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EPIDEMIC SPREAD OF INFLUENZA VIRUSES: THE IMPACT OF TRANSIENT POPULATIONS ON DISEASE DYNAMICS

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Abstract. The recent H1N1 ("swine flu") pandemic and recent H5N1 ("avian flu") outbreaks have brought increased attention to the study of the role of animal populations as reservoirs for pathogens that could invade human populations. It is believed that pigs acquired flu strains from birds and humans, acting as a mixing vessel in generating new influenza viruses. Assessing the role of animal reservoirs, particularly reservoirs involving highly mobile populations (like migratory birds), on disease dispersal and persistence is of interests to a wide range of researchers including public health experts and evolutionary biologists. This paper studies the interactions between transient and resident bird populations and their role on dispersal and persistence. A metapopulation framework based on a system of nonlinear ordinary differential equations is used to study the transmission dynamics and control of avian diseases. Simplified versions of mathematical models involving a limited number of migratory and resident bird populations are analyzed. Epidemiological time scales and singular perturbation methods are used to reduce the dimensionality of the model. Our results show that mixing of bird populations (involving residents and migratory birds) play an important role on the patterns of disease spread.

1. **Introduction.** Wild birds are known reservoirs for diseases like West Nile virus, influenza A virus, enteric bacterial pathogens and drug resistance bacteria. They are often infested by arthropod vectors, which can be dropped along bird migration routes (Reed et al. 2003). Several aspects linked to long distance migration contribute to the acquisition of zoonotic pathogens by migratory birds, that is,

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pathogens that are transmitted from vertebrate animals to humans. One of these aspects is the fact that, for some birds the stress of migration can lead to reactivation of otherwise latent infections (FAO 2006).

Each autumn an estimated 5 billion birds, representing 300 species, migrate from North America to Central and South America and similar numbers travel from Eastern Europe to Africa. Patterns of migration for wild birds are complex and species dependent. In fact, they can be radically different even within populations from the same species (Reed 2003). Migratory bird routes in the Atlantic, Mississippi, Central and Pacific flyways are oriented north to south because the major wetlands in North America run in a similar direction. In contrast, migratory birds in some regions in Europe and Asia tend to move in an east to west fashion, that matches the orientation of major coastlines and topography.

According to the 2006 Food and Agricultural Organization of the United Nations report (FAO 2006), populations of ducks, geese and swans migrate between wetlands in the northern breeding areas and southern non-breading areas and in doing so, regularly cross the borders of two or more countries. Southward migration for these northern breeding species starts in July and increases through the following months. The migration takes them north to reproduction areas at the end of winter, beginning of spring.

Understanding migratory bird patterns and the potential for their contact with domestic birds or poultry (Food and Agricultural Organization of United Nations (FAO) 2005) and even swine populations is of vital importance. We are interested in the interactions between local domestic birds or poultry (resident birds) and migratory birds. There are three issues associated with the control of avian influenza, that need increased attention: information on migration patterns of birds flyways (complex and species dependent), studies on the impact of disease evolution on migration, and studies on the impact of migration on disease distribution.

The movement of diseases via migration birds depends upon the ability of individual birds to migrate after becoming infected with a pathogen (see Olsen et al. 2006). Avian experts agree that sick and dying birds do not spread viruses very far (Normile 2005). It is unknown whether or not migratory birds survive infections to various diseases (Chen et al. 2006). Disease transmission is most common between individuals of the same species. Cross species transmission requires exposure and adaptation . Even adapted domestic birds exhibit high degree of heterogeneity when it comes down to susceptibility and infectivity. Variation is evaluated via the differences in transmission factors, often high between subtypes, and even within each subtype (Boon 2007).

In general the role of migratory birds on disease dynamics is not easy to assess. For example, in the case of the avian flu, it is extremely difficult to know if migratory birds are sparkling new outbreaks in domestic birds or poultry, or whether they pick up the virus from poultry infected by other routes (Butler 2006). In this manuscript a mathematical framework is introduced to study the dynamics of avian diseases within migratory and resident (local) bird populations. The goal here is to assess the impact of interactions between resident and migratory bird species on the dynamics of "communicable" avian diseases like influenza.

2. **Avian and swine influenza.**

2.1. **Avian flu.**

Avian influenza is a non-clinical viral infection of wild birds caused by a group of viruses known as type A influenza. The viruses subtypes are identified

and classified on the basis of two broad types of antigens, hemagglutinan (H) and neuraminidase (N). Among all the type A influenza viruses 15H and 9N antigens have been identified (Friend and Franson 1999). All known subtypes of influenza A viruses can be found in bird populations.

Infected birds shed influenza viruses in their saliva, nasal secretions and feces. Susceptible birds become infected when they have contact with contaminated secretions, excretions or with surfaces that are contaminated with secretions or excretions from infected birds (Center for Disease Control and Prevention (CDC) 2006a).

Wild waterfowls are considered the natural reservoir of all influenza A viruses. They have probably carried influenza viruses, with no apparent harm, for centuries (WHO 2005). Viruses have been recovered from infected waterfowl fecal material for 8 days, from fecal contaminated river water for 4 days, and from poultry houses more than 100 days after flock depopulation for markets (Friend and Franson 1999). It is believed that avian influenza in wild birds cannot be effectively controlled because of the large number of virus subtypes and the high frequency of virus genetic mixing resulting, key to the selection of new subtypes.

Wild birds, especially waterfowl and shorebirds, have long been the focus of concern within the poultry industry. These bird populations are seen as a source for influenza infections in poultry (Friend and Franson 1999). Avian influenza is highly contagious among birds and can make some domesticated birds, including chickens, ducks and turkeys, very sick. Disease-induced death can be high. Domesticated birds may become infected with avian influenza virus through direct contact with infected waterfowl or other infected poultry, or through contact dirt, cages, water or feed, that have been contaminated with the virus (CDC 2006a).

Viruses are classified as having low or high pathogenicity depending on the effects they have on birds (Normile 2005). Low pathogenic avian influenza typically causes mild symptoms that include ruffled feathers and a drop in egg production. Most infections go undetected. Highly pathogenic types spread rapidly through poultry flocks, causing disease affecting multiple organs. In domestic poultry species, turkeys are more commonly infected than for example, chickens, while more influenza viruses have been isolated from ducks. Disease induced mortality in poultry often approaches 100%, within 48 hours (World Health Organization 2005). Considerable circumstantial evidence suggest that migratory birds can introduce low pathogenic H5 and H7 viruses to poultry flocks, forms that can and do mutate into highly pathogenic form (WHO 2005). Mutations from low to high pathogenicity, resulting in bird flu epidemics in poultry, have been documented 19 times since 1959 (Normile 2005). Some migratory birds may be directly spreading H5N1 virus in highly pathogenic forms (WHO 2005). Only some strains of four subtypes of avian influenza viruses have been highly pathogenic in humans they are: H5N1, H7N3, H7N7 and H9N2 (Leong 2008).

2.2. **Swine influenza.** Swine Influenza (swine flu) is a respiratory disease of pigs caused by type A influenza viruses that regularly cause influenza outbreak in pigs. Strains of the H1N1 subtype were found to be circulating in pigs during 1930. Swine flu viruses cause high levels of illness but low death rates in pigs. Pigs can be infected by avian, human and swine influenza viruses. When influenza viruses from different species infect pigs, the viruses can reassort (i.e. swap genes). New virus strains that are a mix of swine, human and/or avian influenza viruses can emerge. Over the years, different variations of swine flu viruses have emerged in this fashion. Currently, there are four main influenza type A virus subtypes that

have been isolated in pigs: H1N1, H1N2, H3N2, and H3N1. However, most of the recently isolated influenza viruses from pigs have been from the H1N1 subtype (CDC 2009a). Recently it was found that H1N1 was the virus associated with the Spanish flu of 1918 (FAS 2009).

Swine flu viruses are thought to spread mostly through close contacts between pigs, but also indirectly (feed, water, etc). Signs of swine flu in pigs include sudden onset of fever, depression, coughing (barking), discharge from the nose or eyes, sneezing, breathing difficulties, eye redness or inflammation, and going off feed. H1N1 and H3N2 swine flu viruses are endemic among pig populations in the United States, a "routine" issue in this industry. Outbreaks among pigs normally occur in colder weather months (late fall and winter) or (sometimes) after the recent introduction of infected pigs into susceptible herds (CDC 2009).

The symptoms of H1N1 flu virus in people are similar to the symptoms of seasonal flu and include fever, cough, sore throat, runny or stuffy nose, body aches, headache, chills and fatigue. A significant number of people who have been infected with this virus also have reported diarrhea and vomiting, uncommon for typical flu symptoms. The spread of the most recent H1N1 virus strain seems to be spreading as actively as seasonal flu (CDC 2009b). Flu viruses are spread primarily, from person to person, as a result of sharing an area that includes coughing or sneezing by sick individuals. Studies have shown that people may be contagious a day before the development of symptoms and for up to 7 days after they get sick. The influenza virus can survive on environmental surfaces and can be viable (infect a person) 2-8 hours after being deposited on such a surface (CDC 2009b).

Pigs are uniquely susceptible to getting flu viruses that infect birds. Experts have long worried that a pig would catch a bird strain of the flu and that the virus would mutate inside the pig to a form that could also be transmitted from mammals to mammals.

