

Chapter 5

Structured Population Models for Vector-Borne Infection Dynamics



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Abstract Dynamical systems provide an appropriate framework to examine whether, where and when a vector species and/or a vector-borne pathogen can establish and spread. Such systems often contain time lags to reflect the transition times from one physiological stage to the next, or from one geographic location to others. We present a brief introduction to dynamical systems generated by delay differential equations with varying delay. We focus on those delay differential equations which are reduced from structured population partial differential equation models, and we discuss the implicit assumption that needs to be made to permit this reduction process. We demonstrate the model formulation from tick population and tick-borne disease infection dynamics, and from bird migration and avian influenza spread dynamics. We show how model parameters, especially time-varying development delays, can be informed from laboratory experiments, field studies and surveillance data, and how these parameters are integrated to a single threshold parameter, the basic reproduction number, to quantify when population establishment and disease persistence are likely.

5.1 Delay Differential Equations for Disease Infection Dynamics

An introduction of mathematical modelling for vector-borne disease infection dynamics often starts with a simplified assumption about the homogeneity in the population in terms of reproduction, transmission contacts and environmental conditions. This assumption yields compartmental systems of ordinary differential equations.

Applications of dynamical systems-based modelling and analysis to informing ecosystem management and disease intervention require however details about

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127

the heterogeneities in the physiological status of the vector species (such as ticks in the context of tick-borne diseases such as Lyme disease) and/or geographical location of the vector species (such as migratory birds in the context of avian influenza spread). Associated with this requirement from applications is the gradually improved surveillance and field observation about these physiological status and/or geographical location. Incorporating these heterogeneities into an infection dynamics model gives rise to structured population and epidemic models which, under the assumption of homogeneity within a particular stage or a spatial segment, can be reduced to a system of delay differential equations (DDEs).

Here we start with a short introduction to the basic model framework and some fundamental results about systems of DDEs. We will then focus on the case of delays which are variable due to climate change and environmental condition variations, and focus on reduction from structured to staged models. We will discuss the definition and calculation of the vector population establishment threshold, the basic reproduction number in vector ecology, and show how this combined with environmental and vector behavior data can be used to produce the vector population establishment risk maps. We will then introduce the concept of monotone maps and threshold dynamics and present two illustrative examples: Lyme tick population dynamics with structured life cycles, and bird migration dynamics and spatially structured models. We will finally touch on the persistence theory and illustrate the theory with two examples: avian influenza spread through bird migration, and Lyme disease dynamics through multi-stage systemic transmission.

5.2 Delay Differential Equations: Setting Up the Model

We start with the logistic equation

$$x'(t) = rx(t)[1 - x(t)/K], \quad r, K > 0;$$

or generally,

$$x'(t) = -d(x) + b(x)$$

with $d(x)$ as the death rate and $b(x)$ as the birth rate.

Examples are when $d(x) = -rx^2/K$ and $b(x) = rx$ (logistic equation, when $K > 0$ is the carrying capacity constant and r is the intrinsic growth rate); when $d(x) = dx$ with a constant $d > 0$ and $b(x) = px e^{-qx}$ (the so-called *Ricker function*, leading to a monostable system); and when $b(x) = px^2 e^{-qx}$ (modelling the Allee effect and leading to a bistable system).

In this model formulation, homogeneity is implicitly assumed: every individual can reproduce, and birth into the population is instantaneous. In most biological populations, however, individuals can reproduce only after maturation. A more realistic formulation posits two classes within the population: immature and mature

(reproducing) individuals. If there is a uniform maturation time (τ), then the equation becomes

$$x'(t) = -dx(t) + \alpha b(x(t - \tau)) \quad (5.1)$$

with the second term being the maturation rate (birth rate at $t - \tau$ times the survival probability α during the maturation). This gives a delay differential equation.

In what follows, we suggest the readers to keep the following reproduction function in mind:

$$b(x) = px e^{-qx}.$$

To uniquely define a solution for all future time $t \geq 0$, we need to specify the initial condition $x(s) = \phi(s)$ for $s \in [-\tau, 0]$ with the initial function ϕ given from the phase space $C := C([-\tau, 0])$. The initial value problem of (5.1) subject to the initial condition can then be solved using the method of steps that solves the initial value problem consequently on the intervals $[0, \tau]$, $[\tau, 2\tau]$, \dots , $[n\tau, (n + 1)\tau]$ for any integer $n > 1$.

