I_1^{bs_2} \neq 0$ , from Equation 3.28,  $S_2^{fms_3}$  can be expressed in terms of  $I_2^{fms_3}$

$$S_2^{fms_3} = x I_2^{fms_3}, \quad (3.37)$$

where

$$x = \frac{\mu_2 + \alpha_2 + \gamma_2 + \epsilon N_1^{bs_2}}{\beta_2 I_1^{bs_2}}. \quad (3.38)$$

Hence, the steady state of the full system  $fms_3$  becomes

$$fms_3 = \begin{pmatrix} S_1^{bs_2} \\ I_1^{bs_2} \\ S_2^{hms_3} \\ I_2^{hms_3} \\ M_2^{hms_3} \\ R_2^{hms_3} \end{pmatrix} = \begin{pmatrix} S_1^{bs_2} \\ I_1^{bs_2} \\ xI_2^{hms_3} \\ I_2^{hms_3} \\ \frac{\Lambda_2 - (\mu_2(x+1) + \alpha_2 + \gamma_2)I_2^{hms_3}}{\mu_2 + \alpha_3 + \gamma_3} \\ \frac{\alpha_3\Lambda_2 + (\alpha_2(\mu_2 + \gamma_3) - \alpha_3(\mu_2(x+1) + \gamma_2))I_2^{hms_3}}{\mu_2(\mu_2 + \alpha_3 + \gamma_3)} \end{pmatrix}, \quad (3.39)$$

with  $N_2 = \frac{\Lambda_2(\mu_2 + \gamma_3)}{\mu_2(\mu_2 + \alpha_3 + \gamma_3)} - \frac{\alpha_2(\mu_2 + \gamma_3) - \alpha_3(\mu_2(x+1) + \gamma_2)}{\mu_2(\mu_2 + \alpha_3 + \gamma_3)} I_2^{hms_3}$ . Substitute the steady state value into Equation 3.29 (or Equation 3.27 for similar result),  $I_2^{hms_3}$  is determined from a quadratic:

$$f(I_2^{hms_3}) = a(I_2^{hms_3})^2 + bI_2^{hms_3} + c = 0 \quad (3.40)$$

with

$$\begin{aligned} a &= \frac{-1}{\mu_2(\mu_2 + \alpha_3 + \gamma_3)} (\mu_2\beta_3x(\mu_2(x+1) + \alpha_2 + \gamma_2) + (\mu_2(x+1) + \alpha_2 + \gamma_2 + \epsilon) \\ &\quad \times (\alpha_2(\mu_2 + \gamma_3) - \alpha_3(\mu_2(x+1) + \gamma_2))), \\ b &= \frac{\Lambda_2}{\mu_2(\mu_2 + \alpha_3 + \gamma_3)} (\mu_2\beta_3x + \epsilon(\mu_2 + \gamma_3) + \alpha_2(\mu_2 + \gamma_3) - \alpha_3(\mu_2(x+1) + \gamma_2) \\ &\quad + (\mu_2 + \gamma_3)(\mu_2(x+1) + \alpha_2 + \gamma_2)), \\ c &= -\frac{\Lambda_2^2(\mu_2 + \gamma_3)}{\mu_2(\mu_2 + \alpha_3 + \gamma_3)}. \end{aligned}$$

Also,

$$\begin{aligned} b^2 - 4ac &= \frac{\Lambda_2^2}{\mu_2^2(\mu_2 + \alpha_3 + \gamma_3)^2} ((\mu_2\beta_3x + \epsilon(\mu_2 + \gamma_3) + \alpha_2(\mu_2 + \gamma_3) \\ &\quad - \alpha_3(\mu_2(x+1) + \gamma_2) + (\mu_2 + \gamma_3)(\mu_2(x+1) + \alpha_2 + \gamma_2))^2 \\ &\quad - 4(\mu_2\beta_3x(\mu_2(x+1) + \alpha_2 + \gamma_2) + (\mu_2(x+1) + \alpha_2 + \gamma_2 + \epsilon) \\ &\quad \times (\alpha_2(\mu_2 + \gamma_3) - \alpha_3(\mu_2(x+1) + \gamma_2)))(\mu_2 + \gamma_3)) \\ &= \frac{\Lambda_2^2}{\mu_2^2(\mu_2 + \alpha_3 + \gamma_3)^2} ((\mu_2\beta_3x - \alpha_2(\mu_2 + \gamma_3) \\ &\quad + \alpha_3(\mu_2(x+1) + \gamma_2) + (\mu_2 + \gamma_3)(\mu_2(x+1) + \alpha_2 + \gamma_2 + \epsilon))^2) \end{aligned}$$

Hence, the roots of Equation 3.40 are real. Similar to the SIR human system, the roots of Equation 3.40 have two cases depending on the value of parameters:

Case (1):

$$\mu\beta_3x(\mu_2(x+1)+\alpha_2+\gamma_2)+(\mu_2(x+1)+\alpha_2+\gamma_2+\epsilon)(\alpha_2(\mu_2+\gamma_3)-\alpha_3(\mu_2(x+1)+\gamma_2)) < 0 \quad (3.41)$$

Case (2):

$$\mu\beta_3x(\mu_2(x+1)+\alpha_2+\gamma_2)+(\mu_2(x+1)+\alpha_2+\gamma_2+\epsilon)(\alpha_2(\mu_2+\gamma_3)-\alpha_3(\mu_2(x+1)+\gamma_2)) > 0 \quad (3.42)$$

Under the condition of Case (1),  $a > 0$ . As  $f(0) = c < 0$ , then Equation 3.40 has one positive and one negative root (which we ignore).

Under the condition of Case (2),  $a < 0$  and  $b > 0$ . Equation 3.40 has two positive roots.

However, by substituting parameter values, we can find that under the condition of Case (1), there are two positive roots of  $M_2^{hms_3}$  and under the condition of Case (2), it has one positive and one negative root of  $M_2^{hms_3}$ . Hence, overall, only one steady state  $fms_3$  exists under  $bs_2$  and it is unique.  $fms_3$  represents the state where infection of (mutated) HPAI is present in the bird system and infection of both AI and mutated AI in the human system.

### 3.2.2 Basic reproduction number

The basic reproduction number for the human SIMR system,  $R_0^{[3]}$ , is defined as the number of humans that are infected by a typical infected human with the mutated virus when all humans are susceptible. The rate at which one infected human infects susceptible humans is  $\frac{\beta_3}{N_2} S_2$ , where  $S_2 = N_2$  if all humans are susceptible. Since the life-time of an infected human is  $\frac{1}{\mu_2 + \alpha_3 + \gamma_3}$ , we have

$$R_0^{[3]} = \frac{\beta_3}{\mu_2 + \alpha_3 + \gamma_3}. \quad (3.43)$$

Recall one of the conditions of existence of  $fms_2$ ,  $\beta_3 - \mu_2 - \alpha_3 - \gamma_3 > 0$  is equivalent to  $R_0^{[3]} > 1$ , thus  $fms_2$  exists for all values of  $R_0^{[1]}$  and for  $R_0^{[3]} > 1$ .

### 3.2.3 Local Stability

Refer to section 3.1.3, we need to determined the stability of each steady state of the human SIMR system. The Jacobian matrix for the human SIMR system is:

$$J_{hm} = \begin{pmatrix} -\mu_2 - \beta_2 \frac{I_1}{N_1} - \beta_3 i & \beta_3 j & -\beta_3 k & \beta_3 j \\ \beta_2 \frac{I_1}{N_1} & -\mu_2 - \alpha_2 - \gamma_2 - \epsilon & 0 & 0 \\ \beta_3 i & -\beta_3 j + \epsilon & \beta_3 k - \mu_2 - \alpha_3 - \gamma_3 & -\beta_3 j \\ 0 & \gamma_2 & \gamma_3 & -\mu_2 \end{pmatrix}, \quad (3.44)$$

where

$$i = \frac{M_2(I_2 + M_2 + R_2)}{N_2^2},$$

$$\begin{aligned}
 j &= \frac{S_2 M_2}{N_2^2}, \\
 k &= \frac{S_2(S_2 + I_2 + R_2)}{N_2^2}.
 \end{aligned}$$

Terms  $i$ ,  $j$  and  $k$  are non-negative.

### Steady state of $hms_1$

At  $hms_1$ , where  $I_1^{hms_2} = 0$  and  $M_1^{hms_2} = 0$ ,

$$i = 0,$$

$$j = 0,$$

$$k = 1.$$

hence the Jacobian matrix becomes

$$J_{hms_1} = \begin{pmatrix} -\mu_2 & 0 & -\beta_3 & 0 \\ 0 & -\mu_2 - \alpha_2 - \gamma_2 - \epsilon & 0 & 0 \\ 0 & \epsilon & \beta_3 - \mu_2 - \alpha_3 - \gamma_3 & 0 \\ 0 & \gamma_2 & \gamma_3 & -\mu_2 \end{pmatrix}. \quad (3.45)$$

The eigenvalues are  $-\mu_2$ ,  $-\mu_2 - \alpha_2 - \gamma_2 - \epsilon$ ,  $\beta_3 - \mu_2 - \alpha_3 - \gamma_3$  and  $-\mu_2$ . They are all negative when  $R_0^{[3]} < 1$ . Therefore,  $hms_1$  is a locally stable steady state when  $R_0^{[3]} < 1$ .

**Steady state of  $hms_2$** 

At  $hms_2$ , where  $I_2^{hms_2} = 0$  and  $M_1^{hms_2} \neq 0$ , the Jacobian matrix becomes

$$J_{hms_2} = \begin{pmatrix} -\mu_2 - \beta_3 i & \beta_3 j & -\beta_3 k & \beta_3 j \\ 0 & -\mu_2 - \alpha_2 - \gamma_2 - \epsilon & 0 & 0 \\ \beta_3 i & -\beta_3 j + \epsilon & \beta_3 k - \mu_2 - \alpha_3 - \gamma_3 & -\beta_3 j \\ 0 & \gamma_2 & \gamma_3 & -\mu_2 \end{pmatrix}, \quad (3.46)$$

where  $i$ ,  $j$  and  $k$  are determined at  $hms_2$ . Let  $A = \mu_2 + \beta_3 i$ ,  $B = \beta_3 j$ ... etc.

Hence the Jacobian matrix becomes

$$J_{hms_2} = \begin{pmatrix} -A & B & -C & B \\ 0 & -D & 0 & 0 \\ E & F & -G & -B \\ 0 & H & I & -J \end{pmatrix}. \quad (3.47)$$

The stability of  $hms_2$  is determined from the characteristic equation

$$g(\lambda) = (a_0 + \lambda)(\lambda^3 + a_1 \lambda^2 + a_2 \lambda + a_3), \quad (3.48)$$

where

$$\begin{aligned} a_0 &= D, \\ a_1 &= A + G + J, \\ a_2 &= AG + AJ + GJ + BI + CE, \\ a_3 &= AGJ + BI(A - E). \end{aligned}$$

Also,

$$\begin{aligned} a_0 a_1 - a_2 &= (A + G + J)(AG + AJ + GJ + BI + CE) - (AGJ + ABI - BEI) \\ &= A(AG + AJ + CE) + (G + J)(AG + AJ + GJ + BI + CE) + BEI. \end{aligned}$$

At  $hms_2$ , Equation 3.29 can be developed into

$$\beta_3 \frac{S_2}{N_2} - \mu_2 - \alpha_3 - \gamma_3 < 0, \quad (3.49)$$

which leads to

$$\beta_3 j - \mu_2 - \alpha_3 - \gamma_3 < 0. \quad (3.50)$$

Thus,  $a_1$ ,  $a_2$ ,  $a_3$  and  $a_0 a_1 - a_2$  are positive. According to the Routh-Hurwitz criteria [8], steady state  $hms_2$  is locally stable when it exists.

### Steady state of $hms_3$

We have not been able to derive the stability criteria for  $hms_3$  in general. However, when we substitute parameter values into  $J_{hms_3}$ , we find that that all four eigenvalues derived are either negative or have negative real parts. Thus, we conjecture that  $hms_3$  is locally stable when it exists.

### 3.2.4 Summary

To sum up, there are three steady states in the bird-human 6-D (mutated) HPAI model, which exist under different conditions.

Steady state  $hms_1$  represents the state where infection of (mutated) HPAI is absent in the human system. Steady state  $hms_1$  exists for all values of  $R_0^{[3]}$  and it is only stable when  $R_0^{[3]}$  is less than 1. Hence, combine this with the stability of  $bs_1$ , we can conclude that the steady state of the full bird-human system  $fms_1$ , which represents the state where infection of (mutated) HPAI

is absent in birds and humans, exists for all values of  $R_0^{[1]}$  and  $R_0^{[3]}$ , but it is only stable when  $R_0^{[1]}$  and  $R_0^{[3]}$  are both under the threshold 1.

Steady state  $hms_2$  represents the state where infections of mutated HPAI are present in humans.  $hms_2$  exists when  $R_0^{[3]}$  is greater than 1 and it is stable when it exists. Hence, combine this with the stability of  $bs_1$ , we can conclude that the steady state of the full bird-human system  $fms_2$ , which represents the state where there is no infection of HPAI in birds, but infections of mutated HPAI are present in humans, exists for all values of  $R_0^{[1]}$  and when  $R_0^{[3]}$  is greater than 1. It is stable when  $R_0^{[1]}$  is less than 1 and  $R_0^{[3]}$  is greater than 1.

Steady state  $hms_3$  represents the state where infection of (mutated) HPAI is present in the humans system. It exists when  $R_0^{[1]} > 1$  and it is stable when it exists. Hence, combine this with the stability of  $bs_2$ , we can conclude that the steady state of the full bird-human system  $fms_3$ , which represents the state where infections of (mutated) HPAI are present in both birds and humans, exists when  $R_0^{[1]}$  is greater than 1 and it is stable when it exists.

### 3.2.5 Numerical Results

Choose different values of  $\beta_1$  (9.6/10.6 day<sup>-1</sup>) and  $\beta_3$  ( $\frac{1}{18}/\frac{2}{3}$  day<sup>-1</sup>) in order to adjust  $R_0^{[1]}$  and  $R_0^{[3]}$  to be less and greater than the threshold 1. Parameter values for birds and humans are shown in Table 2.2 and Table 3.2. Other parameters value and the analytic steady states values calculated from them are shown in Table 3.4.

	Value		$\beta_1 = 9.6$		$\beta_1 = 10.6$	
$\alpha_3$	$0.06 \text{ day}^{-1}$		$\beta_3 = \frac{1}{18}$	$\beta_3 = \frac{2}{3}$	$\beta_3 = \frac{1}{18}$	$\beta_3 = \frac{2}{3}$
$\gamma_3$	$0.05 \text{ day}^{-1}$	$S_2$	200	21.4286	39.9379	16.0142
$\epsilon$	$0.001 \text{ day}^{-1}$	$I_2$	0	0	10.6030	4.2515
		$M_2$	0	21.4286	0.1221	14.4255
		$R_2$	0	71.4286	7.4757	50.9194
		$N_2$	200	114.2857	58.1386	85.6107
		$R_0^{[3]}$	0.4444	5.3333	0.4444	5.3333

Table 3.4: Parameter values and analytic steady state values of the SIMR human systems. Values referenced to [4].

Use Matlab “ode15s” to solve for steady states. The results are shown in Figure 3.6 and 3.7.

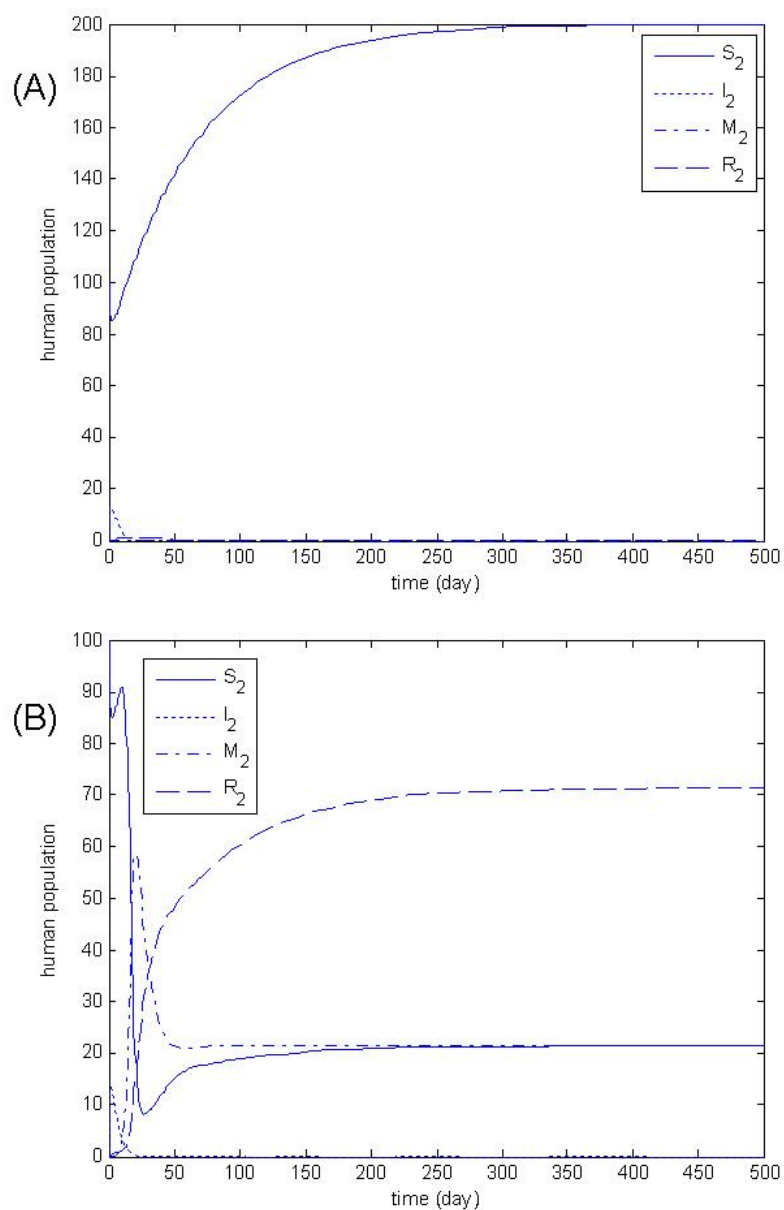


Figure 3.6: Numerical results for the human SIMR system with initial values of  $(S_2, I_2, M_2, R_2) = (100, 0, 0, 0)$  when  $\beta_1 = 9.6$  ( $R_0^{[1]} = 0.96 < 1$ ) up to day 500. Figure (A):  $\beta_3 = \frac{1}{18}$  ( $R_0^{[3]} = 0.4444$ ). Figure (B):  $\beta_3 = \frac{2}{3}$  ( $R_0^{[3]} = 5.3333$ ).

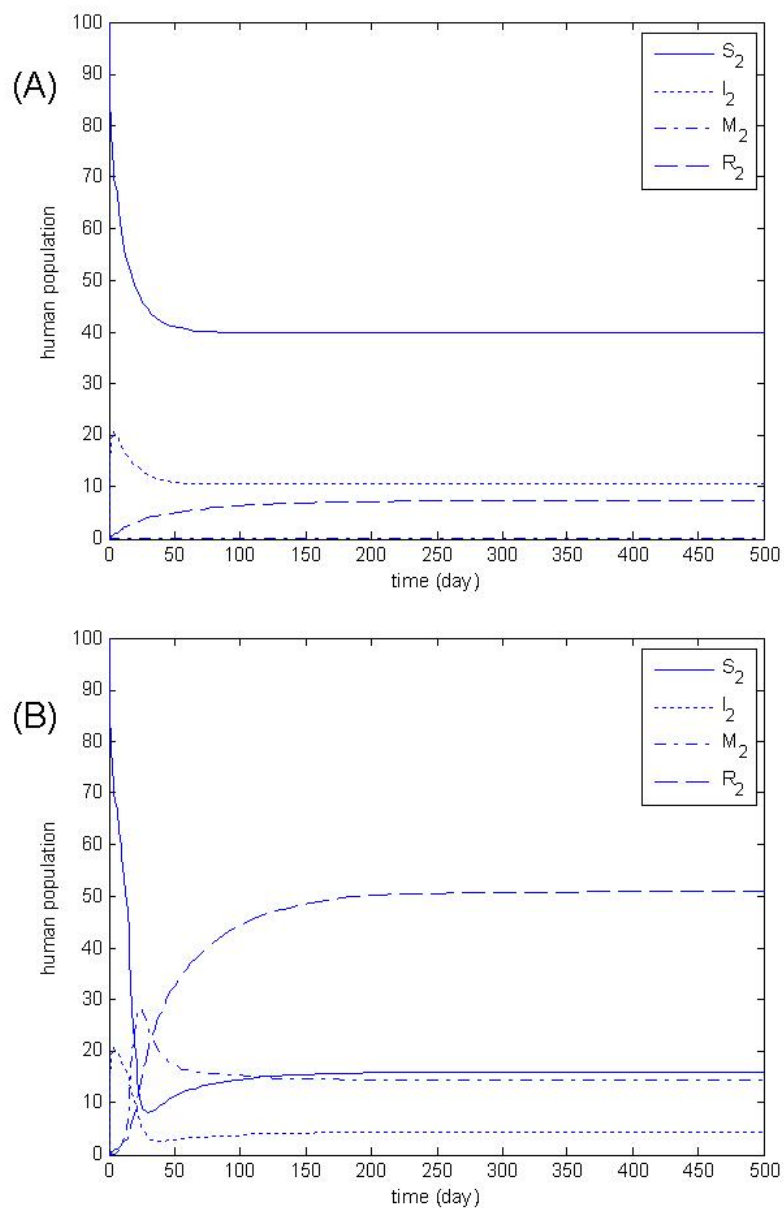


Figure 3.7: Numerical results for the human SIMR system with initial values of  $(S_2, I_2, M_2, R_2) = (100, 0, 0, 0)$  for  $\beta_1 = 10.6$  ( $R_0^{[1]} = 1.06 > 1$ ) up to day 500. Figure (A):  $\beta_3 = \frac{1}{18}$  ( $R_0^{[3]} = 0.4444 < 1$ ). Figure (B):  $\beta_3 = \frac{2}{3}$  ( $R_0^{[3]} = 5.3333 > 1$ ).

In Figure 3.6 (A) when  $\beta_1 = 9.6$  and  $\beta_3 = \frac{1}{18}$  ( $R_0^{[1]} < 1$  and  $R_0^{[3]} < 1$ ), the system approaches  $(S_2, I_2, M_2, R_2) = (200, 0, 0, 0)$  which is the infection free steady state for the human system. In Figure 3.6 (B) when when  $\beta_1 = 9.6$  and  $\beta_3 = \frac{2}{3}$  ( $R_0^{[1]} < 1$  and  $R_0^{[3]} > 1$ ), the system approaches  $(S_2, I_2, M_2, R_2) = (21.43, 0, 21.43, 71.41)$  where only the infection of mutated HPAI is present in the human system.

