DYNAMICS OF LOW AND HIGH PATHOGENIC AVIAN INFLUENZA IN WILD BIRD POPULATION

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Abstract. This chapter introduces an avian influenza model which includes the dynamics of low pathogenic avian influenza (LPAI) and high pathogenic avian influenza (HPAI). The model structures the LPAI-recovered individuals by time-since-recovery and involves the cross-immunity that LPAI infection generates toward the HPAI. Reproduction numbers ($\mathcal{R}_0^{L_w}, \mathcal{R}_0^{H_w}$) and invasion reproduction numbers ($\hat{\mathcal{R}}_{H_w}, \hat{\mathcal{R}}_{L_w}$) of LPAI and HPAI are computed. It is shown that the system has a unique disease-free equilibrium that is locally and globally stable if $\mathcal{R}_0^{L_w} < 1$ and $\mathcal{R}_0^{H_w} < 1$. If $\mathcal{R}_0^{L_w} > 1$ a unique LPAI dominance equilibrium exists. Similarly, if $\mathcal{R}_0^{H_w} > 1$ a unique HPAI dominance equilibrium exists. The equilibria are locally stable if $\hat{\mathcal{R}}_{H_w} < 1$ ($\hat{\mathcal{R}}_{L_w} < 1$ correspondingly). A unique coexistence equilibrium is present if both invasion numbers are larger than one. Simulations show that this coexistence equilibrium can lose stability and coexistence in the form of sustained oscillations is possible. Cross-immunity and duration of protection increase the probability of coexistence. Simulations also show that increasing LPAI transmission increases LPAI prevalence and decreases HPAI prevalence. This observation in part may explain why wild birds which have much higher transmission of LPAI compared to domestic birds also have much lower prevalence of HPAI.

Keywords: mathematical models, age-structured differential equations, reproduction number, invasion number, LPAI, HPAI, H5N1, avian influenza.

AMS Subject Classification: 92D30, 92D40

1. Introduction

Avian (bird) Influenza (flu) viruses belong to a group of viruses called Influenza A. There are three types of influenza viruses: Influenza A, B and C. Influenza A viruses infect many different avian and mammalian species including humans [13]. Humans can be infected with all three types of influenza viruses while birds can be only infected with Influenza A virus [45]. Influenza A strains are classified by their surface proteins: *haemagglutinin* (HA) and *neuraminidase* (NA). Majority of all HA/NA combinations have been isolated in wild birds especially waterfowls and shorebirds [1, 45]. The subtype HA has 16 distinct molecules (H1-H16) and NA has 9 distinct molecules (N1-N9). The H and N combination names the subtype, for instance the virus that caused one of the deadliest pandemics in the history, which is known as the "Spanish Flu," was H1N1 subtype. Two other major influenza pandemics have occurred in the 20^{th} century : "Asian Influenza" caused by H2N2 subtype in 1957 and "Hong Kong Influenza" caused by H3N2 subtype in 1968.

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An influenza pandemic happens when a new influenza subtype spreads in the human population. Influenza viruses have the capability of evolving rapidly and jumping between species. They evolve through two evolutionary mechanisms: *drift* and *shift*. Drift is small and gradual changes on the surface proteins (antigens) which occur both in Influenza A and Influenza B viruses. Shift evolution occurs through reassortment which is the mixing of two influenza strains into a new strain with capabilities of both strains. Since Influenza A viruses infect many different species, shift occurs only in Influenza A type viruses. The research on influenza subtypes H2N2 and H3N2 which caused Asian and Hong Kong influenza respectively, recovered that these subtypes had surface protein genes almost certainly from both influenza virus of avian and human origins [4, 37]. This evidence indicates that antigenic shift occurred through reassortment of both avian and human influenza viruses. On the other hand, influenza subtype H1N1 that caused the "Spanish Flu" was more related to avian influenza than to influenza from any other species which suggested that an avian influenza virus was adapted to human-to-human transmissible pathogen and caused a pandemic [2]. It is highly possible that the next pandemic influenza can be caused by avian influenza.

The pandemic potential of highly pathogenic avian influenza of subtype H5N1 leads to continued concerns. The first human avian influenza case of subtype H5N1 appeared in Hong Kong in 1997, which caused the death of a boy. Since then, as of September 2012, there are total of 608 reported H5N1 human cases worldwide, out of which 359 resulted in death. Even though, the number of H5N1 infected human cases is small, the case fatality rate, which is approximately 60% is very high. Highly pathogenic avian influenza of subtype H5N1 is currently at the top of the list for a pandemic threat. The main reason for the high pandemic potential is that the virus is capable of rapid evolution and at some point might emerge as an effective human-to-human transmissible pathogen and cause a pandemic.

Avian influenza viruses are further classified into two groups based on their ability to cause disease: low pathogenic avian influenza (LPAI) and high pathogenic avian influenza (HPAI). Viruses of most subtypes persist in low pathogenic form, typically producing asymptomatic or mild illness in wild or domestic birds. Studies suggest that LPAI strains from the H5 and H7 subtypes circulating in wild birds can evolve into strains of Highly Pathogenic Avian Influenza (HPAI), after spillover infection to domestic birds [1, 8, 38, 42]. The World Organization for Animal Health (OIE) defines a virus of the H5 or H7 subtype as a *highly pathogenic avian influenza virus* if it can cause at least 75% mortality in 4-week to 8-week old chickens infected intravenously [47, 42].

1.1. **Low Pathogenic Avian Influenza.** The host range of AI in wild birds is not known but some species of aquatic birds (such as ducks, geese, and shorebirds), serve as natural reservoirs of AI viruses [8, 41]. All subtypes of AI viruses isolated this far persist in wild birds as low pathogenic forms. LPAI viruses of the H5 subtype, which is of primary interest here, are generally reported at very low prevalence rates in ducks [23, 33], but the prevalence may vary by location or year. LPAI viruses have been reported in domestic birds, most frequently turkeys, ducks and chickens. Although LPAI viruses of many subtypes can be found in poultry, viruses from the H5 (and H7) subtypes are most frequently reported there [43].

1.2. **High Pathogenic Avian Influenza.** HPAI was first described in poultry in Italy in 1878 [29]. Unlike the low pathogenic influenza, which mostly affects the respiratory tract, the highly pathogenic form infects multiple organs and systems of infected birds. In poultry, HPAI is characterized by high mortality rate, often over 80% within 48 hours. Before 2002, HPAI was rarely found in wild birds. For this reason, it is still an open question whether HPAI viruses are endemic in wild birds. Since 2002, HPAI has been isolated from multiple species of wild birds [41]. The HP H5N1, which is now the main cause of concern, is believed to have emerged from an LPAI virus circulating in chickens sometime in 1996 [46]. After potentially undergoing additional mutation, the HPAI H5N1 virus infected 18 people in Hong Kong in 1997, six of whom died [9]. Since 2003 HPAI H5N1 has been regularly infecting humans primarily though bird-to-human infection. The emergence of a virus that can pass directly from birds to humans showed that pigs are not a necessary link in the chain. Since then, viruses of other subtypes have also made the transition LPAI→HPAI and can pose a significant threat [37].

1.3. **Cross Immunity.** Infection with one strain of Influenza A type viruses provides cross protection against infection with antigenically similar strains. The partial protection offered by the cross immunity is high only if the new strain infecting the host and the strain responsible for immunity are closely related. The protection is ineffective against viruses with major antigenic divergence [6, 7]. However, the unique evolutionary capabilities of Influenza type A viruses (drift and shift) still causes a concern, since prior infection may only reduce the virus spread but can not prevent the infection [10]. Studies in [40] and [10] suggest that prior infection with LPAI provides cross protection against infection with HPAI.

Just before the first H5N1 human case in 1997, there was H5N1 poultry outbreak in chicken farms in Hong Kong. Even though, evidence showed the presence of H5N1 virus, most of the chickens in the poultry markets did not show any symptoms and appeared healthy [39]. Seo and Webster, motivated by this puzzling situation, set up an experiment to test the hypothesis that prior infection with H9N1 (which is LPAI) provides partial protection against highly pathogenic avian H5N1 infections [40]. There are mainly two types of immunity caused by prior infection: cell mediated immunity and antibody mediated immunity. The prior infection with LPAI provides cell mediated immunity toward HPAI [40, 10]. The protection mediated by cellular immune response is established by $CD8^+$ T cells. These findings of the research done by the authors in [40, 10] indicates that it is possible to induce cell mediated immunity toward high pathogenic avian influenza viruses by low pathogenic avian influenza. In terms of control measures, it is promising to develop vaccines that emphasize cell mediated cellular immunity.

1.4. **Mathematical Modeling of Avian Influenza.** Avian influenza is perhaps the most dangerous disease linking humans and animals at present. Because of its deadly pandemic potential, even in its current pre-pandemic stage it has caused significant hardship and economic loss [35]. In the last 5-10 years avian influenza has enjoyed significant attention from mathematical modelers, largely due to its key position among infectious diseases.