3. **Avian influenza and migratory birds.** Wetland or lakes have been associated with the distribution of outbreaks of avian flu in Europe. The disease has emerged in Africa opening a new front that could vastly increase the size of bird reservoir populations (Butler 2006). The close proximity of people and animals, coupled with insufficient surveillance and limited disease control capacities in the rich wetland ecosystems of eastern African countries, are ideal breeding grounds for influenza. Around lakes and wetlands, domestic bird densities are particularly high therefore, the enhancement and strengthening of avian disease surveillance and emergency preparedness in these regions are essential (FAO 2005).

In Asia H5N1 avian influenza spreads through domestic bird populations, wild bird trade and migratory birds. However, outbreaks do not match the migratory patterns of wild birds (Normile 2005). China is the most likely source of emergent and re-emergent HPAI H5N1 influenza viruses (Chen et al. 2006). H5N1 viruses have been found in dead wild birds close to poultry farms (Chen et al 2005) and most recently in Qinghai Lake, one of the most important breeding locations for migratory birds that over-winter in Southeast Asia, Tibet and India (Liu 2005).

In the past only three large die-offs in migratory birds, caused by highly pathogenic viruses, have been documented. The first in South Africa in 1961 (H5N3), the second in Hong Kong in the winter of 2002-2003 (H5N1) (WHO 2005), and the third (April 2005) in Qinghai Lake, an outbreak that killed 5000-6000 migratory water birds (Normile 2005), the first sustained transmission chain within migratory

waterfowl in recent times. Overall 90% of the dead birds in the Qinghai Lake were bar-headed geese. The virus was being transmitted by migratory birds in this lake, suggesting the possibility that H5N1 viruses may possibly be transmitted between migratory birds populations (FAO 2006).

Chen et al. (2006) found that genetic relatedness of gene segments of H5N1 viruses isolated at Poyang and Qinghai Lakes support the hypothesis that migratory birds can transfer the virus over long distances. Ongoing influenza surveillance data show that H5N1 viral strains were present in apparently healthy migratory birds just before the start of their migration trek. These viruses, isolated from apparently healthy migratory ducks, are not invariably fatal. In fact, surviving ducks may shed the virus even 7 days after infection. Subsequent (after April 2005) outbreaks of avian influenza in 13 countries, including Niger and regions in Europe and Asia, seem to have been ignited by strains related to the strain identified in Qinghai Lake (Normile 2006). These findings strongly support the hypothesis that wild birds carry influenza viruses over great distances.

According to Normile (2006) and Chen et al. (2006), the best approach to avert a global threat of avian flu is to control H5N1 virus infections in domestic birds. On the other hand, in China it is believed that circulation among poultry by humans, not re-introduction from wild birds, is what is keeping the virus alive. There has been arguments that the cycle of transmission can be broken if the virus is eradicated from domesticated birds (poultry flocks) (Chen et al. 2006).

4. **Classical mixing.** Migratory birds that visit areas with large resident populations for short periods of times may mix a lot or hardly mix with resident bird populations. In order to look at the impact of strong versus weak mixing regimes, we divide the bird population in two categories: resident birds and migratory birds. Migratory birds are the only ones that are assumed to travel. We let $N_1, ..., N_s$ denote the total population of resident birds of flocks $l = 1, ..., s$ and $N_{s+1}, ..., N_{s+k}$ the total population of migratory birds of flocks $m = s + 1, ..., s + k$. The total population of birds is

$$N = \sum_{r=1}^{s+k} N_r.$$

Within each flock, birds are subdivided into two epidemiological classes, susceptible birds, S_r, and infected birds, I_r, where $r = 1, ..., s+k$. Since migratory birds can get infected by birds in their own flock, by resident birds in a resident bird habitat and by migratory birds of different flocks while visiting the resident birds, the system of non-linear ordinary differential equations that models the interactions of migratory birds is given by

$$\frac{dS_r}{dt} = \Lambda_r - \beta_r S_r \sum_{z=1}^{s+k} P_{rz} \frac{I_z}{N_z} - \mu_r S_r, \tag{1a}$$

$$\frac{dI_r}{dt} = \beta_r S_r \sum_{z=1}^{s+k} P_{rz} \frac{I_z}{N_z} - (\mu_r + d_r) I_r, \tag{1b}$$

where $r = s + 1, ..., s + k$ and P_{rz}'s are the mixing probabilities defined below. On the other hand, since resident birds do not move from their own habitat, the system

corresponding to the interactions of resident birds is given by

$$\frac{dS_r}{dt} = \Lambda_r - \beta_r S_r P_{rr} \frac{I_r}{N_r} - \beta S_r \sum_{z=s+1}^{s+k} P_{rz} \frac{I_z}{N_z} - \mu_r S_r, \tag{2a}$$

$$\frac{dI_r}{dt} = \beta_r S_r P_{rr} \frac{I_r}{N_r} + \beta_r S_r \sum_{z=s+1}^{s+k} P_{rz} \frac{I_z}{N_z} - (\mu_r + d_r) I_r, \tag{2b}$$

where $r = 1, ..., s$. Definition for the parameters are provided in Table 1.

Parameters	Definitions
Λ_r	Birds birth/arrival rate
μ_r	Birds culling/departure mortality rate
d_r	Mortality rate due to disease
β_r	Transmission rate per contact
P_{rz}	Mixing probability between birds from flock r and z

TABLE 1. Parameters Definitions

Two types of mixing probabilities: proportionate and preferred mixing (Jacquez et al. 1988, Blythe et al. 1991, Blythe et al. 1995) are used to illustrate the differences between random versus "preferred" mixing on the patterns of disease spread in bird populations.

4.1. **Preferred mixing.** If birds mix according to preferred mixing (Jacquez et al. 1988, Blythe et al. 1991, Blythe et al 1995) then the mixing probabilities are given by

$$P_{rz} = f_r \delta_{rz} + (1 - f_r) \frac{(1 - f_z) C_z N_z}{\sum_{j=1}^{s+k} (1 - f_j) C_j N_j}.$$

Here, P_{rz} represent the proportion of contacts between birds of flock r and birds of flock z where, $\sum_{z=1}^{s+k} P_{rz} = \sum_{z=1}^{k} P_{rz} + \sum_{z=s+1}^{s+k} P_{rz} = 1$ and r is fixed. δ_{rz} is the delta function, thus f_r denotes the proportion of preferred contacts, that is, "reserve" contacts with your own type while $(1 - f_r) \frac{(1-f_z) C_z N_z}{\sum_{j=1}^{k+s} (1-f_j) C_j N_j}$ denote the rest of the contacts which are distributed via proportionate (random) mixing.

4.2. **Proportionate mixing.** If birds mix according to proportionate mixing (Blythe et al. 1991, Blythe et al. 1995 and Busenberg and Castillo-Chavez 1991) then the mixing probabilities become

$$P_{rz} = \frac{C_z N_z}{\sum_{z=1}^{s+k} C_z N_z},$$

where C_z is the per-capita contact rate of birds of type $z = 1, ..., s + k$ and

$$\sum_{z=1}^{s+k} P_{rz} = 1.$$

5. **Two flock system.** We study the dynamics of bird populations in the case where there are only two interacting bird flock populations: a flock of resident birds (l) and a flock of migratory birds (m). We consider preferred and proportionate mixing. System (1-2) reduces to

$$\begin{aligned}
\frac{dS_l}{dt} &= \Lambda_l - \beta_l S_l \sum_{z=\{l,m\}} P_{lz}\frac{I_z}{N_z} - \mu_l S_l,\\
\frac{dI_l}{dt} &= \beta_l S_l \sum_{z=\{l,m\}} P_{lz}\frac{I_z}{N_z} - (\mu_l + d_l)I_l,\\
\frac{dS_m}{dt} &= \Lambda_m - \beta_m S_m \sum_{z=\{l,m\}} P_{mz}\frac{I_z}{N_z} - \mu_m S_m,\\
\frac{dI_m}{dt} &= \beta_m S_m \sum_{z=\{l,m\}} P_{mz}\frac{I_z}{N_z} - (\mu_m + d_m)I_m.
\end{aligned}$$

Furthermore, under the assumption that migratory birds disperse quickly it is assumed that their disease induced mortality is negligible ($d_m \equiv 0$). Hence, the total population of migratory birds (in this case) is assumed to be constant, $N_m = \frac{\Lambda_m}{\mu_m}$. The assumption that both populations are equally susceptible to infection means that the transmission rates are the same, hence $\beta_m = \beta_l = \beta$. Further it is assumed that the rate of departure of migratory birds is much bigger than the slaughtered or culling rate, that is, $\mu_m >> \mu_l$. These strong simplifying assumptions lead to the following three dimensional system

$$\frac{dI_m}{dt} = \beta(N_m - I_m)\left(P_{mm}\frac{I_m}{N_m} + P_{ml}\frac{I_l}{N_l}\right) - \mu_m I_m, \tag{3a}$$

$$\frac{dS_l}{dt} = \Lambda_l - \beta S_l\left(P_{ll}\frac{I_l}{N_l} + P_{lm}\frac{I_m}{N_m}\right) - \mu_l S_l, \tag{3b}$$

$$\frac{dI_l}{dt} = \beta S_l\left(P_{ll}\frac{I_l}{N_l} + P_{lm}\frac{I_m}{N_m}\right) - (\mu_l + d_l)I_l. \tag{3c}$$

5.1. **Two flock system under proportionate mixing.** For the above case we have that under proportionate mixing the mixing probabilities of the two groups, System (3) are:

$$\begin{aligned}
P_{ll} &= \frac{C_l N_l}{C_m N_m + C_l N_l} = P_{ml},\\
P_{mm} &= \frac{C_m N_m}{C_m N_m + C_l N_l} = P_{lm},\\
P_{lm} &= 1 - P_{ll},\\
P_{ml} &= 1 - P_{mm}.
\end{aligned}$$