In Figure 3.7 (A) where  $\beta_1 = 10.6$  ( $R_0^{[1]} > 1$ ) and  $\beta_3 = \frac{1}{18}$  ( $R_0^{[3]} < 1$ ), the system approaches  $(S_2, I_2, M_2, R_2) = (39.94, 10.6, 0.1221, 7.473)$ . Notice that the number of infected humans with mutated HPAI is 0.1221, which is less than 1. As we mentioned earlier (section 1.2), it presents the mean population in a given area. Since  $R_0^{[3]}$  is less than 1, most of the humans infected with mutated HPAI comes from the mutation for HPAI. When  $R_0^{[3]} < 1$ , by the definition of the basic reproduction number, there should be no infection of mutated HPAI in the human system, thus, the small number of infected humans comes from the mutation of the HPAI viruses. In Figure 3.7 (B) where  $\beta_1 = 10.6$  ( $R_0^{[1]} > 1$ ) and  $\beta_3 = \frac{2}{3}$  ( $R_0^{[3]} > 1$ ), the system approaches  $(S_2, I_2, M_2, R_2) = (16.01, 4.251, 14.43, 50.92)$  where the infection of (mutated) HPAI is present in both birds and humans. We can conclude that the numerical results are consistent with the analytic results.

### 3.2.6 Bifurcation

Similar to the SIR human model, there is a transcritical bifurcation in the human system while  $R_0^{[3]}$  increases through the threshold 1 when  $R_0^{[1]}$  is less than 1. When  $R_0^{[1]}$  and  $R_0^{[3]}$  are both less than 1, there is only one stable

steady state (infection free) exists and when  $R_0^{[1]}$  is less than 1 but  $R_0^{[3]}$  is greater than 1, another stable steady state appears and the infection free steady state become unstable. The bifurcation diagram is shown in Figure 3.8.

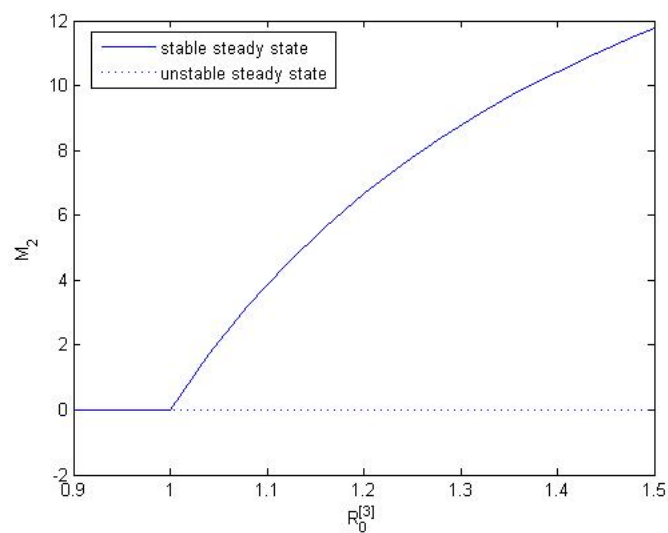


Figure 3.8: Bifurcation diagram of the human SIMR system.



# Chapter 4

## Vaccination

Vaccination against HPAI may not be efficient as the HPAI virus has a high mutation rate. In fact, vaccination is normally not very effective against influenza. However, as we described in the introduction, vaccination is perhaps the most commonly used, effective and cost-effective control measure to prevent contagious diseases. Hence, in this section, we introduce vaccination of humans into the Human (mutated) HPAI system (SIR and SIMR) and keep the bird system unchanged. Note that it is not usual for new borns to be vaccinated against flu. Both the SIR and the SIMR human (mutated) HPAI system with vaccination are combined with the bird HPAI system (Equation (2.1) and (2.2)), hence we have one 5-D and one 6-D bird-human (mutated) HPAI system with vaccination. The steady states of the full bird-human systems with vaccination are combinations of steady states in both the bird and the human systems.

There are two situations of vaccination in the human system: vaccination of immigrants and vaccination of susceptibles. We use BHVI and BHMVI to represent the 5-D and 6-D bird-human models with vaccination of immigrants, and BHVS and BHMVS to represent the 5-D and 6-D bird-human models with vaccination of susceptibles.

## 4.1 Vaccination of immigrants BHVI

In this section, we assume the population classes (susceptible, infected and removed) describe the local population in a city or a country, and the birth rate is taken to mean when a person enters that population. A proportion  $v$  of the immigrant population is vaccinated against either HPAI or mutated HPAI and becomes immune (entering the removed class). Only  $1 - v$  of the immigrant population are susceptible to the viruses. The model of the human part can be expressed as

$$\frac{dS_2}{dt} = \Lambda_2(1 - v) - \mu_2 S_2 - \beta_2 S_2 \frac{I_1}{N_1} - \beta_3 S_2 \frac{I_2}{N_2} \quad (4.1)$$

$$\frac{dI_2}{dt} = \beta_2 S_2 \frac{I_1}{N_1} + \beta_3 S_2 \frac{I_2}{N_2} - (\mu_2 + \alpha_2 + \gamma_2) I_2 \quad (4.2)$$

$$\frac{dR_2}{dt} = v\Lambda_2 + \gamma_2 I_2 - \mu_2 R_2, \quad (4.3)$$

where  $N_2 = S_2 + I_2 + R_2$  and other variables and parameters are the same as in section 3.1. We refer to this as the BHVI system.

### 4.1.1 Steady States

We use  $vihs$  and  $vifs$  to represent the steady state of the human part of the BHVI system and the full BHVI system, respectively.  $vifs$  is derived from Equations (4.1)-(4.3) fixed by the steady state values in the bird system ( $bs_1$  and  $bs_2$ ). At  $vifs$ ,  $S_2^{vihs}$  and  $R_2^{vihs}$  can be rewritten in terms of  $I_2^{vihs}$  and hence the steady state of the full system is

$$vifs = \begin{pmatrix} S_1^{bs} \\ I_1^{bs} \\ S_2^{vihs} \\ I_2^{vihs} \\ R_2^{vihs} \end{pmatrix} = \begin{pmatrix} S_1^{bs} \\ I_1^{bs} \\ \frac{\Lambda_2(1-v) - (\mu_2 + \alpha_2 + \gamma_2)I_2^{vihs}}{\mu_2} \\ I_2^{vihs} \\ \frac{v\Lambda_2 + \gamma_2 I_2^{vihs}}{\mu_2} \end{pmatrix}, \quad (4.4)$$

where  $N_2^{vihs} = \frac{\Lambda_2 - \alpha_2 I_2^{vihs}}{\mu_2}$  for different steady state values of the bird system. Substitute the steady state values into Equation (4.2) and simplify it to obtain a quadratic equation of  $I_2^{vihs}$  (or substitute into Equation (4.1) to get a similar quadratic) as:

$$f(I_2^{vihs}) = a(I_2^{vihs})^2 + bI_2^{vihs} + c = 0, \quad (4.5)$$

where

$$\begin{aligned} a &= \frac{\mu_2 + \alpha_2 + \gamma_2}{\mu_2} \left( \beta_2 \frac{\alpha_2}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} + \alpha_2 - \beta_3 \right), \\ b &= \frac{\Lambda_2}{\mu_2} \left( \beta_3(1-v) - \mu_2 - \alpha_2 - \gamma_2 - \beta_2 \frac{\mu_2 + (2-v)\alpha_2 + \gamma_2}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} \right), \\ c &= \beta_2 \left( \frac{\Lambda_2}{\mu_2} \right)^2 \frac{I_1^{bs}}{N_1^{bs}} (1-v). \end{aligned}$$

Note  $c$  is always positive and the signs of  $a$  and  $b$  are determined by the values of parameters. Also,

$$b^2 - 4ac = \left( \frac{\Lambda_2}{\mu_2} \left( \beta_3(1-v) - \mu_2 - \alpha_2 - \gamma_2 - \beta_2 \frac{\mu_2 + (2-v)\alpha_2 + \gamma_2}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} \right) \right)^2$$

$$\begin{aligned}
& -4 \left( \frac{\mu_2 + \alpha_2 + \gamma_2}{\mu_2} \left( \beta_2 \frac{\alpha_2}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} + \alpha_2 - \beta_3 \right) \right) \left( \beta_2 \left( \frac{\Lambda_2}{\mu_2} \right)^2 \frac{I_1^{bs}}{N_1^{bs}} (1 - v) \right) \\
= & \left( \frac{\Lambda_2}{\mu_2} \right)^2 \left( (\beta_3 - \mu_2 - \alpha_2 - \gamma_2)^2 + \left( \beta_2 \frac{1}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} \right)^2 ((\mu_2 + \gamma_2)^2 \right. \\
& \left. + v\alpha_2(v\alpha_2 + 2(\mu_2 + \alpha_2 + \gamma_2))) + 2\beta_2 \frac{\mu_2 + \gamma_2 + v\alpha_2}{\mu_2} (\beta_3(1 - v) \right. \\
& \left. + \mu_2 + \alpha_2 + \gamma_2) \frac{I_1^{bs}}{N_1^{bs}} \right) > 0,
\end{aligned}$$

which shows that the roots of Equation (4.5) are real for all parameter values.

### Steady States $vifs_1$ and $vifs_2$

The steady states of the BHVI system  $vifs_1$  and  $vifs_2$  are combinations of the steady state of birds  $bs_1$  and the human part  $vihs_1$  and  $vihs_2$  derived with fixed value of  $bs_1$ . At  $bs_1$ , where  $I_1^{bs_1} = 0$ , the coefficients of the quadratic equation  $a$ ,  $b$  and  $c$  can be simplified to

$$\begin{aligned}
a &= \frac{\mu_2 + \alpha_2 + \gamma_2}{\mu_2} (\alpha_2 - \beta_3), \\
b &= \frac{\Lambda_2}{\mu_2} (\beta_3(1 - v) - \mu_2 - \alpha_2 - \gamma_2), \\
c &= 0,
\end{aligned}$$

which gives

$$\begin{aligned}
I_2^{vihs_1} &= 0 \\
I_2^{vihs_2} &= \frac{\Lambda_2(\beta_3(1 - v) - \mu_2 - \alpha_2 - \gamma_2)}{(\beta_3 - \alpha_2)(\mu_2 + \alpha_2 + \gamma_2)}.
\end{aligned}$$

Thus, the first steady state of the BHVI system is

$$vifs_1 = \begin{pmatrix} S_1^{bs_1} \\ I_1^{bs_1} \\ S_2^{vih_{s_1}} \\ I_2^{vih_{s_1}} \\ R_2^{vih_{s_1}} \end{pmatrix} = \begin{pmatrix} \frac{\Lambda_1}{\mu_1} \\ 0 \\ \frac{\Lambda_2(1-v)}{\mu_2} \\ 0 \\ \frac{\Lambda_2 v}{\mu_2} \end{pmatrix}, \quad (4.6)$$

where  $N_2^{vih_{s_1}} = \frac{\Lambda_2}{\mu_2}$ . It represents the absence of (mutated) HPAI in the BHVI system.

The second steady state is

$$vifs_2 = \begin{pmatrix} S_1^{bs_1} \\ I_1^{bs_1} \\ S_2^{vih_{s_2}} \\ I_2^{vih_{s_2}} \\ R_2^{vih_{s_2}} \end{pmatrix} = \begin{pmatrix} \frac{\Lambda_1}{\mu_1} \\ 0 \\ \frac{\Lambda_2(\mu_2 + \gamma_2 + \alpha_2 v)}{\mu_2(\beta_3 - \alpha_2)} \\ \frac{\Lambda_2(\beta_3(1-v) - \mu_2 - \alpha_2 - \gamma_2)}{(\beta_3 - \alpha_2)(\mu_2 + \alpha_2 + \gamma_2)} \\ \frac{\Lambda_2((\beta_3 - \alpha_2)(\mu_2 + \alpha_2 + \gamma_2)v + \gamma_2(\beta_3(1-v) - \mu_2 - \alpha_2 - \gamma_2))}{\mu_2(\beta_3 - \alpha_2)(\mu_2 + \alpha_2 + \gamma_2)} \end{pmatrix}, \quad (4.7)$$

where  $N_2^{vih_{s_2}} = \frac{\beta_3 \Lambda_2 (\mu_2 + \gamma_2 + \alpha_2 v)}{\mu_2 (\beta_3 - \alpha_2) (\mu_2 + \alpha_2 + \gamma_2)}$ . It represents the situation where there is no infection in birds but infections of mutated HPAI are present in humans with vaccination.

Steady state  $vifs_1$  exists for all values of  $R_0^{[1]}$ . Steady state  $vifs_2$  exists for all  $R_0^{[1]}$  values and when  $\beta_3(1-v) - \mu_2 - \alpha_2 - \gamma_2 > 0$ .

**Steady State  $vifs_3$** 

The steady state of the full BHVI system  $vifs_3$  is a combination of steady states of birds  $bs_2$  and humans  $vihs_3$  derived with a fixed value of  $bs_2$ . Similar to the original bird-human system, the roots of Equation 4.5 also have two cases depending on the value of parameters:

Case (1)

$$\beta_2 \frac{\alpha_2}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} + \alpha_2 < \beta_3 \quad (4.8)$$

Case (2)

$$\beta_2 \frac{\alpha_2}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} + \alpha_2 > \beta_3 \quad (4.9)$$

Under the condition of Case (1),  $a < 0$ . As

$$f(0) = \beta_2 \left( \frac{\Lambda_2}{\mu_2} \right)^2 \frac{I_1^{bs}}{N_1^{bs}} (1 - v) > 0, \quad (4.10)$$

Equation 4.5 has one positive root and one negative roots (which we ignore).

Under the condition of Case (2),  $a > 0$  and  $b < 0$ . As  $\sqrt{b^2 - 4ac} < |b|$ , this implies both roots of Equation 3.6 are positive.

Similar to the original human SIR system (refer to section 3.1.1 Steady State  $hs_3$ ), there are two positive values of  $S_2^{vihs_3}$  in Case (1) and one positive and one negative root of  $S_2^{vihs_3}$  in Case (2). Thus, only one steady state  $vihs_3$  exists when  $R_0^{[1]} > 1$  and it is unique. Steady state  $vifs_3$  represents the situation where infection of (mutated) HPAI is present in both the bird and the human system.

### 4.1.2 Basic reproduction number

The basic reproduction number for the human system with vaccination of immigrants,  $R_v^{[2]}$ , is defined as

$$R_v^{[2]} = \frac{\beta_3(1-v)}{\mu_2 + \alpha_2 + \gamma_2}. \quad (4.11)$$

as  $S_2 = \frac{\Lambda_2(1-v)}{\mu_2}$  in the absence of HPAI.

Hence, steady state  $vihs_1$  exists for all values of  $R_0^{[1]}$  and  $R_v^{[2]}$ . Steady state  $vihs_2$  exists for all values of  $R_0^{[1]}$  and when  $R_v^{[2]}$  is greater than 1.

Compare  $R_v^{[2]}$  with  $R_0^{[2]}$ , we have

$$R_v^{[2]} = (1-v)R_0^{[2]}. \quad (4.12)$$

The aim of vaccination is to lower the basic reproduction number  $R_v^{[2]}$  to be under the threshold 1. Thus,

$$v > 1 - \frac{1}{R_0^{[2]}} \quad (4.13)$$

so that  $R_v^{[2]} < 1$ .

### 4.1.3 Local Stability

Refer to section 3.1.3, we need to determine the stability at each steady state of the human system in BHVI. The Jacobian matrix of the human system in BHVI  $J_{vih}$  is the same in the human system of the original bird-human

system, that

$$J_{vih} = \begin{pmatrix} -\mu_2 - \beta_2 \frac{I_1}{N_1} - \beta_3 i & -\beta_3 & \beta_3 k \\ \beta_2 \frac{I_1}{N_1} + \beta_3 i & \beta_3 j - \mu_2 - \alpha_2 - \gamma_2 & -\beta_3 k \\ 0 & \gamma_2 & -\mu_2 \end{pmatrix}, \quad (4.14)$$

where

$$\begin{aligned} i &= \frac{I_2(I_2 + R_2)}{N_2^2}, \\ j &= \frac{S_2(S_2 + R_2)}{N_2^2}, \\ k &= \frac{S_2 I_2}{N_2^2}. \end{aligned}$$

Terms  $i$ ,  $j$  and  $k$  are all non-negative.

### Stability of $vihs_1$

At  $vihs_1$ , where  $I_1^{bs_1}$  and  $I_2^{vihs_1}$  are both zero,

$$\begin{aligned} i &= 0, \\ j &= 1 - v, \\ k &= 0. \end{aligned}$$

Thus,

$$J_{vihs_1} = \begin{pmatrix} -\mu_2 & -\beta_3(1 - v) & 0 \\ 0 & \beta_3(1 - v) - \mu_2 - \alpha_2 - \gamma_2 & 0 \\ 0 & \gamma_2 & -\mu_2 \end{pmatrix}, \quad (4.15)$$

and the eigenvalues are  $-\mu_2$ ,  $\beta_3(1 - v) - \mu_2 - \alpha_2 - \gamma_2$  and  $-\mu_2$ . The eigenvalues are negative if  $R_v^{[2]}$  is less than 1. Therefore,  $vihs_1$  is a locally stable steady state when  $R_v^{[2]}$  is smaller than 1.

**Stability of  $vihs_2$** 

The Jacobian matrix  $J_{vihs_2}$  is in the same form as  $J_{hs_2}$  of the SIR human system (section 3.1.3 Stability of  $hs_2$ ), except  $i$ ,  $j$  and  $k$ . Hence, two systems share the same form of the characteristic equation except  $i$ ,  $j$  and  $k$ . However, terms  $i$ ,  $j$  and  $k$  do not effect the stability of the steady state. Thus, refer to section 3.1.3 (Stability of  $hs_2$ ),  $vihs_2$  is a locally stable steady state when it exists.

**Stability of  $vihs_3$** 

Same as  $vihs_2$ , the Jacobian matrix evaluated at  $vihs_3$  ( $J_{vihs_3}$ ) is in the same form as evaluated at  $fs_3$  ( $J_{hs_3}$ ) except  $i$ ,  $j$  and  $k$ . Hence, two systems share the same form of the characteristic equation except  $i$ ,  $j$  and  $k$ . However, refer to section 3.1.3 (Stability of  $fs_3$ ),  $i$ ,  $j$  and  $k$  do not effect the stability of the steady state. Thus,  $vihs_3$  is a locally stable steady state when it exists.

**4.1.4 Summary**

Over all, there are three steady states in the BHVI system:

Steady state  $vihs_1$  represents the situation where there is no infection of (mutated) HPAI in the human system. It exists for all values of  $R_0^{[1]}$  and  $R_v^{[2]}$ , but it is only stable when  $R_v^{[2]}$  is less than 1. Hence, combine this with

the stability of  $bs_1$ , we can conclude that the steady state of the BHVI system  $vifs_1$ , which represents the situation where there is no infection of mutated HPAI in both the bird and the human system, exists for all values of  $R_0^{[1]}$  and  $R_v^{[2]}$ . It is only stable when  $R_0^{[1]}$  and  $R_v^{[2]}$  are both less than 1.

Steady state  $vih_s2$  represents the situation where infection of (mutated) HPAI is present in humans. It exists for all  $R_0^{[1]}$  and  $R_v^{[2]} > 1$ .  $vih_s2$  is stable when it exists. Hence, combine this with the stability of  $bs_1$ , we can conclude that the steady state of BHVI  $vifs_2$ , which represents the situation where there is no infection of HPAI in birds but infections of (mutated) HPAI are present in humans, exists for all  $R_0^{[1]}$  values and when  $R_v^{[2]}$  is greater than 1.  $vifs_2$  is stable when  $R_0^{[1]}$  is less than 1 and  $R_v^{[2]}$  is greater than 1.

Steady state  $vih_s3$  represents the situation where infection of mutated HPAI is present in humans. It exists when  $R_0^{[1]}$  is greater than 1 and for all values of  $R_v^{[2]}$ .  $vih_s3$  is stable when it exists. Hence, combine this with the stability of  $bs_2$ , we can conclude that the steady state of the BHVI system  $vifs_3$ , which represents the situation where infection of (mutated) HPAI presents in both birds and humans, exists when  $R_0^{[1]}$  is greater than 1 and for all values of  $R_v^{[2]}$ . It is stable when it exists.

#### 4.1.5 Numerical results

Similar to the original bird-human SIR system, choose different values of  $\beta_1$  (9.6/10.6 day<sup>-1</sup>) in order to adjust  $R_0^{[1]}$ . Vaccination only needs to be introduced when there is a chance of an endemic situation, therefore, choose

$\beta_3$  to be  $1.2 \text{ day}^{-1}$  so that  $R_0^{[2]} > 1$ . As Equation 4.12, choose  $v$  to be 0.2 ( $R_v^{[2]} > 1$ ) and 0.85 ( $R_v^{[2]} < 1$ ). For other parameters values refer to Tables 2.2 and 3.2.

The analytic steady state values of the BHVI system are shown in Table 4.1.

	$\beta_1 = 9.6$		$\beta_1 = 10.6$	
	$v = 0.2$	$v = 0.85$	$v = 0.2$	$v = 0.85$
$S_2$ (people)	13	30	9.3217	5.2243
$I_2$ (people)	9.8	0	10.0452	1.652
$R_2$ (people)	46.5333	170	46.6968	171.1011
$N_2$ (people)	69.3333	200	66.0637	177.9771
$R_v^{[2]}$	4.2667	0.8	4.2667	0.8

Table 4.1: Analytic steady state of the BHVI system with parameter values.

We use Matlab “ode15s” to solve the system for steady states. The results are shown in Figures 4.1 and 4.2.