Early models of avian influenza focused on humans, investigating the potential impact of a hypothetical pandemic and exploring strategies for its possible mitigation [12, 15, 14, 27, 32]. Other models focused on the present status quo centered on infection of domestic

birds, and current control strategies which primarily target poultry. For example, a spatial farm-based model treating poultry-farms as units [24] and SIR models for within-flock transmission of H5N1 [44] were developed. Despite the importance of a number of emergent diseases, many of which arise from spillover infections from animals, few models to date involve both animals and humans linked by a pathogen. This situation has been changing recently, particularly in relation to AI. The simplest model that captures a bird-to-human transmission pathway of HPAI involves domestic birds and humans [18]. The dynamics of HPAI in poultry are given by a simple SI model, as infected domestic birds either die from the infection or are culled to prevent further spread. To introduce the model, we denote the number of susceptible domestic birds by $S_d(t)$, and the number of domestic birds infected by HPAI by $I_{H_d}(t)$. Furthermore, we denote susceptible humans by $S(t)$, and humans infected with HPAI by $I(t)$. The AI model consists of the following two systems:

$$\text{(1.1)} \qquad \textbf{Domestic birds:} \qquad \begin{cases} \dfrac{dS_d}{dt} = \Lambda_d - \beta_{H_d} I_{H_d} S_d - \mu_d S_d, \\ \dfrac{dI_{H_d}}{dt} = \beta_{H_d} I_{H_d} S_d - (\mu_d + \nu_{H_d}) I_{H_d} \end{cases}$$

where the parameters for the domestic bird population are: Λ_d – the recruitment rate of domestic birds, μ_d – the natural death rate of domestic birds, β_{H_d} – the transmission coefficient of HPAI among domestic birds, and ν_{H_d} – the death rate of domestic birds due to HPAI.

$$\text{(1.2)} \qquad \textbf{Humans:} \qquad \begin{cases} \dfrac{dS}{dt} = \Lambda - \beta I_{H_d} S - \mu S \\ \dfrac{dI}{dt} = \beta I_{H_d} S - (\nu + \alpha + \mu) I \end{cases}$$

The parameters related to human dynamics are: Λ – the birth/recruitment rate of humans, μ – the natural death rate of humans, β – the transmission coefficient of HPAI from birds to humans, ν – the death rate of humans due to HPAI, and α – the recovery rate. Model (1.1-1.2) has very simple dynamics. However, it fails to capture most of the complexity and characteristic features of AI transmission and evolution. Recognizing the importance of both birds and humans in the transmission and evolution of AI, a number of models involving domestic birds and humans [18, 20, 19, 22] were developed. Some more elaborate models even involve wild birds, as well as domestic birds and humans [28, 26, 16, 3]. These models typically incorporate the hypothetical scenario in which HP H5N1 avian influenza becomes adapted to humans and starts transmitting efficiently from human-to-human. This models the shift evolutionary mechanism. The drift evolutionary mechanism was originally modeled by Pease [36]. Pease's drift model has recently been extensively studied [17, 30]. A novel model combining effects of both drift and shift evolution of influenza A was discussed by Martcheva [31], where it was found that drift evolution may be responsible for the 365-day oscillation of human flu, as well as 365-day oscillations of the number of humans infected with HP H5N1, as observed in data.

In this chapter we investigate the dynamics of LPAI and HPAI in birds. The interaction between LPAI and HPAI in birds has been priorly studied by several authors [**?**, 5] but the effect of cross-immunity that LPAI gives to HPAI has not been investigated.

2. The Model

Influenza strains can compete in two ways: depletion of susceptible hosts, and cross-immunity [6, 7, 34]. Cross-immunity is a mechanism by which infection with one strain provides partial protection against infection with another. A number of references in the biological literature suggest that infection with LPAI can provide partial protection against HP H5N1 both in poultry and in wild birds. Seo and Webster [40] infected a group of chickens with LPAI H9N2 influenza virus. They found that the group infected by H5N1 within 30 days of inoculation by LPAI had a 100% survival rate and reduced clinical signs. As time between the two infections grew, the protection started to fade and the morbidity of infection with HPAI grew. This study suggests that the immunity provided by prior infection with LPAI is temporary, declining with time-since-recovery from LPAI. To incorporate this variability of cross-immunity in wild birds, we let τ be the time-since-recovery from low pathogenic influenza and $q_w(\tau)$ be the variable cross-immunity (high cross-immunity is modeled by low q_w) imparted from LPAI to infection with HPAI. To introduce the model, let the birth/recruitment rate of wild birds be denoted by Λ_w and the natural mortality rate for wild birds by μ_w. The number of susceptible wild birds is $S_w(t)$, the number of LPAI infected wild birds is $I_{L_w}(t)$, and the number of HPAI infected wild birds is $I_{H_w}(t)$. The density of individuals that have recovered from LPAI is $r_{L_w}(\tau, t)$ and the number of individuals that have recovered from HPAI is $R_{H_w}(t)$. The dynamics of LPAI and HPAI in wild birds are captured by the following model

$$
\begin{cases}
\dfrac{dS_w}{dt} &= \Lambda_w - \beta_{11}^L I_{L_w} S_w - \beta_{11}^H I_{H_w} S_w - \mu_w S_w, \\
\dfrac{dI_{L_w}}{dt} &= \beta_{11}^L I_{L_w} S_w - (\mu_w + \alpha_{L_w}) I_{L_w} \\
\dfrac{\partial r_{L_w}}{\partial t} + \dfrac{\partial r_{L_w}}{\partial \tau} &= -q_w(\tau)\beta_{11}^H I_{H_w} r_{L_w} - \mu_w r_{L_w} \\
r_{L_w}(0,t) &= \alpha_{L_w} I_{L_w} \\
\dfrac{dI_{H_w}}{dt} &= \beta_{11}^H I_{H_w} S_w \\
&\quad + \beta_{11}^H I_{H_w} \displaystyle\int_0^\infty q_w(\tau) r_{L_w}(\tau, t) d\tau - (\mu_w + \alpha_{H_w} + \nu_{H_w}) I_{H_w} \\
\dfrac{dR_{H_w}}{dt} &= \alpha_{H_w} I_{H_w} - \mu_w R_{H_w} \, .
\end{cases}
\tag{2.1}
$$

where α_{L_w} and α_{H_w} are the recovery rates for wild birds, and ν_{H_w} is the HPAI-induced mortality. A simplifying assumption is that most wild birds that recover from HPAI do so because they may have had prior exposure to LPAI. This assumption is justified based on the experimental studies that suggest that LPAI strains of the same subtype or different subtype induce partial cross-immunity toward infection with HPAI strains [11, 21]. We make the simplifying assumption that recruitment does not depend upon focal bird numbers. This could be relaxed in future, for instance by introducing a logistic growth term.

In the following section we analyze the dynamics of low pathogenic and high pathogenic avian influenza within the wild bird population. The model that models the interaction

of LPAI and HPAI in poultry is quite similar. Therefore, symmetrical results are true for the domestic bird population.

3. LPAI-HPAI dynamics in wild birds

We study the existence and stability of equilibria of the wild bird system (2.1). To determine the equilibria, we solve the following system which is obtained by setting the time derivatives in (2.1) equal to zero.

$$
\begin{cases}
0 &= \Lambda_w - \beta_{11}^L I_{L_w} S_w - \beta_{11}^H I_{H_w} S_w - \mu_w S_w, \\
0 &= \beta_{11}^L I_{L_w} S_w - (\mu_w + \alpha_{L_w}) I_{L_w} \\
\dfrac{\partial r_{L_w}}{\partial \tau} &= -q_w(\tau)\beta_{11}^H I_{H_w} r_{L_w} - \mu_w r_{L_w} \\
r_{L_w}(0) &= \alpha_{L_w} I_{L_w} \\
0 &= \beta_{11}^H I_{H_w} S_w \\
&\quad + \beta_{11}^H I_{H_w} \displaystyle\int_0^\infty q_w(\tau) r_{L_w}(\tau, t) d\tau - (\mu_w + \alpha_{H_w} + \nu_{H_w}) I_{H_w} \\
0 &= \alpha_{H_w} I_{H_w} - \mu_w R_{H_w} \, .
\end{cases}
\tag{3.1}
$$

The wild bird system has 4 equilibria. The first is the disease-free equilibrium. The second and the third are the LPAI-only and HPAI-only equilibria (i.e. boundary equilibria). The fourth one is the coexistence equilibrium (i.e. interior equilibrium) which represents the state in which both LPAI and HPAI are present in the wild bird population.