5.1.1. *Disease Free Equilibrium, Basic Reproductive Number and Endemic Equilibrium.* The disease free equilibrium (DFE) is $(I_m, S_l, I_l) = \left(0, \frac{\Lambda_l}{\mu_l}, 0\right)$ and the basic reproductive number R_0, the average number of secondary infectious produced by a typical infected individual in a population of susceptibles is (see Appendix A for calculations)

$$R_0^{prop} = \frac{C_l\Lambda_l/\mu_l}{C_m\Lambda_m/\mu_m + C_l\Lambda_l/\mu_l}\left(\frac{\beta}{\mu_l + d_l}\right) + \frac{C_m\Lambda_m/\mu_m}{C_m\Lambda_m/\mu_m + C_l\Lambda_l/\mu_l}\left(\frac{\beta}{\mu_m}\right).$$

That is, R_0^{prop} is a weighted average; weighted by the proportion of migratory and resident birds in the population. The contribution to disease dynamics by migratory birds is $R_0^m = \frac{\beta}{\mu_m}$ while the contribution of resident birds is $R_0^l = \frac{\beta}{\mu_l + d_l}$. Hence, $\frac{1}{\mu_m}$ is the average time spent by migratory birds of flock m in flock or habitat l and $\frac{1}{\mu_l + d_l}$ is the average infectious period of resident birds of flock l. If an arbitrary number of groups of flocks are included ($r = 1, ..., s + k$) then under the above simplifying epidemiological assumption R_0 is given by

$$R_0^{prop} = \sum_{l=1}^{s} \frac{C_l \Lambda_l / \mu_l}{\sum_{r=1}^{s+k} C_r \Lambda_r / \mu_r} \left(\frac{\beta}{\mu_l + d_l} \right) + \sum_{m=s+1}^{s+k} \frac{C_m \Lambda_m / \mu_m}{\sum_{r=1}^{s+k} C_r \Lambda_r / \mu_r} \left(\frac{\beta}{\mu_m} \right).$$

The stability of the DFE depends on the value of R_0. Typically, if $R_0 < 1$, the DFE is locally asymptotically stable while if $R_0 > 1$, it is unstable. The following theorem (two group case) establishes a stronger result, under the assumption that the contact rates are the same for all groups and the departure rate of migratory birds is larger than the sum of the natural and disease related deaths for resident birds.

Theorem 5.1. *Assume $C_m = C_l$, $\Lambda_m = \Lambda_l = \Lambda$ and $\mu_m > \mu_l + d$. If $R_0^{prop} < 1$ then the disease free equilibrium $(0, N^0, 0)$ where $N^0 = \Lambda/\mu_m + \Lambda/\mu_l$ is globally asymptotically stable.*

Proof. Consider new variables $N = N_m + N_l$ and $I = I_m + I_l$ thus, the new system under study is:

$$\begin{aligned} \frac{dN}{dt} &= (\Lambda + \mu_l N_m) - \mu_l N - d_l I_l, \\ \frac{dI}{dt} &= \beta I \left(1 - \frac{I}{N}\right) - \mu_m I + (\mu_m - \mu_l - d_l) I_l, \\ \frac{dI_l}{dt} &= \beta I \left(1 - \frac{N_m}{N}\right) - \beta I \frac{I_l}{N} - (\mu_l + d_l) I_l. \end{aligned}$$

Using

$$\frac{dN}{dt} = N' \leq (\Lambda + \mu_l N_m) - \mu_l N,$$

we can prove that $N(t) \leq N^0 = N_m + N_l^0$ where $N_l^0 = \Lambda/\mu_l$. Consider the Lyapunov function $L(I, I_l) = (\mu_m - \mu_l - d_l) I_l + (\mu_l + d_l) I$, then

$$\begin{aligned} \frac{dL}{dt} &= (\mu_l + d_l)(\beta - \mu_m) I - (\mu_l + d_l) \beta \frac{I^2}{N} + (\mu_m - \mu_l - d_l) \beta I \left(1 - \frac{N_m}{N_0}\right) \\ &\quad + (\mu_m - \mu_l - d_l) \left[\beta I \left(\frac{N_m}{N_0} - \frac{N_m}{N} \right) - \beta I \frac{I_l}{N} \right] \end{aligned}$$

$$\begin{aligned}
&= I[(\mu_l+d_l)\beta-\mu_m(\mu_l+d_l)+\beta\mu_m p-(\mu_l+d_l)\beta p]\\
&\quad -(\mu_l+d_l)\beta\frac{I^2}{N}-(\mu_m-\mu_l-d_l)\left[\beta\frac{N_m(N_0-N)I}{N_0N}+\beta I\frac{I_l}{N}\right]\\
&\leq I((1-p)\beta(\mu_l+d_l)+p\beta\mu_m-\mu_m(\mu_l+d_l))\\
&= I(\mu_l+d_l)\mu_m\left(\frac{\beta}{\mu_m}(1-p)+\left(\frac{\beta}{\mu_l+d_l}\right)p-1\right)\\
&= I(\mu_l+d_l)\mu_m(R_0^{prop}-1)\\
&\leq 0,
\end{aligned}$$

where $p=1-\frac{N_m}{N^0}$. The last inequality holds under the assumption that $R^{prop}<1$. Thus since $L(I,I_l)>0$, $\frac{dL}{dt}\leq 0$ and $\frac{dL}{dt}(0,N^0,0)=0$ by the Krasovskii-Lasalle Principle, the disease free equilibrium $(0,N^0,0)$ is globally asymptotically stable. □

The existence of at least one endemic equilibrium if $R_0^{prop}>1$ is guarantied by the following result.

Theorem 5.2. *Assume $C_l=C_m$. There is at least one endemic equilibrium (I_m^*,S_l^*,I_l^*) for System (3) if $R_0^{prop}>1$.*

Proof. The total population of local birds is governed by

$$\frac{dN_l}{dt}=\Lambda_l-\mu_l S_l-\mu_l I_l-d_l I_l,$$

therefore, we can write

$$\Lambda_l-\mu_l S_l-\mu_l I_l-d_l I_l=0$$

in two forms, that is,

$$\begin{aligned}
S_l &= \frac{\Lambda_l-(\mu_l+d_l)I_1}{\mu_l}\triangleq H_1(I_l), \quad \text{and}\\
N_l &= \frac{\Lambda_l-d_l I_l}{\mu_l}\triangleq H_2(I_l).
\end{aligned}$$

Defined $H(I_l)=N_m+H_2(I_l)$. From $\frac{dI_l}{dt}=0$ and $\frac{dI_m}{dt}=0$, we get

$$\beta H_1(I_l)\frac{I_m+I_l}{H(I_l)} = (\mu_l+d_l)I_l, \quad \text{and} \tag{4}$$

$$\beta(N_m-I_m)\frac{I_m+I_l}{H(I_l)} = \mu_m I_m. \tag{5}$$

Dividing Eq. (4) by Eq. (5), we express I_m in terms of I_l, that is,

$$I_m=\frac{N_m(\mu_l+d_l)I_l}{\mu_m H_1(I_l)+(\mu_l+d_l)I_l}. \tag{6}$$

Therefore, pluging Eq. (6) into Eq. (4) and after canceling I_l (since $I_l=0$ correspond to the DFE), we have $F(I_l)=0$ where

$$F(I_l)=\beta\frac{H_1(I_l)}{H(I_l)}\left(1+\frac{N_m(\mu_l+d_l)}{\mu_m H_1(I_l)+(\mu_l+d_l)I_l}\right)-(\mu_l+d_l).$$

The zeroes of $H_1(I_l) = 0$, $H(I_l) = 0$ and $H_3(I_l) \triangleq \mu_m H_1(I_l) + (\mu_l + d_l)I_l = 0$ are

$$\begin{aligned} \bar{I}_{l1} &= \frac{\Lambda_l}{\mu_l + d_l}, \\ \bar{I}_{l2} &= \frac{\mu_l N_m + \Lambda_l}{d_l} \qquad \text{and} \\ \bar{I}_{l3} &= \frac{\mu_m \Lambda_l}{(\mu_l + d_l)(\mu_m - \mu_l)}, \end{aligned}$$

respectively. If $\bar{I}_{l1} = \min\{\bar{I}_{l1}, \bar{I}_{l2}, \bar{I}_{l3}\}$ then since F is continuous on $\left[0, \frac{\Lambda_l}{\mu_l + d_l}\right]$,

$$\begin{aligned} F(0) &= (\mu_l + d_l)(R_0^{prop} - 1) > 0 \\ \text{and} \qquad F\left(\frac{\Lambda_l}{\mu_l + d_l}\right) &= -(\mu_l + d_l) < 0, \end{aligned}$$

by the Intermediate Value Theorem, there must be at least one positive root $I_l \in \left(0, \frac{\Lambda_l}{\mu_l + d_l}\right)$.

