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AVIAN INFLUENZA DYNAMICS IN WILD BIRDS WITH BIRD MOBILITY AND SPATIAL HETEROGENEOUS ENVIRONMENT

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Abstract. In this paper, we propose a mathematical model to describe the avian influenza dynamics in wild birds with bird mobility and heterogeneous environment incorporated. In addition to establishing the basic properties of solutions to the model, we also prove the threshold dynamics which can be expressed either by the basic reproductive number or by the principal eigenvalue of the linearization at the disease free equilibrium. When the environment factor in the model becomes a constant (homogeneous environment), we are able to find explicit formulas for the basic reproductive number and the principal eigenvalue. We also perform numerical simulation to explore the impact of the heterogeneous environment on the disease dynamics. Our analytical and numerical results reveal that the avian influenza dynamics in wild birds is highly affected by both bird mobility and environmental heterogeneity.

1. **Introduction.** Aquatic birds such as *Anseriformes* (ducks, geese and swans) and *Charadriiformes* (gulls, terns and waders) are the major reservoir of all influenza A viruses, including the highly pathogenic H5N1 AI virus transmitted to humans [9, 17, 22, 36]. Understanding of the ecology of avian influenza (AI) virus and its dynamics in wild birds is useful in predicting influenza dynamics in human population and devising control strategies.

In the context of AI dynamics in wild birds, in addition to transmission of AI from bird to bird, another highly efficient route of transmission is through the excretion of AI virus by infected birds, followed by ingestion of virus in the drinking water of uninfected birds [4, 12, 13, 37]. Laboratory experiments have shown that the persistence of AI virus in water depends on environmental factors such as temperature, pH and salinity [4, 5, 6, 28, 37]. Numerous mathematical modeling studies have already highlighted the importance of such environmental factors in AI dynamics among wild birds [3, 10, 23, 24, 29, 32]. In particular, [32] has shown that even small differences in the environmental condition between two locations (for example, differences in temperature of less than 8^oC) can produce significantly different AI dynamics. In addition, mobility is a common strategy for birds to occupy seasonal habitats [2]. Because of their mobility, birds come across various environmental conditions. Therefore, it is quite obvious to raise the question of how such spatial heterogeneity affects AI dynamics in mobile aquatic wild birds.

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In this study, we propose a dynamic model for the transmission of AI among wild birds that incorporates both mobility of the birds and spatial heterogeneity in the environmental condition. We introduce into the model a spatial diffusion of the bird population and use the experimentally-determined dependence of virus persistence in water upon temperature, pH and salinity. We focus on how spatial diffusion and environmental heterogeneity affect the basic reproductive number and threshold dynamics of the system.

One of the main technical difficulties in our analysis is the lack of compactness of solution maps of the model system (see also [15]). This is because one of the equations, which describes the dynamics of virus particles in water, loses its diffusion term as the diffusion of virus particles is negligible compared to the birds' mobility. To overcome this difficulty, we first prove that the solution maps associated with a *linearized* system around the disease-free equilibrium are κ-condensing, where κ is the Kuratowski measure of non-compactness (see, e.g., [7]). By a generalized Krein-Rutman Theorem, we can show that the principal eigenvalue of the associated eigenvalue problems exists. Next, we prove the solution maps associated with our *model system* are κ-contracting. Thus, we conclude that the solution maps admit a connected global attractor by appealing to some existing results in [21].

The basic reproductive number for an infectious disease, conventionally denoted by $\mathcal{R}_0$, is an important index in epidemiology which predicts whether an infectious disease will die out or persist in the host population. For models given by infinite dimensional systems, such as our model system with spatial structure, identifying $\mathcal{R}_0$ is usually not trivial. For our model, by making use of the abstract results on this topic in [31], we are able to find the so called next generation operator $\mathbf{L}$, and thereby, identify $\mathcal{R}_0$ as the spectral radius of $\mathbf{L}$. We show that $\mathcal{R}_0$ plays a threshold role in the sense that when $\mathcal{R}_0 < 1$, the disease dies out from the birds population while when $\mathcal{R}_0 > 1$, the disease remains persistent. We also carry out model simulations to observe how AI dynamics vary with diffusion rate and spatial heterogeneity of the environmental conditions.

The rest of the paper is organized as follows. The model is formulated in Section 2. The model analysis and simulation results are presented in Sections 3 and 4, respectively. Finally, we state the conclusions of the paper in Section 5.

2. Model.

Suppose $\Omega \subset \mathbb{R}^n$ is a bounded domain which is the habitat of a host (for the AI virus) bird species. We divide the total bird population into susceptible (S), infected (I) and recovered (R) groups. We further consider AI virus concentration in water as V. We introduce the birds' mobility by the spatial diffusion terms in the model. Following [32], we incorporate environmental effects via the spatially-varying viral decay rate $c(x)$, which depends on environmental conditions such as temperature, pH and salinity. The model we consider is as follows:

$$\frac{\partial S(x,t)}{\partial t} = D\Delta S + \lambda - \beta_I SI - \beta_V SV - dS + \eta R, \tag{1}$$

$$\frac{\partial I(x,t)}{\partial t} = D\Delta I + \beta_I SI + \beta_V SV - \gamma I - dI, \tag{2}$$

$$\frac{\partial R(x,t)}{\partial t} = D\Delta R + \gamma I - \eta R - dR, \tag{3}$$

$$\frac{\partial V(x,t)}{\partial t} = \alpha I - c(x)V, \tag{4}$$

with $(x,t) \in \Omega \times (0,\infty)$. Here, D is the diffusion coefficient and Δ is the Laplace operator. As included in the model, the susceptible birds get infected by direct bird-to-bird transmission at rate $\beta_I SI$, and by indirect fecal-oral transmission at rate $\beta_V SV$. The parameters λ, d, γ and η represent the rate of recruitment of susceptible birds, the rate of natural death, the rate of recovery from infection and the rate of immunity loss, respectively. Since AI virus is generally non-pathogenic in wild birds [22], we have ignored disease caused deaths in our model. Infected birds shed virus particles in their feces at rate α.

Here, we use the homogeneous Neumann boundary condition

$$\frac{\partial S(x,t)}{\partial \nu} = \frac{\partial I(x,t)}{\partial \nu} = \frac{\partial R(x,t)}{\partial \nu} = 0,\ x \in \partial\Omega,\ t > 0, \tag{5}$$

and initial conditions

$$S(x,0) = S^0(x),\ I(x,0) = I^0(x),\ R(x,0) = R^0(x),\ V(x,0) = V^0(x),\ x \in \Omega, \tag{6}$$

where $\frac{\partial}{\partial \nu}$ denotes the differentiation along the outward normal ν to $\partial\Omega$. Here we assume that the habitat dependent parameter $c(x)$ is strictly positive and continuous on $\bar{\Omega}$.

3. **Model analysis.** For the sake of convenience, let $(u_1,u_2,u_3,u_4) = (S,I,R,V)$. Then (1)-(4) with (5) and (6) is equivalent to the following system:

$$\begin{cases} \frac{\partial u_1(x,t)}{\partial t} = D\Delta u_1 + \lambda - \beta_I u_1 u_2 - \beta_V u_1 u_4 - d u_1 + \eta u_3, \\ \frac{\partial u_2(x,t)}{\partial t} = D\Delta u_2 + \beta_I u_1 u_2 + \beta_V u_1 u_4 - (\gamma + d) u_2, \\ \frac{\partial u_3(x,t)}{\partial t} = D\Delta u_3 + \gamma u_2 - (\eta + d) u_3, \\ \frac{\partial u_4(x,t)}{\partial t} = \alpha u_2 - c(x) u_4, \end{cases} \tag{7}$$

in $(x,t) \in \Omega \times (0,\infty)$ with the homogeneous Neumann boundary condition

$$\frac{\partial u_i(x,t)}{\partial \nu} = 0,\ x \in \partial\Omega,\ t > 0,\ i = 1,2,3, \tag{8}$$

and initial conditions

$$u_i(x,0) = u_i^0(x),\ x \in \Omega,\ i = 1,2,3,4. \tag{9}$$

3.1. **Existence, uniqueness and positivity of solutions.** Let $\mathbb{X} := C(\bar{\Omega}, \mathbb{R}^4)$ be the Banach space with the supremum norm $\|\cdot\|_{\mathbb{X}}$. Define $\mathbb{X}^+ := C(\bar{\Omega}, \mathbb{R}^4_+)$, then $(\mathbb{X}, \mathbb{X}^+)$ is a strongly ordered spaces. Suppose $T_1(t),\ T_2(t),\ T_3(t) : C(\bar{\Omega}, \mathbb{R}) \to C(\bar{\Omega}, \mathbb{R})$ be the C_0 semigroups associated with $D\Delta - d$, $D\Delta - (\gamma + d)$ and $D\Delta - (\eta + d)$ subject to the Neumann boundary condition, respectively. It then follows that for any $\varphi \in C(\bar{\Omega}, \mathbb{R})$, $t \geq 0$,

$$(T_1(t)\varphi)(x) = e^{-dt} \int_\Omega \Gamma(x,y,t)\varphi(y)dy, \tag{10}$$

$$(T_2(t)\varphi)(x) = e^{-(\gamma+d)t} \int_\Omega \Gamma(x,y,t)\varphi(y)dy, \tag{11}$$

and

$$(T_3(t)\varphi)(x) = e^{-(\eta+d)t} \int_\Omega \Gamma(x,y,t)\varphi(y)dy, \tag{12}$$

where Γ is the Green functions associated with $D\Delta$ subject to the Neumann boundary condition, respectively. Let

$$T_4(t)\varphi = e^{-c(\cdot)t}\varphi. \tag{13}$$

From [26, Section 7.1 and Corollary 7.2.3], it follows that $T_i(t) : C(\bar{\Omega}, \mathbb{R}) \to C(\bar{\Omega}, \mathbb{R})$ is compact and strongly positive, $\forall\ t > 0$ and $i = 1, 2, 3$.