3.1. **Disease-Free Equilibrium.**

The wild-bird-model (2.1) has a disease-free equilibrium (DFE) ε_0 given by

$$\varepsilon_0 = (S_w^*, 0, 0, 0, 0) \, ,$$

where $S_w^* = \frac{\Lambda_w}{\mu_w}$. The basic reproduction number for LPAI in wild birds, denoted by $\mathcal{R}_0^{L_w}$, is given by

$$\mathcal{R}_0^{L_w} = \frac{\beta_{11}^L \Lambda_w}{\mu_w(\mu_w + \alpha_{L_w})} \, ,$$

and the basic reproduction number for HPAI in wild birds, denoted by $\mathcal{R}_0^{H_w}$, is given by

$$\mathcal{R}_0^{H_w} = \frac{\beta_{11}^H \Lambda_w}{\mu_w(\mu_w + \alpha_{H_w} + \nu_{H_w})} \, .$$

These basic reproduction numbers are threshold values which determine whether LPAI or HPAI can invade the disease-free equilibrium.

Theorem 1. *If $\mathcal{R}_0^{L_w} < 1$ and $\mathcal{R}_0^{H_w} < 1$ then the DFE, ε_0, is locally asymptotically stable.*

Proof. Let (u, v, x, y, z) be the perturbations around the steady state. Expressing the perturbations as

$$S_w(t) = S_w^* + u(t) \, , \quad I_{L_w}(t) = v(t) \, , \quad r_{L_w}(\tau, t) = x(\tau, t) \, , \quad I_{H_w}(t) = y(t) \, , \quad R_{H_w}(t) = z(t) \, ,$$

we substitute into the PDE system (2.1). Using the equation for the disease-free equilibrium and dropping the quadratic terms in the perturbations, we obtain the following linear system involving only perturbations.

$$
\begin{aligned}
\frac{du}{dt} &= \beta_{11}^{L} S_w^* v - \beta_{11}^{H} S_w^* y - \mu_w u,\\
\frac{dv}{dt} &= \beta_{11}^{L} S_w^* v - \beta_{11}^{H} S_w^* y - (\mu_w + \alpha_{L_w}) v\\
\frac{\partial x}{\partial t} + \frac{\partial x}{\partial \tau} &= -\mu_w x\\
x(0,t) &= \alpha_{L_w} v\\
\frac{dy}{dt} &= \beta_{11}^{H} S_w^* y - (\mu_w + \alpha_{H_w} + \nu_{H_w}) y\\
\frac{dz}{dt} &= \alpha_{H_w} y - \mu_w z
\end{aligned} \tag{3.2}
$$

To investigate the local stability of the DFE, we study the solutions of the system (3.2). Suppose that the linear system (3.2) has exponential solutions, that is we look for solutions of the following form:

$$
u = \bar{u} e^{\lambda t}\,, \quad v = \bar{v} e^{\lambda t}\,, \quad x = \bar{x}(\tau) e^{\lambda t}\,, \quad y = \bar{y} e^{\lambda t}\,, \quad z = \bar{z} e^{\lambda t}\,. \tag{3.3}
$$

Substituting the above solutions into linearized system (3.2), we get the following eigenvalue problem;

$$
\begin{aligned}
\lambda \bar{u} &= -\beta_{11}^{L} S_w^* \bar{v} - \beta_{11}^{H} S_w^* \bar{y} - \mu_w \bar{u},\\
\lambda \bar{v} &= \beta_{11}^{L} S_w^* \bar{v} - (\mu_w + \alpha_{L_w}) \bar{v}\\
\lambda \bar{y} &= \beta_{11}^{H} S_w^* \bar{y} - (\mu_w + \alpha_{H_w} + \nu_{H_w}) \bar{y}\\
\lambda \bar{z} &= \alpha_{H_w} \bar{y} - \mu_w \bar{z}
\end{aligned} \tag{3.4}
$$

which is combined with the following first order ODE;

$$
\lambda \bar{x} + \frac{d\bar{x}}{d\tau} = -\mu_w \bar{x}\,, \quad \bar{x}(0) = \alpha_{L_w} \bar{v}\,.
$$

Solving the above differential equation, we obtain;

$$
\bar{x} = \alpha_{L_w} \bar{v} e^{-(\lambda + \mu_w)\tau}\,.
$$

Solutions of (3.4) gives the eigenvalues $\{\lambda_i\}_{i=1}^{4}$ of the linearized differential operator in (3.2). The eigenvalue problem (3.4) is linear. The second equation involves only $\bar{v}$ and is independent from $\bar{u}\,,\ \bar{y}$ and $\bar{z}\,$. Similar statement is true for the third equation involving only $\bar{y}$. Solving the second equation we get

$$
\lambda_2 = \beta_{11}^{L} S_w^* - (\mu_w + \alpha_{L_w})\,,
$$

which is negative since $\mathcal{R}_0^{L_w} < 1\,$. Solving the third equation we get $\lambda_3 = \beta_{11}^{L} S_w^* - (\mu_w + \alpha_{H_w} + \nu_{H_w})\,$. Clearly, $\lambda_3 < 0$, since $\mathcal{R}_0^{H_w} < 1\,$. The other two eigenvalues are $\lambda_1 = \lambda_4 = -\mu_w < 0$. □

The basic reproduction number $\mathcal{R}_0^{L_w}$ ($\mathcal{R}_0^{H_w}$) measures the average number of new low (high) pathogenic infections generated by a single wild bird infected with low (high) pathogenic avian influenza in a completely susceptible wild bird population. Thus, Theorem 1 implies that the LPAI and HPAI can be eliminated from the wild bird population if $\mathcal{R}_0^{L_w} < 1$ and $\mathcal{R}_0^{H_w} < 1$ and if initially the number of wild birds infected with LPAI and HPAI are in the the basin of attraction of the DFE.

3.1.1. *Global Stability of the Disease-Free Equilibrium.* Now, we prove the global asymptotic stability of the disease-free equilibrium ε_0.

Theorem 2. *If $\mathcal{R}_0^{L_w} < 1$ and $\mathcal{R}_0^{H_w} < 1$ then the DFE, ε_0, is globally asymptotically stable.*

Proof. From the first equation in the system (2.1) we obtain the following inequality

$$S_w' \leq \Lambda_w - \mu_w S_w.$$

From this inequality we have

$$\limsup_t S_w(t) \leq \frac{\Lambda_w}{\mu_w}. \tag{3.5}$$

Integrating the second equality in system (2.1) we have

$$I_{L_w}(t) = e^{-(\mu_w+\alpha_{L_w})t} I_{L_w}(0) + \beta_{11}^L \int_0^t e^{-(\mu_w+\alpha_{L_w})(t-\sigma)} S_w(\sigma) d\sigma.$$

Changing the variable of integration in the integral, we have

$$I_{L_w}(t) = e^{-(\mu_w+\alpha_{L_w})t} I_{L_w}(0) + \beta_{11}^L \int_0^t e^{-(\mu_w+\alpha_{L_w})\sigma} S_w(t-\sigma) d\sigma.$$

Taking a lim sup of both sides of this equality, we obtain the following inequality:

$$\limsup_t I_{L_w}(t) \leq \frac{\beta_{11}^L \Lambda_w}{\mu_w(\mu_w+\alpha_{L_w})} \limsup_t I_{L_w}(t)$$

where the coefficient infront the lim sup on the right hand side is exactly $\mathcal{R}_0^{L_w}$. Since $\mathcal{R}_0^{L_w} < 1$, this inequality is only possible if $\limsup_t I_{L_w}(t) = 0$. Hence, $I_{L_w}(t) \to 0$ as $t \to \infty$. Next, we integrate the partial differential equation along the characteristic lines. We obtain,

$$r_{L_w}(\tau, t) = \begin{cases} \alpha_{L_w} I_{L_w}(t-\tau) e^{-\int_0^\tau q_w(\sigma) I_{H_w}(t-\tau+\sigma) d\sigma - \mu_w \tau} & \tau < t \\ r^0(\tau - t) e^{-\int_0^t q_w(\tau-t+\sigma) I_{H_w}(\sigma) d\sigma - \mu_w t} & \tau > t \end{cases} \tag{3.6}$$

where $r^0(\tau) = r_{L_w}(\tau, 0)$. Consider the term $\int_0^\infty q_w(\tau) r_{L_w}(\tau, t) d\tau$. We claim

$$\limsup_t \int_0^\infty q_w(\tau) r_{L_w}(\tau, t) d\tau = 0.$$

Indeed, using (3.6) we have

$$\begin{aligned}\limsup_t & \int_0^\infty q_w(\tau) r_{L_w}(\tau,t)d\tau \\ &\leq \alpha_{L_w}\int_0^t q_w(\tau)I_{L_w}(t-\tau)e^{-\mu_w\tau}d\tau + \int_t^\infty q_w(\tau)r^0(\tau-t)e^{-\mu_w t}d\tau \\ &\leq \alpha_{L_w}\int_0^t q_w(\tau)I_{L_w}(t-\tau)e^{-\mu_w\tau}d\tau + e^{-\mu_w t}\int_0^\infty r^0(\tau)d\tau.\end{aligned} \tag{3.7}$$

Taking the lim sup from both sides of the above inequality gives the claim. We denote by

$$Q(t) = \int_0^\infty q_w(\tau) r_{L_w}(\tau,t)d\tau.$$

To conclude the proof, we integrate the equation for high pathogenic influenza and change the variable of integration.