If $\bar{I}_{l2} = \min\{\bar{I}_{l1}, \bar{I}_{l2}, \bar{I}_{l3}\}$ or $\bar{I}_{l3} = \min\{\bar{I}_{l1}, \bar{I}_{l2}, \bar{I}_{l3}\}$ it can also be shown that F has at least one positive root in $I_l \in \left(0, \frac{\Lambda_l}{\mu_l + d_l}\right)$. Hence, the existence of an endemic equilibrium for System (3), has been established whenever $R_0^{prop} > 1$. □

5.2. **Two flock system under preferred mixing.** In the case of a two group model, under preferred mixing, we have

$$\begin{aligned} P_{ll} &= f_l + (1 - f_l)\frac{(1 - f_l)C_l N_l}{(1 - f_m)C_m N_m + (1 - f_l)C_l N_l}, \\ P_{lm} &= (1 - f_l)\frac{(1 - f_m)C_m N_m}{(1 - f_m)C_m N_m + (1 - f_l)C_l N_l}, \\ P_{ml} &= (1 - f_m)\frac{(1 - f_l)C_l N_l}{(1 - f_m)C_m N_m + (1 - f_l)C_l N_l}, \\ P_{mm} &= f_m + (1 - f_m)\frac{(1 - f_m)C_m N_m}{(1 - f_m)C_m N_m + (1 - f_l)C_l N_l}, \end{aligned}$$

Obviously, $P_{ll} + P_{lm} = 1$ and $P_{mm} + P_{ml} = 1$ hold.

5.2.1. *Basic Reproductive Number.* In this case the DFE is $(I_m, S_l, I_l) = \left(0, \frac{\Lambda_l}{\mu_l}, 0\right)$. The basic reproductive number R_0 for the SI model under preferred mixing is given by (see Appendix A for calculations)

$$\begin{aligned} R_0^{pref} &= \frac{1}{2}\left((1 - P_{ml}^0)\frac{\beta}{\mu_m} + (1 - P_{lm}^0)\frac{\beta}{\mu_l + d}\right) \\ &\quad + \frac{1}{2}\sqrt{\left((1 - P_{ml}^0)\frac{\beta}{\mu_m} - (1 - P_{lm}^0)\frac{\beta}{\mu_l + d}\right)^2 + 4\frac{\beta}{\mu_m}P_{ml}^0\frac{\beta}{\mu_l + d}P_{lm}^0}, \end{aligned}$$

where

$$\begin{aligned} P_{ml}^0 &= (1 - f_m)\frac{(1 - f_l)C_l\Lambda_l/\mu_l}{(1 - f_m)C_m\Lambda_m/\mu_m + (1 - f_l)C_l\Lambda_l/\mu_l} \qquad \text{and} \\ P_{lm}^0 &= (1 - f_l)\frac{(1 - f_m)C_m\Lambda_m/\mu_m}{(1 - f_m)C_m\Lambda_m/\mu_m + (1 - f_l)C_l\Lambda_l/\mu_l}. \end{aligned}$$

R_0 is a nonlinear function of the contributions to secondary infections by migratory and resident birds, R_0^m and R_0^l

$$\begin{aligned} R_0^{pref} &= \frac{1}{2}\left[(1-P_{ml}^0)R_0^m + (1-P_{lm}^0)R_0^l\right] \\ &\quad + \frac{1}{2}\sqrt{\left[(1-P_{ml}^0)R_0^m - (1-P_{lm}^0)R_0^l\right]^2 + 4R_0^m P_{ml}^0 R_0^l P_{lm}^0}. \end{aligned}$$

Typically, we expect that if $R_0 < 1$ the DFE is locally asymptotically stable while if $R_0 > 1$ the DFE is unstable. Our simulations support this assertion.

6. **Numerical results.** The results of numerical simulations illustrate and compare the outcomes associated with the two flock system under both mixing regimes. Since the mortality rate due to highly pathogenic avian influenza in poultry (resident birds) is very high, in Figure 1 we only vary the mortality rate due to disease for local birds, d_l. Although research efforts on avian influenza have increase in recent years, little is known about epidemiological parameters in birds and therefore in R_0 (Bouma et al. 2009). Hence, we choose values of the parameters that lead to values of R_0^{prop} and R_0^{pref} both greater than 1 and vary only the proportion of preferred contacts (f's). The rest of the parameters are fixed to $\beta_m = 0.3, \beta_l = 0.6, \mu_m = 0.1, \mu_l = 0.01, \Lambda_m = 100$ and $\Lambda_l = 50$. Therefore, the total population of migratory birds is $\Lambda_m/\mu_m = 1000$ and the total population of resident birds is $\Lambda_l/\mu_l = 5000$. The initial conditions for the epidemiological classes are $S_{l0} = 5000$, $I_{m0} = 20$ and $I_{l0} = 0$.

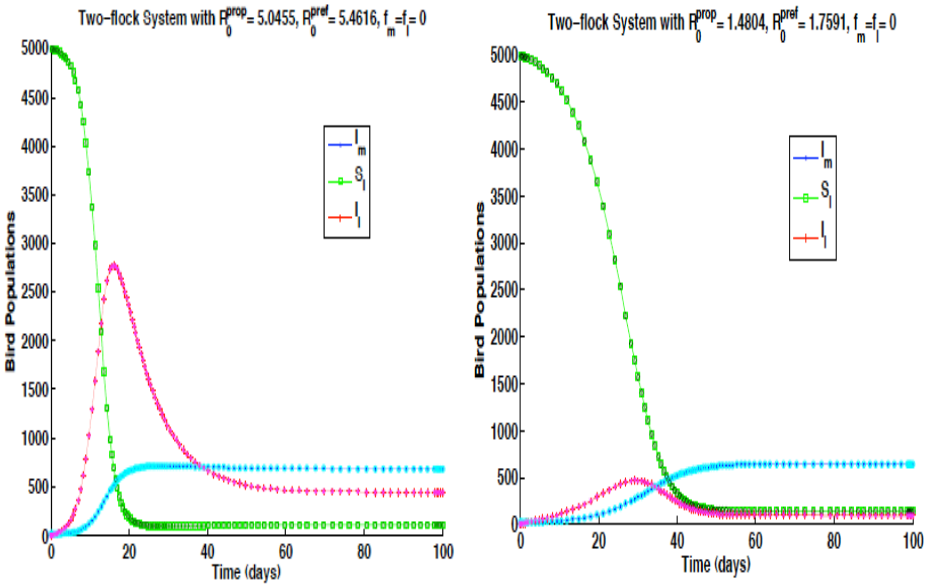

FIGURE 1. Solutions for the two-flock epidemic model under proportionate mixing. The difference between the two figures is the mortality rate due to disease, the figure on the left shows the solutions for $d_l = 0.1$ while the figure on the right shows solutions for $d_l = 0.5$.

If we assume that $d_l = 0.1$ the basic reproductive numbers for migratory and local birds are $R_0^m = 3$ and $R_0^l = 5.45$, respectively (with the parameter values provided above). In 2009 Bouma et al., estimated values of R_0 (e.g. our R_0^l) for H5N1 avian influenza in chickens using experimental transmission studies. The reproduction number for low-dose experiments in unvaccinated birds for fixed infectious periods was 3.4 (95% confidence interval (CI): 1.3-7.6). While Iglesias et al. (2010), estimated R_0 (e.g. our R_0^m) for HPAI in wild birds populations of Europe in 2005-2008, for nine clusters of outbreaks. In this case, the median value of this R_0 was between 1.1 and 3.4. Based on the transmission cycle and models of H5N1, Liu et al (2008) developed a deterministic model focusing on the interaction among poultry, wild birds and environment. Their simulations of R_0 as a function of the death rate of infected poultry (under a specific set of parameter values) lead to a value of the basic reproductive number of at least 3.3. Therefore, our suggested parameter values are indeed reasonable.

Figure 1 shows solutions of the two-flock (one local and one migratory) epidemic model for proportionate mixing. In both figures we vary the local birds disease-induced mortality, d_l. The figure on the left shows the case where $d_l = 0.1$ with $R_0^{prop} = 5.0455$ and $R_0^{pref} = 5.4616$ while the figure on the right shows the case where $d_l = 0.5$ with $R_0^{prop} = 1.4804$ and $R_0^{pref} = 1.7591$. If the disease-induced mortality is 0.5 then infected individuals die so fast that only a small window of time is available to infect others. Hence, when $d_l = 0.5$ we have a smaller (compare to the figure on the left) basic reproductive number and a lower number of infected cases. When $d_l = 0.1$ a larger number of infected cases are recorded and the epidemic takes over in less than 30 days (with a peak at 20 days). Since the average time that migratory birds spend with resident birds is small $\left(\frac{1}{\mu_m} = 10 \text{ days}\right)$ the migratory birds infected population basically remains constant (Bourouiba et al. (2010) estimated an average residence time of 7.58 days using data for bar-headed geese).

Solutions of the two-flock epidemic model under true preferred mixing when $f_m = f_l = 0.5$ or when $f_m = f_l = 0.9$ with $d_l = 0.1$ are presented in Figure 2. On the left, Figure 2 shows the case $f_m = f_l = 0.5$, that is, when half of the contact are reserve for mixing within your own type and the other half are used at random with all other groups. There is not qualitative difference between the left plot in Figure 2, and the left plot in Figure 1. We see a slightly shift on the solutions of local susceptible and infected birds and an increase on the R_0's under preferred mixing from $R_0^{pref} = 5.4616$ for the case $f_m = f_l = 0$ to $R_0^{pref} = 6.8332$ when $f_m = f_l = 0.5$. The figure on the right shows plots for the case $f_m = f_l = 0.9$. In this last case, higher infected levels (higher peak) are seen under preferred mixing. However, there is a significant change in the values of R_0 under preferred mixing when compare to proportionate mixing. When $f_m = f_l = 0.9$, $R_0^{prop} = 5.0455$ but $R_0^{pref} = 8.1164$. Preferred mixing provides a worse epidemic among resident birds. Again, the population of migratory infected birds remains nearly constant.