For every initial value functions $\phi = (\phi_1, \phi_2, \phi_3, \phi_4) \in C(\bar{\Omega}, \mathbb{R}^4)$, we define $F = (F_1, F_2, F_3, F_4) : \mathbb{X}^+ \to \mathbb{X}$ by

$$\begin{aligned} F_1(\phi)(x) &= \lambda - \beta_I \phi_1(x)\phi_2(x) - \beta_V \phi_1(x)\phi_4(x) + \eta\phi_3(x), \\ F_2(\phi)(x) &= \beta_I \phi_1(x)\phi_2(x) + \beta_V \phi_1(x)\phi_4(x), \\ F_3(\phi)(x) &= \gamma\phi_2(x), \\ F_4(\phi)(x) &= \alpha\phi_2(x),\ \forall\ x \in \bar{\Omega}. \end{aligned}$$

Then (7)-(9) can be rewritten as the integral equation:

$$u(t) = T(t)\phi + \int_0^t T(t-s)F(u(s))ds, \tag{14}$$

where

$$u(t) = \begin{pmatrix} u_1(t) \\ u_2(t) \\ u_3(t) \\ u_4(t) \end{pmatrix}, T(t) = \begin{pmatrix} T_1(t) & 0 & 0 & 0 \\ 0 & T_2(t) & 0 & 0 \\ 0 & 0 & T_3(t) & 0 \\ 0 & 0 & 0 & T_4(t) \end{pmatrix}.$$

It is easy to show that

$$\lim_{h \to 0^+} dist(\phi + hF(\phi), \mathbb{X}^+) = 0,\ \forall\ \phi \in \mathbb{X}^+.$$

By [20, Corollary 4], we obtain the following basis results on solutions of (7)-(9)

Theorem 3.1. *For every initial value function $\phi := (\phi_1, \phi_2, \phi_3, \phi_4) \in \mathbb{X}^+$, system (7)-(9) has a unique mild solution $u(x, t, \phi)$ on $[0, \tau_\phi)$ with $u(\cdot, 0, \phi) = \phi$ and $u(\cdot, t, \phi) \in \mathbb{X}^+$, $\forall\ t \in [0, \tau_\phi)$, where $\tau_\phi \leq \infty$.*

Next, we show that the solution of (7)-(9) with initial function $\phi \in \mathbb{X}^+$ actually exists globally, that is, $\tau_\phi = \infty$. To this end, we let

$$W(x, t) := u_1(x, t) + u_2(x, t) + u_3(x, t). \tag{15}$$

Then $W(x, t)$ satisfies the following system

$$\begin{cases} \frac{\partial W(x,t)}{\partial t} = D\Delta W + \lambda - dW,\ x \in \Omega,\ t > 0, \\ \frac{\partial W(x,t)}{\partial \nu} = 0,\ x \in \partial\Omega,\ t > 0, \\ W(x, 0) = W^0(x) \geq 0,\ x \in \Omega. \end{cases} \tag{16}$$

The following result is related to the long-term behavior of the system (16):

Lemma 3.2. [18, Lemma 1] *The system (16) admits a unique positive steady state $w^* := \frac{\lambda}{d}$ which is globally asymptotically stable in $C(\bar{\Omega}, \mathbb{R})$.*

Making use of the above lemma and theorem, we now can confirm global existence of the solution to (7)-(9), as stated in the next theorem.

Theorem 3.3. *For every initial value function $\phi \in \mathbb{X}^+$, system (7)-(9) has a unique solution $u(\cdot, t, \phi)$ on $[0, \infty)$ with $u(\cdot, 0, \phi) = \phi$ and the semiflow $\Psi_t : \mathbb{X}^+ \to \mathbb{X}^+$ generated by (7)-(9) is defined by*

$$\Psi_t(\phi) = (u_1(\cdot, t, \phi), u_2(\cdot, t, \phi), u_3(\cdot, t, \phi), u_4(\cdot, t, \phi)),\ \forall\ x \in \bar{\Omega},\ t \geq 0. \tag{17}$$

Furthermore, the semiflow $\Psi_t : \mathbb{X}^+ \to \mathbb{X}^+$ is point dissipative and the positive orbits of bounded subsets of $\mathbb{X}^+$ for Ψ_t are bounded.

Proof. From (15), (16), Lemma 3.1 and Lemma 3.2, it follows that $u_i(\cdot,t,\phi)$ is bounded on $[0,\tau_\phi)$, $\forall\ i=1,2,3$. Thus, there exists a positive number Q such that the fourth equation of the system (7) is dominated by the equation

$$\frac{\partial v(x,t)}{\partial t}=\alpha Q-\tilde{c}v,\ x\in\Omega,\ t>0, \tag{18}$$

where $\tilde{c}:=\min_{x\in\bar{\Omega}}c(x)$. It is easy to see that $\frac{\alpha Q}{\tilde{c}}$ is globally attractive in $C(\bar{\Omega},\mathbb{R})$ for the scalar equation (18) and hence $u_4(\cdot,t,\phi)$ is bounded on $[0,\tau_\phi)$. Therefore,

$$(u_1(\cdot,t,\phi),u_2(\cdot,t,\phi),u_3(\cdot,t,\phi),u_4(\cdot,t,\phi))$$

is bounded on $[0,\tau_\phi)\ \forall\ \phi\in\mathbb{X}^+$, and hence for $\tau_\phi=\infty$. Thus, system (7)-(9) defines a semiflow $\Psi_t:\mathbb{X}^+\to\mathbb{X}^+$ by

$$\Psi_t(\phi)=(u_1(\cdot,t,\phi),u_2(\cdot,t,\phi),u_3(\cdot,t,\phi),u_4(\cdot,t,\phi)),\ \forall\ \phi\in\mathbb{X}^+.$$

From (15), (16), Lemma 3.1 and Lemma 3.2, it follows that for every initial value function $\phi\in\mathbb{X}^+$ there exists a $t_1:=t_1(\phi)$ such that $u_i(\cdot,t,\phi)\le 2w^*,\ \forall\ t>t_1,\ i=1,2,3$. From the fourth equation of the system (7), it follows that

$$\frac{\partial u_4(x,t)}{\partial t}\le 2\alpha w^*-\tilde{c}u_4,\ t\ge t_1. \tag{19}$$

Since $\frac{2\alpha w^*}{\tilde{c}}$ is globally attractive in $C(\bar{\Omega},\mathbb{R})$ for the scalar equation $\frac{\partial v(x,t)}{\partial t}=2\alpha w^*-\tilde{c}v$. By (19), it follows that there is a $t_2(\phi)>t_1$ such that $u_4(x,t)\le\frac{4\alpha w^*}{\tilde{c}},\ \forall\ t\ge t_2(\phi)$. Therefore, the solution semiflow $\Psi_t:\mathbb{X}^+\to\mathbb{X}^+$ is point dissipative. Furthermore, the positive orbits of bounded subsets of $\mathbb{X}^+$ for Ψ_t are bounded. □

3.2. **The basic reproductive number.** The basic reproductive number, which is defined as the average number of secondary infections generated by a single infected individual introduced into a completely susceptible population, is one of the important quantities in epidemiology. In this subsection, we will identify the basic reproductive number for the model system (7)-(9).