There are some important properties of DDEs, including the non-existence and possible non-uniqueness of backward extensions from an initial condition, the eventual compactness, non-negativeness and boundedness of the (forward) solutions when the feedback function b is appropriately given. The solutions then give a semiflow in C which has a global attractor. The standard notation x_t is used to denote the segment x on the interval $[t - \tau, t]$ translated into the initial interval $[-\tau, 0]$, i.e.,

$$x_t(s) = x(t + s), s \in [-\tau, 0].$$

Fundamental results can be found in [15]; see also [6, 8, 9, 13, 14, 19, 21, 30, 37] for a collection of textbooks and references.

The local stability of the model system at a given equilibrium x^* is determined by the stability of the zero solution of the linear system describing the perturbation $x(t)$ around x^* :

$$x'(t) = -dx(t) + \alpha b'(x^*)x(t - \tau).$$

The linearization at the zero equilibrium $x^* = 0$ generates a positive semigroup (since $b'(0) > 0$) and hence the stability of this equilibrium is determined by the real eigenvalue of the characteristic equation (Corollary 3.2 of [30])

$$\lambda = -d + \alpha b'(x^*)e^{-\lambda\tau}.$$

So if $\alpha b'(0) < d$ then $x^* = 0$ is locally asymptotically stable. We can also easily check that when $\alpha b'(0) < d$ the system has no positive equilibrium. On the other hand, if $\alpha b'(0) > d$ then there is a positive equilibrium x^* which maybe locally

asymptotically stable or unstable, but the zero equilibrium becomes unstable. In some cases, we can also make conclusions regarding the global attractivity of the positive equilibrium using the monotone dynamical systems theory [30]. This is particularly true when the positive equilibrium is within the interval where the function b remains monotonically increasing. In the case where $b'(x^*) < 0$ at the positive equilibrium x^* , we have the situation of a negative feedback around this equilibrium and a Hopf bifurcation of periodic solutions may take place. This is a typical example of delay-induced nonlinear oscillations. Figure 5.1 gives an illustration of possible scenarios of model dynamics, depending on the location of the intersections between the death rate dx and the maturation rate function $\alpha b(x)$.

Note also that the survival probability during the maturation period may depend on the maturation delay τ , the stability analysis of the characteristic equation involving delay-dependent coefficients is very complicated, and the global Hopf bifurcation (the birth, death and global continuation of local Hopf bifurcation) has