Figure 3 on the left shows the solutions of the two-flock epidemic model for $f_m = f_l = 0.999$ with disease induced mortality $d_l = 0.1$. Even though in this case most contacts are only within your own type, we see that slight random mixing can still trigger an epidemic. The figure on the right show solutions where $f_m = f_l \approx 1$, that is under complete preferred mixing. In this last case a higher number of local infected birds are reported, $I_l = 4202$. Therefore, contacts under preferred mixing

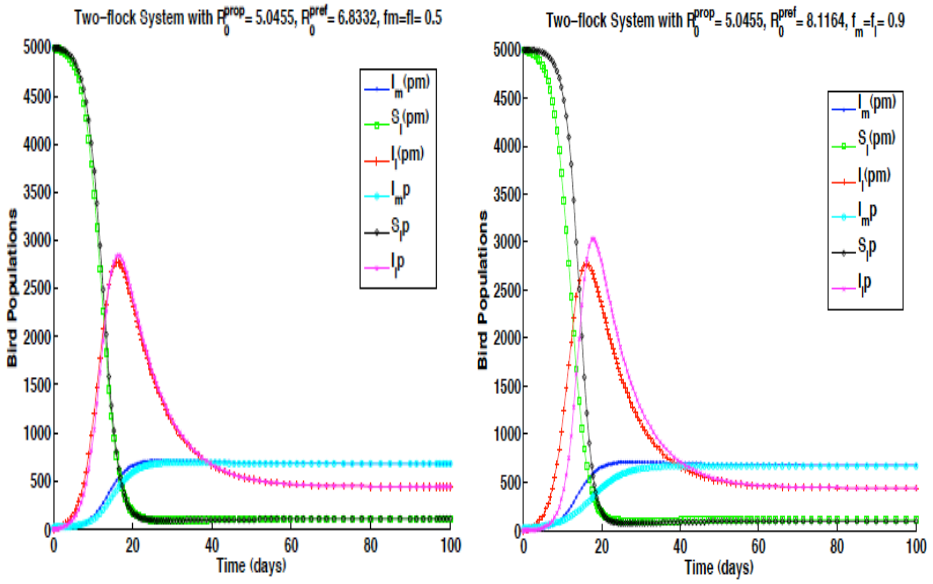

FIGURE 2. Solutions for the two-flock epidemic model for both proportionate and preferred mixing. The figure on the left shows solutions for $f_m = f_l = 0.5$ while the figure on the right show solutions for $f_m = f_l = 0.9$. As the proportion of contact with your own type increases the number of infected increases as well.

$f_l = f_r$	R_0^{prop}	R_0^{pref}
0	5.0455	5.4616
0.5	5.0455	6.8332
0.9	5.0455	8.1164
0.999	5.0455	8.4511
≈ 1	5.0455	8.4545

TABLE 2. R_0^{prop} and R_0^{pref} for different values of preferred contacts, f_r.

generate worse outbreaks in infected domestic birds. However, the epidemic takes longer (days) before it becomes established in resident bird populations. Therefore, in this situation, it may be possible to put in place control measures in time to prevent further damage. Table 2 summarizes the values found for R_0 for different values of the proportion of preferred contacts, f_r with parameters: $d_l = 0.1, \beta_m = 0.3, \beta_l = 0.6, \mu_m = 0.1, \mu_l = 0.01, \Lambda_m = 100$ and $\Lambda_l = 50$.

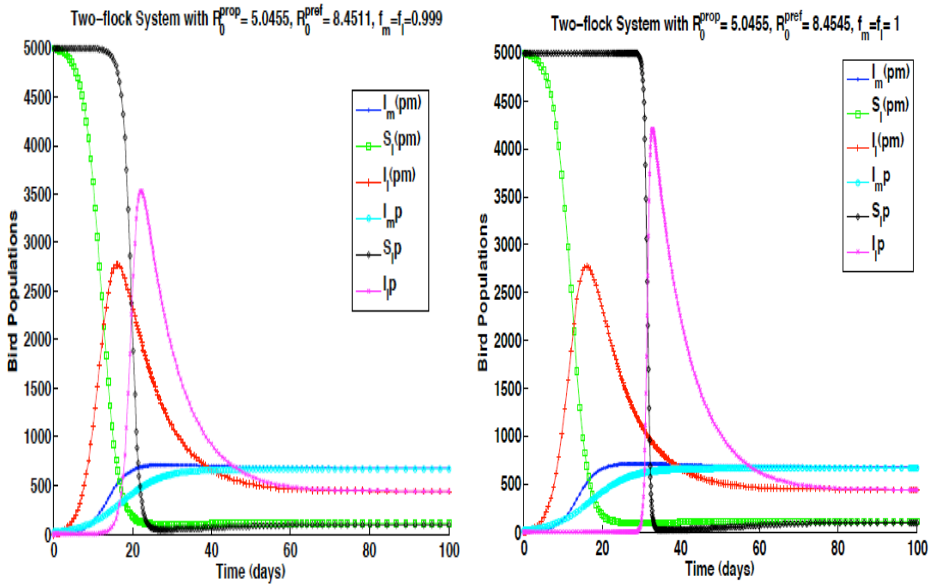

FIGURE 3. Solutions for the two-flock epidemic model for both proportionate and preferred mixing. The figure on the left shows solutions for $f_m = f_l = 0.999$. The figure on the right show solutions completely preferred mixing for $f_m = f_l \approx 1$. In this case higher reported cases are shown with 4202 local infected birds.

Figure 4 shows R_0^{prop} and R_0^{pref} as a function of the R_0's of migratory birds and resident birds, that is, R_0^m and R_0^l respectively. All other parameters are fixed to $\beta_m = \beta_l = 0.4, \mu_l = 0.01, d_l = 0.1, \Lambda_m = 7.5, \Lambda_l = 50$ and $f_m = f_l = 0.999$. For proportionate mixing Figure (4) on the left shows that for small values of R_0^m, as R_0^l increases, R_0^{prop} also increases. For the case of preferred mixing the figure on the right also shows that if $R_0^l > 1$, there is always an epidemic outbreak among local and migratory birds even when $R_0^m < 1$, that is, $R_0^{pref} > 1$. Thus, an epidemic among domestic birds is sufficient to maintain the epidemic among all bird populations, that is, under preferred mixing. Therefore, R_0^{pref} can be larger when R_0^m and R_l vary, thus preferred mixing indeed will generate higher disease levels than just proportionate mixing. This is particularly interesting because it shows that one could reduced influenza prevalence among migratory birds if the main host were indeed to be the population of resident birds.

7. **Dynamics analysis for a three flock system.** A three flock system that includes one resident and two migratory bird populations under proportionate mixing is considered under the assumption that disease induced mortality for migratory birds is negligible ($d_m \equiv 0$), that all populations are equally susceptible to infections ($\beta_l = \beta_{m_1} = \beta_{m_2} = \beta$), and that departure rates for migratory birds are the same

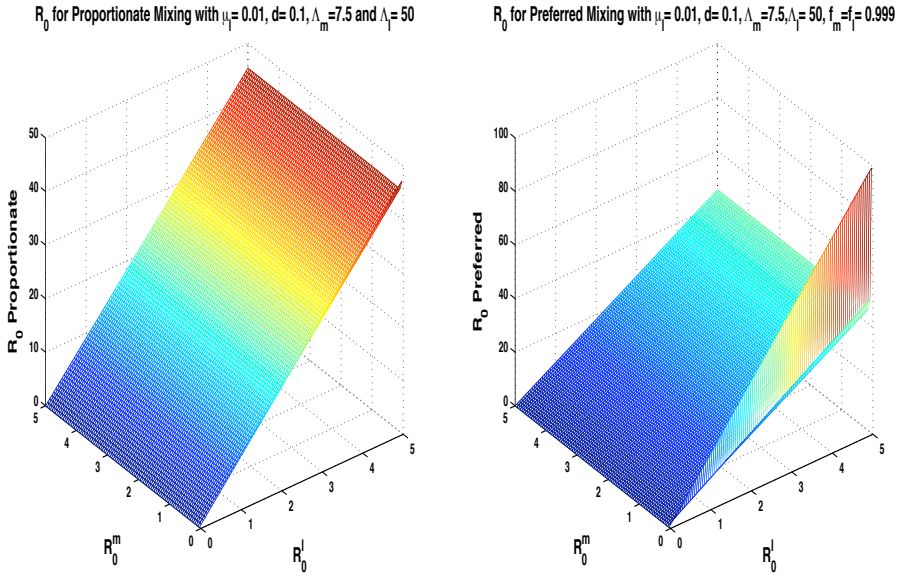

FIGURE 4. The graphs shows R_0^{prop} and R_0^{pref} as a function of $\beta = \beta_m = \beta_l$ and μ_m.

($\mu_{m_1} = \mu_{m_2} = \mu$), System (1-2) becomes

$$\frac{dS_l}{dt} = \Lambda_l - \beta S_l \sum_{z=\{l,m_1,m_2\}} P_{lz}\frac{I_z}{N_z} - \mu_l S_l, \tag{7a}$$

$$\frac{dI_l}{dt} = \beta S_l \sum_{z=\{l,m_1,m_2\}} P_{lz}\frac{I_z}{N_z} - (\mu_l + d_l) I_l, \tag{7b}$$

$$\frac{dS_{m_1}}{dt} = \Lambda_{m_1} - \beta S_{m_1} \sum_{z=\{l,m_1,m_2\}} P_{m_1 z}\frac{I_z}{N_z} - \mu S_{m_1}, \tag{7c}$$

$$\frac{dI_{m_1}}{dt} = \beta S_{m_1} \sum_{z=\{l,m_1,m_2\}} P_{m_1 z}\frac{I_z}{N_z} - \mu I_{m_1}, \tag{7d}$$

$$\frac{dS_{m_2}}{dt} = \Lambda_{m_2} - \beta S_{m_2} \sum_{z=\{l,m_1,m_2\}} P_{m_2 z}\frac{I_z}{N_z} - \mu S_{m_2}, \tag{7e}$$

$$\frac{dI_{m_2}}{dt} = \beta S_{m_2} \sum_{z=\{l,m_1,m_2\}} P_{m_2 z}\frac{I_z}{N_z} - \mu I_{m_2}, \tag{7f}$$

where

$$P_{rz} = \frac{C_z N_z}{\sum_{z=1}^{s+k} C_z N_z} \tag{8}$$

with $r \in \{l, m_1, m_2\}$.