Obviously $E_0=(w^*,0,0,0)$ is the disease free equilibrium of (7) where $w^*=\frac{\lambda}{d}$. Note that by Lemma 3.2, w^* is the unique positive equilibrium of (16) and is globally asymptotically stable in $C(\bar{\Omega},\mathbb{R})$. Linearizing system (7)-(9) at E_0, we get the following system for the infection related variables u_2 and u_4:

$$\begin{cases}\frac{\partial u_2(x,t)}{\partial t}=D\Delta u_2+\beta_I w^*u_2+\beta_V w^*u_4-(\gamma+d)u_2,\ x\in\Omega,\ t>0,\\ \frac{\partial u_4(x,t)}{\partial t}=\alpha u_2-c(x)u_4,\ x\in\Omega,\ t>0,\\ \frac{\partial u_2(x,t)}{\partial\nu}=\frac{\partial u_4(x,t)}{\partial\nu}=0,\ x\in\partial\Omega,\ t>0.\end{cases} \tag{20}$$

We first consider the following generalized version of the system (20):

$$\begin{cases}\frac{\partial u_2(x,t)}{\partial t}=D\Delta u_2+\beta_I H(x)u_2+\beta_V H(x)u_4-(\gamma+d)u_2,\ x\in\Omega,\ t>0,\\ \frac{\partial u_4(x,t)}{\partial t}=\alpha u_2-c(x)u_4,\ x\in\Omega,\ t>0,\\ \frac{\partial u_2(x,t)}{\partial\nu}=\frac{\partial u_4(x,t)}{\partial\nu}=0,\ x\in\partial\Omega,\ t>0\end{cases} \tag{21}$$

where $H(x)>0,\ \forall\ x\in\bar{\Omega}$.

Substituting $u_i(x,t)=e^{\mu t}\psi_i(x)$, $i=2,4$, into (21) leads to the following associated eigenvalue problem:

$$\begin{cases}\mu\psi_2(x)=D\Delta\psi_2+\beta_I H(x)\psi_2+\beta_V H(x)\psi_4-(\gamma+d)\psi_2,\ x\in\Omega,\\ \mu\psi_4(x)=\alpha\psi_2-c(x)\psi_4,\ x\in\Omega,\\ \frac{\partial\psi_2(x)}{\partial\nu}=\frac{\partial\psi_4(x)}{\partial\nu}=0,\ x\in\partial\Omega.\end{cases} \tag{22}$$

It is easy to see that the system (21) is co-operative, but its solution map is not compact since the second equation in (21) has no diffusion term. The following lemma deals with the existence of the principal eigenvalue of (22).

Lemma 3.4. *For $H(x) > 0,\ \forall\ x \in \bar{\Omega}$, the eigenvalue problem (22) has a principal eigenvalue, denoted by $\mu(H)$ which is associated with a strongly positive eigenfunction.*

Proof. Let $\mathbb{Y} = C(\bar{\Omega}, \mathbb{R}^2)$. For every initial value function $\phi = (\phi_2, \phi_4) \in \mathbb{Y}$, the solution map $\Pi_t : \mathbb{Y} \to \mathbb{Y}$ associated with the linear system (21) is defined by

$$\Pi_t(\phi) = (u_2(\cdot, t, \phi), u_4(\cdot, t, \phi)),\ \forall\ \phi \in \mathbb{Y},\ t \geq 0.$$

By the same argument as that in the proof of Lemma 3.5 in the next subsection, we can show that for each $t > 0$, Π_t is an κ-contraction on $\mathbb{Y}$ in the sense that

$$\kappa(\Pi_t B) \leq e^{-\tilde{c}t}\kappa(B),$$

for any bounded set B in $\mathbb{Y}$, where $\tilde{c} := \min_{x\in\bar{\Omega}} c(x) > 0$ and κ is the Kuratowski measure of non-compactness as defined in (28).

From the discussions above, it is easy to see that the solution map Π_t generated by (21) is κ-condensing in the sense that

$$\kappa(\Pi_t B) < \kappa(B),\ \text{for any bounded set } B \text{ in } \mathbb{Y} \text{ with } \kappa(B) > 0,\ t > 0.$$

Note that (21) is a cooperative system. By the generalized Krein-Rutman Theorem (see, e.g., [16, Lemma 2.2]) and [11, Chapter II.14], the equation (22) has a principal eigenvalue, denoted by $\mu(H)$, with an associated eigenvector $\psi^* = (\psi_2^*, \psi_4^*) \gg 0$. □

With the above preparation, we can now employ the ideas and theory in [8, 18, 31, 33, 35] to the linearized system (20) to define the basic reproductive number for the system (7)-(9). Assume that population is near the disease free equilibrium $(w^*, 0, 0, 0)$. Let $\varphi := (\varphi_2, \varphi_4)$ be the spatial distribution of (u_2, u_4) and $S(t)\varphi$ be the solution semiflow generated by the following linear system:

$$\begin{cases} \frac{\partial u_2(x,t)}{\partial t} = D\Delta u_2 - (\gamma + d)u_2,\ x \in \Omega,\ t > 0, \\ \frac{\partial u_4(x,t)}{\partial t} = \alpha u_2 - c(x)u_4,\ x \in \Omega,\ t > 0, \\ \frac{\partial u_2(x,t)}{\partial \nu} = \frac{\partial u_4(x,t)}{\partial \nu} = 0,\ x \in \partial\Omega,\ t > 0, \\ u_2(x, 0) = \varphi_2(x),\ u_4(x, 0) = \varphi_4(x),\ x \in \Omega. \end{cases} \tag{23}$$

Let $T_2(t)$ and $T_4(t)$ be the semigroup defined in (11) and (13), respectively. From the first two equations of (23), it follows that $u_2(\cdot, t, \varphi) = T_2(t)\varphi_2$ and

$$\begin{aligned} u_4(\cdot, t, \varphi) &= T_4(t)\varphi_4 + \int_0^t T_4(t-s)[\alpha u_2(\cdot, s, \varphi)]ds \\ &= e^{-c(\cdot)t}\varphi_4 + \int_0^t e^{-c(\cdot)(t-s)}[\alpha T_2(s)\varphi_2]ds. \end{aligned}$$

That is,

$$S(t)\varphi := \left(T_2(t)\varphi_2, e^{-c(\cdot)t}\varphi_4 + \int_0^t e^{-c(\cdot)(t-s)}[\alpha T_2(s)\varphi_2]ds\right).$$

It then follows that $S(t)$ is a positive C_0-semigroup on $C(\bar{\Omega}, \mathbb{R}^2)$ and $S(t)\varphi$ represents the spatial distribution of u_2 and u_4 at time $t > 0$.

Let C be the positive linear operator on $C(\bar{\Omega}, \mathbb{R}^2)$ defined by

$$C(\varphi)(x) := (C_2(\varphi)(x), 0),\ \forall\ \varphi := (\varphi_2, \varphi_4) \in C(\bar{\Omega}, \mathbb{R}^2),\ x \in \bar{\Omega}, \tag{24}$$

where

$$C_2(\varphi)(x) := \beta_I w^* \varphi_2 + \beta_V w^* \varphi_4.$$

Then, at time $t > 0$ and location x, there will be $C_2(S(t)\varphi)(x)$ individuals added per unit time into the u_2 compartment, and hence $C(S(t)\varphi)(x)$ accounts for the infection force at time t and location x. Thus, the spatial distribution of total new infected individuals caused by the initial infective distribution $\varphi = (\varphi_2, \varphi_4)$ is

$$\begin{aligned} &\int_0^\infty C_2(S(t)\varphi)\,dt = C_2\left(\int_0^\infty S(t)\varphi\,dt\right) \\ = \;& \beta_I w^* \int_0^\infty T_2(t)\varphi_2 dt \\ & + \beta_V w^* \int_0^\infty \left[e^{-c(\cdot)t}\varphi_4 + \int_0^t e^{-c(\cdot)(t-s)}(\alpha T_2(s)\varphi_2)ds\right] dt. \end{aligned} \tag{25}$$

Along the line of [29] where no spatial factor is considered, we can define the next generation operator $\mathbf{L}$ by

$$\mathbf{L}(\varphi) := \left(C_2\left(\int_0^\infty S(t)\varphi dt\right), 0\right) = C\left(\int_0^\infty S(t)\varphi dt\right) \tag{26}$$

By [31], the basic reproductive number for system (7)-(9) is given by the spectral radius of $\mathbf{L}$, that is,

$$\mathcal{R}_0 := r(\mathbf{L}) \tag{27}$$

Also, by the general results in [31] and the same arguments as in [35, Lemma 2.2], we have the following conclusion on $\mathcal{R}_0$ and $\mu(w^*)$.

Proposition 1. *$\mathcal{R}_0 - 1$ and $\mu(w^*)$ have the same sign.*

3.3. **Threshold dynamics.** In this subsection, we show that $\mathcal{R}_0$ is, in fact, a threshold index for disease persistence. Since the last equation in (7) has no diffusion term, its solution map Ψ_t is not compact. In order to overcome this problem, we introduce the Kuratowski measure of non-compactness (see [7]), κ, which is defined by

$$\kappa(B) := \inf\{r : B \text{ has a finite cover of diameter } < r\}, \tag{28}$$

for any bounded set B. We set $\kappa(B) = \infty$ whenever B is unbounded. It is easy to see that B is precompact (i.e., $\bar{B}$ is compact) if and only if $\kappa(B) = 0$.