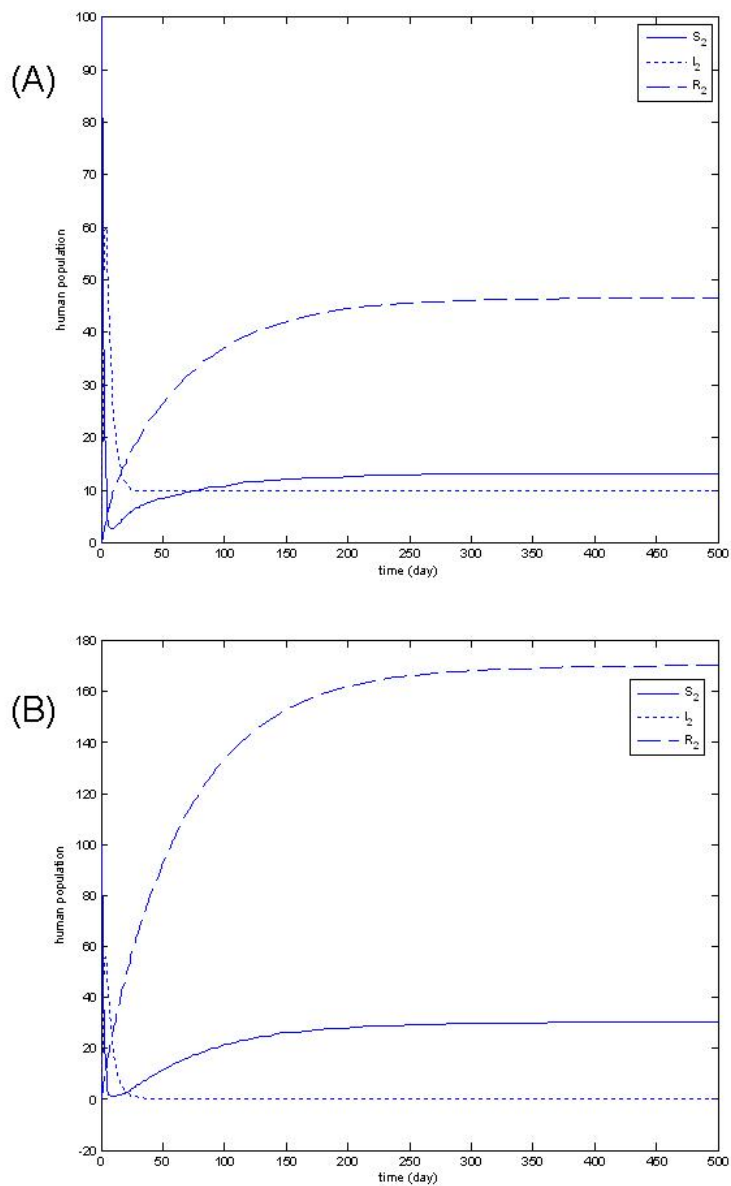


Figure 4.1: Numerical results for the human part of the BHVI system with initial values of  $(S_2, I_2, R_2) = (100, 0, 0)$  when  $\beta_1 = 9.6$  in the first 500 days. Figure (A):  $v = 0.2$  ( $R_v^{[2]} = 4.2667 > 1$ ). Figure (B):  $v = 0.85$  ( $R_v^{[2]} = 0.8 < 1$ ).

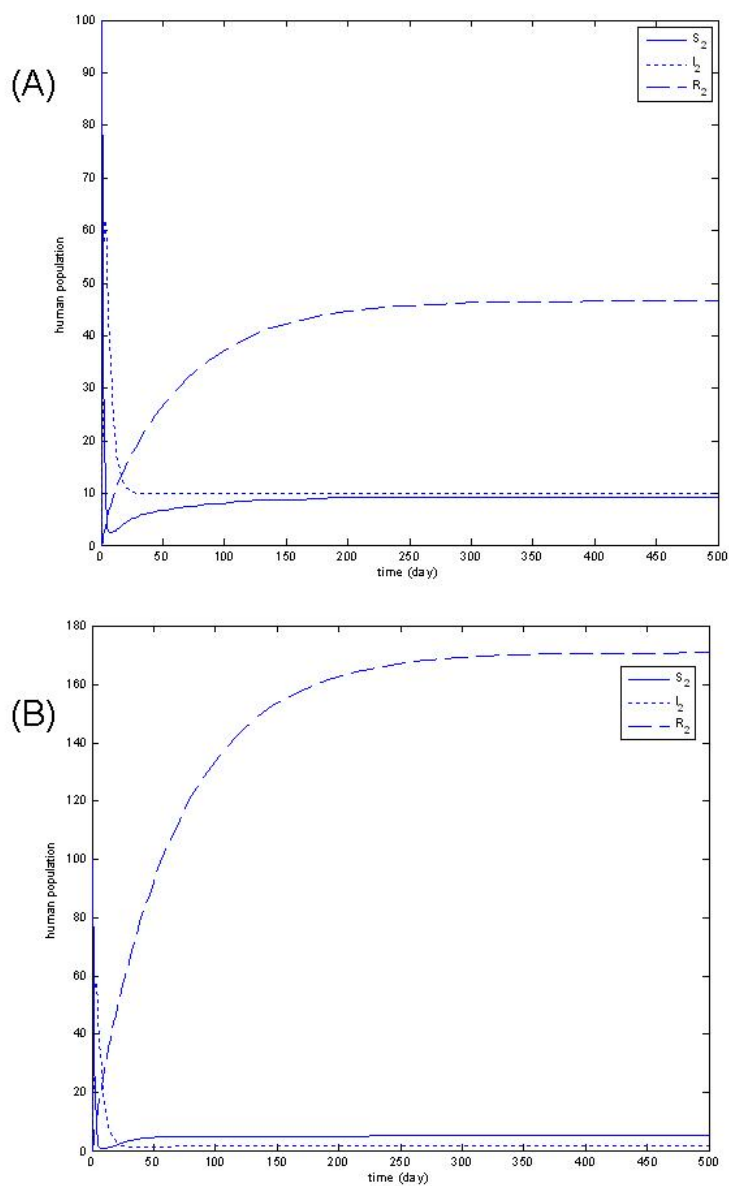


Figure 4.2: Numerical results for the human part of the BHVI system with initial values of  $(S_2, I_2, R_2) = (100, 0, 0)$  when  $\beta_1 = 10.6$  in the first 500 days. Figure (A):  $v = 0.2$  ( $R_v^{[2]} = 4.2667 > 1$ ). Figure (B):  $v = 0.85$  ( $R_v^{[2]} = 0.8 < 1$ ).

In Figure 4.1 (B) when  $\beta_1 = 9.6$  and  $v = 0.85$  ( $R_0^{[1]} < 1$  and  $R_v^{[2]} < 1$ ), the system approaches  $(S_2, I_2, R_2) = (29.98, 0, 169.9)$  which is the infection free steady state of the BHVI system. In Figure 4.1 (A) when  $\beta_1 = 9.6$  and  $v = 0.2$  ( $R_0^{[1]} < 1$  and  $R_v^{[2]} > 1$ ), the system approaches  $(S_2, I_2, R_2) = (13, 9.8, 46.51)$  where there is no infection of HPAI in birds but infection of (mutated) HPAI is present in humans.

In Figure 4.2 (B) when  $\beta_1 = 10.6$  and  $v = 0.85$  ( $R_0^{[1]} > 1$  and  $R_v^{[2]} < 1$ ), the system approaches  $(S_2, I_2, R_2) = (5.224, 1.652, 171)$ . In Figure 4.1 (A) when  $\beta_1 = 10.6$  and  $v = 0.2$  ( $R_0^{[1]} > 1$  and  $R_v^{[2]} > 1$ ), the system approaches  $(S_2, I_2, R_2) = (9.319, 10.05, 46.67)$ . Infection of (mutated) HPAI is always present in birds and humans when  $R_0^{[1]} < 1$ .

#### 4.1.6 Comparison

Compare the numerical results in BHVI with the original bird-human system:

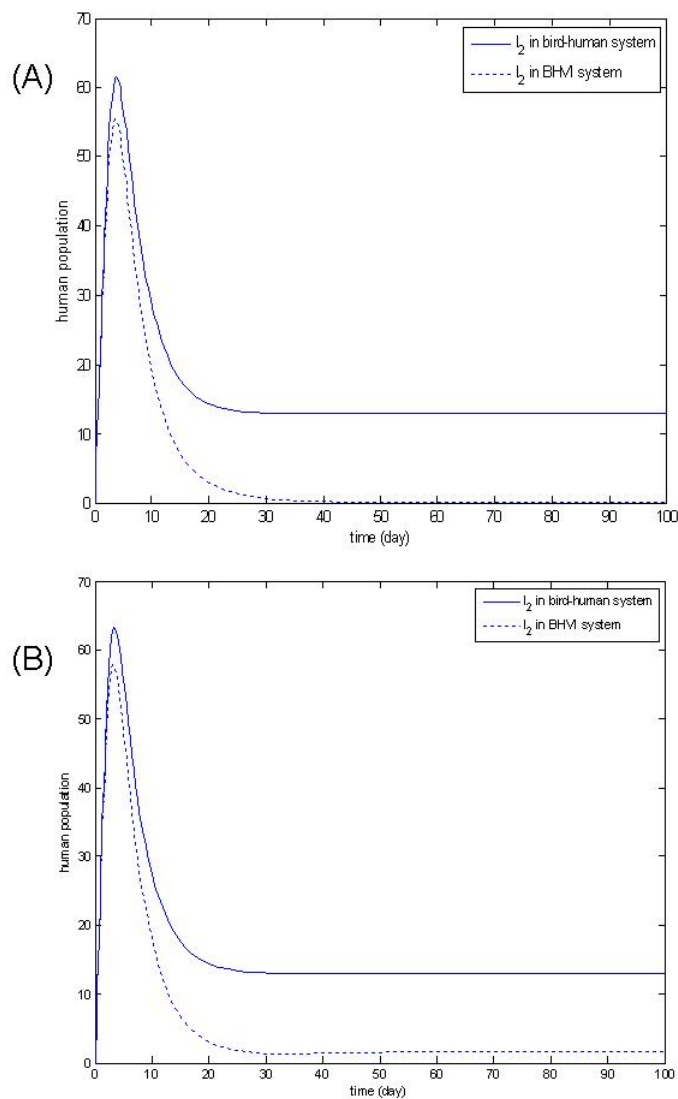


Figure 4.3: The number of infected humans in the bird-human and BHVI system. Figure (A) represents the situation when  $\beta_1 = 9.6$ ,  $\beta_3 = 1.2$  and  $v = 0.2$ . Figure (B) represents the situation when  $\beta_1 = 10.6$ ,  $\beta_3 = 1.2$  and  $v = 0.85$ .

In Figure 4.8, we can see that there are reductions in the number of infected humans in both cases ((A) and (B)). The gaps are not only appear at the peak of the curves, there are even more at the steady state. The higher percentage of immigrants vaccinated, the lower number of infected people we will get.

## 4.2 Vaccination of immigrants BHMVI

Similar to the BHVI system, we assume the population classes (susceptible, infected with HPAI, infected with mutated HPAI and removed) describe the local population in a city or a country, and the birth rate is taken to mean when a person enters that population. A proportion  $v$  of the immigrant population are vaccinated against (mutated) HPAI and become immune (entering the removed class). Only  $1 - v$  of the immigrant population are susceptible to the viruses. The model equations of the human part are:

$$\frac{dS_2}{dt} = \Lambda_2(1 - v) - \mu_2 S_2 - \beta_2 S_2 \frac{I_1}{N_1} - \beta_3 S_2 \frac{M_2}{N_2} \quad (4.16)$$

$$\frac{dI_2}{dt} = \beta_2 S_2 \frac{I_1}{N_1} - (\mu_2 + \alpha_2 + \gamma_2) I_2 - \epsilon I_2 \quad (4.17)$$

$$\frac{dM_2}{dt} = \beta_3 S_2 \frac{M_2}{N_2} + \epsilon I_2 - (\mu_2 + \alpha_3 + \gamma_3) M_2 \quad (4.18)$$

$$\frac{dR_2}{dt} = \Lambda_2 v + \gamma_2 I_2 + \gamma_3 M_2 - \mu_2 R_2. \quad (4.19)$$

The total number of humans is

$$N_2 = S_2 + I_2 + M_2 + R_2. \quad (4.20)$$

### 4.2.1 Basic reproduction number

The basic reproduction number for the human system with vaccination,  $R_v^{[3]}$ , is defined as

$$R_v^{[3]} = \frac{\beta_3(1-v)}{\mu_2 + \alpha_3 + \gamma_3}. \quad (4.21)$$

as  $S_2 = \frac{\Lambda_2(1-v)}{\mu_2}$  in the absence of (mutated) HPAI.

Compare  $R_v^{[3]}$  with  $R_0^{[3]}$ , we have

$$R_v^{[3]} = (1-v)R_0^{[3]}. \quad (4.22)$$

If the vaccination rate

$$v > 1 - \frac{1}{R_0^{[3]}}, \quad (4.23)$$

then  $R_v^{[3]}$  is less the threshold 1.

### 4.2.2 Numerical results

Similar to the BHVI system, choose different values of  $\beta_1$  (9.6/10.6 day<sup>-1</sup>) in order to adjust  $R_0^{[1]}$ . Vaccination only needs to be introduced when there is a chance of an endemic situation, therefore, choose  $\beta_3$  to be 0.6133 day<sup>-1</sup> so that  $R_0^{[3]} > 1$ ; as Equation 4.12, choose  $v$  to be 0.2 ( $R_v^{[3]} > 1$ ) and 0.85 ( $R_v^{[3]} < 1$ ). Use all other parameter values in Tables 2.2 and 3.4.

We use Matlab “ode15s” to solve for steady states. The results are shown in Figures 4.4 and 4.5.

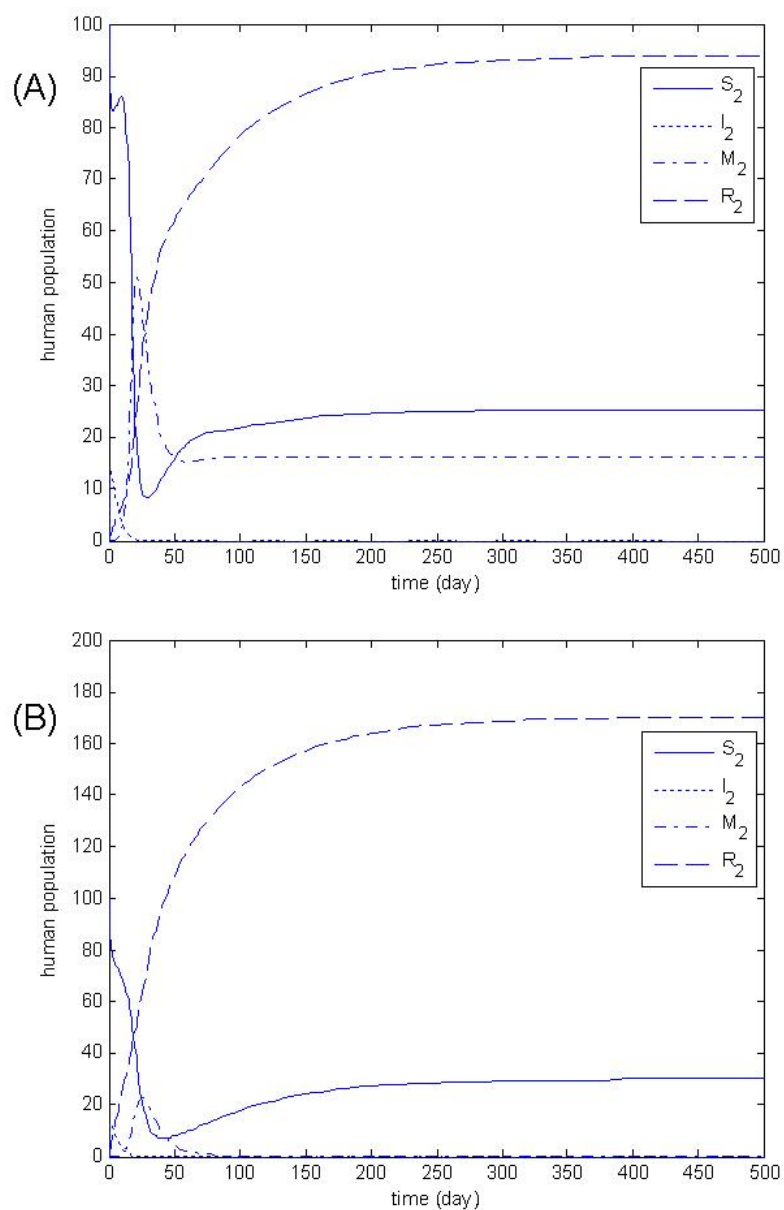


Figure 4.4: Numerical results for the human part of the BHMVI system with initial values of  $(S_2, I_2, M_2, R_2) = (100, 0, 0, 0)$  when  $\beta_1 = 9.6$  in the first 500 days. Figure (A):  $v = 0.2$  ( $R_v^{[3]} = 4.2667 > 1$ ). Figure (B):  $v = 0.85$  ( $R_v^{[3]} = 0.8 < 1$ ).

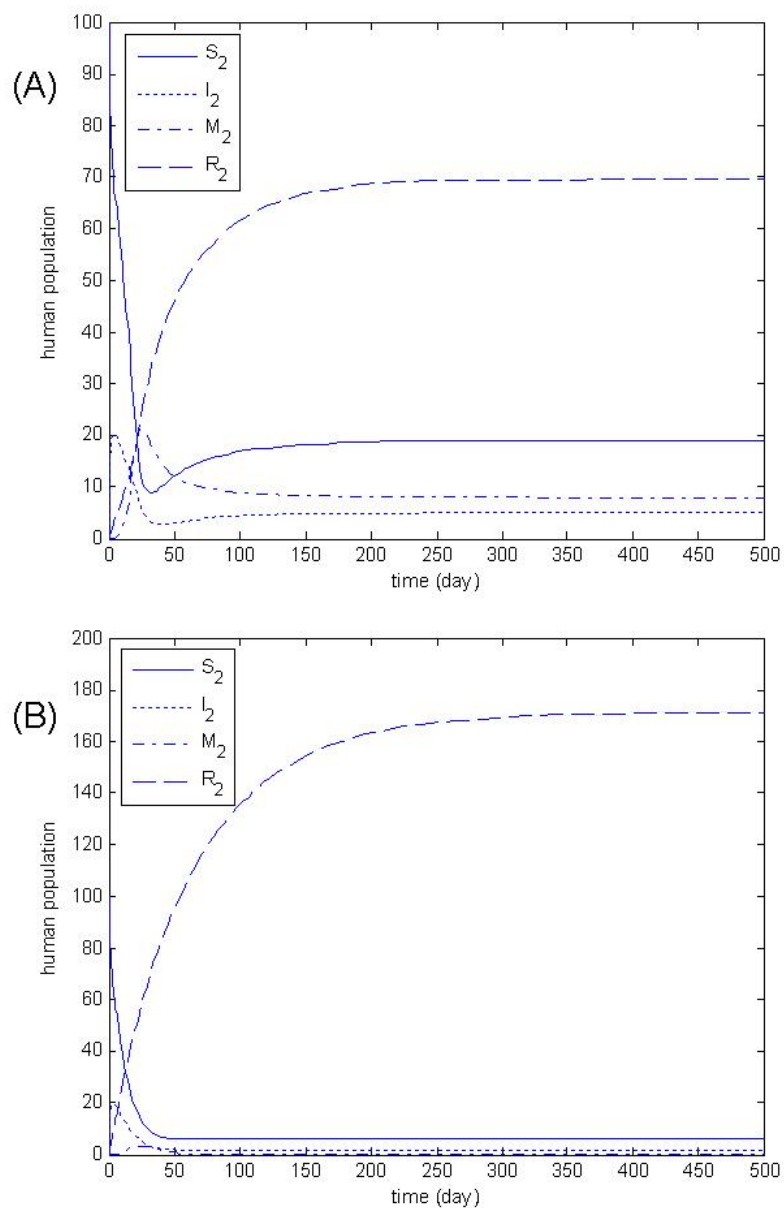


Figure 4.5: Numerical results for the human part of the BHMVI system with initial values of  $(S_2, I_2, M_2, R_2) = (100, 0, 0, 0)$  when  $\beta_1 = 10.6$  in the first 500 days. Figure (A):  $v = 0.2$  ( $R_v^{[3]} = 4.2667 > 1$ ). Figure (B):  $v = 0.85$  ( $R_v^{[3]} = 0.8 < 1$ ).

In Figure 4.4 (B) when  $R_0^{[1]} < 1$  and  $R_v^{[3]} < 1$ , the numerical results reach to an infection free steady state for the human part of the BHMVI system. In Figure 4.4 (A) when when  $R_0^{[1]} < 1$  and  $R_v^{[3]} > 1$ , the system approaches to the steady state where infection of mutated HPAI is present in humans.

In Figure 4.5 when  $R_0^{[1]} > 1$ , in both cases of  $R_v^{[3]}$ , the system approaches non-zero steady state which represent the infection of (mutated) HPAI is present in bird and humans. When  $R_0^{[1]} > 1$  and  $R_v^{[3]} < 1$ , the numerical result shows that the number of infected human with mutated HPAI is greater than 0 but less than 1, where most of infected human with mutated HPAI comes from the mutation of the HPAI viruses.

### 4.3 Vaccination of susceptibles BHVS

Instead of vaccinating the immigrants, vaccinating the susceptible population at a constant rate  $\nu \text{ day}^{-1}$  is also an option. The equations of the human part can be expressed as:

$$\frac{dS_2}{dt} = \Lambda_2 - \nu S_2 - \mu_2 S_2 - \beta_2 S_2 \frac{I_1}{N_1} - \beta_3 S_2 \frac{I_2}{N_2} \quad (4.24)$$

$$\frac{dI_2}{dt} = \beta_2 S_2 \frac{I_1}{N_1} + \beta_3 S_2 \frac{I_2}{N_2} - (\mu_2 + \alpha_2 + \gamma_2) I_2 \quad (4.25)$$

$$\frac{dR_2}{dt} = \nu S_2 + \gamma_2 I_2 - \mu_2 R_2. \quad (4.26)$$

The total population of humans ( $N_2$ ) is

$$N_2 = S_2 + I_2 + R_2. \quad (4.27)$$

### 4.3.1 Steady States

We use  $vshs$  and  $vsfs$  to represent the steady state of the human part of the BHVS system and the full BHVS system, respectively.  $vshs$  are derived from Equation (4.24)-(4.26) fixed by the steady state values in the bird system ( $bs_1$  and  $bs_2$ ). At the steady state of the BHVS system,  $S_2^{vshs}$  and  $R_2^{vshs}$  can be rewritten in terms of  $I_2^{vshs}$  and hence the steady state of the whole system is

$$vsfs = \begin{pmatrix} S_1^{bs} \\ I_1^{bs} \\ S_2^{vshs} \\ I_2^{vshs} \\ R_2^{vshs} \end{pmatrix} = \begin{pmatrix} S_1^{bs} \\ I_1^{bs} \\ \frac{\Lambda_2 - (\mu_2 + \alpha_2 + \gamma_2)I_2^{vshs}}{\mu_2 + \nu} \\ I_2^{vshs} \\ \frac{\nu\Lambda_2 - (\nu(\mu_2 + \alpha_2 + \gamma_2) - \gamma_2(\mu_2 + \nu))I_2^{vshs}}{\mu_2(\mu_2 + \nu)} \end{pmatrix}, \quad (4.28)$$

where  $N_2^{vshs} = \frac{\Lambda_2 - \alpha_2 I_2^{vshs}}{\mu_2}$ . Substitute the steady state values in terms of  $I_2^{vshs}$  into Equation (4.25) and simplify, it becomes a quadratic equation in  $I_2^{vshs}$  (or substitute into Equation (4.24) to get a similar quadratic):

$$f(I_2^{vshs}) = a(I_2^{vshs})^2 + bI_2^{vshs} + c = 0, \quad (4.29)$$

where

$$\begin{aligned} a &= (\mu_2 + \alpha_2 + \gamma_2) \left( \beta_2 \frac{\alpha_2}{\mu_2(\mu_2 + \nu)} \frac{I_1^{bs}}{N_1^{bs}} + \frac{\alpha_2}{\mu_2} - \frac{\beta_3}{\mu_2 + \nu} \right), \\ b &= \Lambda_2 \left( \frac{\beta_3}{\mu_2 + \nu} - \frac{\mu_2 + \alpha_2 + \gamma_2}{\mu_2} - \beta_2 \frac{\mu_2 + 2\alpha_2 + \gamma_2}{\mu_2(\mu_2 + \nu)} \frac{I_1^{bs}}{N_1^{bs}} \right), \\ c &= \beta_2 \frac{\Lambda_2^2}{\mu_2(\mu_2 + \nu)} \frac{I_1^{bs}}{N_1^{bs}}. \end{aligned}$$

Note  $c$  is always positive and the signs of  $a$  and  $b$  are determined by the value of the parameters. Also,

$$b^2 - 4ac = \left( \Lambda_2 \left( \frac{\beta_3}{\mu_2 + \nu} - \frac{\mu_2 + \alpha_2 + \gamma_2}{\mu_2} - \beta_2 \frac{\mu_2 + 2\alpha_2 + \gamma_2}{\mu_2(\mu_2 + \nu)} \frac{I_1^{bs}}{N_1^{bs}} \right) \right)^2$$

$$\begin{aligned}
& -4 \left( (\mu_2 + \alpha_2 + \gamma_2) \left( \beta_2 \frac{\alpha_2}{\mu_2(\mu_2 + \nu)} \frac{I_1^{bs}}{N_1^{bs}} + \frac{\alpha_2}{\mu_2} - \frac{\beta_3}{\mu_2 + \nu} \right) \right) \\
& \left( \beta_2 \frac{\Lambda_2^2}{\mu_2(\mu_2 + \nu)} \frac{I_1^{bs}}{N_1^{bs}} \right) \\
= & \Lambda_2^2 \left( \left( \frac{\beta_3}{\mu_2 + \nu} - \frac{\mu_2 + \alpha_2 + \gamma_2}{\mu_2} \right)^2 + \left( \beta_2 \frac{\mu_2 + \gamma_2}{\mu_2(\mu_2 + \nu)} \frac{I_1^{bs}}{N_1^{bs}} \right)^2 \right. \\
& \left. + 2\beta_2 \frac{\mu_2 + \gamma_2}{\mu_2(\mu_2 + \nu)} \left( \frac{\beta_3}{\mu_2 + \nu} + \frac{\mu_2 + \alpha_2 + \gamma_2}{\mu_2} \right) \frac{I_1^{bs}}{N_1^{bs}} \right) > 0,
\end{aligned}$$

which shows that the roots of Equation (4.29) are real for all parameter values.