The time evolution of the migratory (transient populations) epidemiological bird classes $S_{m_1}, S_{m_2}, I_{m_1}$ and I_{m_2} are much faster than those of the resident bird populations S_l and I_l. Migratory birds by assumption spend short periods of time at

different locations (along migration routes) as opposed to resident birds. Using singular perturbation theory, it is shown with the help of a Dulac function, that when $R_0^3 \leq 1$, the DFE is globally asymptotically stable, where R_0^3 is the basic reproductive number for the three flock system that is given by (17). It is also shown that the endemic equilibria is globally asymptotically stable when $R_0^3 > 1$.

7.1. **Re-scaling the model equations.** Time is re-scaled by letting $\tau = \left(\frac{\beta\mu}{\beta+\mu}\right) t$. The state variables are re-scaled by $\frac{1}{\Theta_i}$, where $\Theta_i = \frac{\Lambda_i}{\mu_i}$ is the total asymptotic population size for migratory birds ($i \in \{l, m_1, m_2\} = \{1, 2, 3\}$). The re-scaled non-dimensional variables are: $x_i = \frac{1}{\Theta_i} S_i$ and $y_i = \frac{1}{\Theta_i} I_i$. The re-scaled model equations for System (7) with Expression (8) can be written as

$$\begin{aligned}
\frac{dx_1}{d\tau} &= \alpha(1-x_1) - \frac{\eta x_1}{\Omega_1(x_1+y_1)+1}(y_1 + k_2 y_2 + k_3 y_3), && \text{(9a)}\\
\frac{dy_1}{d\tau} &= \frac{\eta x_1}{\Omega_1(x_1+y_1)+1}(y_1 + k_2 y_2 + k_3 y_3) - \gamma y_1, && \text{(9b)}\\
\epsilon\ \frac{dx_2}{d\tau} &= m(1-x_2) - \frac{\Omega_1 x_2}{\Omega_1(x_1+y_1)+1}(y_1 + k_2 y_2 + k_3 y_3), && \text{(9c)}\\
\epsilon\ \frac{dy_2}{d\tau} &= \frac{\Omega_1 x_2}{\Omega_1(x_1+y_1)+1}(y_1 + k_2 y_2 + k_3 y_3) - m y_2, && \text{(9d)}\\
\epsilon\ \frac{dx_3}{d\tau} &= m(1-x_3) - \frac{\Omega_1 x_3}{\Omega_1(x_1+y_1)+1}(y_1 + k_2 y_2 + k_3 y_3), && \text{(9e)}\\
\epsilon\ \frac{dy_3}{d\tau} &= \frac{\Omega_1 x_3}{\Omega_1(x_1+y_1)+1}(y_1 + k_2 y_2 + k_3 y_3) - m y_3, && \text{(9f)}
\end{aligned}$$

where

$$\epsilon = \frac{\mu}{\beta+\mu}, \quad \alpha = \mu_1\left(\frac{\beta+\mu}{\beta\mu}\right), \quad m = \frac{\mu}{\beta}, \quad \Omega_i = \frac{C_i\Theta_i}{C_2\Theta_2 + C_3\Theta_3}, \quad k_i = \frac{\Omega_i}{\Omega_1},$$

$$\eta = \Omega_1\left(\frac{\beta+\mu}{\mu}\right) \quad \text{and} \quad \gamma = (\mu_1 + d_1)\left(\frac{\beta+\mu}{\beta\mu}\right).$$

The terms in the right hand side of System (9) all have the same order of magnitude whenever $\epsilon = \mu/(\beta+\mu) << 1$ which is the case since $\mu << \beta$. Therefore, x_2, y_2, x_3 and y_3 are fast variables and x_1 and y_1 are slow variables. In addition, since the total populations of migratory birds are constant we can reduce the fast variables to two by letting $x_2 = 1 - y_2$ and $x_3 = 1 - y_3$ in the y_2 and y_3 equations. Hence, System (9) is reduced from six to four equations (two fast variables and two slow variables), that is,

$$\begin{aligned}
\frac{dx_1}{d\tau} &= \alpha(1-x_1) - \frac{\eta x_1}{\Omega_1(x_1+y_1)+1}(y_1 + k_2 y_2 + k_3 y_3), && \text{(10a)}\\
\frac{dy_1}{d\tau} &= \frac{\eta x_1}{\Omega_1(x_1+y_1)+1}(y_1 + k_2 y_2 + k_3 y_3) - \gamma y_1, && \text{(10b)}\\
\epsilon\ \frac{dy_2}{d\tau} &= \frac{\Omega_1(1-y_2)}{\Omega_1(x_1+y_1)+1}(y_1 + k_2 y_2 + k_3 y_3) - m y_2, && \text{(10c)}\\
\epsilon\ \frac{dy_3}{d\tau} &= \frac{\Omega_1(1-y_3)}{\Omega_1(x_1+y_1)+1}(y_1 + k_2 y_2 + k_3 y_3) - m y_3. && \text{(10d)}
\end{aligned}$$

7.2. **Dynamics on the slow manifold.** We solve for the quasi-steady states y_2 and y_3 in terms of x_1 and y_1 from

$$\frac{\Omega_1(1-y_2)}{\Omega_1(x_1+y_1)+1}(y_1+k_2y_2+k_3y_3)-my_2 = 0, \tag{11}$$

$$\frac{\Omega_1(1-y_3)}{\Omega_1(x_1+y_1)+1}(y_1+k_2y_2+k_3y_3)-my_3 = 0. \tag{12}$$

Letting $z=k_2y_2+k_3y_3$ and adding k_2 times Eq. (11) with k_3 times Eq. (12) yields

$$z^2+Bz-C=0, \tag{13}$$

where

$$B=y_1+m\left((x_1+y_1)+\frac{1}{\Omega_1}\right)-\frac{1}{\Omega_1} \quad \text{and} \quad C=\frac{y_1}{\Omega_1}.$$

Eq. (13) has only one positive solution given by

$$z(x_1,y_1)=\frac{-B+\sqrt{B^2+4C}}{2}.$$

Therefore, the quasi-steady states y_2 and y_3 in term of x_1 and y_1 are given by

$$y_2=y_3=\frac{\Omega_1(y_1+z(x_1,y_1))}{\Omega_1(y_1+z(x_1,y_1))+m(\Omega_1(x_1+y_1)+1)}. \tag{14}$$

Therefore, substitution of Eq. (14) into System (10) gives the reduced system

$$\frac{dx_1}{d\tau} = \alpha(1-x_1)-\frac{\eta x_1}{\Omega_1(x_1+y_1)+1}(y_1+z(x_1,y_1)), \tag{15a}$$

$$\frac{dy_1}{d\tau} = \frac{\eta x_1}{\Omega_1(x_1+y_1)+1}(y_1+z(x_1,y_1))-\gamma y_1. \tag{15b}$$

If (x_1,y_1) is an equilibrium for System (15) then $y_1=U(1-x_1)$, where $U=\mu_1/(\mu_1+d_1)$. Hence, x_1 is given by

$$\frac{\eta x_1}{\Omega_1(x_1+U(1-x_1))+1}(U(1-x_1)+z)-\alpha(1-x_1)=0. \tag{16}$$

The stability of the DFE $(x_1^0,y_1^0)=(1,0)$ can be easily established by the eigenvalues of the Jacobian matrix of System (15) around the DFE. This matrix has two eigenvalues, $\lambda_1=-\alpha<0$ and $\lambda_2=\frac{\eta}{1+\Omega_1}\left(1+\frac{1}{m(\Omega_1+1)-1}\right)-\gamma$. Therefore we conclude that, $\lambda_2<0$ whenever

$$R_0^3=\frac{C_1\Theta_1}{\sum_{i=1}^3 C_i\Theta_i}\left(\frac{\beta}{\mu_l+d_l}\right)+\frac{C_2\Theta_2}{\sum_{i=1}^3 C_i\Theta_i}\left(\frac{\beta}{\mu}\right)+\frac{C_3\Theta_3}{\sum_{i=1}^3 C_i\Theta_i}\left(\frac{\beta}{\mu}\right)<1. \tag{17}$$

To show the existence of endemic equilibria, dividing Eq. (16) by $1-x_1$ we obtain

$$0=\frac{\eta x_1}{\Omega_1(x_1+U(1-x_1))+1}\left(U+\frac{z}{1-x_1}\right)-\alpha.$$

Thus, we define

$$Q(x_1)=\frac{\eta x_1}{\Omega_1(x_1+U(1-x_1))+1}\left(U+\frac{z}{1-x_1}\right)-\alpha.$$

Observe that $Q(0)=-\alpha<0$, and that

$$Q(1)=\lim_{x_1\to 1}\left[\frac{\eta}{1+\Omega_1}\left(U+\frac{z}{1-x_1}\right)-\alpha\right].$$