(3.8)

$$\begin{aligned}I_{H_w}(t) &= e^{-(\mu_w+\alpha_{H_w}+\nu_{H_w})t}I_{H_w}(0) + \beta_{11}^H\int_0^t e^{-(\mu_w+\alpha_{H_w}+\nu_{H_w})\sigma}S_w(t-\sigma)I_{H_w}(t-\sigma)d\sigma \\ &+\beta_{11}^H\int_0^t e^{-(\mu_w+\alpha_{H_w}+\nu_{H_w})\sigma}Q(t-\sigma)I_{H_w}(t-\sigma)d\sigma.\end{aligned}$$

Taking lim sup of both sides of the above equality, we have

$$\limsup_t I_{H_w}(t) \leq \frac{\beta_{11}^H\Lambda_w}{\mu_w(\mu_w+\alpha_{H_w}+\nu_{H_w})}\limsup_t I_{H_w}(t).$$

The coefficient on the right-hand side infront $\limsup_t I_{H_w}(t)$ is exactly $\mathcal{R}_0^{H_w}$. Since $\mathcal{R}_0^{H_w} < 1$, the only way the above inequality can hold is if $\limsup_t I_{H_w}(t) = 0$, that is if $I_{H_w}(t) \to 0$ as $t \to \infty$. That completes the proof.

□

3.2. **LPAI-only and HPAI-only Equilibria.** We study the competition of the low and high pathogenic avian influenza in wild bird population. Like basic reproduction number, the invasion number is a threshold quantity that determines if one pathogen can invade the other pathogen's equilibrium. The invasion numbers are very useful in understanding the dynamics between low and high pathogens in wild bird population. We denote by $\hat{\mathcal{R}}_{L_w}$ the invasion number of LPAI when the system is at HPAI-only equilibrium. The invasion number of LPAI is

$$\hat{\mathcal{R}}_{L_w} = \frac{\beta_{11}^L\left(\mu_w+\alpha_{H_w}+\nu_{H_w}\right)}{\beta_{11}^H(\mu_w+\alpha_{L_w})} = \frac{\mathcal{R}_0^{L_w}}{\mathcal{R}_0^{H_w}}.$$

The invasion number $\hat{\mathcal{R}}_{L_w}$ gives the ability of LPAI to invade the HPAI-only equilibrium which is measured as the secondary infections one LPAI-infected wild bird can produce in a wild bird population where HPAI is at equilibrium. We denote by $\hat{\mathcal{R}}_{H_w}$ the invasion number of HPAI. Similar definition is true for the invasion number of HPAI. The invasion

number of HPAI is

$$\begin{aligned}\hat{\mathcal{R}}_{H_w} &= \frac{\beta_{11}^H \hat{S}_w + \beta_{11}^H \displaystyle\int_0^\infty q_w(\tau)\hat{r}_w d\tau}{\mu_w + \alpha_{H_w} + \nu_{H_w}} \\ &= \frac{\mathcal{R}_0^{H_w}}{\mathcal{R}_0^{L_w}}\left(1 + \frac{\alpha_{L_w}\mu_w}{\alpha_{L_w}+\mu_w}(\mathcal{R}_0^{L_w}-1)\int_0^\infty q_w(\tau)e^{-\mu_w\tau}d\tau\right).\end{aligned} \tag{3.9}$$

The wild bird system (2.1) has two boundary equilibria: LPAI-only and HPAI-only equilibria. We denote the LPAI-only equilibrium by $(\hat{S}_w, \hat{I}_{L_w}\hat{r}_{L_w}, 0, 0)$ and the HPAI-only equilibrium by $(\tilde{S}_w, 0, 0, \tilde{I}_{H_w}\tilde{R}_{H_w})$. In the following two theorems we prove the existence of boundary equilibria.

Theorem 3. *If $\mathcal{R}_0^{L_w} > 1$, then there exists a unique LPAI-only equilibrium $(\hat{S}_w, \hat{I}_{L_w}\hat{r}_{L_w}, 0, 0)$ in which $\hat{S}_w = \frac{\mu_w+\alpha_{L_w}}{\beta_{11}^L}$, $\hat{I}_{L_w} = \frac{\mu_w}{\beta_{11}^L}\left(\mathcal{R}_0^{L_w}-1\right)$ and $\hat{r}_{L_w} = \alpha_{L_w}\hat{I}_{L_w}e^{-\mu_w\tau}$.*

Proof. To find the LPAI-only equilibrium, we look for time-independent solutions of the form $(\hat{S}_w, \hat{I}_{L_w}\hat{r}_{L_w}(\tau), 0, 0)$. We set the time derivatives in wild bird system (2.1) equal to zero and obtain the following system for the LPAI-only equilibrium.

$$\begin{aligned} 0 &= \Lambda_w - \beta_{11}^L \hat{I}_{L_w}\hat{S}_w - \mu_w\hat{S}_w \\ 0 &= \beta_{11}^L \hat{I}_{L_w}\hat{S}_w - (\mu_w+\alpha_w)\hat{I}_{L_w} \\ \frac{d\hat{r}_{L_w}}{d\tau} &= \mu_w\hat{r}_{L_w} \\ \hat{r}_{L_w}(0) &= \alpha_{L_w}\hat{I}_{L_w}\end{aligned} \tag{3.10}$$

The system consists of one first order ODE whose initial condition depends on the solution $\hat{I}_{L_w}$ and two algebraic equations. The second equation can be rewritten as

$$0 = \left(\beta_{11}^L\hat{S}_w - (\mu_w+\alpha_w)\right)\hat{I}_{L_w}.$$

Solving for $\hat{S}_w$ we get,

$$\hat{S}_w = \frac{\mu_w+\alpha_w}{\beta_{11}^L}.$$

Substituting the expression for $\hat{S}_w$ into the first equation and solving it for $\hat{I}_{L_w}$ we get,

$$\hat{I}_{L_w} = \frac{\Lambda_w}{\mu_w+\alpha_{L_w}} - \frac{\mu_w}{\beta_{11}^L}.$$

Since the basic reproduction number for LPAI is $\mathcal{R}_0^{L_w} = \frac{\beta_{11}^L\Lambda_w}{\mu_w(\mu_w+\alpha_{L_w})}$, we rearrange the terms in $\hat{I}_{L_w}$ by factoring out $\frac{\mu_w}{\beta_{11}^L}$ to obtain

$$\hat{I}_{L_w} = \frac{\mu_w}{\beta_{11}^L}\left(\mathcal{R}_0^{L_w}-1\right).$$

Finally we solve the differential equation $\frac{d\hat{r}_{L_w}}{d\tau} = -\mu_w\hat{r}_{L_w}$ with $\hat{r}_{L_w}(0) = \alpha_{L_w}\hat{I}_{L_w}$ whose solution is

$$\hat{r}_{L_w}(\tau) = \alpha_{L_w}\hat{I}_{L_w}e^{-\mu_w\tau}$$

□

Theorem 4. *If $\mathcal{R}_0^{H_w} > 1$, then there exists a unique HPAI-only equilibrium $(\tilde{S}_w, 0, 0, \tilde{I}_{H_w}\tilde{R}_{H_w})$ where $\tilde{S}_w = \frac{\mu_w+\alpha_{L_w}+\nu_{H_w}}{\beta_{11}^H}$, $\hat{I}_{H_w} = \frac{\mu_w}{\beta_{11}^H}\left(\mathcal{R}_0^{H_w} - 1\right)$ and $\tilde{R}_{H_w} = \frac{\alpha_{H_w}}{\beta_{11}^H}\left(\mathcal{R}_0^{H_w} - 1\right)$.*

Proof. Proof is very similar to the proof of Theorem 3, and will not be repeated. □

Theorem 5. *The LPAI-only equilibrium is locally asymptotically stable if $\hat{\mathcal{R}}_{H_w} < 1$ and unstable if $\hat{\mathcal{R}}_{H_w} > 1$.*

Proof. As before, we start by linearizing the system. We denote by (u, v, x, y, z) the perturbations around the steady state and set

$$S_w(t) = \hat{S}_w + u(t)\,, I_{L_w}(t) = \hat{I}_{L_w} + v(t)\,, r_{L_w}(\tau, t) = \hat{r}_{L_w}(\tau) + x(\tau, t)\,, I_{H_w}(t) = y(t)\,, R_{H_w}(t) = z(t)\,.$$

Substituting the above expressions onto (2.1), we obtain the following linear system for perturbations.

$$\begin{aligned}
&\frac{du}{dt} &&= -\beta_{11}^L \hat{I}_{L_w} u - \beta_{11}^L \hat{S}_w v - \beta_{11}^H \hat{S}_w y - \mu_w u,\\
&\frac{dv}{dt} &&= \beta_{11}^L \hat{I}_{L_w} u + \beta_{11}^L \hat{S}_w v - (\mu_w + \alpha_{L_w}) v\\
&\frac{\partial x}{\partial t} + \frac{\partial x}{\partial \tau} &&= -\beta_{11}^H \hat{r}_{L_w} q_w(\tau) y - \mu_w x\\
&x(0,t) &&= \alpha_{L_w} v\\
&\frac{dy}{dt} &&= \beta_{11}^H \hat{S}_w y + \beta_{11}^H y \int_0^\infty q_w(\tau)\hat{r}_{L_w} d\tau - (\mu_w + \alpha_{H_w} + \nu_{H_w}) y\\
&\frac{dz}{dt} &&= \alpha_{H_w} y - \mu_w z
\end{aligned} \tag{3.11}$$