### Steady States $vsfs_1$ and $vsfs_2$

The steady states of the full system  $vsfs_1$  and  $vsfs_2$  are combinations of the steady states of the bird  $bs_1$  and human in the BHVS ( $vshs_1$  and  $vshs_2$ ) system derived with fixed values of  $bs_1$ . At  $bs_1$ , where  $I_1^{bs_1} = 0$ , the coefficients of the quadratic equation  $a$ ,  $b$  and  $c$  can be simplified as

$$\begin{aligned}
a &= \frac{(\mu_2 + \alpha_2 + \gamma_2)(\mu_2(\alpha_2 - \beta_3) + \nu\alpha_2)}{\mu_2(\mu_2 + \nu)}, \\
b &= \frac{\Lambda_2(\mu_2\beta_3 - (\mu_2 + \nu)(\mu_2 + \alpha_2 + \gamma_2))}{\mu_2(\mu_2 + \nu)}, \\
c &= 0,
\end{aligned}$$

which gives

$$\begin{aligned}
I_2^{vshs_1} &= 0 \\
I_2^{vshs_2} &= \frac{\Lambda_2(\mu_2\beta_3 - (\mu_2 + \nu)(\mu_2 + \alpha_2 + \gamma_2))}{(\mu_2(\beta_3 - \alpha_2) - \nu\alpha_2)(\mu_2 + \alpha_2 + \gamma_2)}.
\end{aligned}$$

Thus, steady state values of  $S_2$  and  $R_2$  can be derived from them. The first steady state of the BHVS system is

$$vsfs_1 = \begin{pmatrix} S_1^{bs_1} \\ I_1^{bs_1} \\ S_2^{vshs_1} \\ I_2^{vshs_1} \\ R_2^{vshs_1} \end{pmatrix} = \begin{pmatrix} \frac{\Lambda_1}{\mu_1} \\ 0 \\ \frac{\Lambda_2}{\mu_2 + \nu} \\ 0 \\ \frac{\nu \Lambda_2}{\mu_2(\mu_2 + \nu)} \end{pmatrix}, \quad (4.30)$$

where  $N_2^{vshs_1} = \frac{\Lambda_2}{\mu_2}$ . It is the infection free steady state.

The second steady state is

$$vsfs_2 = \begin{pmatrix} S_1^{bs_1} \\ I_1^{bs_1} \\ S_2^{vshs_2} \\ I_2^{vshs_2} \\ R_2^{vshs_2} \end{pmatrix} = \begin{pmatrix} \frac{\Lambda_1}{\mu_1} \\ 0 \\ \frac{\Lambda_2(\mu_2 + \gamma_2)}{\mu_2(\beta_3 - \alpha_2) - \nu\alpha_2} \\ \frac{\Lambda_2(\mu_2\beta_3 - (\mu_2 + \nu)(\mu_2 + \alpha_2 + \gamma_2))}{(\mu_2(\beta_3 - \alpha_2) - \nu\alpha_2)(\mu_2 + \alpha_2 + \gamma_2)} \\ \frac{\Lambda_2(\gamma_2(\beta_3 - \mu_2 - \alpha_2 - \gamma_2) + \nu(\mu_2 + \alpha_2 + \gamma_2))}{(\mu_2 + \alpha_2 + \gamma_2)(\mu_2(\beta_3 - \alpha_2) - \nu\alpha_2)} \end{pmatrix}, \quad (4.31)$$

where  $N_2^{vshs_2} = \frac{\Lambda_2\beta_3(\mu_2 + \gamma_2)}{(\mu_2 + \alpha_2 + \gamma_2)(\mu_2(\beta_3 - \alpha_2) - \nu\alpha_2)}$ . There is no infection in birds but there are infections of mutated HPAI in humans.

Steady state  $vsfs_1$  exists for all  $R_0^{[1]}$  values. Steady state  $vsfs_2$  exists for all  $R_0^{[1]}$  and when  $\mu_2\beta_3 - (\mu_2 + \nu)(\mu_2 + \alpha_2 + \gamma_2) > 0$ .

### Steady States $vsfs_3$

The steady state of the BHVS system  $vsfs_3$  is a combination of the steady state of birds  $bs_2$  and humans in BHVS ( $vshs_3$ ) fixed by the value of  $bs_2$ . The roots of Equation 4.29 have two cases depending on the value of parameters:

Case (1)

$$\beta_2 \frac{\alpha_2}{\mu_2(\mu_2 + \nu)} \frac{I_1^{bs}}{N_1^{bs}} + \frac{\alpha_2}{\mu_2} < \frac{\beta_3}{\mu_2 + \nu} \quad (4.32)$$

Case (2)

$$\beta_2 \frac{\alpha_2}{\mu_2(\mu_2 + \nu)} \frac{I_1^{bs}}{N_1^{bs}} + \frac{\alpha_2}{\mu_2} > \frac{\beta_3}{\mu_2 + \nu} \quad (4.33)$$

Under the condition of Case (1),  $a < 0$ . Because

$$f(0) = \beta_2 \frac{\Lambda_2^2}{\mu_2(\mu_2 + \nu)} \frac{I_1^{bs}}{N_1^{bs}} > 0, \quad (4.34)$$

Equation 4.29 has one positive root and one negative root (which we ignore).

Under the condition of Case (2),  $a > 0$  and  $b < 0$ . Thus,  $\sqrt{b^2 - 4ac} < |b|$ , which implies two roots of Equation 4.29 are positive.

However, similar to section 3.2.1 (Steady state  $fs_3$ ), in Case (1), there are two positive real roots of  $S_2^{vshs_3}$  and in Case (2), there is one positive and one negative real root of  $S_2^{vshs_3}$ . Thus, we can conclude that only one steady state  $vshs_3$  exists for  $bs_2$  and it is unique.

$vshs_3$  represents the situation where infection of (mutated) HPAI is present in both the bird and the human systems. It exists when  $R_0^{[1]} > 1$ .

### 4.3.2 Basic reproduction number

The basic reproduction number for the human system,  $R_\nu^{[2]}$ , is defined as

$$R_\nu^{[2]} = \frac{\mu_2 \beta_3}{(\mu_2 + \nu)(\mu_2 + \alpha_2 + \gamma_2)}. \quad (4.35)$$

Compare it with the basic reproduction number in the original human system  $R_0^{[2]}$ , we have

$$R_\nu^{[2]} = \frac{\mu_2}{\mu_2 + \nu} R_0^{[2]}. \quad (4.36)$$

In order to keep  $R_\nu^{[2]}$  under the threshold 1, we need

$$\nu > \mu_2(R_0^{[2]} - 1). \quad (4.37)$$

Recall one of the conditions for the existence of  $vsfs_2$  is  $\mu_2\beta_3 - (\mu_2 + \nu)(\mu_2 + \alpha_2 + \gamma_2) > 0$ , which is equivalent to  $R_\nu^{[2]} > 1$ . Thus,  $vsfs_2$  exists for all values of  $R_0^{[1]}$  and when  $R_\nu^{[2]}$  is greater than 1.

### 4.3.3 Local Stability

Refer to section 3.1.3, we need to determined the stability at each steady state of the human system in BHVS in order to determine the stability of the whole system. The Jacobian matrix of the human system  $J_{vsh}$  is

$$J_{vsh} = \begin{pmatrix} -\mu_2 - \nu - \beta_2 \frac{I_1}{N_1} - \beta_3 i & -\beta_3 j & \beta_3 k \\ \beta_2 \frac{I_1}{N_1} + \beta_3 i & \beta_3 j - \mu_2 - \alpha_2 - \gamma_2 & -\beta_3 k \\ \nu & \gamma_2 & -\mu_2 \end{pmatrix}, \quad (4.38)$$

where

$$\begin{aligned} i &= \frac{I_2(I_2 + R_2)}{N_2^2}, \\ j &= \frac{S_2(S_2 + R_2)}{N_2^2}, \\ k &= \frac{S_2 I_2}{N_2^2}. \end{aligned}$$

Terms  $i$ ,  $j$  and  $k$  are non-negative.

**Stability of  $vshs_1$** 

At  $vshs_1$ , where  $I_1^{bs_1}$  and  $I_2^{vshs_1}$ ,

$$\begin{aligned} i &= 0, \\ j &= \frac{\mu_2}{\mu_2 + \nu}, \\ k &= 0, \end{aligned}$$

and

$$J_{vshs_1} = \begin{pmatrix} -\mu_2 - \nu & -\beta_3 \frac{\mu_2}{\mu_2 + \nu} & 0 \\ 0 & \beta_3 \frac{\mu_2}{\mu_2 + \nu} - \mu_2 - \alpha_2 - \gamma_2 & 0 \\ \nu & \gamma_2 & -\mu_2 \end{pmatrix}. \quad (4.39)$$

Thus, the eigenvalues of  $J_{vshs_1}$  are  $-\mu_2 - \nu$ ,  $\beta_3 \frac{\mu_2}{\mu_2 + \nu} - \mu_2 - \alpha_2 - \gamma_2$  and  $-\mu_2$ . They are all negative if  $R_\nu^{[2]}$  is less than 1. Thus,  $vshs_1$  is locally stable when  $R_\nu^{[2]} < 1$ .

**Stability of  $vshs_2$** 

The Jacobian matrix evaluated at  $vshs_2$  ( $I_1^{bs_1} = 0$  and  $I_2^{vshs_2} \neq 0$ ) is

$$J_{vshs_2} = \begin{pmatrix} -\mu_2 - \nu - \beta_3 i & -\beta_3 j & \beta_3 k \\ \beta_3 i & \beta_3 j - \mu_2 - \alpha_2 - \gamma_2 & -\beta_3 k \\ \nu & \gamma_2 & -\mu_2 \end{pmatrix}. \quad (4.40)$$

The characteristic equation then becomes

$$\lambda^3 + a_0 \lambda^2 + a_1 \lambda + a_2 = 0 \quad (4.41)$$

where

$$a_0 = 2\mu_2 + \nu + \beta_3 i + \mu_2 + \alpha_2 + \gamma_2 - \beta_3 j,$$

$$a_1 = (\mu_2 + \nu + \beta_3 i)\mu_2 + (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j)(2\mu_2 + \beta_3 i) + \beta_3 k\gamma_2 + \beta_3^2 ij \\ + \nu(\mu_2 + \alpha_2 + \gamma_2 - \beta_3(j+k)),$$

$$a_2 = (\mu_2 + \nu)(\beta_3 k\gamma_2 + (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j)\mu_2) + (\mu_2 + \alpha_2 + \gamma_2)(\mu_2 \beta_3 i - \nu \beta_3 k).$$

Also,

$$a_0 a_1 - a_2 = (2\mu_2 + \nu + \beta_3 i + \mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) ((\mu_2 + \nu + \beta_3 i)\mu_2 \\ + (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j)(2\mu_2 + \beta_3 i) + \beta_3 k\gamma_2 + \beta_3^2 ij + \nu(\mu_2 + \alpha_2 \\ + \gamma_2 - \beta_3(j+k))) - ((\mu_2 + \nu)(\beta_3 k\gamma_2 + (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j)\mu_2) \\ + (\mu_2 + \alpha_2 + \gamma_2)(\mu_2 \beta_3 i - \nu \beta_3 k)) \\ = (\mu_2 + \nu) ((\mu_2 + \nu + \beta_3 i)\mu_2 + (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j)(2\mu_2 + \beta_3 i) \\ + \beta_3^2 ij + \nu(\mu_2 + \alpha_2 + \gamma_2 - \beta_3(j+k))) + (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) \\ (\beta_3 i\mu_2 + (\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j)(2\mu_2 + \beta_3 i) + \beta_3 k\gamma_2 + \beta_3^2 ij \\ + \nu(\mu_2 + \alpha_2 + \gamma_2 - \beta_3(j+k))) + \mu_2 ((\mu_2 + \nu + \beta_3 i)\mu_2 \\ + 2\mu_2(\mu_2 + \alpha_2 + \gamma_2 - \beta_3 j) + \beta_3 k\gamma_2 + \nu(\mu_2 + \alpha_2 + \gamma_2 - \beta_3(j+k))) \\ + (\mu_2 + \alpha_2 + \gamma_2)\nu\beta_3 k$$

At the steady state, Equation 4.26 can be rearranged to

$$\nu S_2 + \gamma_2 I_2 = \mu_2 R_2, \quad (4.42)$$

which gives

$$\frac{\nu S_2}{N_2} < \frac{\mu_2 R_2}{N_2}. \quad (4.43)$$

Thus,

$$\frac{\mu_2(R_2 + I_2)}{N_2} > \frac{\nu S_2}{N_2}$$

$$\Rightarrow \quad \mu_2 i > \nu k$$

at steady state. Thus, refer to section 3.1.3 Steady state of  $fs_2$ , terms  $a_0$ ,  $a_1$ ,  $a_2$  and  $a_0 a_1 - a_2 > 0$  are all positive. Therefore, steady state  $vshs_2$  is locally stable when it exists.

### Stability of $vshs_3$

The Jacobian matrix  $J_{vshs_3}$  is in the same form as  $J_{vshs_2}$ , apart from  $i$ ,  $j$ ,  $k$  and  $I_1^{bs_2} \neq 0$ . Thus, the characteristic equation of  $J_{vshs_3}$  is similar to the one of  $J_{vshs_2}$  and steady state  $vshs_3$  is locally stable when it exists.

### 4.3.4 Summary

Over all, there are three steady states in the BHVS system:

Steady state  $vshs_1$  represents the situation where there is no infection of mutated HPAI in the human system. It exists for all values of  $R_0^{[1]}$  and  $R_\nu^{[2]}$ , but it is stable only when  $R_\nu^{[2]} < 1$ . Hence, combining this with the stability of  $bs_1$ , we can conclude that the steady state of the BHVS system  $vshs_1$ , which is the infection free steady state, exists for all values of  $R_0^{[1]}$  and  $R_\nu^{[2]}$ . It is stable only when  $R_0^{[1]}$  and  $R_\nu^{[2]}$  are both less than 1.

Steady state  $vshs_2$  represents the situation where there are infections of (mutated) HPAI present in humans. It exists for all  $R_0^{[1]}$  values and when  $R_\nu^{[2]}$  is greater than 1.  $vshs_2$  is stable when it exists. Hence, combining this

with the stability of  $bs_1$ , we can conclude that the steady state of the BHVS system  $vsfs_2$ , which represents the situation where there is no infection of HPAI infection in birds but infections of (mutated) HPAI are present in humans, exists for all  $R_0^{[1]}$  values and when  $R_\nu^{[2]}$  is greater than 1.  $vsfs_2$  is stable when  $R_0^{[1]} < 1$  and  $R_\nu^{[2]} > 1$ .

Steady state  $vshs_3$  represents the situation where infections of (mutated) HPAI are present in humans. It exists when  $R_0^{[1]}$  is greater than 1 and for all values of  $R_\nu^{[2]}$ . It is stable when it exists. Hence, combining this with the stability of  $bs_2$ , we can conclude that the steady state of the BHVS system  $vsfs_3$ , which represents the situation where infections of (mutated) HPAI are present in both birds and humans, exists when  $R_0^{[1]} > 1$  and for all values of  $R_\nu^{[2]}$ . It is stable when it exists.

### 4.3.5 Numerical results

In order to check the analytic results with the numerical results, choose different values of  $\beta_1$  ( $9.6/10.6 \text{ day}^{-1}$ ) to adjust  $R_0^{[1]}$ . Vaccination only needs to be introduced when there is a chance of an endemic situation, therefore, choose  $\beta_3$  to be  $1.2 \text{ day}^{-1}$  for  $R_0^{[2]} > 1$ . Also, choose  $\nu$  to be 0.01 ( $R_\nu^{[2]} > 1$ ) and 0.1 ( $R_\nu^{[2]} < 1$ ). other parameters values are in Table 2.2 and 3.2.

The analytic steady states values of BHVS are shown in Table 5.1.

Matlab “ode15s” was used to solve for steady states. The results are shown in Figure 4.6 and 4.7.

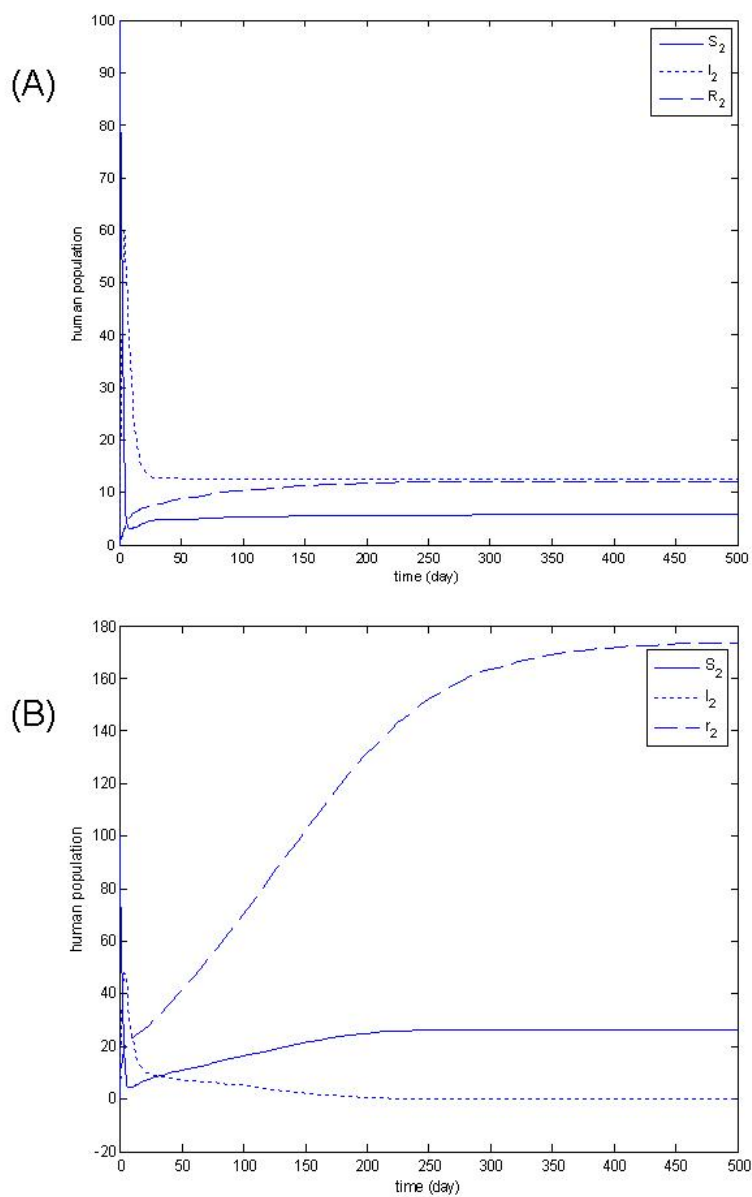


Figure 4.6: Numerical results for the BHVS system with initial values of  $(S_2, I_2, R_2) = (100, 0, 0)$  for  $\beta_1 = 9.6$  ( $R_v^{[1]} < 1$ ) in the first 500 days. Figure (A):  $\nu = 0.01$  ( $R_v^{[2]} = 3.2 > 1$ ). Figure (B):  $\nu = 0.1$  ( $R_v^{[2]} = 0.6957 < 1$ ).