Recall that for any $\phi(\cdot) = (\phi_1(\cdot), \phi_2(\cdot), \phi_3(\cdot), \phi_4(\cdot)) \in \mathbb{X}^+$, the semiflow associated with system (7)-(9) is defined by

$$\Psi_t(\phi) = (u_1(\cdot, t, \phi), u_2(\cdot, t, \phi), u_3(\cdot, t, \phi), u_4(\cdot, t, \phi)),\ \forall\ \phi \in \mathbb{X}^+,\ t \geq 0.$$

The following Lemma is concerned with the non-compactness of Ψ_t (see also [15]).

Lemma 3.5. *Ψ_t is κ-contraction on $\mathbb{X}^+$ in the sense that there is a $\tilde{c} > 0$ such that*

$$\kappa(\Psi_t B) \leq e^{-\tilde{c}t}\kappa(B),\ \textit{for any bounded set } B \subset \mathbb{X}^+.$$

Further, Ψ_t is κ-contracting on $\mathbb{X}^+$ in the sense that

$$\lim_{t\to\infty} \kappa(\Psi_t B) = 0,\ \textit{for any bounded set } B \subset \mathbb{X}^+.$$

Proof. It is easy to see that $u_4(\cdot, t, \phi)$ satisfies the following equations:

$$\begin{cases} \frac{\partial u_4(t)}{\partial t} = -c(\cdot)u_4(\cdot, t, \phi) + \alpha u_2(\cdot, t, \phi),\ t > 0, \\ u_4(0) = \phi_4, \end{cases} \tag{29}$$

Then

$$u_4(\cdot,t,\phi) = e^{-c(\cdot)t}\phi_4 + \alpha\int_0^t e^{-c(\cdot)(t-s)}u_2(\cdot,s,\phi)ds.$$

Motivated by the discussion above, we define the following operators:

$$L(t)\phi = (0,0,0,e^{-c(\cdot)t}\phi_4),$$

and

$$Q(t)\phi = (u_1(\cdot,t,\phi), u_2(\cdot,t,\phi), u_3(\cdot,t,\phi), \alpha\int_0^t e^{-c(\cdot)(t-s)}u_2(\cdot,s,\phi)ds)$$

for any $\phi = (\phi_1,\phi_2,\phi_3,\phi_4) \in \mathbb{X}^+$. It is easy to see that

$$\Psi_t(\phi) = L(t)\phi + Q(t)\phi,\ \forall\phi \in \mathbb{X}^+,\ t\ \geq 0.$$

Consequently, we have

$$\kappa(\Psi_t B) \leq \kappa(L(t)B) + \kappa(Q(t)B),\ \forall t \geq 0,$$

for any bounded set $B \subset \mathbb{X}^+$. It is easy to see that $Q(t) : \mathbb{X}^+ \to \mathbb{X}^+$ is compact for each $t > 0$ and hence $\kappa(Q(t)B) = 0,\ \forall\ t \geq 0$.

It is easy to see that there exists a real number $\tilde{c} := \min_{x\in\bar{\Omega}} c(x) > 0$ such that $c(\cdot) \geq \tilde{c}$ and it then follows that

$$\sup_{\phi\in\mathbb{Y}}\frac{\|L(t)\phi\|}{\|\phi\|} \leq \sup_{\phi\in\mathbb{Y}}\frac{\|e^{-c(\cdot)t}\phi_4\|}{\|\phi\|} \leq \sup_{\phi\in\mathbb{Y}}\frac{\|e^{-\tilde{c}t}\phi_4\|}{\|\phi\|} \leq e^{-\tilde{c}t},$$

and hence $\|L(t)\| \leq e^{-\tilde{c}t}$. Consequently,

$$\kappa(\Psi_t B) \leq \kappa(L(t)B) + \kappa(Q(t)B) \leq \|L(t)\|\kappa(B) + 0 \leq e^{-\tilde{c}t}\kappa(B),\ \forall\ t > 0.$$

Thus, Ψ_t is κ-contraction of order $e^{-\tilde{c}t}$ on $\mathbb{X}^+$. This implies Ψ_t is κ-contracting on $\mathbb{X}^+$. □

Theorem 3.6. *Ψ_t admits a connected global attractor on $\mathbb{X}^+$.*

Proof. By Lemma 3.3, it follows that Ψ_t is point dissipative on $\mathbb{X}^+$ and that the positive orbits of bounded subsets of $\mathbb{X}^+$ for Ψ_t are bounded. Furthermore, Ψ_t is κ-contracting on $\mathbb{X}^+$ by Lemma 3.5. By [21, Theorem 2.6], Ψ_t has a global attractor that attracts each bounded set in $\mathbb{X}^+$. □

The following results will play an important role in establishing the persistence of (7)-(9).

Lemma 3.7. *Suppose $u(x,t,\phi)$ is the solution of system (7)-(9) with $u(\cdot,0,\phi) = \phi \in \mathbb{X}^+$.*

(i) *If there exists some $t_0 \geq 0$ such that $u_i(\cdot,t_0,\phi) \not\equiv 0$, for some $i \in \{2,3\}$, then $u_i(x,t,\phi) > 0,\ \forall\ x \in \bar{\Omega},\ t > t_0$;*

(ii) *If there exists some $t_0 \geq 0$ such that $u_2(\cdot,t_0,\phi) \not\equiv 0$ and $u_4(\cdot,t_0,\phi) \not\equiv 0$, then $u_4(x,t,\phi) > 0,\ \forall\ x \in \bar{\Omega},\ t > t_0$;*

(iii) *For any $\phi \in \mathbb{X}^+$, we always have $u_1(x,t,\phi) > 0,\ \forall\ x \in \bar{\Omega},\ t > 0$ and*

$$\liminf_{t\to\infty} u_1(\cdot,t,\phi) \geq \frac{\lambda}{2w^*\beta_I + 4\frac{\alpha w^*}{\tilde{c}}\beta_V + d},$$

where $\tilde{c} := \min_{x\in\bar{\Omega}} c(x)$ and $w^* := \frac{\lambda}{d}$.

Proof. It is easy to see that u_2 and u_3 satisfy the following inequality:

$$\begin{cases} \frac{\partial u_2(x,t)}{\partial t} \geq d\Delta u_2(x,t) - (\gamma + d)u_2(x,t), \ x \in \Omega, \ t > 0, \\ \frac{\partial u_2}{\partial \nu} = 0, \ x \in \partial\Omega, \ t > 0. \end{cases}$$

and

$$\begin{cases} \frac{\partial u_3(x,t)}{\partial t} \geq d\Delta u_3(x,t) - (\eta + d)u_3(x,t), \ x \in \Omega, \ t > 0, \\ \frac{\partial u_3}{\partial \nu} = 0, \ x \in \partial\Omega, \ t > 0. \end{cases}$$

By the similar arguments as in [14, Lemma 2.1] and [34, Proposition 3.1], it follows from the strong maximum principle (see, e. g., [25, p. 172, Theorem 4]) and the Hopf boundary lemma (see, e.g., [25, p. 170, Theorem 3]) that part (i) is valid.

From the last equation of (7), we get that

$$u_4(x,t) = \alpha e^{-c(x)t} \int_{t_0}^{t} u_2(x,s)e^{c(x)s}ds + e^{-c(x)(t-t_0)}u_4(x,t_0), \ x \in \Omega, \ t \geq t_0.$$

This implies that part (ii) is valid.

From (15), (16), Lemma 3.1 and Lemma 3.2, it follows that there exists a $t_1 > 0$ such that $u_2(x,t) \leq 2w^*, \ \forall \ t \geq t_1$. From the last equation of (7), we get

$$\frac{\partial u_4(x,t)}{\partial t} \leq 2\alpha w^* - \tilde{c}u_4, \ t \geq t_1,$$

where $\tilde{c} := \min_{x\in\bar{\Omega}} c(x)$. Thus, there exists $t_2 \geq t_1$ such that $u_4(x,t) \leq 4\frac{\alpha w^*}{\tilde{c}}, \ t \geq t_2$. The first equation of (7) gives

$$\begin{cases} \frac{\partial u_1(x,t)}{\partial t} \geq D\Delta u_1 + \lambda - (2w^*\beta_I + 4\frac{\alpha w^*}{\tilde{c}}\beta_V + d)u_1, \\ \frac{\partial u_1}{\partial \nu} = 0, \ x \in \partial\Omega, \ t > t_2. \end{cases}$$

Therefore,

$$\liminf_{t\to\infty} u_1(\cdot,t,\phi) \geq \frac{\lambda}{2w^*\beta_I + 4\frac{\alpha w^*}{\tilde{c}}\beta_V + d},$$

which completes the proof. □

Now we prove the main result of this section, which shows that $\mathcal{R}_0$ is a threshold index for disease persistence.