$$x'(t) = -dx(t) + \alpha b(x(t - \tau))$$

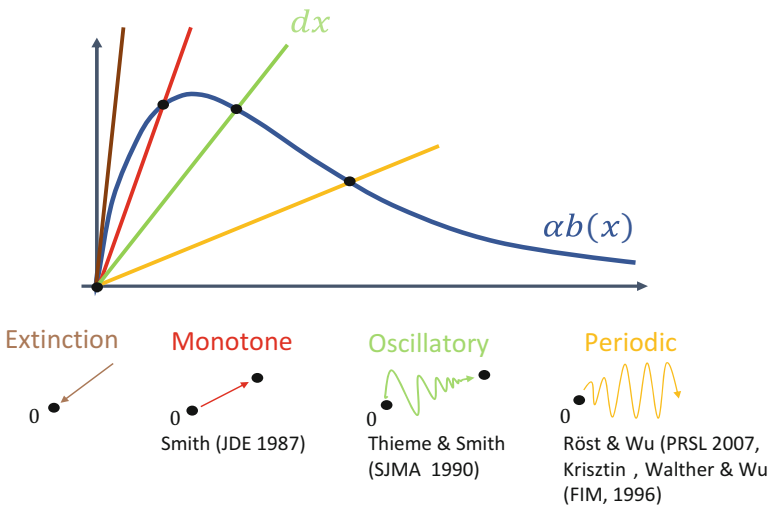


Fig. 5.1 The global dynamics of the delay differential equation $x'(t) = -dx(t) + \alpha b(x(t - \tau))$ with a constant delay $\tau > 0$. Depending on the relative value of $\alpha b'(0)$ and d , the model may have one or two non-negative equilibria. The positive equilibrium, if it exists and is within the interval where the function b is increasing, is the global attractor for all solutions of the equation with non-trivial non-negative initial value (using the monotone dynamical system theory [29]). When this positive equilibrium value is in the interval when the function b is decreasing and when the delay is small, this equilibrium remains stable (using the dynamical system theory in [31] for semiflows which are order-preserving with respect to the so-called exponential ordering). This equilibrium however can lose its stability through the mechanism of Hopf bifurcations. Under certain technical conditions, one can show that the bifurcated periodic solutions are stable [26], and the structure of the global attractor can be described as in [18]

been recently studied in [27, 28]. See also [40] for some further extensions when the scalar equation is replaced by a system of delay differential equations.

A question arises: *What happens if the delay is not a constant, but for example, temporally periodic (maturation regulated by the seasonal variation of the environment)? If this delay is given by $\tau(t)$, would the model become*

$$x'(t) = -dx(t) + \alpha b(x(t - \tau(t)))?$$

A positive answer was suggested and used in a number of studies including [11]. However, this answer ignored a key factor as explained below.

To understand why the general answer to the above question should be negative, we call attention to the warning statement in the textbook [8] that one should appropriately start with the description of population dynamics at the individual level or to derive from a probabilistic formulation the system for the matured population dynamics with variable delay.

Let us take the approach using reduction by integration along characteristics of individual-based models. We define $u(t, a)$ as the population density at time t and age a . The dynamics is described by the basic evolutionary operator

$$\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a} \right) u(t, a) = -\mu(a)u(t, a)$$

subject to boundary condition

$$u(t, 0) = b(M(t)),$$

where the reproductive population is given by

$$M(t) = \int_{\tau(t)}^{\infty} u(t, a) da.$$

Under the assumption that $\mu(a)$ is stage-dependent (not age-dependent) (that is, $\mu(a) = \mu_m$ for a constant independent of the age variable $a \geq \tau(t)$, and $\mu(a) = \mu_i$ for $a < \tau(t)$), we can use integration along characteristics to obtain

$$M'(t) = -\mu_m M(t) + (1 - \tau'(t))e^{-\mu_i \tau(t)} b(M(t - \tau(t))).$$

Note that a factor $(1 - \tau'(t))$ appears, which is one only when the delay is a constant.

An interesting problem for future studies is whether we can transfer the above model with variable delay to a periodic DDE model with a constant delay, with a transformation that is guided by, and can provide with, biological insights into the maturation process with variable maturation time.

5.3 Lyme Tick Population Dynamics

An example to illustrate the importance of considering structured population modelling and variable developmental delays is Lyme disease transmission dynamics.

Lyme disease spread involves complex interaction of a spirochete, multiple vertebrate hosts, and a vector with a two (or three)-year life cycle strongly influenced by the season rhythm. The black-legged tick, *Ixodes scapularis* Say, is the primary vector of *Borrelia burgdorferi*, the bacterial agent of Lyme disease, in eastern and mid-western United States. Northward invasive spread of the tick vectors from United States endemic foci to non-endemic Canadian habitats has been a public health concern. A mathematical model to faithfully describe the development of tick populations and the pathogen spread dynamics is needed to understand the invasion pattern and predict Lyme infection risk under projected environmental condition variations.

In [38], a system of ordinary differential equations with periodic coefficients was proposed for the tick population dynamics. Such a model implicitly makes an assumption of exponentially distributed development delays. However, tick development delay is normally concentrated around a particular value though this value depends on the historical environment conditions up to the time of the completion of the development. A more appropriate model would require the use of time-varying development delay.

An attempt was made in [39] which carefully follows the development of tick populations from one stage to another. In the formulated model, the development delay is not a constant but rather a periodic function of the time due to seasonality in the environmental conditions. The model parameters were estimated from many years of surveillance, lab test and field data, and the theory of Floquet multipliers of periodic systems was used to calculate the threshold condition for the tick population dynamics. In the next subsections, we will introduce the model and some relevant analyses.