We expect that the solutions are exponential and seek for solutions of the form (3.3). Substituting the these solutions (3.3) into linearized system (3.11), we get the following linear eigenvalue problem which consists of algebraic equations and a differential equation. The algebraic equations can be represented in the following matrix form

$$A\omega = \lambda\omega \tag{3.12}$$

where $\omega = (\bar{u}\,, \bar{v}\,, \bar{y}\,, \bar{z})^T$ and the matrix A is;

$$A = \begin{pmatrix} -\beta_{11}^L \hat{I}_{L_w} - \mu_w & -\beta_{11}^L \hat{S}_w & -\beta_{11}^H \hat{S}_w & 0\\ \beta_{11}^L \hat{I}_{L_w} & \beta_{11}^L \hat{S}_w - (\mu_w + \alpha_{L_w}) & 0 & 0\\ 0 & 0 & D & 0\\ 0 & 0 & \alpha_{H_w} & -\mu_w \end{pmatrix}$$

where $D = \beta_{11}^H \hat{S}_w + \beta_{11}^H \int_0^\infty q_w(\tau)\hat{r}_{L_w} d\tau - (\mu_w + \alpha_{H_w} + \nu_{H_w})$. The differential equation is:

$$\lambda\bar{x} + \frac{d\bar{x}}{d\tau} = -\beta_{11}^H \hat{r}_{L_w} q_w(\tau)\bar{y} - \mu_w \bar{x}\,, \quad \bar{x}(0) = \alpha_{L_w}\bar{v}\,.$$

We solve the non-homogeneous differential equation by first multiplying with the integral factor $e^{(\lambda+\mu_w)\tau}$. We then integrate and obtain the following solution;

$$\bar{x}(\tau) = \alpha_{L_w}\bar{v}e^{-(\lambda+\mu_w)\tau} - \int_0^\tau \beta_{11}^H \hat{r}_{L_w} q_w(s)\bar{y}e^{-(\lambda-\mu_w)(\tau-s)}ds\,.$$

The LPAI-only equilibrium is stable, if and only if the eigenvalues $\{\lambda_i\}_{i=1}^4$ of the algebraic eigenvalue problem (3.12) are all negative. The third equation in (3.12) involves only $\bar{y}$. We solve the third equation and obtain

$$\lambda_3 = \beta_{11}^H \hat{S}_w + \beta_{11}^H \int_0^\infty q_w(\tau)\hat{r}_{L_w}d\tau - (\mu_w + \alpha_{H_w} + \nu_{H_w})\,.$$

The eigenvalue $\lambda_3 < 3$ if $\hat{R}_{H_w} < 1$. We see that eigenvalue $\lambda_4 = -\mu_w$. Note that $\beta_{11}^L \hat{S}_w - (\mu_w + \alpha_{L_w}) = 0$ Thus, the characteristic equation for eigenvalues λ_1 and λ_2 is;

$$\lambda^2 + \lambda\left(\beta_{11}^H \hat{I}_{L_w} + \mu_w\right) + \beta_{11}^L \hat{S}_w \beta_{11}^L \hat{I}_{L_w} = 0$$

Since $\lambda_1 + \lambda_2 < 0$ and $\lambda_1\lambda_2 > 0$, there are either $\lambda_1 < 0$ and $\lambda_2 < 0$ or two complex conjugate eigenvalues that satisfy $\Re\lambda_1 < 0$, $\Re\lambda_2 < 0$. □

Theorem 6. *The HPAI-only equilibrium is locally asymptotically stable if* $\hat{\mathcal{R}}_{L_w} < 1$ *and unstable if* $\hat{\mathcal{R}}_{L_w} > 1$.

Proof. Proof of Theorem 6 is very similar to the proof of Theorem 5, and will be omitted. □

3.3. **Coexistence Equilibrium.** In this subsection, we investigate the existence, uniqueness and the stability of the coexistence equilibrium (i.e. interior equilibrium). We denote the coexistence equilibrium by $(S_w^{**}, I_{L_w}^{**}, r_{L_w}^{**}, I_{H_w}^{**}, R_{H_w}^{**})$. Coexistence equilibrium represents the state for which both low pathogenic and high pathogenic avian influenza are endemic in the wild bird population. We first show the existence and uniqueness of the coexistence equilibrium by the following theorem.

Theorem 7. *There exists a unique coexistence equilibrium* $(S_w^{**}, I_{L_w}^{**}, r_{L_w}^{**}, I_{H_w}^{**}, R_{H_w}^{**})$ *iff* $\hat{\mathcal{R}}_{L_w} > 1$, *and* $\hat{\mathcal{R}}_{H_w} > 1$.

Proof. The coexistence equilibrium satisfies the following steady state equation

$$\begin{cases} 0 &= \Lambda_w - \beta_{11}^L I_{L_w}^{**} S_w^{**} - \beta_{11}^H I_{H_w}^{**} S_w^{**} - \mu_w S_w^{**}, \\ 0 &= \beta_{11}^L I_{L_w}^{**} S_w^{**} - (\mu_w + \alpha_{L_w}) I_{L_w}^{**} \\ \dfrac{dr_{L_w}^{**}}{d\tau} &= -q_w(\tau)\beta_{11}^H I_{H_w}^{**} r_{L_w}^{**} - \mu_w r_{L_w}^{**} \\ r_{L_w}^{**}(0) &= \alpha_{L_w} I_{L_w}^{**} \\ 0 &= \beta_{11}^H I_{H_w}^{**} S_w^{**} + \beta_{11}^H I_{H_w}^{**} \displaystyle\int_0^\infty q_w(\tau) r_{L_w}^{**}(\tau)d\tau - (\mu_w + \alpha_{H_w} + \nu_{H_w}) I_{H_w}^{**} \\ 0 &= \alpha_{H_w} I_{H_w}^{**} - \mu_w R_{H_w}^{**} \end{cases} \tag{3.13}$$

Solving the second equation for S_w^{**}, we get;

$$S_w^{**} = \frac{\mu_w + \alpha_{L_w}}{\beta_{11}^L}\,.$$

We then substitute the expression for S_w^{**} to the first equation and solve for $I_{L_w}^{**}$ and obtain:

$$I_{L_w}^{**} = \mu_w \left(\mathcal{R}_0^{L_w} - 1\right) - \frac{\beta_{11}^H}{\beta_{11}^L} I_{H_w}^{**} .$$

To determine $r_{L_w}^{**}$, we solve the differential equation

$$\frac{dr_{L_w}^{**}}{d\tau} = -q_w(\tau)\beta_{11}^H I_{H_w}^{**} r_{L_w}^{**} - \mu_w r_{L_w}^{**} , \quad r_{L_w}^{**}(0) = \alpha_{L_w} I_{L_w}^{**}$$

and obtain

$$r_{L_w}^{**} = \alpha_{L_w} I_{L_w}^{**} e^{-\mu_w \tau - \beta_{11}^H I_{H_w}^{**} \int_0^\tau q_w(s)ds} .$$

Substituting the expressions for S_w^{**} and $r_{L_w}^{**}$ into the fourth equation, we see that $I_{H_w}^{**}$ satisfies the equation $F(I_{H_w}^{**}) = 0$ where $F(x)$ is the following monotone decreasing function

(3.14)

$$F(x) = \frac{\beta_{11}^H}{\beta_{11}^L}(\mu_w + \alpha_{L_w}) + \frac{\beta_{11}^H}{\beta_{11}^L}\alpha_{L_w}\left(\mu_w(\mathcal{R}_0^{L_w} - 1) - \beta_{11}^H x\right) \int_0^\infty q_w(\tau) e^{-\mu_w \tau - \beta_{11}^H x \int_0^\tau q_w(s)ds} d\tau - (\mu_w + \alpha_{H_w} + \nu_{H_w}).$$

There exists a unique positive $I_{H_w}^{**}$ in the interval $(0, \hat{I}_{L_w})$ such that $F(I_{H_w}^{**}) = 0$, since

$$\begin{aligned} F(0) &= \frac{\beta_{11}^H}{\beta_{11}^L}(\mu_w + \alpha_{L_w}) + \frac{\beta_{11}^H}{\beta_{11}^L}\left(\mu_w(\mathcal{R}_0^{L_w} - 1)\right) \int_0^\infty q_w(\tau) e^{-\mu_w \tau} d\tau - (\mu_w + \alpha_{H_w} + \nu_{H_w}) \\ &= \beta_{11}^H \hat{S}_w + \beta_{11}^H \int_0^\infty q_w(\tau)\hat{r}_{L_w}(\tau)d\tau - (\mu_w + \alpha_{H_w} + \nu_{H_w}) \\ &= (\mu_w + \alpha_{H_w} + \nu_{H_w})(\hat{\mathcal{R}}_{H_w} - 1) \\ &> 0 \end{aligned}$$

and

$$\begin{aligned} F(\hat{I}_{L_w}) &= \frac{\beta_{11}^H}{\beta_{11}^L}(\mu_w + \alpha_{L_w}) - (\mu_w + \alpha_{H_w} + \nu_{H_w}) \\ &= (\mu_w + \alpha_{H_w} + \nu_{H_w})\left(\frac{1}{\hat{\mathcal{R}}_{L_w}} - 1\right) \\ &< 0. \end{aligned}$$