Theorem 3.8. *Suppose $u(x,t,\phi)$ is the solution of system (7)-(9) with $u(\cdot,0,\phi) = \phi \in \mathbb{X}^+$. Then the following statements hold.*

(i) *If $\mathcal{R}_0 < 1$, then the disease free equilibrium $(w^*,0,0,0)$ is globally attractive in $\mathbb{X}^+$;*

(ii) *If $\mathcal{R}_0 > 1$, then system (7)-(9) admits at least one positive steady state $\hat{u}(x)$ and there exists a $\sigma > 0$ such that for any $\phi \in \mathbb{X}^+$ with $\phi_i(\cdot) \not\equiv 0$ for $i = 2,3,4$, we have*

$$\liminf_{t\to\infty} u_i(x,t) \geq \sigma, \ \forall \ i = 1,2,3,4,$$

uniformly for all $x \in \bar{\Omega}$.

Proof. We first assume that $\mathcal{R}_0 < 1$. By Lemma 1, it implies that $\mu(w^*) < 0$. By the continuity, there is a $\rho_0 > 0$ such that $\mu(w^* + \rho_0) < 0$. From (15), (16), Lemma 3.1 and Lemma 3.2, it follows that there is a $t_0 := t_0(\phi)$ such that

$$u_1(x,t,\phi) \leq w^* + \rho_0, \ \forall \ t \geq t_0, \ x \in \bar{\Omega}.$$

From the second and the last equations of (7), we get the following system:

$$\begin{cases} \frac{\partial u_2(x,t)}{\partial t} \leq D\Delta u_2 + \beta_I(w^* + \rho_0)u_2 + \beta_V(w^* + \rho_0)u_4 - (\gamma + d)u_2, \\ \frac{\partial u_4(x,t)}{\partial t} = \alpha u_2 - c(x)u_4, \\ \frac{\partial u_i(x,t)}{\partial \nu} = 0, \ x \in \partial\Omega, \ t > 0, \ i = 2, 4 \end{cases} \tag{30}$$

and initial conditions.

By Lemma 3.4, there is a strongly positive eigenfunction $\hat{\psi} := (\hat{\psi}_2, \hat{\psi}_4)$ corresponding to $\mu(w^* + \rho_0)$. Since for any given $\phi \in \mathbb{X}^+$, there exists some $a > 0$ such that $(u_2(x, t_0, \phi), u_4(x, t_0, \phi)) \leq ae^{\mu(w^*+\rho_0)t_0}\hat{\psi}(x), \ \forall\, x \in \bar{\Omega}$. Note that the following linear system

$$\begin{cases} \frac{\partial u_2(x,t)}{\partial t} = D\Delta u_2 + \beta_I(w^* + \rho_0)u_2 + \beta_V(w^* + \rho_0)u_4 - (\gamma + d)u_2, \ x \in \Omega, \ t > 0, \\ \frac{\partial u_4(x,t)}{\partial t} = \alpha u_2 - c(x)u_4, \ x \in \Omega, \ t > 0, \\ \frac{\partial u_i(x,t)}{\partial \nu} = 0, \ x \in \partial\Omega, \ t > 0, \ i = 2, 4, \end{cases} \tag{31}$$

admits a solution $ae^{\mu(w^*+\rho_0)t}\hat{\psi}(x), \ \forall\, t \geq t_0$. The comparison principle implies that

$$(u_2(x, t, \phi), u_4(x, t, \phi)) \leq ae^{\mu(w^*+\rho_0)t}\hat{\psi}(x), \ \forall\, t \geq t_0,$$

and it then follows that $\lim_{t\to\infty}(u_2(x, t, \phi), u_4(x, t, \phi)) = 0$ uniformly for $x \in \bar{\Omega}$. Then, the equation for u_3 is asymptotic to

$$\begin{cases} \frac{\partial u_3(x,t)}{\partial t} = D\Delta u_3 - (\eta + d)u_3, \ x \in \Omega, \ t > 0, \\ \frac{\partial u_3(x,t)}{\partial \nu} = 0, \ x \in \partial\Omega, \ t > 0. \end{cases} \tag{32}$$

Thus, $\lim_{t\to\infty} u_3(x, t, \phi) = 0$ uniformly for $x \in \bar{\Omega}$, by the theory for asymptotically autonomous semiflows (see, e.g., [30, Corollary 4.3]). Hence, it then follows that the equation for u_1 is asymptotic to (16). This implies that $\lim_{t\to\infty} u_1(x, t, \phi) = w^*$ uniformly for $x \in \bar{\Omega}$, by Lemma 3.2 and the theory for asymptotically autonomous semiflows (see, e.g., [30, Corollary 4.3]). Thus Part (i) is proved.

We consider the case where $\mathcal{R}_0 > 1$. By Lemma 1, it implies that $\mu(w^*) > 0$. Let

$$\mathbb{W}_0 = \{\phi \in \mathbb{X}^+ : \phi_2(\cdot) \not\equiv 0 \text{ and } \phi_3(\cdot) \not\equiv 0 \text{ and } \phi_4(\cdot) \not\equiv 0\},$$

and

$$\partial\mathbb{W}_0 = \mathbb{X}^+ \backslash \mathbb{W}_0 = \{\phi \in \mathbb{X}^+ : \phi_2(\cdot) \equiv 0 \text{ or } \phi_3(\cdot) \equiv 0 \text{ or } \phi_4(\cdot) \equiv 0\}.$$

By Lemma 3.7, it follows that for any $\phi \in \mathbb{W}_0$, we have $u_i(x, t, \phi) > 0, \ \forall\, x \in \bar{\Omega}, \ t > 0, \ i = 2, 3, 4$. In other words, $\Psi_t\mathbb{W}_0 \subseteq \mathbb{W}_0, \ \forall\, t \geq 0$.

Let

$$M_\partial := \{\phi \in \partial\mathbb{W}_0 : \Psi_t\phi \in \partial\mathbb{W}_0, \forall\, t \geq 0\},$$

and $\omega(\phi)$ be the omega limit set of the orbit $O^+(\phi) := \{\Psi_t\phi : t \geq 0\}$.

Claim: $\omega(\psi) = \{(w^*, 0, 0, 0)\}, \ \forall\, \psi \in M_\partial$.

Since $\psi \in M_\partial$, we have $\Psi_t\psi \in M_\partial, \ \forall\, t \geq 0$. Thus $u_2(\cdot, t, \psi) \equiv 0$ or $u_3(\cdot, t, \psi) \equiv 0$ or $u_4(\cdot, t, \psi) \equiv 0, \ \forall\, t \geq 0$. In case where $u_2(\cdot, t, \psi) \equiv 0, \ \forall\, t \geq 0$. From the third and fourth equations of (7), it is easy to see that $\lim_{t\to\infty} u_3(x, t, \phi) = \lim_{t\to\infty} u_4(x, t, \phi) = 0$ uniformly for $x \in \bar{\Omega}$. Thus, u_1 is asymptotic to (16) and $\lim_{t\to\infty} u_1(x, t, \phi) = w^*$ uniformly for $x \in \bar{\Omega}$, by Lemma 3.2 and the theory for asymptotically autonomous semiflows (see, e.g., [30, Corollary 4.3]). In case where $u_2(\cdot, \tilde{t}_0, \psi) \not\equiv 0$, for some $\tilde{t}_0 \geq 0$. Then Lemma 3.7 implies that $u_2(x, t, \psi) > 0, \ \forall\, x \in \bar{\Omega}, \forall\, t > \tilde{t}_0$. Hence, $u_3(\cdot, t, \psi) \equiv 0, \ \forall\, t > \tilde{t}_0$ or $u_4(\cdot, t, \psi) \equiv 0, \ \forall\, t > \tilde{t}_0$. In case where $u_4(\cdot, t, \psi) \equiv 0, \ \forall\, t > \tilde{t}_0$. From the last equation of (7), it follows that

$u_2(\cdot,t,\psi)\equiv 0,\ \forall\ t>\tilde{t}_0$, which is a contradiction. Hence, $u_4(\cdot,\tilde{t}_1,\psi)\not\equiv 0$, for some $\tilde{t}_1>\tilde{t}_0$. Then Lemma 3.7 implies that $u_4(x,t,\psi)>0,\ \forall\ x\in\bar{\Omega},\forall\ t>\tilde{t}_1$. Hence, $u_3(\cdot,t,\psi)\equiv 0,\ \forall\ t>\tilde{t}_1$. From the third equation of (7), it follows that $u_2(\cdot,t,\psi)\equiv 0,\ \forall\ t>\tilde{t}_1$, which is a contradiction. Hence, $\omega(\psi)=\{(w^*,0,0,0)\},\ \forall\ \psi\in M_\partial$.

Since $\mu(w^*)>0$, there exists a sufficiently small positive number δ_0 such that $\mu(w^*-\delta_0)>0$.