5.3.1 Model Formulation and Objective

We now describe key ingredients in the aforementioned model study.

- Model formulation: a general dynamic population model where the development time from one life stage to the next has considerable variation due to temperature change.
- Key assumptions: the transition time between two consecutive stages is constant when the temperature is fixed; the correlation between the fixed temperature and the transition time can be determined from lab data; the temperature in a considered region varies periodically (annually); and therefore the transition time between two consecutive stages (in the considered region) is a temporally varying periodic function (of the time).

- **Model variables:** The life cycle of a population is divided into n stages, with each stage embodying a specific point of the life of the individual. Let x_j ($1 \leq j \leq n$) be the size of subpopulations at the j th stage, with stages in order of increasing maturity (e.g., egg, larvae, nymphs, adult...), except x_1 which is the size of the mature subpopulation who are able to produce offspring (egg-laying females).
- **Objective:** To formulate a closed system for the dynamics of $(x_1(t), \dots, x_n(t))$ in order to predict the tick establishment risk.

Age-structured model, the starting point: We start with the population's chronological age variable a (time since being produced as an egg), and describe the evolution of $\rho(t, a)$, the density of the female population, by

$$\begin{cases} (\frac{\partial}{\partial t} + \frac{\partial}{\partial a})\rho(t, a) = -\mu(t, a)\rho(t, a), \\ \rho(0, a) = \phi(a), \quad a \geq 0 \quad (\text{Initial Condition}), \\ \rho(t, 0) = b(x_1(t)), \quad t \geq 0 \quad (\text{Boundary Condition}). \end{cases}$$

Here μ is the death rate. Integrating along characteristics yields

$$\rho(t, a) = \begin{cases} \rho(0, a-t)e^{-\int_0^t \mu(r, a-t+r) dr}, & 0 \leq t \leq a, \\ \rho(t-a, 0)e^{-\int_0^a \mu(t-a+r, r) dr}, & a < t. \end{cases}$$

A natural question then arises: *What kind of homogeneity needs to be assumed to permit the reduction from a structured population PDE model to a stage-structured DDE model?*

It turns out that the stage-homogeneity assumption about the mortality rate $\mu(t, a)$ given below is (mathematically) sufficient and (practically) justified by how the lab and field observation data is collected. This stage-homogeneity assumption states that each mortality rate in a given stage is a constant independent of the ages within the given stage, but the mortality rates can vary from one stage to another. This is described by

$$\mu(t, a) = \begin{cases} \mu_1(x_1(t)), & a \in [A_n(t), \infty), \\ \mu_i(x_i(t)), & a \in [A_{i-1}(t), A_i(t)], \quad i = 2, \dots, n, \end{cases}$$

where $A_{i-1}(t)$ and $A_i(t)$ are the time-dependent minimum and maximum ages of those individuals who are developing within the specific i th stage, and

$$\begin{cases} x_1(t) = \int_{A_n(t)}^{\infty} \rho(t, a) da \\ x_i(t) = \int_{A_{i-1}(t)}^{A_i(t)} \rho(t, a) da, \quad i = 2, \dots, n. \end{cases}$$

Under this stage-homogeneity assumption, we have from the evolution equation the following

$$\begin{aligned} x_1'(t) &= \int_{A_n(t)}^{\infty} \{(\partial_t + \partial_a)\rho(t, a) - \partial_a\rho(t, a)\} da - \rho(t, A_n(t))A_n'(t) \\ &= \rho(t, \infty) + \rho(t, A_n(t)) - \int_{A_n(t)}^{\infty} \mu(t, a)\rho(t, a) da - \rho(t, A_n(t))A_n'(t) \\ &= \rho(t, A_n(t))(1 - A_n'(t)) - \int_{A_n(t)}^{\infty} \mu(t, a)\rho(t, a) da \\ &= \rho(t, A_n(t))(1 - A_n'(t)) - \mu_1(x_1(t))x_1(t). \end{aligned}$$