□

3.3.1. **Stability of the Coexistence Equilibrium:** To investigate the stability of coexistence equilibrium $(S_w^{**}, I_{L_w}^{**}, r_{L_w}^{**}, I_{H_w}^{**}, R_{H_w}^{**})$ we start by linearizing the system (2.1). We set

$$S_w(t) = S_w^{**} + u(t) , \quad I_{L_w}(t) = I_{L_w}^{**} + v(t) , \quad r_{L_w}(\tau, t) = r_{L_w}^{**} + x(\tau, t) , \quad I_{H_w}(t) = I_{H_w}^{**} + y(t) ,$$

$R_{H_w}(t) = R_{H_w}^{**} + z(t)$. Substituting into the equations of the system (2.1) and using the equation (3.13) for coexistence equilibrium, we get the following linear system after dropping the quadratic terms in perturbations:

$$\frac{du}{dt} = -\beta_{11}^{L} S_w^{**} v - \beta_{11}^{L} I_{L_w}^{**} u - \beta_{11}^{H} I_{H_w}^{**} u - \beta_{11}^{H} S_w^{**} y - \mu_w u \tag{3.15}$$

$$\frac{dv}{dt} = \beta_{11}^{L} S_w^{**} v + \beta_{11}^{L} I_{L_w}^{**} u - (\mu_w + \alpha_{L_w}) v \tag{3.16}$$

$$\frac{\partial x}{\partial t} + \frac{\partial x}{\partial \tau} = -q_w(\tau)\beta_{11}^{H} r_{L_w}^{**} y - q_w(\tau)\beta_{11}^{H} I_{H_w}^{**} x - \mu_w x \tag{3.17}$$

$$x(0,t) = \alpha_{L_w} v$$

$$\frac{dy}{dt} = \beta_{11}^{H} I_{H_w}^{**} u + \beta_{11}^{H} S_w^{**} y + \beta_{11}^{H} I_{H_w}^{**} \int_0^\infty q_w(\tau) x(\tau, t) d\tau \tag{3.18}$$

$$+ \beta_{11}^{H} y \int_0^\infty q_w(\tau) r_{L_w}^{**} d\tau - (\mu_w + \alpha_{H_w} + \nu_{H_w}) y$$

$$\frac{dz}{dt} = \alpha_{H_w} y - \mu_w z \tag{3.19}$$

We look for exponential solutions of the system (3.15)-(3.19). Substituting (3.3) into (3.15)-(3.19), we get the following eigenvalue problem:

$$\lambda \bar{u} = -\beta_{11}^{L} S_w^{**} \bar{v} - \beta_{11}^{L} I_{L_w}^{**} \bar{u} - \beta_{11}^{H} I_{H_w}^{**} \bar{u} - \beta_{11}^{H} S_w^{**} \bar{y} - \mu_w \bar{u} \tag{3.20}$$

$$\lambda \bar{v} = \beta_{11}^{L} S_w^{**} \bar{v} + \beta_{11}^{L} I_{L_w}^{**} \bar{u} - (\mu_w + \alpha_{L_w}) \bar{v} \tag{3.21}$$

$$\lambda \bar{x} + \frac{d\bar{x}}{d\tau} = -q_w(\tau)\beta_{11}^{H} r_{L_w}^{**} \bar{y} - q_w(\tau)\beta_{11}^{H} I_{H_w}^{**} \bar{x} - \mu_w \bar{x} \tag{3.22}$$

$$\bar{x}(0) = \alpha_{L_w} \bar{v}$$

$$\lambda \bar{y} = \beta_{11}^{H} I_{H_w}^{**} \bar{u} + \beta_{11}^{H} S_w^{**} \bar{y} + \beta_{11}^{H} I_{H_w}^{**} \int_0^\infty q_w(\tau) \bar{x}(\tau) d\tau \tag{3.23}$$

$$+ \beta_{11}^{H} \bar{y} \int_0^\infty q_w(\tau) r_{L_w}^{**} d\tau - (\mu_w + \alpha_{H_w} + \nu_{H_w}) \bar{y}$$

$$\lambda \bar{z} = \alpha_{H_w} \bar{y} - \mu_w \bar{z} \tag{3.24}$$

We solve the non-homogeneous differential equation (3.22), by first multiplying with the integrating factor;

$$e^{(\lambda+\mu_w)\tau + \beta_{11}^{H} I_{H_w}^{**} \int_0^\tau q_w(s) ds}.$$

We then integrate both sides from 0 to τ and use the initial condition $\bar{x}(0) = \alpha_{L_w} \bar{v}$ to obtain:

$$\bar{x}(\tau) = \alpha_{L_w} \bar{v} e^{-(\lambda+\mu_w)\tau - \beta_{11}^{H} I_{H_w}^{**} \int_0^\tau q_w(s) ds} - \beta_{11}^{H} \bar{y} f(\tau)\,, \tag{3.25}$$

where

$$f(\tau) = \int_0^\tau q_w(s) r_{L_w}^{**}(s) e^{-(\lambda+\mu_w)(\tau-s) - \beta_{11}^{H} I_{H_w}^{**} \int_s^\tau q_w(\sigma) d\sigma}. \tag{3.26}$$

Since $\beta_{11}^L S_w^{**} - (\mu_w + \alpha_{L_w}) = 0$, equation (3.21) reduces to

$$\lambda \bar{v} = \beta_{11}^L I_{L_w}^{**} \bar{u}\,. \tag{3.27}$$

Similarly using the equation of coexistence equilibrium (3.13), from (3.23) we see that $\beta_{11}^H S_w^{**} + \beta_{11}^H \int_0^\infty q_w(\tau) r_{L_w}^{**} d\tau - (\mu_w + \alpha_{H_w} + \nu_{H_w}) = 0$. Hence, (3.23) reduces to

$$\lambda \bar{y} = \beta_{11}^H I_{H_w}^{**} \bar{u} + \beta_{11}^H I_{H_w}^{**} \int_0^\infty q_w(\tau) \bar{x}(\tau) d\tau\,. \tag{3.28}$$

Substituting the solution for $\bar{x}(\tau)$, (3.25), into the reduced equation for $\bar{y}$ (3.28), we obtain the following equation for $\bar{y}$ which involves only $\bar{u}$ and $\bar{v}$

$$\lambda \bar{y} = \beta_{11}^H I_{H_w}^{**} \bar{u} + A(\lambda)\bar{v} - \beta_{11}^H I_{H_w}^{**} \beta_{11}^H B(\lambda) \bar{y} \tag{3.29}$$

where

$$A(\lambda) = \alpha_{L_w} \beta_{11}^H I_{H_w}^{**} \int_0^\infty \left(q_w(\tau) e^{-(\lambda+\mu_w)\tau - \beta_{11}^H I_{H_w}^{**} \int_0^\tau q_w(s) ds} \right) d\tau\,. \tag{3.30}$$

and

$$B(\lambda) = \int_0^\infty q_w(\tau) f(\tau) d\tau\,. \tag{3.31}$$

Combining these reduced equations for (3.27) and (3.29) together with (3.20), we get the following eigenvalue problem;

$$\begin{aligned} \lambda \bar{u} &= -\beta_{11}^L S_w^{**} \bar{v} - \beta_{11}^L I_{L_w}^{**} \bar{u} - \beta_{11}^H I_{H_w}^{**} \bar{u} - \beta_{11}^H S_w^{**} \bar{y} - \mu_w \bar{u} \\ \lambda \bar{v} &= \beta_{11}^L I_{L_w}^{**} \bar{u} \\ \lambda \bar{y} &= \beta_{11}^H I_{H_w}^{**} \bar{u} + A(\lambda)\bar{v} - \beta_{11}^H I_{H_w}^{**} \beta_{11}^H B(\lambda) \bar{y}\,. \end{aligned} \tag{3.32}$$

This system will have non-zero solution for $(\bar{u}, \bar{v}, \bar{y})$ if the determinant of this system is zero, that is, if