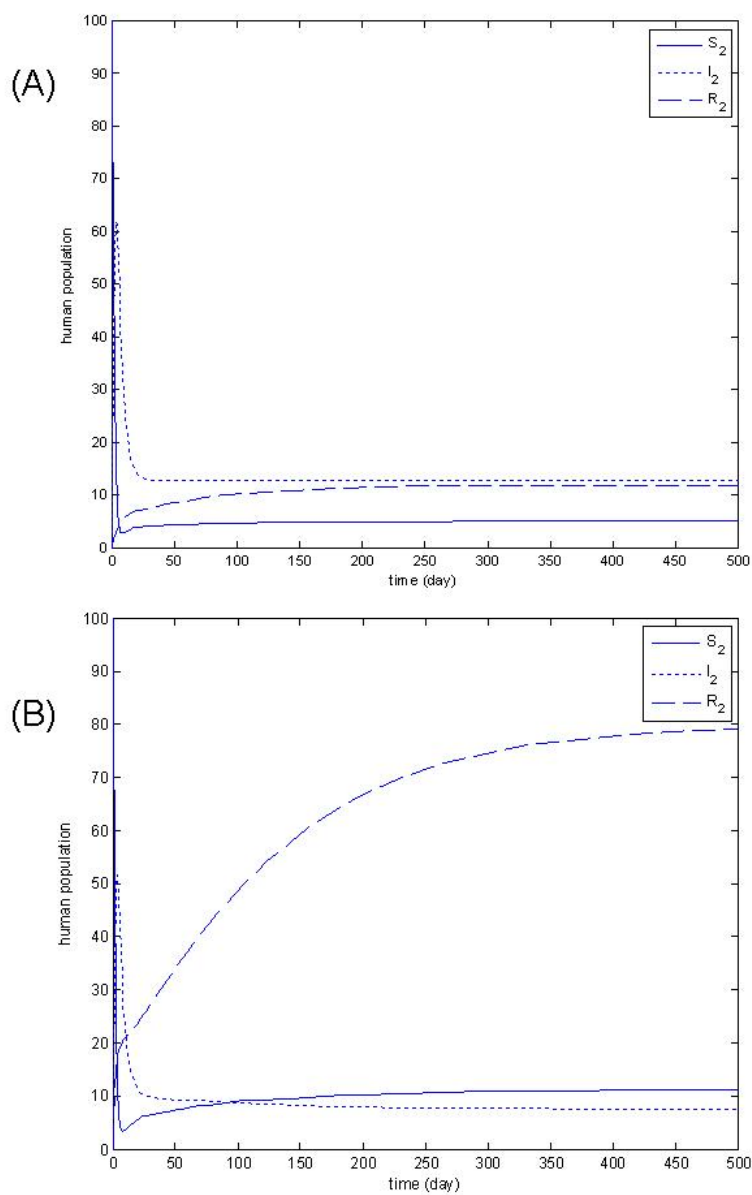


Figure 4.7: Numerical results for the BHVS system with initial values of  $(S_2, I_2, R_2) = (100, 0, 0)$  for  $\beta_1 = 10.6$  ( $R_v^{[1]} < 1$ ) in the first 500 days. Figure (A):  $\nu = 0.01$  ( $R_v^{[2]} = 3.2 > 1$ ). Figure (B):  $\nu = 0.1$  ( $R_v^{[2]} = 0.6957 < 1$ ).

	$\beta_1 = 9.6$		$\beta_1 = 10.6$	
	$\nu = 0.01$	$\nu = 0.1$	$\nu = 0.01$	$\nu = 0.1$
$S_2$ (people)	5.7692	26.087	4.9723	11.2182
$I_2$ (people)	12.6923	0	12.7809	7.5996
$R_2$ (people)	12.3077	173.913	11.8354	79.8546
$N_2$ (people)	30.7692	200	29.5886	98.6724
$R_\nu^{[2]}$	3.2	0.6957	3.2	0.6957

Table 4.2: Analytic steady state of the BHVS system with parameter values.

In Figure 4.6 (B) when  $\beta_1 = 9.6$  and  $\nu = 0.1$  ( $R_0^{[1]} < 1$  and  $R_\nu^{[2]} < 1$ ), the system approaches  $(S_2, I_2, R_2) = (26.09, 0, 173.4)$  which is the infection free steady state. In Figure 4.6 (A) when  $\beta_1 = 9.6$  and  $\nu = 0.01$  ( $R_0^{[1]} < 1$  and  $R_\nu^{[2]} > 1$ ), the system approaches  $(S_2, I_2, R_2) = (5.767, 12.69, 12.3)$  where there is no infection of HPAI in birds but infection of (mutated) HPAI presents in humans.

In Figure 4.7 (B) when  $\beta_1 = 10.6$  and  $\nu = 0.1$  ( $R_0^{[1]} > 1$  and  $R_\nu^{[2]} < 1$ ), the system approaches  $(S_2, I_2, R_2) = (11.17, 7.621, 79.08)$ . In Figure 4.7 (A) when  $\beta_1 = 10.6$  and  $\nu = 0.01$  ( $R_0^{[1]} > 1$  and  $R_\nu^{[2]} > 1$ ), the system approaches  $(S_2, I_2, R_2) = (4.971, 12.78, 11.83)$ . In either case, the system always reach the steady state where infections of (mutated) HPAI are present in both birds and humans.

### 4.3.6 Comparison

Compare the numerical results in this model with the original bird-human system:

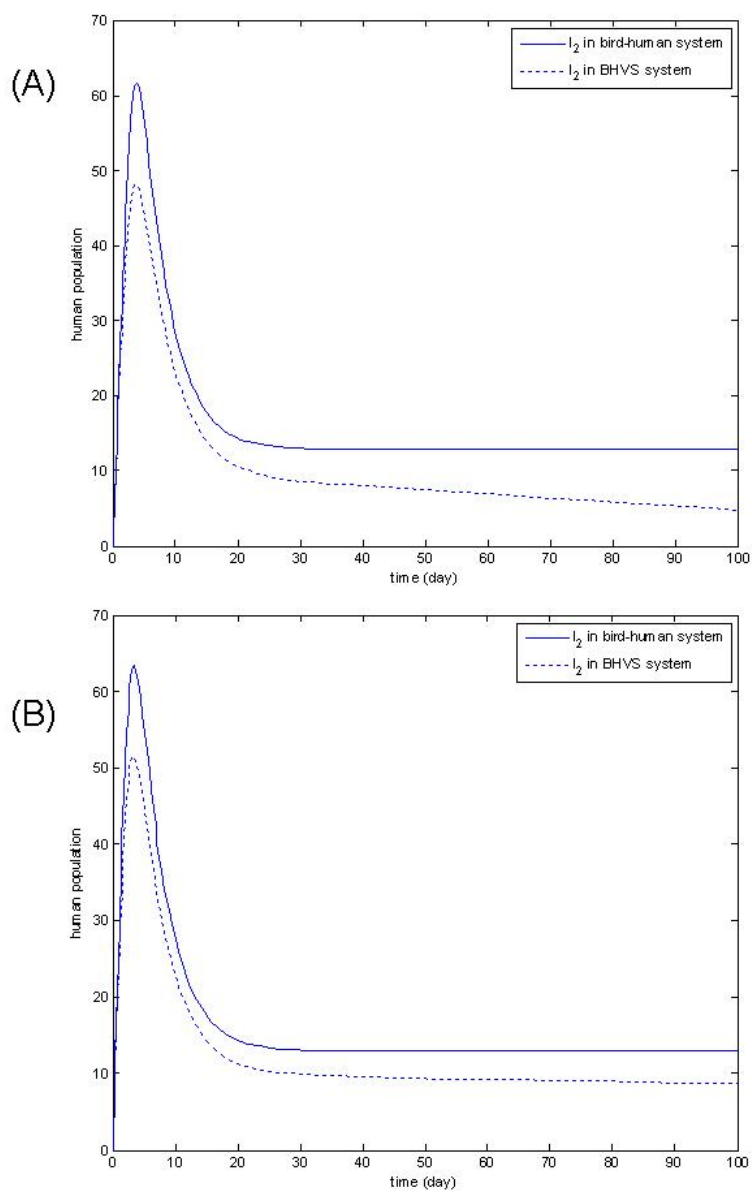


Figure 4.8: The number of infected humans in the original bird-human and the BHVS system. Figure (A) represents the situation when  $\beta_1 = 9.6$ ,  $\beta_3 = 1.2$  and  $v = 0.01$ . Figure (B) represents the situation when  $\beta_1 = 10.6$ ,  $\beta_3 = 1.2$  and  $v = 0.1$ .

In Figure 4.8, we can see that there are reductions in the number of infected humans in both cases ((A) and (B)). The higher percentage of susceptibles vaccinated, the lower number of infected people we will get.

## 4.4 Vaccination of susceptibles BHMVS

Similar to the BHVS model, susceptible humans are vaccinated at a constant rate  $\nu$  day<sup>-1</sup> in this BHMVS system. The model equations of the human part are:

$$\frac{dS_2}{dt} = \Lambda_2 - (\nu + \mu_2)S_2 - \beta_2 S_2 \frac{I_1}{N_1} - \beta_3 S_2 \frac{M_2}{N_2} \quad (4.44)$$

$$\frac{dI_2}{dt} = \beta_2 S_2 \frac{I_1}{N_1} - (\mu_2 + \alpha_2 + \gamma_2)I_2 - \epsilon I_2 \quad (4.45)$$

$$\frac{dM_2}{dt} = \beta_3 S_2 \frac{M_2}{N_2} + \epsilon I_2 - (\mu_2 + \alpha_3 + \gamma_3)M_2 \quad (4.46)$$

$$\frac{dR_2}{dt} = \nu S_2 + \gamma_2 I_2 + \gamma_3 M_2 - \mu_2 R_2. \quad (4.47)$$

The total number of humans is

$$N_2 = S_2 + I_2 + M_2 + R_2. \quad (4.48)$$

### 4.4.1 Basic reproduction number

The basic reproduction number for the human system,  $R_\nu^{[3]}$ , is defined as

$$R_\nu^{[3]} = \frac{\mu_2 \beta_3}{(\mu_2 + \nu)(\mu_2 + \alpha_3 + \gamma_3)}. \quad (4.49)$$

Compare it with the basic reproduction number in the original human system  $R_0^{[3]}$ , we have

$$R_\nu^{[3]} = \frac{\mu_2}{\mu_2 + \nu} R_0^{[3]}. \quad (4.50)$$

In order to keep  $R_\nu^{[3]}$  under the threshold 1, we need

$$\nu > \mu_2(R_0^{[3]} - 1). \quad (4.51)$$

#### 4.4.2 Numerical results

Similar to the BHVI system, choose different values of  $\beta_1$  (9.6/10.6 day<sup>-1</sup>) in order to adjust  $R_0^{[1]}$ . Vaccination only needs to be introduced when there is a chance of an endemic situation, therefore, choose  $\beta_3$  to be  $\frac{2}{3}$  day<sup>-1</sup> so that  $R_0^{[3]} > 1$ . Also, choose  $\nu$  to be 0.01 ( $R_\nu^{[3]} > 1$ ) and 0.1 ( $R_\nu^{[3]} < 1$ ). Use all other parameter values in Tables 2.2 and 3.4.

Use MATLAB “ode15s” to solve for steady states. The results are shown in Figures 4.4 and 4.5.

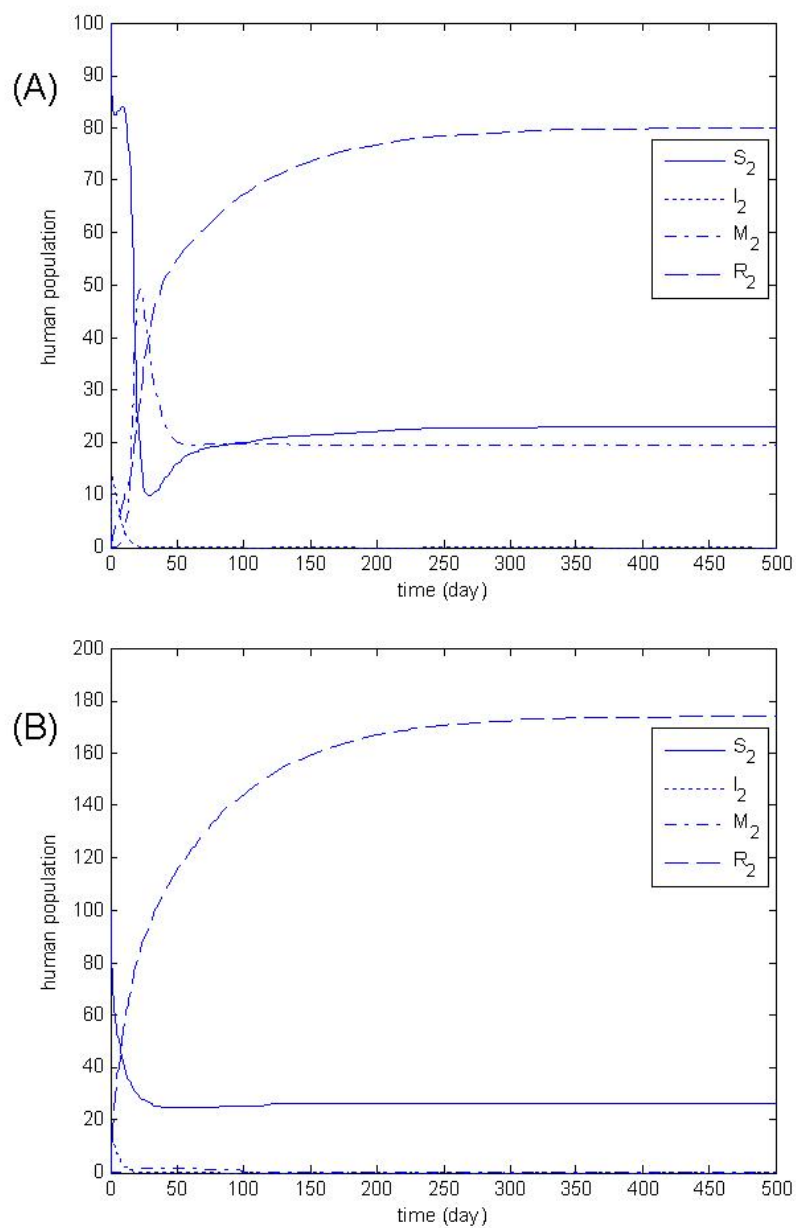


Figure 4.9: Numerical results for the human system in BHMVI with initial values of  $(S_2, I_2, M_2, R_2) = (100, 0, 0, 0, 0)$  when  $\beta_1 = 9.6$  in the first 500 days. Figure (A):  $v = 0.2$  ( $R_v^{[3]} = 4.2667 > 1$ ). Figure (B):  $v = 0.85$  ( $R_v^{[3]} = 0.8 < 1$ ).

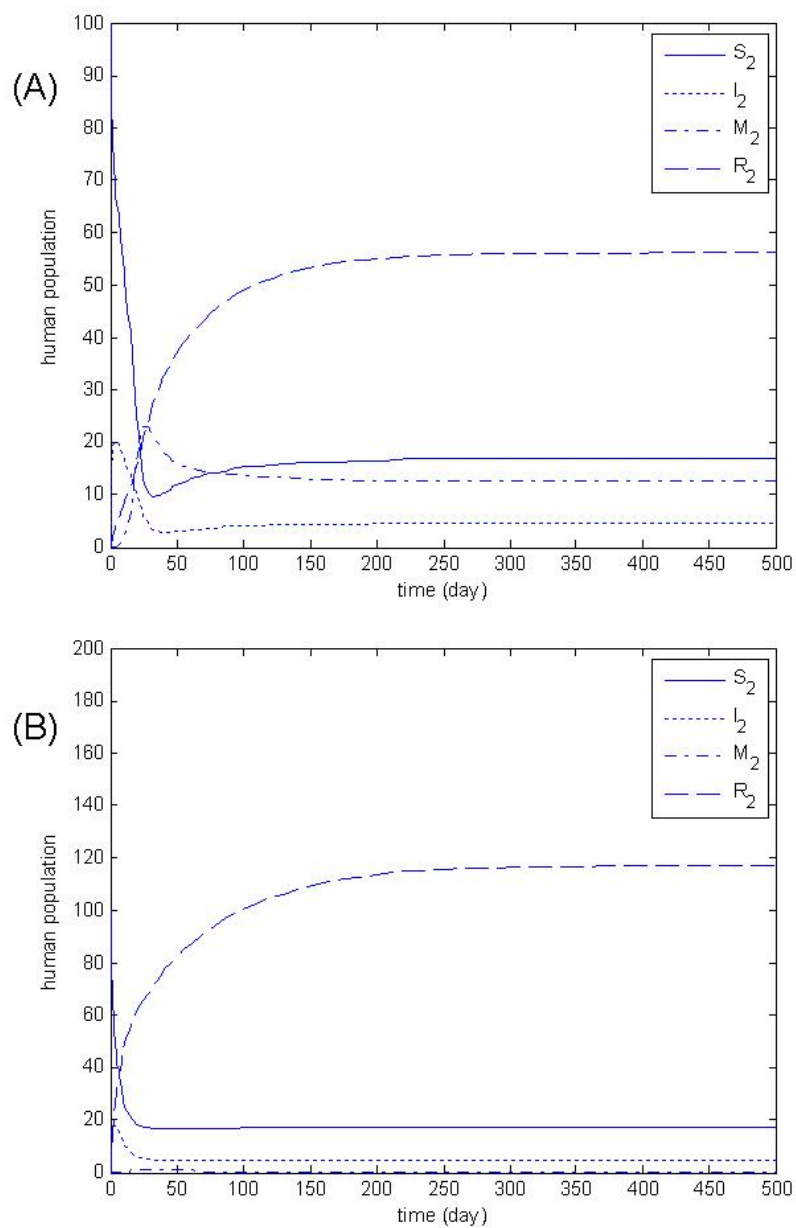


Figure 4.10: Numerical results for the human system in BHMVI with initial values of  $(S_2, I_2, M_2, R_2) = (100, 0, 0, 0, 0)$  when  $\beta_1 = 10.6$  in the first 500 days. Figure (A):  $v = 0.2$  ( $R_v^{[3]} = 4.2667 > 1$ ). Figure (B):  $v = 0.85$  ( $R_v^{[3]} = 0.8 < 1$ ).

In Figure 4.9 (B) when  $\beta_1 = 9.6$  and  $v = 0.85$  ( $R_0^{[1]} < 1$  and  $R_v^{[3]} < 1$ ), the system reaches an infection free steady state of the BHMVI system. In Figure 4.9 (A) when  $\beta_1 = 9.6$  and  $v = 0.2$  ( $R_0^{[1]} < 1$  and  $R_v^{[3]} > 1$ ), there is no infection of HPAI in birds, but infections of mutated HPAI are present in humans.

In Figure 4.10 when  $R_0^{[1]} > 1$ , in both cases of  $R_v^{[3]}$ , the system approaches the non-zero steady state which represents the infections of (mutated) HPAI are present in bird and humans. When  $R_0^{[1]} > 1$  and  $R_v^{[3]} < 1$ , by the definition of the basic reproduction number, there is no infection of mutated HPAI in humans. However, the numerical result shows that the number of infected human with mutated HPAI is greater than 0 but less than 1. Hence, this small amount of infected human with mutated HPAI can be seen as zero and it comes from the mutation of the HPAI viruses.

## 4.5 Vaccine immigrants vs Vaccine susceptibles BHVI vs BHVS

In order to compare two strategies, firstly, we fix the basic reproduction numbers ( $R_v^{[2]}$  and  $R_\nu^{[2]}$ ) to be equal. Choose  $v = 0.8208$  in BHVI where 82.08% of the immigrants are going to be vaccinated and  $\nu = 0.0692 \text{ day}^{-1}$  in BHVS where 6.92% of the susceptible population is going to be vaccinated each day, so that  $R_v^{[2]} \approx R_\nu^{[2]} \approx 0.95$ , the numerical results are shown in Figures 4.11 and 4.12.

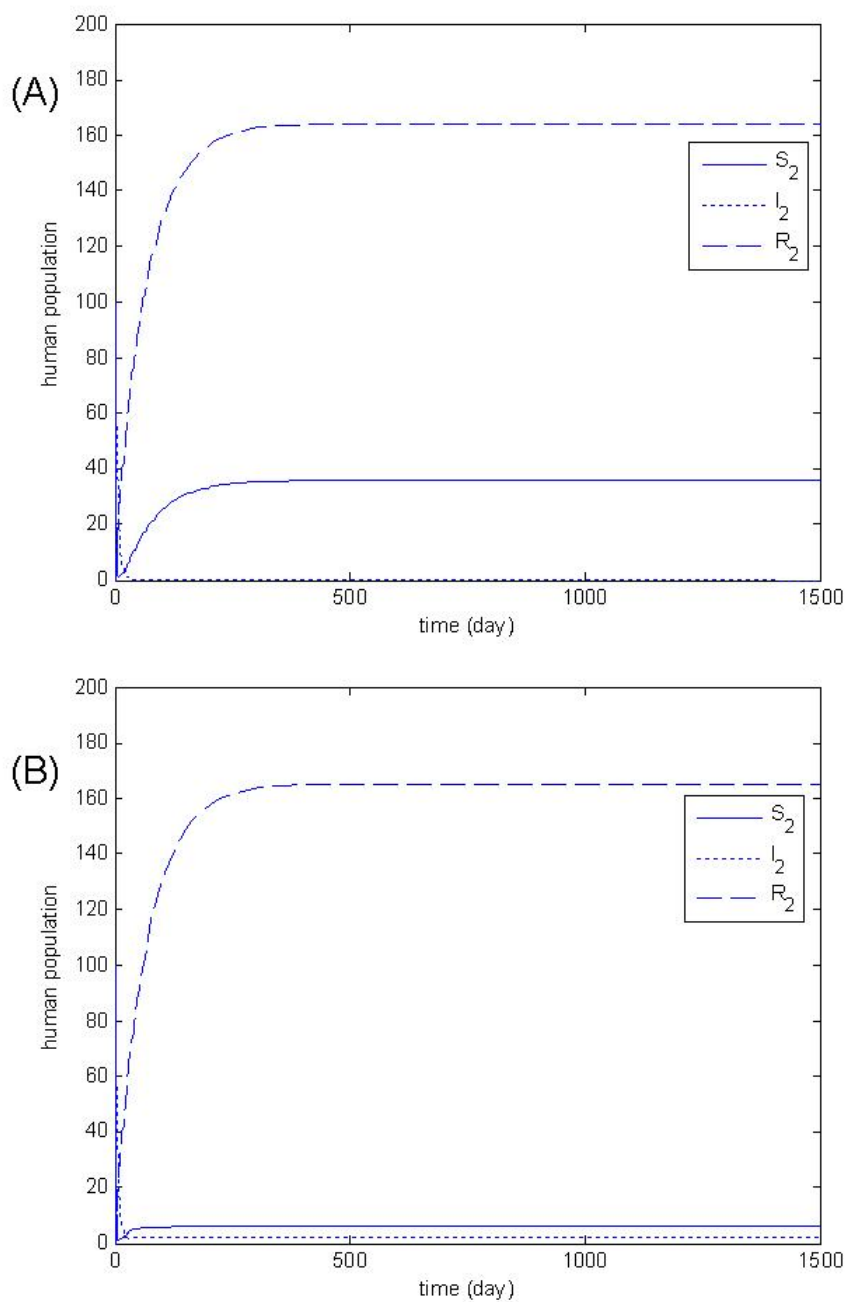


Figure 4.11: Numerical results of the BHVI system when  $R_v^{[2]} \approx 0.95$ . Figure (A) shows when  $R_0^{[1]} = 0.96 < 1$  and Figure (B) shows when  $R_0^{[1]} = 1.06 > 1$ .