Similarly, for $i = 2, \dots, n$, we have

$$x_i'(t) = \rho(t, A_{i-1}(t))(1 - A_{i-1}'(t)) - \rho(t, A_i(t))(1 - A_i'(t)) - \mu_i(x_i(t))x_i(t).$$

Therefore, we obtain the closed system:

$$\begin{cases} x_1'(t) = \rho(t, A_n(t))(1 - A_n'(t)) - \mu_1(x_1(t))x_1(t), \\ x_i'(t) = \rho(t, A_{i-1}(t))(1 - A_{i-1}'(t)) - \rho(t, A_i(t))(1 - A_i'(t)) - \mu_i(x_i(t))x_i(t). \end{cases} \quad (5.2)$$

Note also that x_1 is decoupled from other equations in system (2).

With appropriate assumptions on b and μ_i , we can obtain the non-negativeness, boundedness and the existence of the global compact attractor.

We now address the *practical problem: How to calculate $A_i(t)$ and $\rho(t, A_i(t))$ from the available data?* To answer this question, we let $\tau_i(t)$ represent the length of time that a tick is developed at time t into the $(i + 1)$ -stage from a tick at the previous i -stage at time $t - \tau_i(t)$. Much of the qualitative analysis requires the condition

$$1 - \tau_i'(t) \geq 0. \quad (5.3)$$

It is important, for resolving the above practical problem, that we note $\tau_i(t)$ can be approximated from lab data. An illustration is given in Fig. 5.2, see also [22–24] for some of the lab data discussions.

Equally importantly, from the biological interpretations between maturation age and chronological ages, we can calculate $A_i(t)$ iteratively from $\tau_i(t)$ using the following formula (formula (9) in [39]):

$$A_i(t) = \sum_{j=2}^i \tau_j \left(t - \sum_{k=j+1}^i \tau_k \left(t - \sum_{l=k+1}^i \tau_l (t - \dots - \tau_{i-1}(t - \tau_i(t))) \right) \right).$$

With the above discussions, we can then substitute

$$\rho(t, A_i(t)) = \rho(t - A_i(t), 0)\alpha_i(t, t - A_i(t))$$

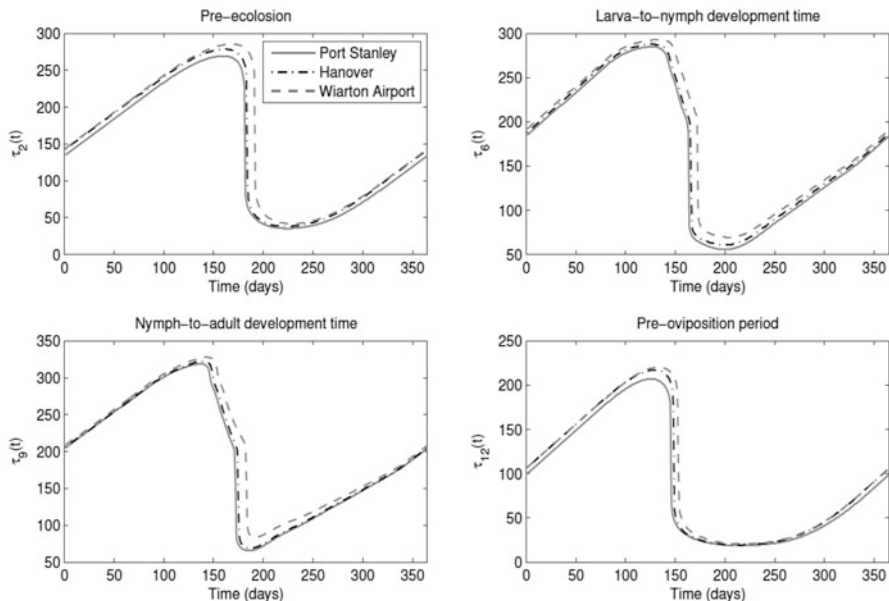


Fig. 5.2 Samples of time-varying development delays, using temperature data during 1971–2000, in Port Stanley, Hanover and Warton Airport weather stations (Figure is taken from [39])

to the equation (5.2) coupled with the reproduction condition

$$\rho(t, 0) = b(x_n(t))$$

to get a closed system. Here $\alpha_i(t, t - A_i(t))$ ($i = 2, \dots, n$) can now be calculated and represents the density-dependent survival probability of an egg who was born at time $t - A_i(t)$ and is able to live until time t when the egg matures (fully) to the i th stage.