Claim: $(w^*,0,0,0)$ is a uniform weak repeller for $\mathbb{W}_0$ in the sense that

$$\limsup_{t\to\infty}\|\Psi_t\phi-(w^*,0,0,0)\|\geq\delta_0,\ \forall\ \phi\in\mathbb{W}_0.$$

Suppose, by contradiction, there exists $\phi_0\in\mathbb{W}_0$ such that

$$\limsup_{t\to\infty}\|\Psi_t\phi_0-(w^*,0,0,0)\|<\delta_0.$$

Then, there exists $t_2>0$ such that $u_1(x,t,\phi_0)>w^*-\delta_0,\ \forall\ t\geq t_2,\ x\in\bar{\Omega}$. Thus, $u_2(x,t,\phi_0)$ and $u_4(x,t,\phi_0)$ satisfy

$$\begin{cases}\frac{\partial u_2(x,t)}{\partial t}\geq D\Delta u_2+\beta_I(w^*-\delta_0)u_2+\beta_V(w^*-\delta_0)u_4-(\gamma+d)u_2,\ x\in\Omega,\ t>0,\\ \frac{\partial u_4(x,t)}{\partial t}=\alpha u_2-c(x)u_4,\ x\in\Omega,\ t>0,\\ \frac{\partial u_2(x,t)}{\partial\nu}=\frac{\partial u_4(x,t)}{\partial\nu}=0,\ x\in\partial\Omega,\ t>0.\end{cases}\tag{33}$$

By Lemma 3.4, we can let $\tilde{\psi}:=(\tilde{\psi}_2,\tilde{\psi}_4)$ be the strongly positive eigenfunction corresponding to $\mu(w^*-\delta_0)>0$. Since $u_i(x,t,\phi_0)>0,\ \forall\ x\in\bar{\Omega},\ t>0,\ i=2,4$, there exists $\epsilon_0>0$ such that $(u_2(x,t_1,\phi_0),u_4(x,t_1,\phi_0)\geq\epsilon_0e^{\mu(w^*-\delta_0)t_1}\tilde{\psi}$. Note that $\epsilon_0e^{\mu(w^*-\delta_0)t}\tilde{\psi}$ is a solution of the following linear system:

$$\begin{cases}\frac{\partial u_2(x,t)}{\partial t}=D\Delta u_2+\beta_I(w^*-\delta_0)u_2+\beta_V(w^*-\delta_0)u_4-(\gamma+d)u_2,\ x\in\Omega,\ t>0,\\ \frac{\partial u_4(x,t)}{\partial t}=\alpha u_2-c(x)u_4,\ x\in\Omega,\ t>0,\\ \frac{\partial u_2(x,t)}{\partial\nu}=\frac{\partial u_4(x,t)}{\partial\nu}=0,\ x\in\partial\Omega,\ t>0.\end{cases}\tag{34}$$

The comparison principle implies that

$$(u_2(x,t,\phi_0),u_4(x,t,\phi_0))\geq\epsilon_0e^{\mu(w^*-\delta_0)t}\tilde{\psi},\ \forall\ t\geq t_1,\ x\in\bar{\Omega}.$$

Since $\mu(w^*-\delta_0)>0$, it follows that $u_2(x,t,\phi_0)$ and $u_4(x,t,\phi_0)$ are unbounded as $t\to\infty$. This contradiction proves the claim.

Define a continuous function $p:\mathbb{X}^+\to[0,\infty)$ by

$$p(\phi):=\min\{\min_{x\in\bar{\Omega}}\phi_2(x),\ \min_{x\in\bar{\Omega}}\phi_3(x),\ \min_{x\in\bar{\Omega}}\phi_4(x)\},\ \forall\ \phi\in\mathbb{X}^+.$$

By Lemma 3.7, it follows that $p^{-1}(0,\infty)\subseteq\mathbb{W}_0$ and p has the property that if $p(\phi)>0$ or $\phi\in\mathbb{W}_0$ with $p(\phi)=0$, then $p(\Psi_t\phi)>0,\ \forall\ t>0$. That is, p is a generalized distance function for the semiflow $\Psi_t:\mathbb{X}^+\to\mathbb{X}^+$ (see, e.g., [27]). From the above claims, it follows that any forward orbit of Ψ_t in M_∂ converges to $(w^*,0,0,0)$ which is isolated in $\mathbb{X}^+$ and $W^s(w^*,0,0,0)\cap\mathbb{W}_0=\emptyset$, where $W^s(w^*,0,0,0)$ is the stable set of $(w^*,0,0,0)$ (see [27]). It is obvious that there is no cycle in M_∂ from $(w^*,0,0,0)$ to $(w^*,0,0,0)$. By [27, Theorem 3], it follows that there exists an $\tilde{\sigma}>0$ such that

$$\min_{\psi\in\omega(\phi)}p(\psi)>\tilde{\sigma},\ \forall\ \phi\in\mathbb{W}_0.$$

Hence, $\liminf_{t\to\infty} u_i(\cdot,t,\phi) \geq \tilde{\sigma},\ \forall\ \phi \in \mathbb{W}_0,\ i = 2,3,4$. From Lemma 3.7, there exists an $0 < \sigma \leq \tilde{\sigma}$ such that

$$\liminf_{t\to\infty} u_i(\cdot,t,\phi) \geq \sigma,\ \forall\ \phi \in \mathbb{W}_0,\ i = 1,2,3,4.$$

Hence, the uniform persistence stated in the conclusion (ii) are valid. By [21, Theorem 3.7 and Remark 3.10], it follows that $\Psi_t : \mathbb{W}_0 \to \mathbb{W}_0$ has a global attractor A_0. Since the set $\mathbb{W}_0$ is convex and the solution maps Ψ_t are κ-condensing (see Lemma 3.5), it then follows from [21, Theorem 4.7] that Ψ_t has an equilibrium $\tilde{u}(\cdot) \in \mathbb{W}_0$. Furthermore, Lemma 3.7 implies that $\tilde{u}(\cdot)$ is a positive steady state of (7)-(9). This completes the proof. □

3.4. **Homogeneous environment: $c(x) = c$.** In this subsection, we discuss the special case when $c(x) = c$, a positive constant. The space independence will allow us to obtain more explicit results on extinction and persistence of the disease (see also [38, Lemma 3.1]).

First, we consider $\mu^* := \mu(w^*)$, the principal eigenvalue of the eigenvalue problem:

$$\begin{cases} \mu\psi_2(x) = D\Delta\psi_2 + \beta_I w^*\psi_2 + \beta_V w^*\psi_4 - (\gamma+d)\psi_2,\ x \in \Omega, \\ \mu\psi_4(x) = \alpha\psi_2 - c\psi_4,\ x \in \Omega, \\ \frac{\partial\psi_2(x)}{\partial\nu} = \frac{\partial\psi_4(x)}{\partial\nu} = 0,\ x \in \partial\Omega. \end{cases} \tag{35}$$

Note that the eigenvalue-eigenfunction problem

$$\begin{cases} \mu\phi(x) = D\Delta\phi(x),\ x \in \Omega, \\ \frac{\partial\phi(x)}{\partial\nu} = 0,\ x \in \partial\Omega. \end{cases} \tag{36}$$

has a unique (up to scalar multiple) positive eigenfunction $\phi^0(x) = 1$ with the associated eigenvalue being $\mu^0 = 0$. Suppose that $(\psi_2^*, \psi_4^*) \gg 0$ is the eigenfunction (unique up to scalar multiple) of (35) associated to μ^*. From the second equation of (35), it follows that

$$\psi_4^*(x) = \frac{\alpha}{\mu^* + c}\psi_2^*(x).$$

Plugging this into the first equation of (35) leads to

$$\begin{cases} \left[\mu^* - \beta_I w^* - \beta_V w^* \frac{\alpha}{\mu^*+c} + (\gamma+d)\right]\psi_2^*(x) = D\Delta\psi_2^*(x),\ x \in \Omega, \\ \frac{\partial\psi_2^*(x)}{\partial\nu} = 0,\ x \in \partial\Omega. \end{cases} \tag{37}$$

Since $\psi_2^*(x) > 0$ in $x \in \Omega$, by the uniqueness of $\phi^0(x) = 1$, we conclude that $\mu^* - \beta_I w^* - \beta_V w^* \frac{\alpha}{\mu^*+c} + (\gamma+d) = \mu^0 = 0$. Hence, μ^* is a real root of the quadratic equation

$$P(\mu) := \mu^2 + [c - \beta_I w^* + (\gamma+d)]\mu - [\beta_I w^* c + \beta_V w^* \alpha - (\gamma+d)c] = 0. \tag{38}$$