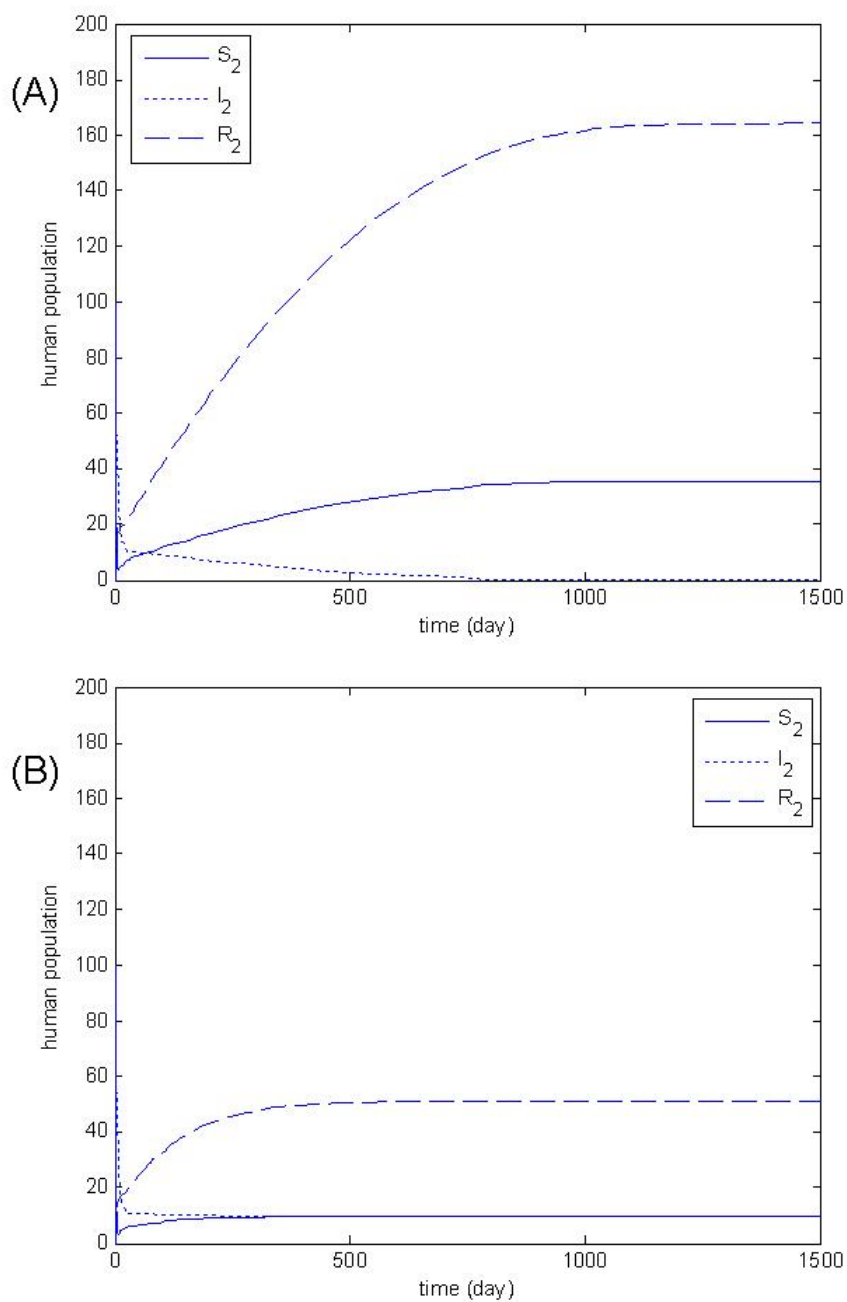


Figure 4.12: Numerical results of the BHVs system when  $R_\nu^{[2]} \approx 0.95$ . Figure (A) shows when  $R_0^{[1]} = 0.96 < 1$  and Figure (B) shows when  $R_0^{[1]} = 1.06 > 1$ .

Under the condition of the same value of the basic reproduction number ( $R_v^{[2]}$  and  $R_\nu^{[2]}$ ), as they are less than the threshold value 1, both systems (BHVI and BHVS) reach the infection free steady state where the number of infected humans is zero when  $R_0^{[1]} < 1$  (Figure 4.11 (A) and Figure 4.12 (A)). Infection is present in both systems when  $R_0^{[1]} > 1$  ((Figure 4.11 (B) and Figure 4.12 (B))). The results are consistent with the results we have before.

The numerical results show that when  $R_0^{[1]} < 1$ , an average of 2.65% the whole population (117 people in total) have to be vaccinated each day (3.1 people) so that the system could reach the infection free steady state ( $R_v^{[2]} \approx R_\nu^{[2]} \approx 0.95$ ) in the BHVI system, where only an average of 1.48% (101 people in total) in the BHVS system (1.49 people per day). When  $R_0^{[1]} > 1$ , 2.97% of the whole population (99 in total) need to be vaccinated each day (2.94 people) so that  $R_v^{[2]} \approx R_\nu^{[2]} \approx 0.95$  in BHVI and 1.97% (69 people in) in BHVS (1.35 people per day). (Refer to Table 4.3)

	bird-human 5-D	BHVI $\nu = 0.8208$	BHVS $\nu = 0.0692$
$R_0^{[1]} < 1$	0	2.65%	1.48%
$R_0^{[1]} > 1$	0	2.97%	1.97%

Table 4.3: The mean percentage vaccinated in the population to achieve  $R_v^{[2]} \approx R_\nu^{[2]} \approx 0.95$  in both vaccine systems. In the numerical results that produced by “ode15s” in MATLAB, at each time step, we first calculate the percentage of vaccinated susceptibles in the population, and then find the average percentage.

However, when  $R_0^{[1]} < 1$ , even though the systems reach the infection free steady state, it takes around 300 to 400 days in the BHVI system and more

than 1000 days in the BHVS to do so. In this case, the strategy of vaccination of immigrants has the advantage over the other.

In controlling of the maximum number of infecteds, the strategy of vaccination of susceptibles (BHVS) has 28.4091 when  $R_0^{[1]} < 1$  and 33.1262 when  $R_0^{[1]} > 1$ . That is almost half the number as in the BHVI system (Table 4.4).

	bird-human 5-D	BHVI $v = 0.8208$	BHVS $\nu = 0.0692$
$R_0^{[1]} < 1$	61.564	55.6951	28.4091
$R_0^{[1]} > 1$	63.3308	58.0504	33.1262

Table 4.4: The maximum number of infected humans of the original bird-human 5-D system, the BHVI system and the BHVS system.



# Chapter 5

## Quarantine & Treatment

When a contagious, severe and previously unknown (or partially known) disease becomes endemic or epidemic, the most usual and effective prevention is quarantine. Keeping infected people together or in isolation from susceptibles is able to lower the contact rate between infected and susceptible people and it is more convenient for the infected people getting medication.

In this chapter, we introduce quarantine of infected humans at a fixed rate  $\rho$  at each time step in the bird-human 5-D and 6-D (mutated) HPAI system, named BHQT and BHMQT, respectively. We form a new compartment group  $Q$  of those quarantined people, so that the two systems are of “SIQR” and “SIMQR” type.

Under normal circumstance, people under quarantine with treatment would have a lower additional death rate and higher recovery rate than the in-

fectured people without quarantine. Therefore, in the model of bird-human-quarantine-treatment (BHQT) system, we have a lower additional death rate ( $\alpha_3 < \alpha_2$ ) and a higher recovery rate ( $\gamma_3 > \gamma_2$ ) than in the infected class.

The bird-human system under quarantine without treatment (BHQ) is a special case of BHQT, where  $\alpha_3 = \alpha_2$  and  $\gamma_3 = \gamma_2$ .

## 5.1 The BHQT system

There are four compartments of the population in this BHQT system: human susceptible ( $S_2$ ), human infected with (mutated) HPAI ( $I_2$ ), human quarantined ( $Q_2$ ) and human removed ( $R_2$ ). The model equations are:

$$\frac{dS_2}{dt} = \Lambda_2 - \mu_2 S_2 - \beta_2 S_2 \frac{I_1}{N_1} - \beta_3 S_2 \frac{I_2}{N_2}, \quad (5.1)$$

$$\frac{dI_2}{dt} = \beta_2 S_2 \frac{I_1}{N_1} + \beta_3 S_2 \frac{I_2}{N_2} - (\mu_2 + \alpha_2 + \gamma_2 + \rho) I_2, \quad (5.2)$$

$$\frac{dQ_2}{dt} = \rho I_2 - (\mu_2 + \alpha_3 + \gamma_3) Q_2, \quad (5.3)$$

$$\frac{dR_2}{dt} = \gamma_2 I_2 + \gamma_3 Q_2 - \mu_2 R_2. \quad (5.4)$$

where the total population of humans ( $N_2$ ) is

$$N_2 = S_2 + I_2 + Q_2 + R_2. \quad (5.5)$$

### 5.1.1 Steady States

Let  $qths$  and  $qtfs$  represents the steady state of the human part of the BHQT and the full BHQT system.  $qths$  is derived from Equation (5.1)-(5.4) fixed by the steady state values in the bird system ( $bs_1$  and  $bs_2$ ). At the steady state of the full system,  $S_2^{qts}$  and  $R_2^{qts}$  can be rewritten in terms of  $I_2^{qts}$  and hence the steady state of the full system is

$$qtfs = \begin{pmatrix} S_1^{bs} \\ I_1^{bs} \\ S_2^{qths} \\ I_2^{qths} \\ Q_2^{qths} \\ R_2^{qths} \end{pmatrix} = \begin{pmatrix} S_1^{bs} \\ I_1^{bs} \\ \frac{\Lambda_2 - (\mu_2 + \alpha_2 + \gamma_2 + \rho)I_2^{qths}}{\mu_2} \\ I_2^{qths} \\ \frac{\rho}{\mu_2 + \alpha_3 + \gamma_3} I_2^{qths} \\ \frac{1}{\mu_2} \left( \gamma_2 + \gamma_3 \frac{\rho}{\mu_2 + \alpha_3 + \gamma_3} \right) I_2^{qths} \end{pmatrix}, \quad (5.6)$$

where  $N_2^{qths} = \frac{1}{\mu_2} (\Lambda_2 - \alpha_2 + \alpha_3 \frac{\rho}{\mu_2 + \alpha_3 + \gamma_3}) I_2^{qths}$ . Substitute the steady state values into Equation (5.2) and simplify to obtain a quadratic equation in  $I_2^{qts}$  (or substitute into Equation (5.1) to get a similar quadratic):

$$f(I_2^{qts}) = a(I_2^{qts})^2 + bI_2^{qts} + c = 0, \quad (5.7)$$

where

$$\begin{aligned} a &= \frac{\mu_2 + \alpha_2 + \gamma_2 + \rho}{\mu_2} \left( \left( \beta_2 \frac{I_1^{bs}}{N_1^{bs}} \frac{1}{\mu_2} + 1 \right) \left( \frac{\alpha_3 \rho}{\mu_2 + \alpha_3 + \gamma_3} + \alpha_2 \right) - \beta_3 \right), \\ b &= \frac{\Lambda_2}{\mu_2} \left( \beta_3 - \mu_2 - \alpha_2 - \gamma_2 - \rho - \beta_2 \frac{I_1^{bs}}{N_1^{bs}} \frac{1}{\mu_2} \left( \mu_2 + 2\alpha_2 + \gamma_2 + \rho + \frac{\alpha_3 \rho}{\mu_2 + \alpha_3 + \gamma_3} \right) \right), \\ c &= \beta_2 \left( \frac{\Lambda_2}{\mu_2} \right)^2 \frac{I_1^{bs}}{N_1^{bs}}. \end{aligned}$$

Note  $c$  is non-negative and the signs of  $a$  and  $b$  are determined by the values of the parameters. Also,

$$b^2 - 4ac = \left( \frac{\Lambda_2}{\mu_2} \right)^2 \left( (\beta_3 - \mu_2 - \alpha_2 - \gamma_2 - \rho)^2 + \left( \beta_2 \frac{\mu_2 + \gamma_2 + \rho}{\mu_2} \frac{I_1^{bs}}{N_1^{bs}} \right)^2 \right)$$

$$+2\beta_2 \frac{\mu_2 + \gamma_2 + \frac{\rho(\mu_2 + \gamma_3)}{\mu_2 + \alpha_3 + \gamma_3}}{\mu_2} (\beta_3 + \mu_2 + \alpha_2 + \gamma_2 + \rho) \frac{I_1^{bs}}{N_1^{bs}} > 0,$$

which shows that the roots of Equation (5.7) are real for all parameters values.

### Steady States $qtfs_1$ and $qtfs_2$

The steady states of the full system  $qtfs_1$  and  $qtfs_2$  are combinations of the steady state of the bird system  $bs_1$  and the steady states of the human system in HBQT ( $qths_1$  and  $qths_2$ ) derived with fixed value of  $bs_1$ . At  $bs_1$ , where  $I_1^{bs_1} = 0$ , the coefficients of the quadratic equation  $a$ ,  $b$  and  $c$  can be simplified to

$$\begin{aligned} a &= \frac{\mu_2 + \alpha_2 + \gamma_2 + \rho}{\mu_2} \left( \alpha_2 + \frac{\alpha_3 \rho}{\mu_2 + \alpha_3 + \gamma_3} - \beta_3 \right), \\ b &= \frac{\Lambda_2}{\mu_2} (\beta_3 - \mu_2 - \alpha_2 - \gamma_2 - \rho), \\ c &= 0, \end{aligned}$$

which gives

$$\begin{aligned} I_2^{qt_s1} &= 0 \\ I_2^{qt_s2} &= \frac{\Lambda_2 (\beta_3 - \mu_2 - \alpha_2 - \gamma_2 - \rho)}{((\beta_3 - \alpha_2)(\mu_2 + \alpha_3 + \gamma_3) - \alpha_3 \rho)(\mu_2 + \alpha_2 + \gamma_2 + \rho)} \end{aligned}$$

Thus, the steady state values can be developed as:

$$qtfs_1 = \begin{pmatrix} S_1^{bs_1} \\ I_1^{bs_1} \\ S_2^{qths_1} \\ I_2^{qths_1} \\ Q_2^{qths_1} \\ R_2^{qths_1} \end{pmatrix} = \begin{pmatrix} \frac{\Lambda_1}{\mu_1} \\ 0 \\ \frac{\Lambda_2}{\mu_2} \\ 0 \\ 0 \\ 0 \end{pmatrix}, \quad (5.8)$$

where  $N_2^{qths_1} = \frac{\Lambda_2}{\mu_2}$ . It is the infection free steady state. The other steady state

$$qtfs_2 = \begin{pmatrix} S_1^{bs_1} \\ I_1^{bs_1} \\ S_2^{qths_2} \\ I_2^{qths_2} \\ Q_2^{qths_2} \\ R_2^{qths_2} \end{pmatrix} = \begin{pmatrix} \frac{\Lambda_1}{\mu_1} \\ 0 \\ \frac{\Lambda_2((\mu_2+\gamma_2)(\mu_2+\alpha_3+\gamma_3)+\rho(\mu_2+\gamma_3))}{\mu_2((\beta_3-\alpha_2)(\mu_2+\alpha_3+\gamma_3)-\alpha_3\rho)} \\ \frac{\Lambda_2(\beta_3-\mu_2-\alpha_2-\gamma_2-\rho)(\mu_2+\alpha_3+\gamma_3)}{((\beta_3-\alpha_2)(\mu_2+\alpha_3+\gamma_3)-\alpha_3\rho)(\mu_2+\alpha_2+\gamma_2+\rho)} \\ \frac{\Lambda_2(\beta_3-\mu_2-\alpha_2-\gamma_2-\rho)\rho}{((\beta_3-\alpha_2)(\mu_2+\alpha_3+\gamma_3)-\alpha_3\rho)(\mu_2+\alpha_2+\gamma_2+\rho)} \\ \frac{\Lambda_2(\beta_3-\mu_2-\alpha_2-\gamma_2-\rho)(\gamma_2(\mu_2+\alpha_3+\gamma_3)+\gamma_3\rho)}{\mu_2((\beta_3-\alpha_2)(\mu_2+\alpha_3+\gamma_3)-\alpha_3\rho)(\mu_2+\alpha_2+\gamma_2+\rho)} \end{pmatrix}, \quad (5.9)$$

where  $N_2^{qths_2} = \frac{\beta_3\Lambda_2((\mu_2+\gamma_2)(\mu_2+\alpha_3+\gamma_3)+\rho(\mu_2+\gamma_3))}{\mu_2((\beta_3-\alpha_2)(\mu_2+\alpha_3+\gamma_3)-\alpha_3\rho)(\mu_2+\alpha_2+\gamma_2+\rho)}$ . There is no infection of HPAI in birds but there are infections of mutated HPAI in humans.

Steady state  $qtfs_1$  exists for all values of  $R_0^{[1]}$  and  $R_0^{[2]}$ . Steady state  $qtfs_2$  exists for all  $R_0^{[1]}$  and  $\beta_3 - \mu_2 - \alpha_2 - \gamma_2 - \rho > 0$ .

### Steady States $qtfs_3$

The steady state of the full system  $qtfs_3$  is a combination of the steady state of birds  $bs_2$  and the steady state of the human system in BHQT derived with

a fixed value of  $bs_2$ . It represents the situation where infections are present in both the bird and human systems. The roots of Equation 5.7 depend on the values of parameters  $a$ ,  $b$  and  $c$ . There are two cases:

Case (1)

$$\left( \beta_2 \frac{I_1^{bs}}{N_1^{bs}} \frac{1}{\mu_2} + 1 \right) \left( \frac{\alpha_3 \rho}{\mu_2 + \alpha_3 + \gamma_3} + \alpha_2 \right) < \beta_3 \quad (5.10)$$

Case (2)

$$\left( \beta_2 \frac{I_1^{bs}}{N_1^{bs}} \frac{1}{\mu_2} + 1 \right) \left( \frac{\alpha_3 \rho}{\mu_2 + \alpha_3 + \gamma_3} + \alpha_2 \right) > \beta_3 \quad (5.11)$$

Under the condition of Case (1),  $a < 0$ . Because

$$f(0) = \beta_2 \left( \frac{\Lambda_2}{\mu_2} \right)^2 \frac{I_1^{bs}}{N_1^{bs}} > 0, \quad (5.12)$$

Equation 5.7 has one positive root and one negative root (which we ignore).

Under the condition of Case (2),  $a > 0$  and  $b < 0$ . Thus,  $\sqrt{b^2 - 4ac} < |b|$ , which implies two roots of Equation 5.7 are positive.

However, numerical results shows that, in Case (1), there are two positive real roots of  $S_2^{qths_3}$  and in Case (2), there is one positive and one negative real root of  $S_2^{qths_3}$ . Thus, we conjecture that only one steady state  $qtfs_3$  exist for  $bs_2$  and it is unique. Steady state  $qtfs_3$  only exists when  $R_0^{[1]}$  greater than 1.

### 5.1.2 Basic reproduction number

The basic reproduction number for the human system,  $R_q^{[2]}$ , is defined as

$$R_q^{[2]} = \frac{\beta_3}{\mu_2 + \alpha_2 + \gamma_2 + \rho}. \quad (5.13)$$

Recall one of the conditions for the existence of  $qtfs_2$  is  $\beta_3 - \mu_2 - \alpha_2 - \gamma_2 - \rho > 0$ , which is equivalent to  $R_q^{[2]} > 1$ . Thus, we can conclude that  $qtfs_2$  exist for all  $R_0^{[1]}$  values and  $R_q^{[2]} > 1$ .

Compare it with the basic reproduction number in the original bird-human system ( $R_0^{[2]}$ ), we have

$$R_q^{[2]} = \frac{\mu_2 + \alpha_2 + \gamma_2}{\mu_2 + \alpha_2 + \gamma_2 + \rho} R_0^{[2]}. \quad (5.14)$$

The basic reproduction number  $R_q^{[2]}$  is under the threshold 1 when

$$\rho > (\mu_2 + \alpha_2 + \gamma_2)(R_0^{[2]} - 1). \quad (5.15)$$

### 5.1.3 Local Stability

Refer to section 3.1.3, we need to determined the stability at each steady state of the human system. The Jacobian matrix of the human system  $J_h$  is

$$J_{qth} = \begin{pmatrix} -\mu_2 - \beta_2 \frac{I_1}{N_1} - \beta_3 i & -\beta_3 j & \beta_3 k & \beta_3 k \\ \beta_2 \frac{I_1}{N_1} + \beta_3 i & \beta_3 j - \mu_2 - \alpha_2 - \gamma_2 - \rho & -\beta_3 k & -\beta_3 k \\ 0 & \rho & -\mu_2 - \alpha_3 - \gamma_3 & 0 \\ 0 & \gamma_2 & \gamma_3 & -\mu_2 \end{pmatrix}, \quad (5.16)$$

where

$$\begin{aligned} i &= \frac{I_2(I_2 + Q_2 + R_2)}{N_2^2}, \\ j &= \frac{S_2(S_2 + Q_2 + R_2)}{N_2^2}, \\ k &= \frac{S_2 I_2}{N_2^2}. \end{aligned}$$

The terms  $i$ ,  $j$  and  $k$  are non-negative.

**Stability of  $qths_1$** 

At  $qths_1$ ,

$$i = 0,$$

$$j = 1,$$

$$k = 0,$$

and

$$J_{qths_1} = \begin{pmatrix} -\mu_2 & -\beta_3 & 0 & 0 \\ 0 & \beta_3 - \mu_2 - \alpha_2 - \gamma_2 - \rho & 0 & 0 \\ 0 & \rho & -\mu_2 - \alpha_3 - \gamma_3 & 0 \\ 0 & \gamma_2 & \gamma_3 & -\mu_2 \end{pmatrix}, \quad (5.17)$$

Thus, the eigenvalues of  $J_h^{bs_1}$  are  $-\mu_2$ ,  $\beta_3 - \mu_2 - \alpha_2 - \gamma_2 - \rho$ ,  $-\mu_2 - \alpha_3 - \gamma_3$  and  $-\mu_2$ . They are all negative if  $R_q^{[2]} < 1$ . Thus, we can conclude that  $qths_1$  is locally stable when  $R_q^{[2]}$  less than 1.