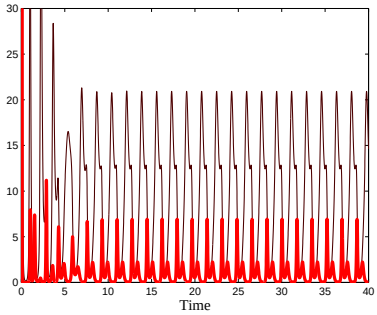
$$\begin{vmatrix} -\lambda - \beta_{11}^L I_{L_w}^{**} - \beta_{11}^H I_{H_w}^{**} - \mu_w & -\beta_{11}^L S_w^{**} & \beta_{11}^H S_w^{**} \\ \beta_{11}^L I_{L_w}^{**} & -\lambda & 0 \\ \beta_{11}^H I_{H_w}^{**} & A(\lambda) & -\lambda - \beta_{11}^H I_{H_w}^{**} B(\lambda) \end{vmatrix} = 0. \tag{3.33}$$

From the determinant, we obtain the characteristic equation for the eigenvalue problem (3.32):

$$\begin{aligned} &\lambda^3 + \lambda^2 \left(\beta_{11}^H I_{H_w}^{**} \beta_{11}^H B(\lambda) + \beta_{11}^L I_{L_w}^{**} + \beta_{11}^H I_{H_w}^{**} + \mu_w \right) \\ &+\lambda \left[\left(\beta_{11}^L I_{L_w}^{**} + \beta_{11}^H I_{H_w}^{**} + \mu_w \right) \left(\beta_{11}^H I_{H_w}^{**} \beta_{11}^H B(\lambda) \right) + \beta_{11}^H S_w^{**} \beta_{11}^H I_{H_w}^{**} + \beta_{11}^L S_w^{**} \beta_{11}^L I_{L_w}^{**} \right] \\ &+\beta_{11}^H S_w^{**} \beta_{11}^L I_{L_w}^{**} A(\lambda) + \beta_{11}^H I_{H_w}^{**} \beta_{11}^H B(\lambda) \beta_{11}^L S_w^{**} \beta_{11}^L I_{L_w}^{**} = 0. \end{aligned}$$

This characteristic equation has roots with positive real parts. Thus instability and oscillations occur. We show that sustained oscillations are possible in the system (2.1) by demonstrating it with a specific example in the next section.

FIGURE 1. The number of wild birds infected with LPAI (thin line) and the number of wild birds infected with HPAI (thick line) exhibit oscillations.



4. Numerical Simulations

In this section, we perform several numerical simulations of the model (2.1). We obtain the approximate solution of the system (2.1) by constructing an implicit finite difference method. We discretize the domain $D = \{(\tau, t) : 0 \leq \tau \leq A\,,\ 0 \leq t \leq T\}$ by taking equal step sizes in both t and τ direction. Thus, $\Delta t = \Delta\tau$.

In all simulations, we choose the cross-immunity function $q_w(\tau)$ to be the following step function;

$$q_w(\tau) = \begin{cases} 0 & \text{if } \tau \leq a \\ q & \text{if } \tau > a \end{cases} \tag{4.1}$$

where a is an arbitrary constant. Since the variable τ is the time-since-recovery from low pathogenic avian influenza, this cross immunity function $q_w(\tau)$ means that the wild birds are fully protected from HPAI for a period of time a. After that period a, the protection wanes. This is a reasonable assumption for low pathogenic and high pathogenic influenza in the avian population, and it is in agreement with the results of the study by [40].

The first question that we address with simulations is whether system can (2.1) can exhibit oscillations in which both the LPAI and the HPAI oscillate at non-zero values. To address this question, we analyze the characteristic equation. With the above choice of $q_w(\tau)$, we compute the integrals in $f(\tau)$, $A(\lambda)$, and $B(\lambda)$ and get;

$$f(\tau) = q\alpha_{L_w} I^{**}_{L_w} \frac{1}{\lambda}\left(e^{\lambda\tau} - e^{\lambda a}\right) e^{-(\lambda+\mu_w)\tau - \beta^H_{11} I^{**}_{H_w} q(\tau - a)}$$

and

$$A(\lambda) = \frac{\beta^H_{11} I^{**}_{H_w} \alpha_{L_w} q e^{-(\lambda+\mu_w)a}}{\lambda + \mu_w + \beta^H_{11} I^{**}_{L_w} q}$$

and

$$B(\lambda) = \frac{q^2 \alpha_{L_w} I^{**}_{L_w} e^{-\mu_w a}}{(\lambda + \mu_w + \beta^H_{11} I^{**}_{L_w} q)(\mu_w + \beta^H_{11} I^{**}_{L_w} q)}.$$

After analyzing the characteristics equation we find parameters of the model (2.1), whose solutions exhibits oscillations. These parameters are given in Table 1. To illustrate the oscillations, we simulate the solutions of the wild bird system (2.1) using an implicit finite difference method. Time is measured in years, and the final time for the simulations

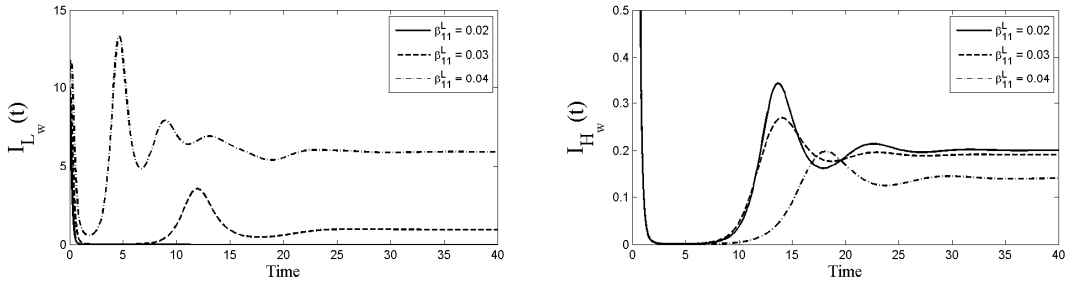
are $T = 40$ and $A = 30$. The number of wild birds infected with LPAI and the number of wild birds infected with HPAI, which exhibit sustained oscillations, are plotted in Figure 1. The Figure shows that the oscillations in LPAI have a much larger amplitude than the oscillations of LPAI suggesting that the instability of the dynamics of LPAI is more pronounced. Furthermore, the oscillations in HPAI follow the oscillations of LPAI with the peak in HPAI occurring right after the drop in LPAI. This behavior partly reminds of a Lotka-Volterra predator-prey dynamics where the oscillations in the predator follow the oscillations of the prey with 1/4 of a turn. This analogy is perhaps not surprising since HPAI infects individuals recovered from LPAI.

TABLE 1. Parameter values of the wild birds model (2.1) which exhibits oscillations.

Prameter	Value	Parameter	Value	Parameter	Value
Λ_w	1020	β_{11}^L	0.1278	$r_{L_w}(\tau, 0)$	$28/T$
μ_w	1/2	β_{11}^H	0.7140	$I_{H_w}(0)$	2
ν_{H_w}	460.925	$S_w(0)$	2000	q	1
α_{H_w}	365/7	$I_{L_w}(0)$	10	a	0.25
α_{L_w}	365/7				

The next question we address is how changes in the transmission of LPAI affect the competition of the strains. To investigate the impact of β_{11}^L, we obtain the approximate solutions of the system (2.1) for three different values of β_{11}^L. We fix all other parameters and change only β_{11}^L. The results show that increasing β_{11}^L increases the LPAI prevalence and decreases the HPAI prevalence. We plot $I_{L_w}(t)$ and $I_{H_w}(t)$ in Figure 2.

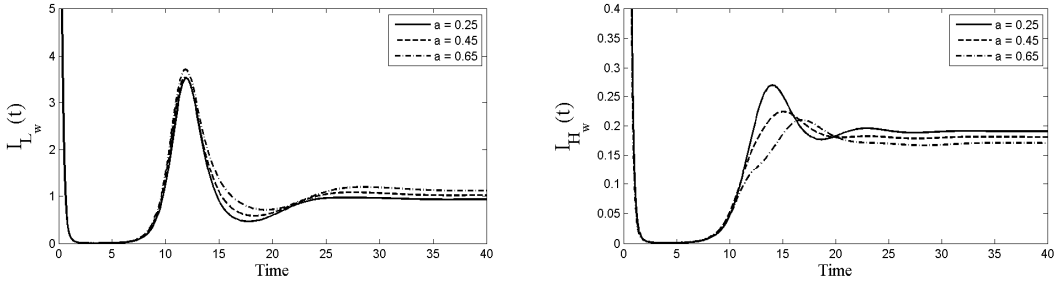
FIGURE 2. LPAI and HPAI prevalence for three different values of β_{11}^L



System (2.1) can model the dynamics of LPAI and HPAI in both wild and domestic birds. The observation that increasing transmission increases prevalence of LPAI and decreases prevalence of HPAI may shed light on why wild birds have lower prevalence of HPAI compared to domestic birds. The immunity created by circulating LPAI protects wild birds from HPAI. In contrast, domestic birds are protected from LPAI and consequently, they experience much more serious symptoms from HPAI and HPAI has much higher prevalence in domestic birds, particularly in the poultry population of some countries.