We show that μ^* is the larger root of equation (38). Suppose that μ is a root of (38). Obviously, $P(-c) = -\beta_V w^* \alpha < 0$ and hence $\mu \neq -c$, that is, $\mu + c \neq 0$. Let $\psi^0(x) = \frac{\alpha}{\mu+c}\phi^0(x)$. Then μ is an eigenvalue of (35) with eigenfunction $(\phi^0(x), \psi^0(x))$. Thus, $\mu \leq \mu^*$ since μ^* is the principal eigenvalue of (35). This

shows that μ^* is the maximum root of equation (38), and hence

$$\begin{aligned}\mu^* &= \frac{1}{2}\Big[-[c-\beta_I w^*+(\gamma+d)] \\ &\quad +\sqrt{[c-\beta_I w^*+(\gamma+d)]^2+4[\beta_I w^* c+\beta_V w^*\alpha-(\gamma+d)c]}\Big] \\ &= \frac{1}{2}\Big[-[c-\beta_I w^*+(\gamma+d)] \\ &\quad +\sqrt{[c-\beta_I w^*+(\gamma+d)]^2+4(\gamma+d)c[\mathcal{R}_0^*-1]}\Big] \end{aligned} \tag{39}$$

where

$$\mathcal{R}_0^* = \frac{\beta_I w^*}{\gamma+d}+\frac{\alpha}{c}\frac{\beta_V w^*}{\gamma+d}.$$

Next, we show that the basic reproductive number $\mathcal{R}_0$ is indeed identical to $\mathcal{R}_0^*$ in this case. To this end, we use the idea in [35, Theorem 2.1] to consider the following operator obtained by perturbing $\mathbf{L}$:

$$\mathbf{L}_\epsilon(\varphi) = C^\epsilon\left(\int_0^\infty S(t)\varphi dt\right),\ \forall\ \varphi := (\varphi_2,\varphi_4)\in C(\bar\Omega,\mathbb{R}^2),$$

where $\epsilon>0$ is a constant and

$$C^\epsilon(\varphi) = \epsilon\varphi + C(\varphi),\ \forall\ \varphi := (\varphi_2,\varphi_4)\in C(\bar\Omega,\mathbb{R}^2),$$

Then $\mathbf{L}_\epsilon$ is a *strongly positive* linear operator. Moreover, by $\int_\Omega \Gamma(x,y,t)dy = 1,\ \forall\ x\in\Omega,\ t>0$, it is easy to see that

$$\mathbf{L}_\epsilon(\hat z) = J_\epsilon z,\ \forall\ z=(z_2,z_4)^T\in\mathbb{R}^2,$$

where $\hat z$ means the constant function taking value z on $\bar\Omega$ and

$$J_\epsilon = \begin{pmatrix} \frac{\beta_I w^*}{\gamma+d}+\frac{\alpha}{c}\frac{\beta_V w^*}{\gamma+d}+\frac{\epsilon}{\gamma+d} & \frac{\beta_V w^*}{c} \\ \frac{\alpha}{c}\frac{\epsilon}{\gamma+d}+\frac{\epsilon}{\gamma+d} & \frac{\epsilon}{c}\end{pmatrix}.$$

Since each element of matrix J_ϵ is positive, its spectral radius $r(J_\epsilon)$ is an eigenvalue corresponding to which there is a positive eigenvector in $\mathbb{R}^2$. Straightforward calculation shows that

$$r(J) = r(J_0) = \frac{\beta_I w^*}{\gamma+d}+\frac{\alpha}{c}\frac{\beta_V w^*}{\gamma+d} = \mathcal{R}_0^*.$$

If we can prove that

$$r(\mathbf{L}_\epsilon) = r(J_\epsilon),\quad \text{for}\ \epsilon>0, \tag{40}$$

then by letting $\epsilon\to 0^+$, we would obtain

$$\mathcal{R}_0 = r(\mathbf{L}) = r(\mathbf{L}_0) = r(J_0) = \frac{\beta_I w^*}{\gamma+d}+\frac{\alpha}{c}\frac{\beta_V w^*}{\gamma+d} = \mathcal{R}_0^*. \tag{41}$$

Unfortunately, we are unable to prove (40). The main difficulty is that, like $\mathbf{L}$, $\mathbf{L}_\epsilon$ is not compact; otherwise the uniqueness of the positive eigenvector associated with $r(\mathbf{L}_\epsilon)$ would immediately confirm (40). Note that the formulas (39) and (41) coincide with the conclusion of Proposition 1. This makes us conjecture that (40) holds.

Below we provide an alternative way to confirm (41). Assume that initially there is no virus in the host population and a single infective individual is brought into the host population with the probability of landing at the location x being $\varphi_2(x)\ge 0$ (hence $0\le\varphi_2(x)\le 1$ and $\int_\Omega \varphi_2(x)\,dx = 1$). This corresponds to $\varphi_4 = 0$. By (25),

the spatial distribution of total new infected individuals caused by such a single infective individual is given by

$$\beta_I w^* \int_0^\infty (T_2(t)\varphi_2)(x)dt + \beta_V w^* \int_0^\infty \int_0^t e^{-c(t-s)}(\alpha T_2(s)\varphi_2)(x)\, ds\, dt. \tag{42}$$

Summing up the above over the spatial domain, we then obtain the total new infected individuals caused by the single infective individual as

$$\begin{aligned}
&\int_\Omega \left[\beta_I w^* \int_0^\infty (T_2(t)\varphi_2)(x)\, dt + \beta_V w^* \int_0^\infty \int_0^t e^{-c(t-s)}(\alpha T_2(s)\varphi_2)(x)\, ds\, dt\right] dx \\
&= \beta_I w^* \int_\Omega \int_0^\infty \int_\Omega e^{-(\gamma+d)t}\Gamma(x,y,t)\varphi(y)dy\, ds\, dt \\
&\quad + \alpha\beta_V w^* \int_\Omega \int_0^\infty \int_0^t e^{-c(t-s)} \int_\Omega e^{-(\gamma+d)s}\Gamma(x,y,s)\varphi_2(y)\, dy\, ds\, dt\, dx.
\end{aligned} \tag{43}$$

Making use of $\int_\Omega \Gamma(x,y,t)dx = \int_\Omega \Gamma(x,y,t)dy = 1$ and $\int_\Omega \varphi_2(x)\, dx = 1$, as well as changing the orders of integrals in the above, we can show that the above quantity involving multiple intergrals actually is equal to

$$\frac{\beta_I w^*}{\gamma+d} + \frac{\alpha}{c}\frac{\beta_V w^*}{\gamma+d}.$$

On the other hand, by the biological definition of the basic reproductive number, (43) is nothing but $\mathcal{R}_0$. This confirms (41).

4. **Simulation results.** For simplicity we consider $\Omega = [0, L] \subset \mathbb{R}$. Furthermore, we can take $L = 1$ by transforming $D \to D/L^2$ and $c(x) \to c(xL)$. We obtained the model parameters from the literature (See Table 1). It is quite difficult to obtain the actual function c depending on the spatial variable x. In fact, it varies from location to location and also from time to time. For illustration purposes, we consider a linearly decay function of temperature, i.e. $T(x)$, to represent the spatial variation of the environment: $T(0) = T_0$ and $T(1) = T_1$ stand for temperatures of a warmer place and a cooler place, respectively, while the temperature in between is given by $T(x) = (T_1 - T_0)x + T_0$. Then as obtained in [32], the decay rate of viral particles, $c(x)$ is given by the following relation:

$$c(x) = \frac{\ln 10}{e^{aT(x)+b}}, \tag{44}$$

where a and b are constants (See Table 1).

By taking different values of D and different temperature profiles, T, we study how the diffusion and the spatial heterogeneity of the environmental condition impact AI dynamics. Numerical solutions are obtained by using the method of lines to derive a system of ODEs, which are solved using MATLAB software.

As a case study, we consider spatial temperature variation in Canada [1]. As given in [1], the mean annual temperature in Canada varies from 13^oC at some places along the southern border to -18^oC in the north. Therefore we take $T_0 = 13^o$C and $T_1 = -18^o$C for our base case computation, while the base case value of the scaled diffusion coefficient is fixed at $D = 5 \times 10^{-4}$. We simulate the model for a six month time-frame, and analyze the spatial distribution of avian influenza prevalence (%) at the end of six months. Initially, birds are assumed to live locally in the middle of the domain (Fig. 1). We then observe how the spatial diffusion and the spatial environmental heterogeneity will drive the dynamics of avian influenza

among these birds. We emphasize that this case study is not intended as a model of AI in Canada, but simply illustrates the pattern and magnitude of the effects we are studying.