**Stability of  $qths_2$** 

The Jacobian matrix at  $qths_2$  is

$$J_{qths_2} = \begin{pmatrix} -\mu_2 - \beta_3 i & -\beta_3 j & \beta_3 k & \beta_3 k \\ \beta_3 i & \beta_3 j - \mu_2 - \alpha_2 - \gamma_2 - q & -\beta_3 k & -\beta_3 k \\ 0 & q & -\mu_2 - \alpha_3 - \gamma_3 & 0 \\ 0 & \gamma_2 & \gamma_3 & -\mu_2 \end{pmatrix}, \quad (5.18)$$

where  $i$ ,  $j$  and  $k$  are evaluated at  $qths_2$ . Let  $A = -J_{qth}^{qths_2}(1, 1)$ ,  $B = -J_{qth}^{qths_2}(1, 3)$ , ... etc.,  $J_{qth}^{qths_2}$  can be rewritten as

$$J_{qths_2} = \begin{pmatrix} -A & -B & C & C \\ D & -E & -C & -C \\ 0 & F & -G & 0 \\ 0 & H & I & -J \end{pmatrix}. \quad (5.19)$$

The characteristic equation is

$$\lambda^4 + a_0\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0 \quad (5.20)$$

where

$$a_0 = A + E + G + J,$$

$$a_1 = AE + GJ + (A + E)(G + J) + CF + CH + BD,$$

$$a_2 = (G + J)(AE + BD) + GJ(A + E) + CF(A + I + J - D) + CH(A + G - D)$$

$$a_3 = GJ(AE + BD) + C(F(J + I) + GH)(A - D).$$

Since  $A = D + J$ ,

$$a_2 = (G + J)(AE + BD + CH) + GJ(A + E) + CF(I + 2J),$$

$$a_3 = J(G(AE + BD) + C(F(J + I) + GH)).$$

Thus,  $a_0$ ,  $a_1$ ,  $a_2$  and  $a_3$  are all positive. We need to check the sign of  $a_0a_1a_2 - a_2^2 - a_3a_0^2$  in order to determine the stability of  $qts_2$ . Firstly, evaluate  $a_0a_1a_2 - a_2^2$  that

$$\begin{aligned} a_0a_1a_2 - a_2^2 &= a_2(a_0a_1 - a_2) \\ &= a_2((A + E + G + J)(AE + GJ + (A + E)(G + J) + CF + CH \\ &\quad + BD) - (AE(G + J) + GJ(A + E) + 2CFJ + CH(G + J) + \end{aligned}$$

$$\begin{aligned}
& BD(G + J) + CFI)) \\
= & a_2((A + E)(AE + (A + E)(G + J) + CF + CH + BD) + \\
& (G + J)(GJ + (A + E)(G + J)) + CF(G - J - I)).
\end{aligned}$$

Since  $G = J + I + \alpha_3$ ,  $a_0a_1a_2 - a_2^2$  is positive. Then, check the whole expression  $a_0a_1a_2 - a_2^2 - a_3a_0^2$ . Note  $a_3$  has a common factor  $J$  and hence  $a_3a_0^2$  can be rewrite as

$$\begin{aligned}
a_3a_0^2 &= a_3(A + E + G + J)^2 \\
&= a_3((A + E)^2 + (A + E)(G + J)) + a_3((G + J)^2 + (A + E)(G + J)).
\end{aligned}$$

Then,

$$\begin{aligned}
& a_0a_1a_2 - a_2^2 - a_3a_0^2 \\
= & ((G + J)(AE + BD + CH) + GJ(A + E) + CF(I + 2J))(((A + E) \\
& (AE + (A + E)(G + J) + CF + CH + BD) + (G + J)(GJ + (A + E)(G + J)) \\
& + CF(G - J - I))) - (J(G(AE + BD) + C(F(J + I) + GH))((A + E)^2 \\
& + (G + J)^2 + 2(A + E)(G + J)) \\
= & G(AE + BD)((A + E)(AE + (A + E)(G + J) + CF + CH + BD) \\
& + (A + E)(G^2 + J^2 + GJ) + CF(G - J - I))J(AE + BD)((A + E) \\
& (AE + (A + E)(G + J) + CF + CH + BD) + (A + E)J^2 \\
& + CF(G - J - I)) + CH(G + J)((A + E)(AE + CF + CH + BD) \\
& + (A + E)(AJ + G(A - J) + E(G + J)) + (A + E)(G^2 + J^2 + GJ) \\
& + CF(G - J - I)) + GJ(A + E)((A + E)^2(G + J) + (G + J) \\
& (GJ + (A + E)(G + J)) + CF(G - J - I)) + CFJ((A + E) \\
& (AE + (A + E)(G + J) + CF + CH + BD) + (G + J)(GJ + (A + E) \\
& (G + J)) + CF(G - J - I)) + CF(I + J)((A + E)(AE + (A + E - 2J)
\end{aligned}$$

$$(G + J) + CF + CH + BD) + (G + J)(GJ) + (G + J)^2(A + E - J) \\ + CF(G - J - I)).$$

Hence, the term  $a_0a_1a_2 - a_2^2 - a_3a_0^2$  is positive. By the Routh-Hurwitz criteria [4], steady state  $qths_2$  is locally stable when it exists.

### Stability of $qths_3$

At  $qths_3$ , the Jacobian matrix is of the same form as  $J_{qths_2}$ , only with  $i, j, k$  evaluated at different steady state and  $I_1^{bs_2} \neq 0$ . Hence, the results of the characteristic equation at  $qths_3$  are the same as at  $qths_2$  and thus, we can conclude that steady state  $qths_3$  is also locally stable when it exists.

## 5.1.4 Summary

Over all, there are three steady states in the BHQT system:

Steady state  $qths_1$  represents the situation where there is no infection of mutated HPAI in the human system. It exists for all values of  $R_0^{[1]}$  and  $R_q^{[2]}$ , but it is stable only when  $R_q^{[2]} < 1$ . Hence, combine this with the stability of  $bs_1$ , we can conclude that the steady state of BHQT  $qtfs_1$ , which represents the situation where there is no infection of (mutated) HPAI in both the bird and the human system, exists for all values of  $R_0^{[1]}$  and  $R_q^{[2]}$ . It is stable only when  $R_0^{[1]} < 1$  and  $R_q^{[2]} < 1$ .

Steady state  $qths_2$  represents the situation where there is infection of mutated HPAI presents in humans. It exists for all  $R_0^{[1]}$  and  $R_q^{[2]} > 1$ .  $qths_2$  is stable when it exists. Hence, combining this with the stability of  $bs_1$ , we can conclude that the steady state of BHQT  $qtfs_2$ , which represents the situation where there is no infection of HPAI in birds and infections of (mutated) HPAI are present in humans, exists for all  $R_0^{[1]}$  and  $R_q^{[2]} > 1$ . It is stable when  $R_0^{[1]} < 1$  and  $R_q^{[2]} > 1$ .

Steady state  $qths_3$  represents the situation where infections of (mutated) HPAI are present in humans. It exists when  $R_0^{[1]} > 1$  and is stable when it exists. Hence, combine this with the stability of  $bs_2$ , we can conclude that the steady state of BHQT  $qtfs_3$ , which represents the situation where infections of (mutated) HPAI are present in both birds and humans, exists when  $R_0^{[1]} > 1$  and all values of  $R_q^{[2]}$ . It is stable when it exists.

### 5.1.5 Numerical results

In order to check the analytic results with numerical results, choose different values of  $\beta_1$  ( $9.6/10.6 \text{ day}^{-1}$ ) to adjust  $R_0^{[1]}$ . Assume quarantine is only needed when there is a chance of an endemic in the human system, therefore, choose  $\beta_3$  to be  $1.2 \text{ day}^{-1}$  for  $R_0^{[2]} > 1$ ; as  $R_q^{[2]} = \frac{\mu_2 + \alpha_2 + \gamma_2}{\mu_2 + \alpha_2 + \gamma_2 + \rho} R_0^{[2]}$ , choose  $\rho$  to be  $0.03$  ( $R_q^{[2]} > 1$ ) and  $1$  ( $R_q^{[2]} < 1$ ); let the additional death rate and recovery rate to be  $0.15 \text{ day}^{-1}$  and  $0.04 \text{ day}^{-1}$ , respectively; other parameters value refer to Table 2.2 and 3.2.

The analytic steady states (section 5.1.1) values are shown in Table 5.1.

	$\beta_1 = 9.6$		$\beta_1 = 10.6$	
	$\rho = 0.03$	$\rho = 1$	$\rho = 0.03$	$\rho = 1$
$S_2$ (people)	6.7581	200	5.7946	26.7048
$I_2$ (people)	11.3672	0	11.4238	2.122
$Q_2$ (people)	1.6635	0	1.6718	10.3511
$R_2$ (people)	12.0141	0	12.074	29.0177
$N_2$ (people)	31.8028	200	30.9642	68.1956
$R_q^{[2]}$	4.7059	0.9796	4.7059	0.9796

Table 5.1: Analytic steady state of the BHVI system with parameter values.

Use MATLAB “ode15s” to solve for steady states. The results are shown in Figures 5.1 and 5.2.

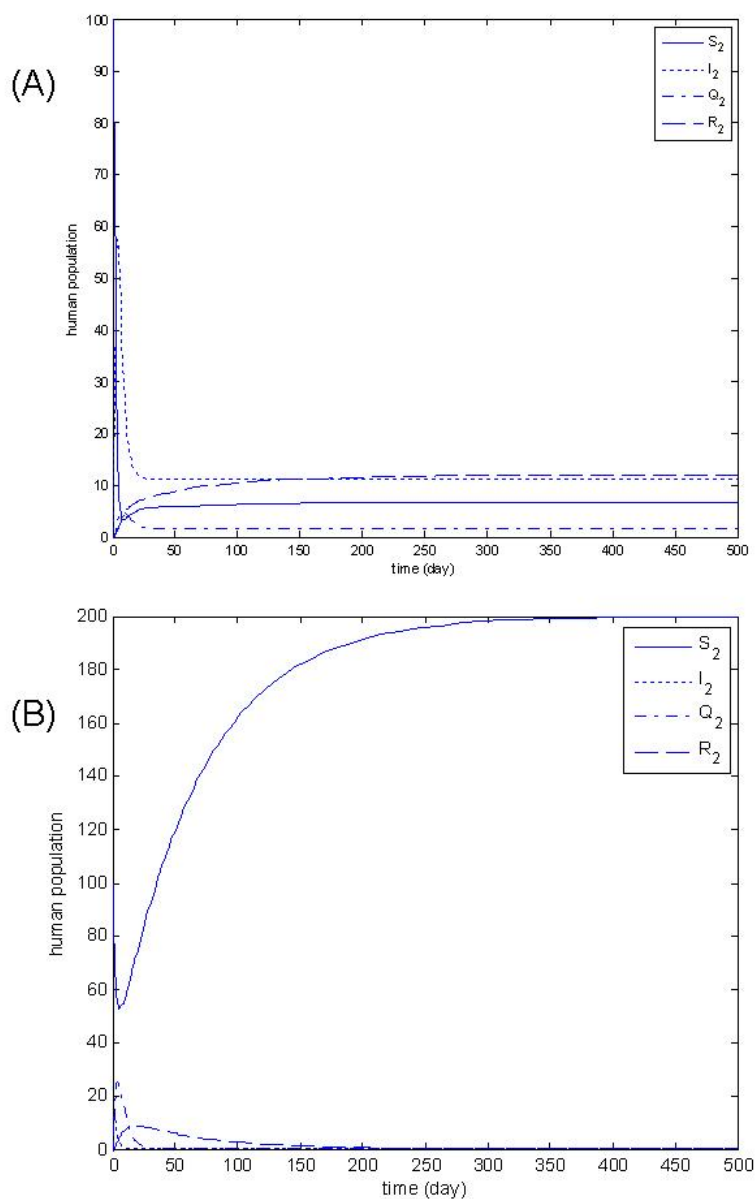


Figure 5.1: Numerical results for the BHQT system with initial values of  $(S_2, I_2, Q_2, R_2) = (100, 0, 0, 0)$  for  $\beta_1 = 9.6$  in the first 500 days. Figure (A):  $\rho = 0.03$  ( $R_q^{[2]} = 4.7059 > 1$ ). Figure (B):  $\rho = 1$  ( $R_q^{[2]} = 0.9796 < 1$ ).

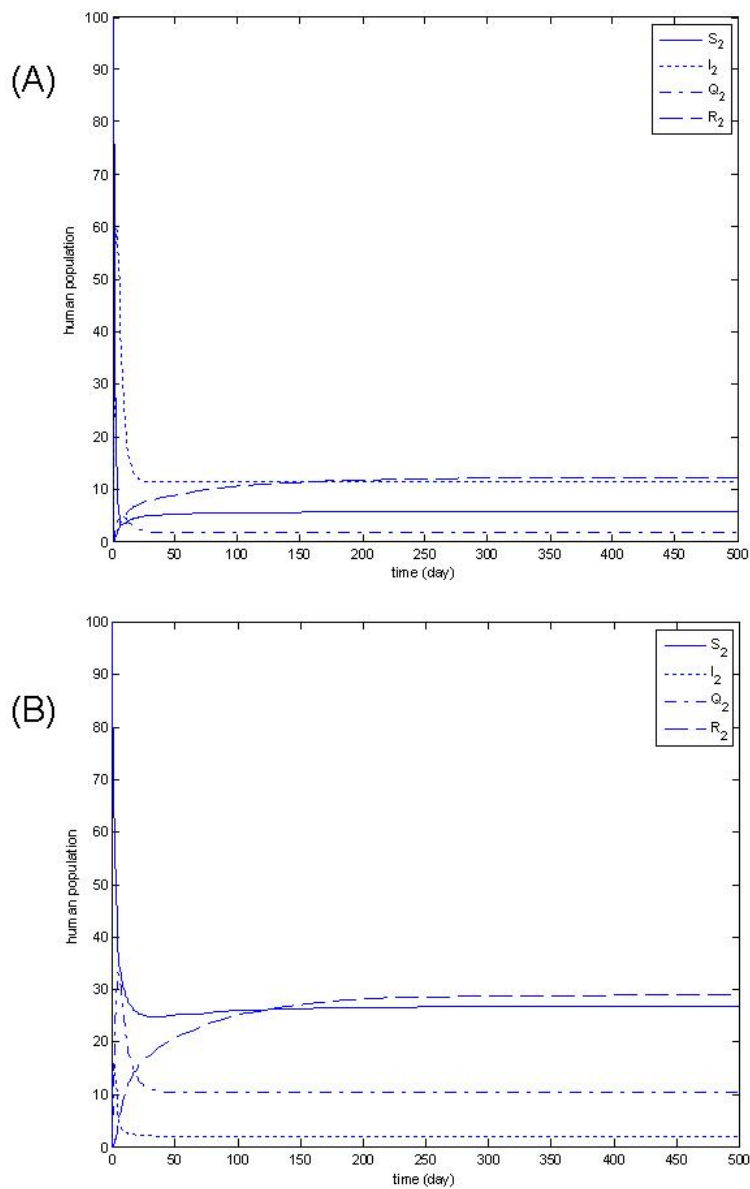


Figure 5.2: Numerical results for the BHQT system with initial values of  $(S_2, I_2, Q_2, R_2) = (100, 0, 0, 0)$  for  $\beta_1 = 10.6$  in the first 500 days. Figure (A):  $\rho = 0.03$  ( $R_q^{[2]} = 4.7059 > 1$ ). Figure (B):  $\rho = 1$  ( $R_q^{[2]} = 0.9796 < 1$ ).

In Figure 5.1 (B) when  $\beta_1 = 9.6$  and  $\rho = 1$  ( $R_0^{[1]} < 1$  and  $R_q^{[2]} < 1$ ), the system approaches  $(S_2, I_2, Q_2, R_2) = (200, 0, 0, 0)$  which is the infection free steady state for the BHVS system. In Figure 5.1 (A) when  $\beta_1 = 9.6$  and  $\rho = 0.03$  ( $R_0^{[1]} < 1$  and  $R_q^{[2]} > 1$ ), the system approaches  $(S_2, I_2, Q_2, R_2) = (6.757, 11.37, 1.663, 12.01)$  where there is no infection of HPAI in bird but infection of (mutated) HPAI in humans.

In Figure 5.2 (B) when  $\beta_1 = 10.6$  and  $\rho = 1$  ( $R_0^{[1]} > 1$  and  $R_q^{[2]} < 1$ ), the system approaches  $(S_2, I_2, Q_2, R_2) = (26.7, 2.122, 10.35, 29.01)$ . In Figure 5.1 (A) when  $\beta_1 = 9.6$  and  $\rho = 0.03$  ( $R_0^{[1]} < 1$  and  $R_q^{[2]} > 1$ ), the system approaches  $(S_2, I_2, Q_2, R_2) = (5.795, 11.42, 1.672, 12.07)$ . In both case, infection of (mutated) HPAI is always present in the bird and the human system.

## 5.2 The BHMQT system

Similar to the BHQI model, another population compartment  $Q$  is introduced into the SIMR human model. Infected humans with (mutated) HPAI are quarantined and treated at rate  $\rho_1$  and  $\rho_2$  each day. Since there are two types of influenza (HPAI or mutated HPAI), there might be different symptoms in the population. Hence,  $\rho_1$  and  $\rho_2$  may not be equal to each other. Note that we also quarantine the people who are infected with HPAI even they are not contagious to other susceptible humans, because they may be difficult to distinguish. The model equations are:

$$\frac{dS_2}{dt} = \Lambda_2 - \mu_2 S_2 - \beta_2 S_2 \frac{I_1}{N_1} - \beta_3 S_2 \frac{M_2}{N_2} \quad (5.21)$$

$$\frac{dI_2}{dt} = \beta_2 S_2 \frac{I_1}{N_1} - (\mu_2 + \alpha_2 + \gamma_2 + \rho_1 + \epsilon) I_2 \quad (5.22)$$

$$\frac{dM_2}{dt} = \beta_3 S_2 \frac{M_2}{N_2} + \epsilon I_2 - (\mu_2 + \alpha_3 + \gamma_3 + \rho_2) M_2 \quad (5.23)$$

$$\frac{dQ_2}{dt} = \rho_1 I_2 + \rho_2 M_2 - (\mu_2 + \alpha_4 + \gamma_4) Q_2, \quad (5.24)$$

$$\frac{dR_2}{dt} = \gamma_2 I_2 + \gamma_3 M_2 + \gamma_4 Q_2 - \mu_2 R_2. \quad (5.25)$$

The total number of humans is

$$N_2 = S_2 + I_2 + M_2 + Q_2 + R_2. \quad (5.26)$$

### 5.2.1 Basic reproduction number

The basic reproduction number for the human system,  $R_q^{[3]}$ , is defined as

$$R_q^{[3]} = \frac{\beta_3}{\mu_2 + \alpha_3 + \gamma_3 + \rho_2}. \quad (5.27)$$

Compare it with the basic reproduction number in the original human system

$R_0^{[3]}$ , we have

$$R_q^{[3]} = \frac{\mu_2 + \alpha_3 + \gamma_3}{\mu_2 + \alpha_3 + \gamma_3 + \rho_2} R_0^{[2]}. \quad (5.28)$$

$R_q^{[3]}$  is under the threshold 1 when

$$\rho_2 > (\mu_2 + \alpha_3 + \gamma_3)(R_0^{[3]} - 1). \quad (5.29)$$

### 5.2.2 Numerical results

Similar to the BHQT system, choose different values of  $\beta_1$  (9.6/10.6 day<sup>-1</sup>) to adjust  $R_0^{[1]}$ . Assume quarantine is only needed when there is a chance

of an endemic in the human system, therefore, choose  $\beta_3$  to be  $\frac{2}{3}$  day<sup>-1</sup> for  $R_0^{[3]} > 1$ . Choose  $\rho_1$  to be 0.01. In order to keep  $R_q^{[3]}$  the same as  $R_q^{[2]}$  (to compare), choose  $\rho_2$  to be  $\frac{1}{60}$  ( $R_q^{[3]} > 1$ ) and 0.555498 ( $R_q^{[3]} < 1$ ). Let the  $\alpha_4$  and  $\gamma_4$  to be 0.15 day<sup>-1</sup> and 0.04 day<sup>-1</sup>, respectively; other parameter values remain the same as before.

Use MATLAB “ode15s” solve for steady states. The results are shown in Figures 5.3 and 5.4.

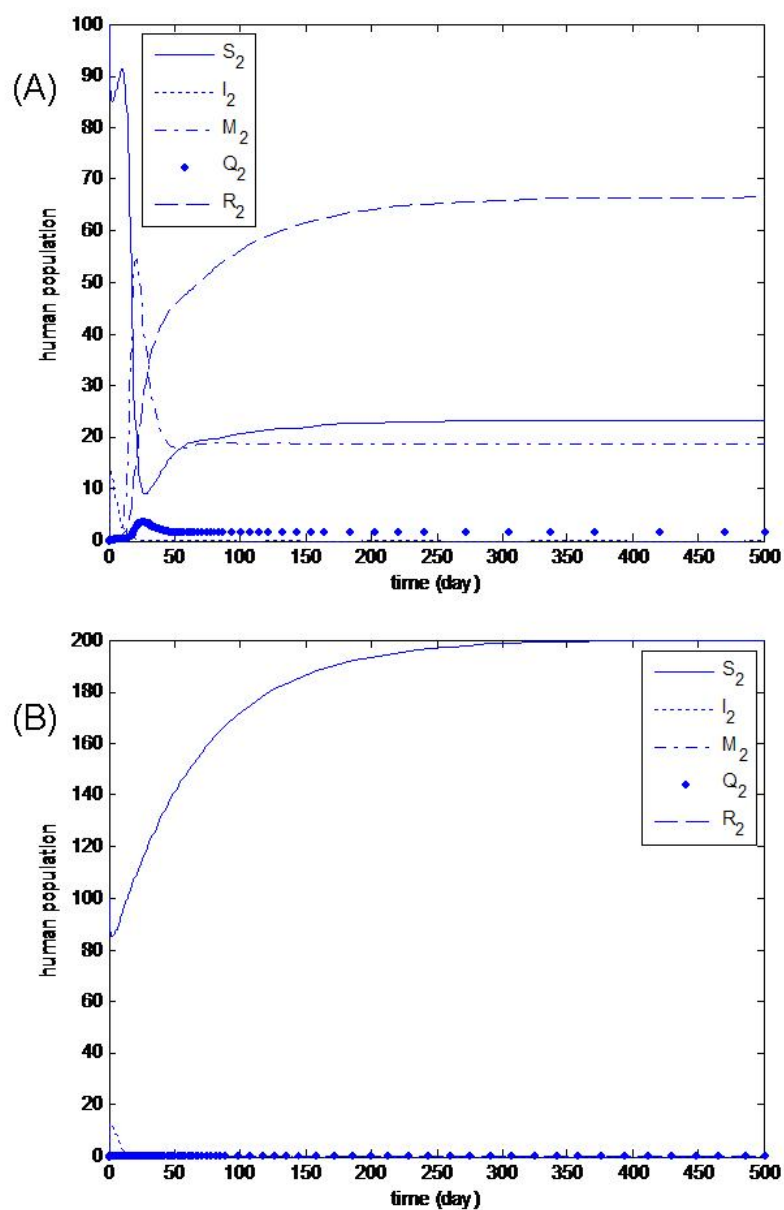


Figure 5.3: Numerical results for the BHMQT system with initial values of  $(S_2, I_2, M_2, Q_2, R_2) = (100, 0, 0, 0, 0)$  for  $\beta_1 = 9.6$  in the first 500 days. Figure (A):  $\rho_2 = \frac{1}{60}$  ( $R_q^{[3]} = 4.7059 > 1$ ). Figure (B):  $\rho_2 = 0.5555498$  ( $R_q^{[3]} = 0.9796 < 1$ ).