Since $\lim_{x_1\to 1} C = 0$ and $\lim_{x_1\to 1} B = m\left(1+\frac{1}{\Omega_1}\right) - \frac{1}{\Omega_1}$ then

$$\lim_{x_1\to 1}\left(\frac{z}{1-x_1}\right) = \lim_{x_1\to 1}\left(-\frac{C'}{B}\right) = \frac{U}{m(1+\Omega_1)-1},$$

and

$$Q(1) = \frac{\eta U m}{m(1+\Omega_1)-1} - \alpha = R_0^3 - 1.$$

where R_0^3 is given in Eq. (17). Thus, $Q(1) > 0$ if $R_0^3 > 1$. The Intermediate Value Theorem guaranties the existence of at least one endemic equilibria. To show uniqueness, we consider an equivalent system of System (15) by introducing $K = x_1 + y_1$,

$$\frac{dK}{dt} = \alpha(1-K) + (\alpha-\gamma)y_1 \triangleq f(K, y_1), \tag{18a}$$

$$\frac{dy_1}{dt} = \frac{\eta(K-y_1)}{\Omega_1 K + 1}(y_1 + z(K, y_1)) - \gamma y_1 \triangleq g(K, y_1). \tag{18b}$$

Thus the system will be studied in the region $0 \le y_1 \le K \le 1$. To solve for the equilibria of the equivalent system we set both equations in System (18) equal to zero. $f(K, y_1) = 0$ provides $K = 1 + y_1 - (\gamma/\alpha)y_1$ and substitution of this expression into $g(K, y_1) = 0$ gives:

$$y_1\left[\frac{\eta(K-y_1)}{\Omega_1 K + 1}(1 + z(K, y_1)) - \gamma\right] = 0.$$

The non-zero equilibrium is given by

$$G(y_1) \triangleq \left[\frac{\eta(1-\frac{\gamma}{\alpha}y_1)}{\Omega_1(1+y_1-\frac{\gamma}{\alpha}y_1)+1}(1+z(y_1)) - \gamma\right] = 0$$

thus,

$$\begin{aligned} G'(y_1) &= -\left(\frac{\eta\Omega_1(1-(\gamma/\alpha)y_1)}{[\Omega_1(1+y_1-(\gamma/\alpha)y_1+1]^2}\right)(1+z(y_1)) \\ &\quad -\frac{\eta(1-(\gamma/\alpha)y_1)}{\Omega_1(1+y_1-(\gamma/\alpha)y_1)+1}\left[\frac{2}{\Omega_1}\left(\frac{1+(B+2/\Omega_1)(B^2+4C)^{-1/2}}{(B+\sqrt{B^2+C})^2}\right)\right] \\ &< 0, \end{aligned}$$

where $B(y_1) = y_1 + m(1 + y_1 - (\gamma/\alpha)y_1 + 1/\Omega_1) - 1/\Omega_1$, $C(y_1) = y_1/\Omega_1$. If $1 - (\gamma/\alpha)y_1 < 0$, then $K - y_1 = 1 - (\gamma/\alpha)y_1 < 0$, then $K < y_1$ which is impossible because $K = x_1 + y_1 > y_1$. Therefore, since $G(y_1)$ is monotone there exist only one endemic equilibria of System (18). Hence, we have a established the following result:

Theorem 7.1. *If $R_0^3 > 1$ there exist a unique equilibrium (x_1^*, y_1^*) of System (15). In addition, if $R_0^3 < 1$ the equilibrium $(x_1^0, y_1^0) = (1, 0)$ of System (15) is globally asymptotically stable while if $R_0^3 > 1$ the unique endemic equilibria is (x_1^*, y_1^*) is globally asymptotically stable.*

Proof. The arguments above has shown existence of the unique endemic equilibrium and the local stability of the DFE. To show global stability, a Dulac function is used to rule out the existence of closed orbit:

$$V(K, y_1) = \frac{1}{y_1}$$

defined inside the first quadrant. The divergence is

$$\begin{aligned}
&\frac{\partial}{\partial K}\left(\frac{f(K,y_1)}{y_1}\right)+\frac{\partial}{\partial y_1}\left(\frac{g(K,y_1)}{y_1}\right)\\
=\;& -\frac{\eta}{\Omega_1 K+1}\left[\left(1+\frac{z}{y_1}\right)+(K-y_1)\left(\frac{2}{\Omega_1\sqrt{B^2+4C}}\right)\left(\frac{1+B+\frac{2}{\Omega_1}}{(B+\sqrt{B^2+4C})^2}\right)\right]\\
&-\frac{\alpha}{y_1}-\gamma<0.
\end{aligned}$$

Therefore, there are no closed orbits for System (18). Since $R_0^3 > 1$, $(1,0)$ is a saddle point and its stable manifolds are on $y_1 = 0$. Hence, since there are no limit cycles by the Poincaré-Bendixson Theorem, the DFE $(x_1^0, y_1^0) = (1,0)$ is globally asymptotically stable if $R_0^3 < 1$ and the endemic equilibrium is globally asymptotically stable if $R_0^3 > 1$. □

8. **Dynamics of the full system.** Using the approach in Song et al. (2002) and Hoppensteadt (1974) it can be shown that when $R_0^3 < 1$ the DFE of the full system (7) is globally asymptotically stable and when $R_0^3 > 1$ the endemic equilibria of the full system is globally asymptotically stable provided that ϵ is small. Here, we only use numerical simulations to illustrate this result. Figure 5 provides solutions for the approximation of the full model, Model (7) and those obtained under our quasi-steady state approximation provided by Equations (14) when slow variables evolve according to the reduced system, System (18). Solutions for the fast variables I_{m1} and I_{m2} are provided when $\epsilon = \frac{\mu}{\beta+\mu}$ varies. All parameters except for β were fixed: $\mu_l = 0.01, d_l = 0.1, \Lambda_l = 50, \Lambda_{m1} = 60, \Lambda_{m2} = 100, C_l = 30, C_{m1} = 10$ and $C_{m2} = 15$. Therefore, the total population of resident birds is $\Lambda_l/\mu_l = 5000$, of migratory birds of flock m_1 is $\Lambda_{m_1}/\mu_{m1} = 600$ and the total population of migratory bird of flock m_2 is $\Lambda_{m2}/\mu_{m2} = 1000$. The initial conditions for the reduced system, System (15) are set to $x_1 = 0.975$ and $y_1 = 0.02$ while the initial conditions for the epidemiological classes of the full system (7) are set to $S_l^0 = 4875$, $I_l^0 = 100$, $I_{m1}^0 = 341$ and $I_{m2}^0 = 568$. Values for β are set to 0.4, 0.8 and 1.5 and the corresponding ϵ values of are 0.2, 0.111 and 0.0625. Figure 5 shows that the smaller the value of ϵ the better the approximation to the full model by the reduced model.

9. **Discussion.** Our metapopulation model can be modified to incorporate the seasonality of avian influenza, for instance, by letting the β's be periodic functions of time. If we choose one patch (local bird) for wintering and the other patch for breeding, then the seasonality of migration can also be studied in addition to the study of the interactions of residence and migratory birds. Without distinguishing residence and migratory birds, recent contributions of Gourley et al. (2010) emphasized spatiotemporal distributions of migratory birds. Except for the wintering and breeding grounds, Gourley et al. considered multiple stopovers for the migratory birds on their flyway.

In this paper, a general metapopulation framework is introduced for the study of the dynamics of epidemics that result from weak or strong interactions between migratory and resident birds. The analysis is, in fact, carried out in the case of two and three interacting flocks of birds. Specifically, we focus on the epidemics driven by the interactions of one or two migratory bird flocks (short residence-times) and one resident populations of birds, under two forms of mixing. We observe that the