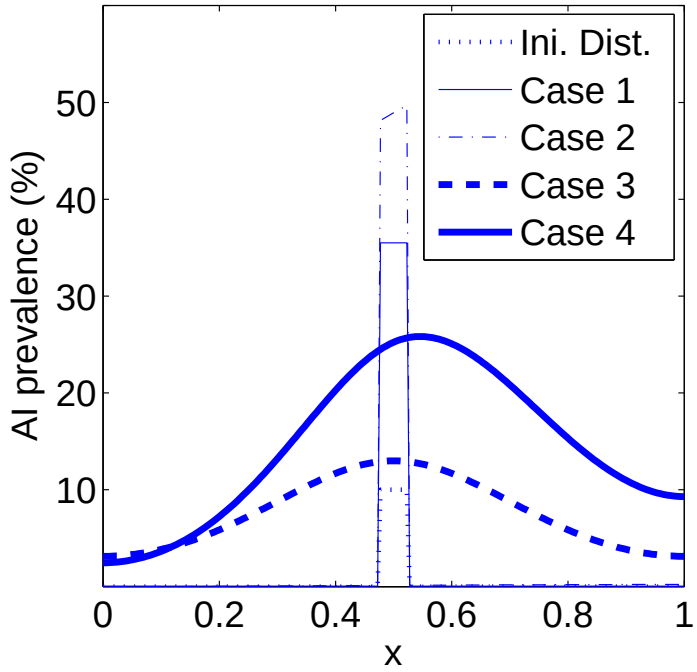

FIGURE 1. Distribution of AI prevalence (%) among wild birds in a six month period for a model without spatial diffusion and spatial environmental heterogeneity (case 1), with spatial environmental heterogeneity only (case 2), with spatial diffusion only (case 3), and with both spatial diffusion and spatial environmental heterogeneity (case 4). The dotted line indicates the initial distribution.

We present spatial distributions of AI prevalence (%) predicted by the model for different cases (Fig. 1): (i) neither spatial diffusion nor spatial environmental heterogeneity, (ii) with spatial environmental heterogeneity only, (iii) with spatial diffusion only, and (iv) with both spatial diffusion and spatial environmental heterogeneity. We can clearly see a significant effect of both diffusion and environmental heterogeneity. As expected, without spatial diffusion, AI accumulates locally. While the AI prevalence without diffusion shown in Fig. 1 is at $T = 5^o$C, the level of AI prevalence is set by the value of T considered: the lower the temperature the higher the prevalence level, as the infectious viruses persist longer in cold temperatures. When diffusion is introduced without any environmental heterogeneity, AI spreads out symmetrically on both sides from the initial location. AI becomes asymmetrically distributed across the spatial domain if spatial environmental heterogeneity is taken into account in addition to diffusion.

We now fix the temperature distribution as $T_0 = 13^oC, \Delta T = T_1 - T_0 = -31^oC$ and observe how the spatial distribution of AI prevalence changes with the diffusion

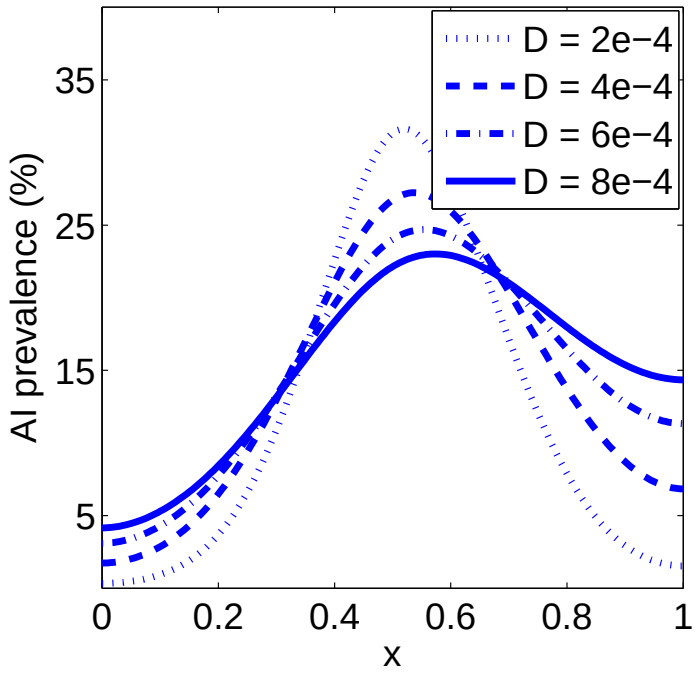

FIGURE 2. Distribution of AI prevalence (%) among wild birds in a six month period for various spatial diffusion constants, $D = 2 \times 10^{-4}, 4\times10^{-4}, 6\times10^{-4}$ and 8×10^{-4}, with a fixed $T_0 = 13^oC, \Delta T = T_1 - T_0 = -31^oC$.

coefficient $D = 2 \times 10^{-4}, 4 \times 10^{-4}, 6 \times 10^{-4}$ and 8×10^{-4} (Fig. 2). A higher diffusion coefficient has tendency to increase AI prevalence towards the boundary while decreasing the prevalence in the middle as seen in Fig. 2. However, due to the spatial environmental heterogeneity, the effect of diffusion is more pronounced at the cooler boundary than the warmer boundary and the prevalence remains higher at cooler places, again due to longer persistence of viruses at low temperatures.

In Fig. 3, we show a spatial distribution of AI prevalence for different temperature profiles while fixing the diffusion constant at $D = 5 \times 10^{-4}$. Here, in each case we force the temperature in the middle of the domain to be always the same (5^oC), and then from the middle of the domain the temperature linearly increases to the $x = 0$ boundary and linearly decreases to the $x = 1$ boundary so that $\Delta T = 5, 15, 25$ and 35^oC. AI prevalence is clearly affected by spatial environmental heterogeneity with a positive correlation between heterogeneity in environment and heterogeneity in the AI distribution. The results shown in Fig. 3 reveal that this effect is more sensitive at cooler places than warmer places.

5. **Conclusion.** In this paper, we presented a transmission dynamic model of avian influenza among wild birds. The novelty of the model is that it includes both spatial diffusion of birds and spatial heterogeneity of the environment, which are critical in understanding AI dynamics and devising control strategies. The environmental heterogeneity was introduced into the model based on the experimentally-observed

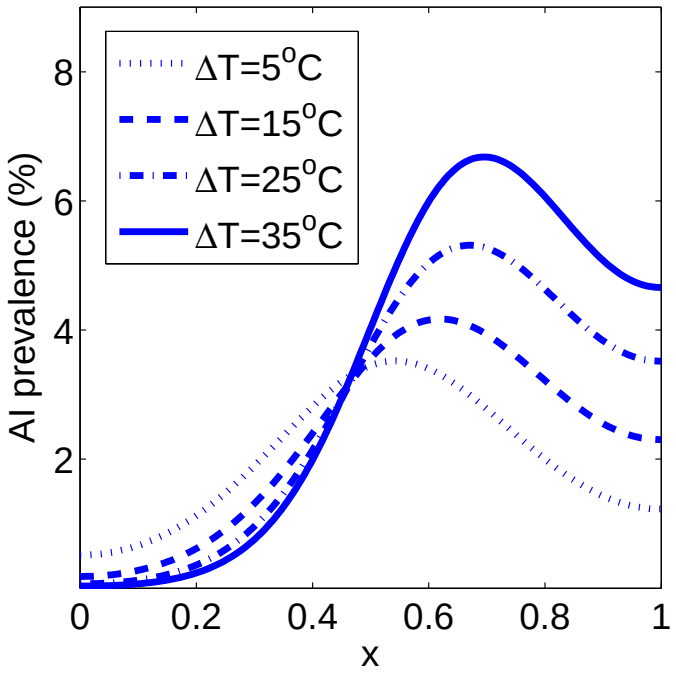

FIGURE 3. Distribution of AI prevalence (%) among wild birds in a six month period for various temperature profiles with a fixed diffusion constant $D = 5 \times 10^{-4}$.

dependence of virus persistence on the environmental factors such as temperature, pH and salinity. Mathematical analysis of the model allowed us to achieve a formula for the basic reproductive number and a threshold condition for the disease to die out. We found that the reproductive number is independent of the diffusion coefficient in the absence of environmental heterogeneity. However, diffusion comes into play to define the reproductive number due to spatial heterogeneity in the environmental condition.

We performed model simulations for various diffusion constants and environmental conditions. Our results show that the dynamics of AI prevalence among wild birds is highly affected by both bird diffusion and environmental heterogeneity. While diffusion has a tendency to spread AI across a larger space, the environmental heterogeneity brings an asymmetrical nature to the AI distribution. In our model, we have introduced only spatial heterogeneity. However, the environmental condition, for example temperature, varies widely even within a short period. Therefore, further extension of our work would be to analyze the effects of spatio-temporal variations of the environmental conditions on AI dynamics in wild birds.

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TABLE 1. Model parameters

Parameter	Description	Value	Reference
λ	Recruitment rate of susceptible birds	60 (0-100) [birds day^{-1}]	[3, 32]
d	Natural death rate	0.1 (0.05-0.3) [year^{-1}]	[3, 2]
β_I	Direct transmission rate	1.00×10^{-9} [bird^{-1}day^{-1}]	[32]
β_V	Indirect transmission rate	1.97×10^{-9} [virion^{-1}day^{-1}]	[32]
η	Immunity loss rate	0.038 [day^{-1}]	[32]
γ	Recovery rate	0.14 [day^{-1}]	[19, 37, 36]
α	Viral shedding rate	1×10^3 [virion bird^{-1} day^{-1}]	[23]
D	Diffusion coefficient		varied
a	In $c(x)$	-0.12	[32]
b	In $c(x)$	5.10	[32]

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