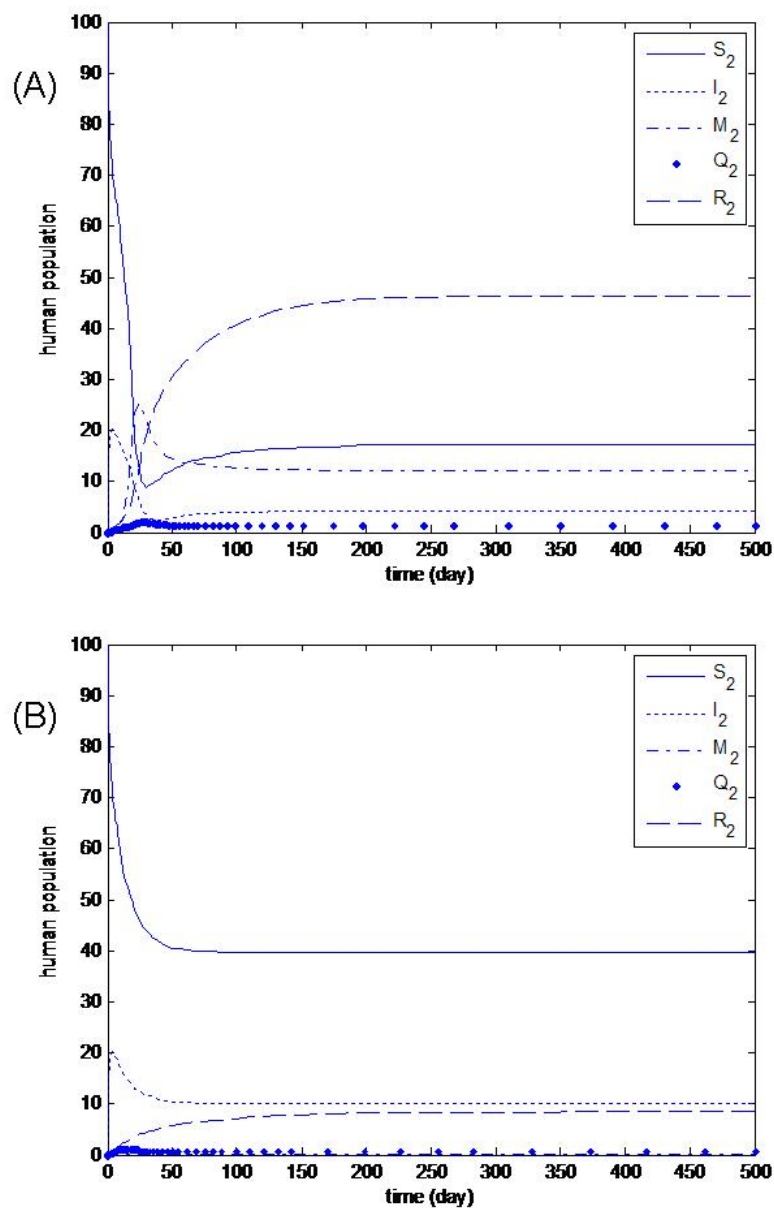


Figure 5.4: Numerical results for the BHMQT system with initial values of  $(S_2, I_2, M_2, Q_2, R_2) = (100, 0, 0, 0, 0)$  for  $\beta_1 = 10.6$  in the first 500 days. Figure (A):  $\rho = \frac{1}{60}$  ( $R_q^{[3]} = 4.7059 > 1$ ). Figure (B):  $\rho_2 = 0.5555498$  ( $R_q^{[3]} = 0.9796 < 1$ ).

In Figure 5.3 (B) when  $R_0^{[1]} < 1$  and  $R_q^{[3]} < 1$ , the system reaches an infection free steady state for the BHMQT system. In Figure 5.3 (A) when  $R_0^{[1]} < 1$  and  $R_q^{[3]} > 1$ , there is no infection of HPAI in birds but infections of mutated HPAI are present in humans. The quarantined class, hence is not empty at steady state.

In Figure 5.4 when  $R_0^{[1]} > 1$ , in both cases of  $R_q^{[3]}$ , the system approaches the non-zero steady state which represents infections of (mutated) HPAI are present in birds and humans. When  $R_0^{[1]} > 1$  and  $R_q^{[3]} < 1$ , the numerical results show that the number of infected human with mutated HPAI is greater than 0 but less than 1. Most of this small amount infected human with mutated HPAI comes from the mutation of the HPAI viruses. The quarantined class is also non-empty in both cases.

### 5.3 Quarantine for limited times BHQT

The analytical and numerical results we have for the BHQT system are calculated in the situation where quarantine exists for all time  $t$ . However, in real world, quarantine can not be brought into effect forever. Therefore, in this section, we first simulate the endemic situation for a short period of time without quarantine, and then add quarantine into the system (quarantine rate is non-zero) for a limited time (e.g. 14 days). Using all parameter values as before and the quarantine rate  $\rho = 1$ , we have the results in Figures 5.5 and 5.6.

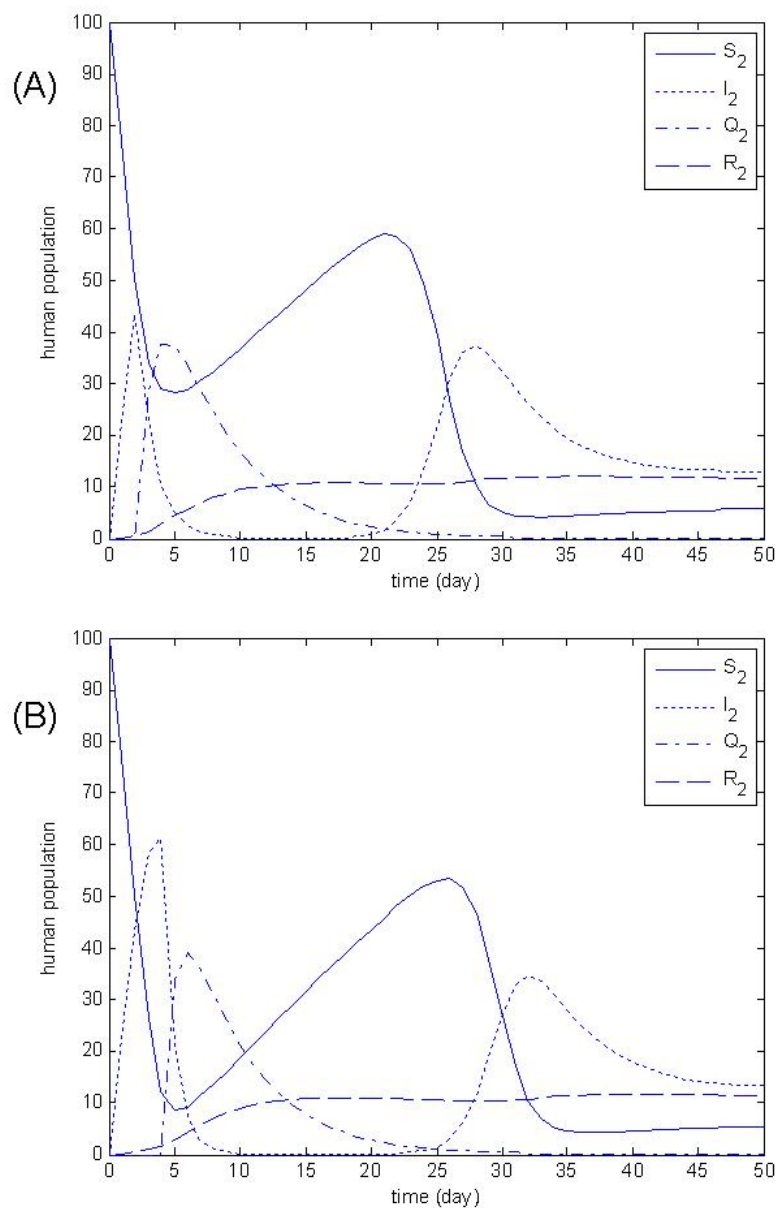


Figure 5.5: Numerical results for the BHQT system when quarantine is introduced for limited times when  $R_0^{[1]} < 1$  and  $R_q^{[2]} < 1$ . Figure (A): quarantine starts when the endemic just begins (on day 2). Figure (B): quarantine starts when the number of infected humans reach the peak (on day 4).

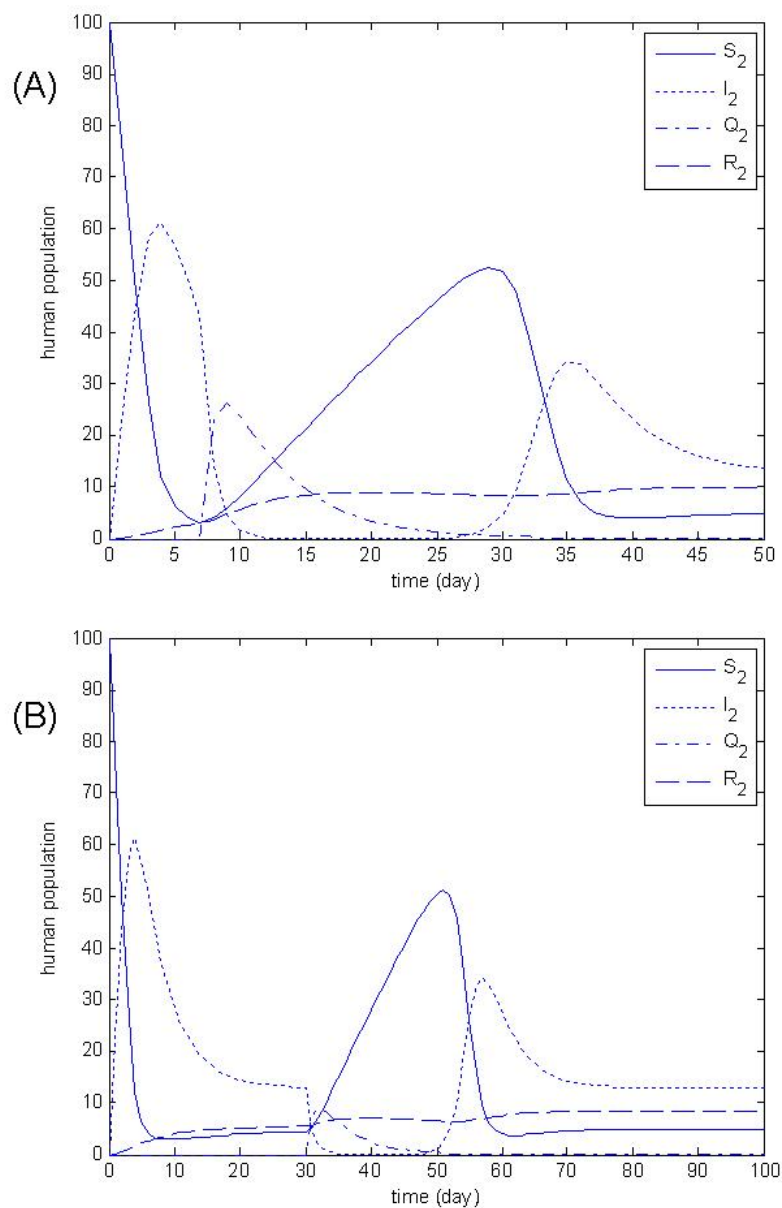


Figure 5.6: Numerical results for the BHQT system when quarantine is introduced for limited times when  $R_0^{[1]} < 1$  and  $R_q^{[2]} < 1$ . Figure (A): quarantine starts when the number of infected humans starts climbing down the hill (on day 7). Figure (B): quarantine starts when the system reaches the steady state (on day 12).

In all figures, after quarantine is launched, the number of infected humans decreases sharply till it reaches nearly zero and holds for a small amount of time (approximate 14 days which equals the quarantine time). The number of susceptible humans, in the meanwhile, increases dramatically. After quarantine has been stopped, the number of infected humans starts to rise again and reaches another peak in about 10 days, just a little bit lower than the first one. The systems reaches a steady state after the second peak.

Theoretically, in the case of the quarantine rate  $\rho = 1$ ,  $R_q^{[2]} < 1$ , which means the system should reach to the infection free steady state when the system is quarantined for all  $t$ . In our numerical results, shortly after quarantine launches, the number of infected humans decreases and reaches to nearly zero ( $\ll 1$ ). Even though it is a small number, we can not assume that the infection is stopped, it is only in controlled.

More over, the numerical results also suggest that this steady state is not stable after quarantine stopped. That is because the number of infected humans is not exactly zero. The large number of susceptible humans in the population results the number of infected human rises to the second peak. The infection free steady state under quarantine is not a stable steady state.

To prevent this situation, we have to abate the number of susceptible humans to a reasonable value so that an infected human may not contact and transmit the virus in the same rate. Consider the models we present so far, vaccination is a useful strategy of transferring susceptible individuals into the removed class and it has no time limitation. Hence, we consider adding vaccination with quarantine in our model.

Compare two strategies of vaccination (section 4.5), vaccination of susceptibles requires less numbers of vaccinated to lower the basic reproduction number, but it takes a longer time to reach steady state. However, in our case, the number of infected humans is already small. Hence, vaccination of susceptibles is a better choice. The model becomes:

$$\frac{dS_2}{dt} = \Lambda_2 - (\nu + \mu_2)S_2 - \beta_2 S_2 \frac{I_1}{N_1} - \beta_3 S_2 \frac{I_2}{N_2}, \quad (5.30)$$

$$\frac{dI_2}{dt} = \beta_2 S_2 \frac{I_1}{N_1} + \beta_3 S_2 \frac{I_2}{N_2} - (\mu_2 + \alpha_2 + \gamma_2 + \rho)I_2, \quad (5.31)$$

$$\frac{dQ_2}{dt} = \rho I_2 - (\mu_2 + \alpha_3 + \gamma_3)Q_2, \quad (5.32)$$

$$\frac{dR_2}{dt} = \nu S_2 + \gamma_2 I_2 + \gamma_3 Q_2 - \mu_2 R_2. \quad (5.33)$$

where the total population of humans ( $N_2$ ) is

$$N_2 = S_2 + I_2 + Q_2 + R_2. \quad (5.34)$$

The basic reproduction number of this system is

$$R_{q\nu}^{[2]} = \frac{\mu_2 \beta_3}{(\mu_2 + \nu)(\mu_2 + \alpha_2 + \gamma_2 + \rho)}. \quad (5.35)$$

Choose  $\nu = 0.1$ , the numerical results are shown in Figures 5.7 and 5.8.

As in the figures, after we introduce vaccination into the BHQT system, the number of infected humans does not rise again. It approaches the infection free steady state.

To sum up, in the situation where endemic influenza occurs in the human system but not in the bird system, control by quarantine of infecteds for a limited time may stop the infection. But it is not stable. Other strategies such as vaccination of susceptibles could insure safety.

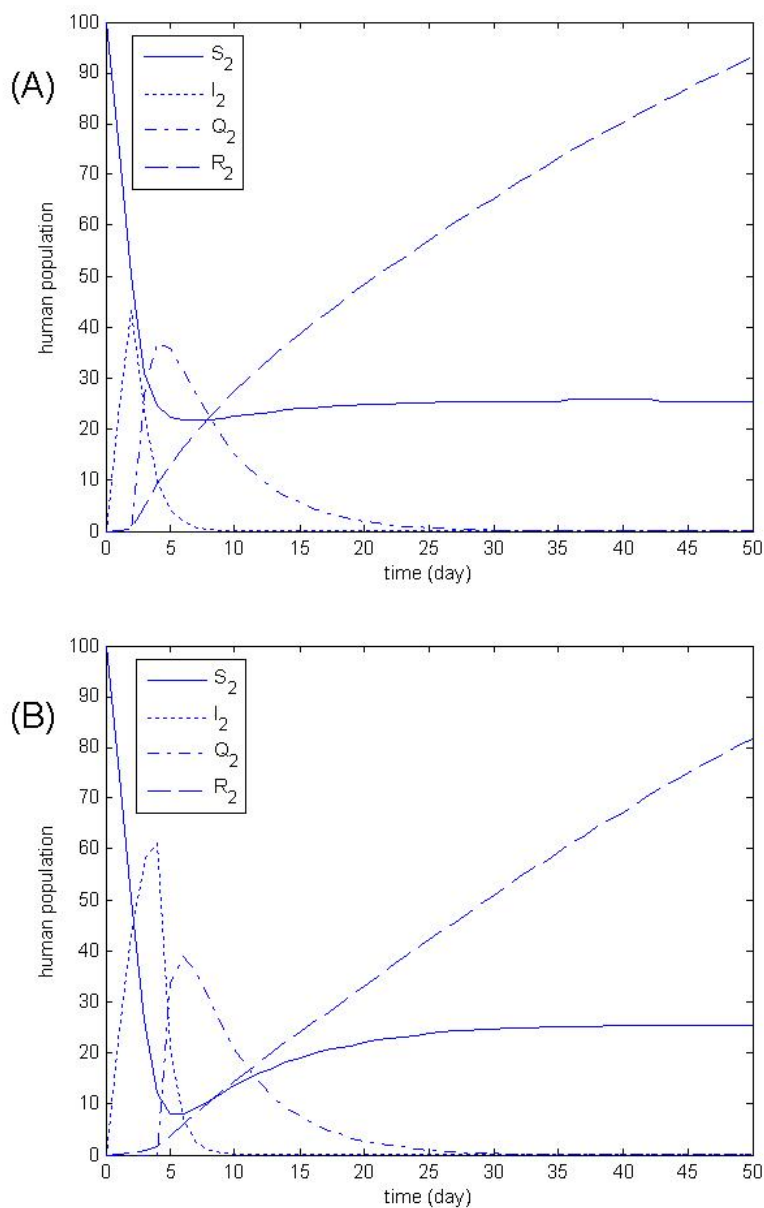


Figure 5.7: Numerical results for the BHQT system with vaccination of susceptibles when quarantine is introduced for limited times and vaccination is introduced for all the time ( $R_0^{[1]} < 1$  and  $R_{qv}^{[2]} < 1$ ). Figure (A): quarantine starts when the endemic just begins (on day 2). Figure (B): quarantine starts when the number of infected humans reach the peak (on day 4).

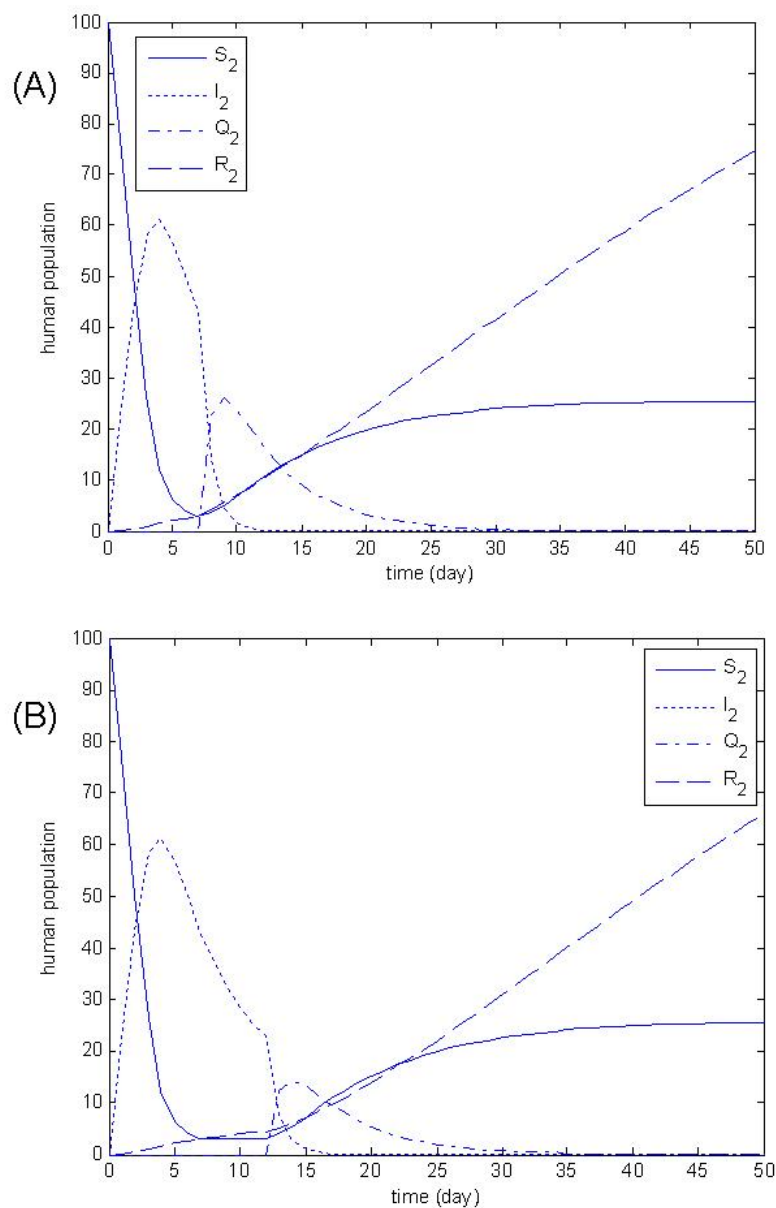


Figure 5.8: Numerical results for the BHQT system with vaccination of susceptibles when quarantine is introduced for limited times and vaccination is introduced for all the time ( $R_0^{[1]} < 1$  and  $R_{qv}^{[2]} < 1$ ). Figure (A): quarantine starts when the number of infected humans climbing down the hill (on day 7). Figure (B): quarantine starts when the system reach the steady state (on day 12)



# Chapter 6

## Conclusion

In this thesis, we have constructed bird-human models of high pathogenic avian influenza and its mutated form. We have also introduced possible control measures into the systems.

We have found analytically and numerically that in both the bird-human 5-D and 6-D models, when the bird system has no infection, the human system could either be infection free if the basic reproduction number in humans ( $R_0^{[2]}$  and  $R_0^{[3]}$ ) is less than 1, or endemic if  $R_0^{[2]} / R_0^{[3]}$  is greater than 1. When there is an endemic infection in birds, an endemic infection is always present in humans.

In both vaccination of immigrants and susceptibles, vaccinating an appropriate number of susceptible humans could bring down the basic reproduction number ( $R_v$  and  $R_\mu$ ) so that the system is infection free in the long term

when there is no infection in birds. But if there is infection in birds, an endemic infection is always present in humans.

When comparing two vaccination strategies that lower the basic reproduction number to the same value, the strategy of vaccination of susceptibles results in fewer people to vaccinated, but vaccination of immigrants approaches the steady state much faster and has the advantage in time.

Under quarantine, the systems have similar outcomes as under vaccination. However, when quarantine is time-limited, numerical results show that the infection free steady state is not stable as the quarantine cannot last for all time. A hybrid of the model with quarantine and vaccination of susceptibles is able to prevent this situation.

For further research and studies, we could look at the models (BHMVI, BHMVS and BHMQT) analytically to compare with their numerical results. Also, more practical numbers could be gathered for numerical results in the vaccination and quarantine parts. A more precise comparison of hybrids between quarantine with vaccination of immigration and quarantine with vaccination of susceptibles could be looked at.

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