Another question of interest is how the duration of cross-immunity affects the LPAI and HPAI prevalence. Since we assume that LPAI provides full protection against HPAI for $\tau \in [0, a]$, it is interesting to know how the length of this protection affects the dynamics. We take three different values of a and plot $I_{L_w}(t)$ and $I_{H_w}(t)$ in Figure 3. We observe that increasing duration of cross-immunity decreases the prevalence of HPAI among wild bird populations. What is unexpected is that cross-immunity also increases the prevalence of LPAI, even though it does not directly affect LPAI. The change in LPAI is at least as pronounced as the change in HPAI.

FIGURE 3. Effect of cross-immunity on HPAI prevalence



Another question that we consider is the impact of LPAI and HPAI transmission rates β_{11}^H and β_{11}^L on the HPAI prevalence at coexistence equilibrium. To investigate this topic, we consider the equation for the $I_{H_w}^{**}$. The HPAI prevalence in the coexistence equilibrium satisfies the equation $F(I_{H_w}^{**}) = 0$ given in (3.14) which involves the following integral

$$C = \int_0^\infty q_w(\tau) e^{-\mu_w \tau - \beta_{11}^H I_{H_w}^{**} \int_0^\tau q_w(s) ds} d\tau \,.$$

We compute the integral $C(\lambda)$ by taking $q_w(\tau)$ to be the step function in (4.1) and obtain

$$C = \frac{q e^{-\mu_w a}}{\mu_w + \beta_{11}^H I_{H_w}^{**} q}.$$

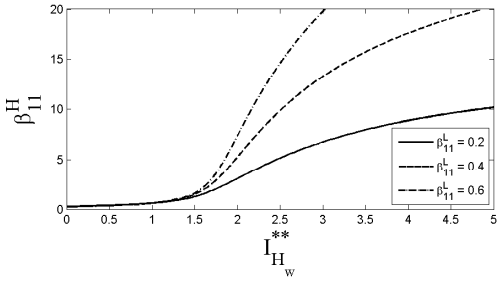
Thus, the HPAI coexistence equilibrium, $I_{H_w}^{**}$ satisfies

(4.2)

$$\frac{\beta_{11}^H}{\beta_{11}^L}(\mu_w + \alpha_{L_w}) + \frac{\beta_{11}^H}{\beta_{11}^L}\alpha_{L_w}\left(\mu_w(\mathcal{R}_0^{L_w} - 1) - \beta_{11}^H I_{H_w}^{**}\right)\frac{q e^{-\mu_w a}}{\mu_w + \beta_{11}^H I_{H_w}^{**} q} - (\mu_w + \alpha_{H_w} + \nu_{H_w}) = 0$$

We plot (4.2) for several values of β_{11}^L in Figure 4 . We consider how the two transmission rates impact $I_{H_w}^{**}$. We notice that for low values of HPAI transmission rate and low HPAI prevalence, the HPAI prevalence does not depend on the transmission rate of LPAI. However, as the HPAI prevalence increases it becomes more and more sensitive to the LPAI transmission rate. A surprising conclusion is that for higher HPAI prevalences, the HPAI prevalence depends significantly on the LPAI transmission rate β_{11}^L. It is further clear that increase in β_{11}^H increases the HPAI prevalence $I_{H_w}^{**}$ while increase in the LPAI transmission rate β_{11}^L decreases HPAI prevalence $I_{H_w}^{**}$. This observation again suggests that higher transmission of LPAI in wild birds may be responsible for lower prevalence of HPAI.

FIGURE 4. HPAI coexistence equilibrium

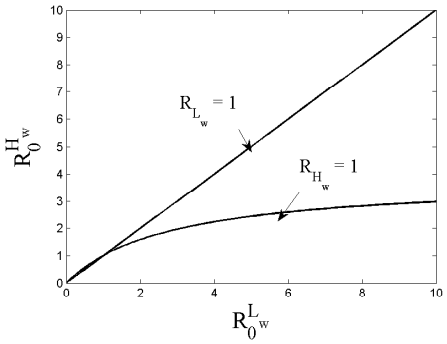


Finally, we recall that HPAI is locally stable if $\hat{\mathcal{R}}_{L_w} < 1$, and LPAI is locally stable if $\hat{\mathcal{R}}_{H_w} < 1$. We notice that the two invasion numbers can be written as function of the two reproduction numbers:

$$\hat{\mathcal{R}}_{L_w} = h(\mathcal{R}_0^{L_w}, \mathcal{R}_0^{H_w}) \qquad \hat{\mathcal{R}}_{H_w} = g(\mathcal{R}_0^{L_w}, \mathcal{R}_0^{H_w}).$$

Therefore, we can plot the curves $h(\mathcal{R}_0^{L_w}, \mathcal{R}_0^{H_w}) = 1$ and $g(\mathcal{R}_0^{L_w}, \mathcal{R}_0^{H_w}) = 1$ in the $(\mathcal{R}_0^{L_w}, \mathcal{R}_0^{H_w})$ plane. The figure we obtain is given in Figure 5. The figure shows that the

FIGURE 5. The regions of coexistence and dominance



area in the $(\mathcal{R}_0^{L_w}, \mathcal{R}_0^{H_w})$ plane where HPAI dominates is the largest. HPAI dominates whenever $\mathcal{R}_0^{H_w} > \mathcal{R}_0^{L_w}$. The area where LPAI dominates is below the lower curve. The area where LPAI and HPAI coexist is the area between the curves. This area is larger if q is larger and when a is smaller. That is to say that coexistence is more likely if the full immunity provided by LPAI is shorter.

5. Discussion

This chapter introduces a LPAI-HPAI avian influenza model. HPAI-infected individuals can infect individuals recovered from LPAI at some reduced infectivity. However, we assume that LPAI-infected individuals cannot infect HPAI-recovered individuals. Furthermore, LPAI-recovered individuals are structured by time-since-recovery and the immunity to HAPI created by prior infection by LPAI wanes as the time-since-recovery increases. This model describes the HPAI-LPAI dynamics in both domestic and wild birds.

We find that the system has a unique disease-free equilibrium. We define the reproduction numbers for the LPAI and HPAI. If both reproduction number are smaller than one, then we show that the disease-free equilibrium is both locally and globally stable. If one of the reproduction numbers is greater than one, then the disease-free equilibrium is unstable. Furthermore, we find that if the reproduction number of LPAI is greater than one, there is a unique LPAI-only equilibrium. Similarly, if the reproduction number of HPAI is greater than one, there is a unique HPAI-only equilibrium. We define the invasion reproduction numbers of LPAI and HPAI. The invasion reproduction number of LPAI is greater than one if and only if the reproduction number of LPAI is greater then the reproduction number of HPAI. We prove that the LPAI-only equilibrium is locally asymptotically stable if the HPAI invasion number is smaller than one, that if the HPAI cannot invade the equilibrium of the LPAI. Similarly we prove that the HPAI-only equilibrium is locally asymptotically stable if the LPAI invasion number is smaller than one, that is the LPAI cannot invade the equilibrium of the HPAI. This is to say that HAPI dominates in the population and drives LPAI to extinction if and only if HAPI reproduction number is larger than the LPAI reproduction number. HPAI dominates for more values of the reproduction numbers than LPAI and every time the reproduction number of HPAI is larger than the reproduction number of LPAI; however, we believe that for realistic parameter values LPAI has a higher reproduction number, particularly in wild birds.

Finally we show that if both invasion numbers are larger than one coexistence equilibrium is present. The mechanism of coexistence is cross-immunity. We show that the coexistence equilibrium is unique. In addition, we show through simulations that the coexistence equilibrium may lose stability and coexistence in the form of sustained oscillations is possible. In this case HPAI's peak follows right after the LPAI's peak.

Simulations also suggest that increasing the transmission coefficient of LPAI increases the prevalence of LPAI and decreases the prevalence of HPAI. Furthermore, increasing the transmission coefficient of HPAI and decreasing the transmission coefficient of LPAI both increase the HPAI prevalence. Based on these simulations we conclude that higher transmission of LPAI in wild birds may be responsible for the lower prevalence of HPAI compared to poultry. Finally, assuming that LPAI protects against HPAI completely for a period of time, we investigate the effect the duration of protection has on the LPAI and HPAI prevalence. We find that increasing the duration of protection has an impact on both the LPAI prevalence and the HPAI prevalence. In particular, it increases the LPAI prevalence and decreases the HPAI prevalence.

Several articles have investigated the dynamics of LPAI and HPAI before [28, 5]. However, the effects of cross-immunity and duration of protection have not been studied. In this article we investigate these effects as well as how transmission impacts the prevalence of LPAI and HPAI. Furthermore, prior studies have found that ODE models with cross-immunity have note been able to exhibit sustain oscillations [6, 7]. To generate oscillations in the multi-strain influenza dynamics, a quarantine state was introduced in [34]. Here, we have used a different approach to model the oscillations in avian influenza dynamics, namely, we have introduced a time-since-recovery independent variable. We show via simulations that the coexistence equilibrium can be destabilized and coexistence in the form of sustained oscillation is possible.

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