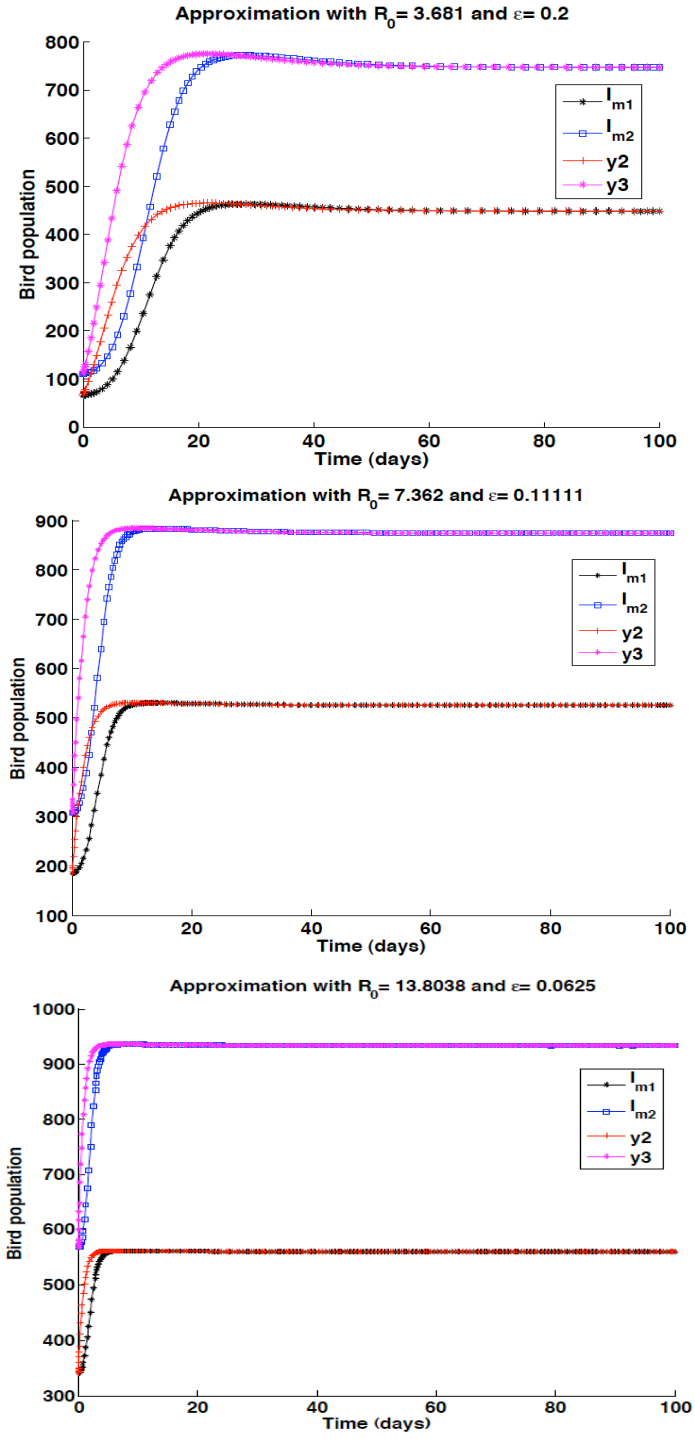

FIGURE 5. The full model (7) is compared with the reduced model (15) for three different values of ϵ. The smaller the value of ϵ the better the approximation.

mixing regime not only impacts the value of the basic reproductive number (as expected) but also the duration of the epidemic. We also explore the case when disease (HPAI avian influenza) seriously impact the ability of local populations to survive. That is, we study the impact of high-mortality rates in local populations under two mixing regimes. It is observed that preferred mixing triggers a stronger epidemic (larger R_0 and higher number of infected resident birds) although it takes a longer period of time to be established in the resident bird population. Thus, control measures may be achieved in a timely manner under preferred mixing. The reduction of the avian flu epidemic may be achieved by effectively controlling the interactions between migratory and resident bird populations along migration routes. Persistence of H5N1 in poultry populations poses risks for human health. One of this risks comes from infections acquired directly from poultry, resulting in *severe* disease. Other risks come from the likelihood that the virus would change to a highly infection human form that could spread easily from person to person. Therefore, as concluded by Normile (2006) and Cheng et al (2006), the cycle of transmission between all of these populations should be broken if the virus is to be eradicated from poultry flocks.

Appendix A. **Next generator operator.** In 1990 Dieckmann et al. defined R_0 as the spectral radius of the next generator matrix. R_0 is typically found by calculating the eigenvalues of the Jacobian matrix at the DFE equilibrium, where the largest positive eigenvalue is R_0 (Castillo-Chavez et al. 2002). Here, the general idea of the next generator approach is explained following the work of van den Driessche and Watmough (2002).

The total population is divided in compartments according to their epidemiological status, that is, susceptible, exposed, infected, recovered and treated among others such that $x = (x_1, x_2, x_3, ...x_n)^t$ where $x_i \geq 0$ represent the number of individuals in each compartment. These compartments are further divided, $\mathcal{M}_i(x)$ corresponds to the rate of appearance of new infections into each compartment whereas $\mathcal{D}_i(x)^+$ is the transfer of individuals into each compartment by all other means and $\mathcal{D}_i(x)^-$ is the transfer of individuals out of each compartment. Therefore, disease transmission model correspond to the following system of equations:

$$\dot{x_i} = f(x_i) = \mathcal{M}_i(x) - \mathcal{D}_i(x), \qquad i = 1, ..., n \tag{19}$$

where $\mathcal{D}_i(x) = \mathcal{D}_i^+(x) - \mathcal{D}_i^-(x)$. Thus, if x_0 is the DFE of System (19) with Jacobian matrices

$$M = \left[\frac{\partial \mathcal{M}_i}{\partial x_j}(x_0)\right] \quad \text{and} \quad D = \left[\frac{\partial \mathcal{D}_i}{\partial x_j}(x_0)\right] \qquad \text{with} \qquad 1 \leq i, j \leq m$$

then

$$R_0 = \rho(MD^{-1})$$

where $\rho(A)$ denotes the spectral radius of A.

A.1. R_0 **for the case of proportionate mixing.** To obtain the R_0 of the two-flock epidemic model with proportionate mixing we let the vector of new infections be:

$$\mathcal{M} = \begin{bmatrix} \beta(N_m - I_m)\left(\frac{I_m + I_l}{N_m + N_l}\right) \\ 0 \\ \beta S_l \left(\frac{I_m + I_l}{N_m + N_l}\right) \end{bmatrix}$$

whereas

$$\mathcal{D} = \begin{bmatrix} \mu_m I_m \\ -\Lambda_l + \beta S_l (N_m - I_m)\left(\frac{I_m + I_l}{N_m + N_l}\right) + \mu_l S_l \\ (\mu_l + d) I_l \end{bmatrix}.$$

Thus, after computing the Jacobian matrices of $\mathcal{M}$ and $\mathcal{D}$, evaluating them at the DFE $x_0 = \left(0, \frac{\Lambda_l}{\mu_l}, 0\right)$, and doing some simplifications we obtain

$$M = \begin{bmatrix} \beta T_m & \beta T_m \\ \beta T_l & \beta T_l \end{bmatrix} \quad \text{and} \quad D = \begin{bmatrix} \mu_m & 0 \\ 0 & \mu_l + d \end{bmatrix},$$

where

$$\begin{aligned} T_m &= \frac{C_m \Lambda_m / \mu_m}{C_m \Lambda_m / \mu_m + C_l \Lambda_l / \mu_l} \qquad \text{and} \\ T_l &= \frac{C_l \Lambda_l / \mu_l}{C_m \Lambda_m / \mu_m + C_l \Lambda_l / \mu_l}. \end{aligned}$$

Therefore,

$$MD^{-1} = \begin{bmatrix} \frac{\beta T_m}{\mu_m} & \frac{\beta T_m}{\mu_l + d} \\ \frac{\beta T_l}{\mu_m} & \frac{\beta T_l}{\mu_l + d} \end{bmatrix}$$

and the basic reproductive number is

$$R_0^{prop} = \rho(MD^{-1}) = T_m \frac{\beta}{\mu_m} + T_l \frac{\beta}{\mu_l + d}.$$

A.2. R_0 **for the case of preferred mixing.** For the case of preferred mixing, the vector of new infections is:

$$\mathcal{M} = \begin{bmatrix} \beta(N_m - I_m)\left((1 - P_{ml})\frac{I_l}{N_l} + P_{ml}\frac{I_m}{N_m}\right) \\ 0 \\ \beta S_l \left((1 - P_{lm})\frac{I_l}{N_l} + P_{lm}\frac{I_m}{N_m}\right) \end{bmatrix}$$

whereas

$$\mathcal{D} = \begin{bmatrix} \mu_m I_m \\ -\Lambda_l + \beta S_l \left((1 - P_{lm})\frac{I_l}{N_l} + P_{lm}\frac{I_m}{N_m}\right) + \mu_l S_l \\ (\mu_l + d) I_l \end{bmatrix}.$$

Thus, after obtaining the Jacobian matrices of $\mathcal{M}$ and $\mathcal{D}$ evaluating them at the DFE $x_0 = \left(0, \frac{\Lambda_l}{\mu_l}, 0\right)$ and doing some simplifications, we obtain

$$M = \begin{bmatrix} \beta(1 - P^0_{ml}) & \beta P^0_{lm} \\ \beta P^0_{ml} & \beta(1 - P^0_{lm}) \end{bmatrix} \quad \text{and} \quad D = \begin{bmatrix} \mu_m & 0 \\ 0 & \mu_l + d \end{bmatrix},$$

where

$$\begin{aligned} P^0_{ml} &= (1 - f_m)\frac{(1 - f_l) C_l \Lambda_l / \mu_l}{(1 - f_m) C_m \Lambda_m / \mu_m + (1 - f_l) C_l \Lambda_l / \mu_l} \qquad \text{and} \\ P^0_{lm} &= (1 - f_l)\frac{(1 - f_m) C_m \Lambda_m / \mu_m}{(1 - f_m) C_m \Lambda_m / \mu_m + (1 - f_l) C_l \Lambda_l / \mu_l}. \end{aligned}$$

Therefore,

$$MD^{-1} = \begin{bmatrix} \frac{\beta}{\mu_m}(1-P^0_{ml}) & \frac{\beta}{\mu_l+d}P^0_{lm} \\ \frac{\beta}{\mu_m}P^0_{ml} & \frac{\beta}{\mu_l+d}(1-P^0_{lm}) \end{bmatrix}$$

and the basic reproductive number is $R_0^{pref} = \rho(MD^{-1})$, where

$$\begin{aligned} R_0^{pref} &= \frac{1}{2}\left((1-P^0_{ml})\frac{\beta}{\mu_m} + (1-P^0_{lm})\frac{\beta}{\mu_l+d}\right) \\ &\quad + \frac{1}{2}\sqrt{\left((1-P^0_{ml})\frac{\beta}{\mu_m} - (1-P^0_{lm})\frac{\beta}{\mu_l+d}\right)^2 + 4\frac{\beta}{\mu_m}P^0_{ml}\frac{\beta}{\mu_l+d}P^0_{lm}}. \end{aligned}$$

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