5.3.2 The Ecological Threshold: Calculating Future Generation of Egg-Laying Females

To answer the question whether the population can grow and establish in the environment, we linearize the system at the zero solution to check if the population will undergo exponential growth from a small population. This leads to the introduction of the basic reproduction number R_0 .

In particular, the linearized system at the zero solution has a one-dimensional decoupled subsystem

$$x_1'(t) = a(t)x_1(t - A_n(t)) - \mu_1(0)x_1(t),$$

with $a(t) = b'(0)\alpha_n(t, t - A_n(t))(1 - A'_n(t))$ being the change rate of egg-laying females at time t that depends on the number of egg-laying females at time $t - A_n(t)$.

To define the basic reproduction number, we examine the future generation of egg-laying female ticks. We assume that

$$h(t) := t - A_n(t) \text{ is a strictly increasing function of } t.$$

Integration yields

$$x_1(t) = \int_{-\infty}^t e^{-\mu_1(0)(t-s)} a(s)x_1(s - A_n(s))ds.$$

This allows us to look at the number of newly generated egg-laying females per unit time at time t , from an initial introduction of the egg-laying females with an initial distribution of $x(s), s \in R$ (Fig. 5.3).

More specifically, for a fixed time t , the cohort of egg-laying females will produce some newborns who will eventually become egg-laying females at the future time

$$h^{-1}(t) := \tilde{t}, \text{ where } h(\tilde{t}) = \tilde{t} - A_n(\tilde{t}).$$

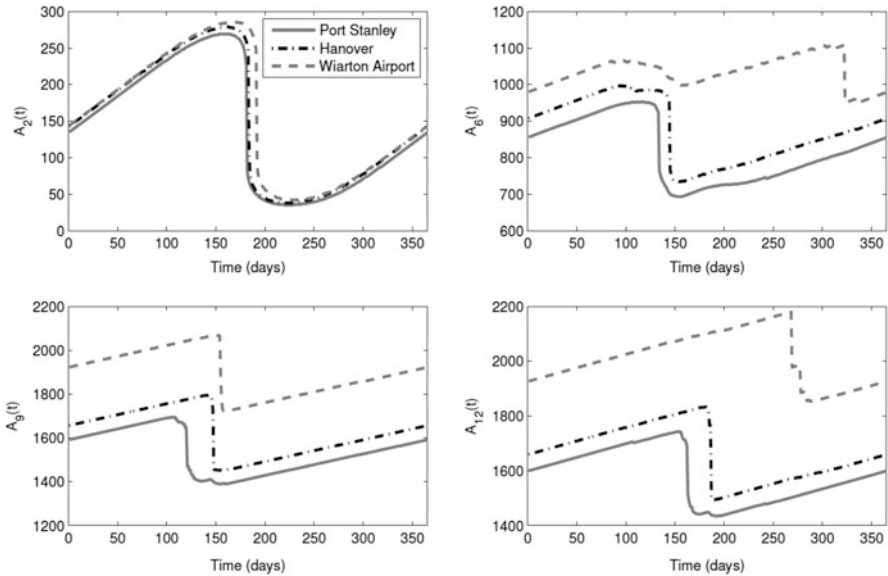


Fig. 5.3 Calculation of $A_{i-1}(t)$ and $A_i(t)$, the time-dependent minimum and maximum ages of those individuals who are developing within the specific i th stage. The calculations are based on the time-varying development delays for the period 1971–2000, in Port Stanley, Hanover and Warton Airport weather stations (Figure is taken from [39])

At this future time, we have

$$\frac{d}{dt}x_1(\tilde{t}) = \frac{d}{d\tilde{t}}x_1(\tilde{t})\frac{d\tilde{t}}{dt} = [a(\tilde{t})x_1(h(\tilde{t})) - \mu_1(0)x_1(\tilde{t})]\frac{1}{1 - A'_n(\tilde{t})}.$$

We write

$$\frac{d}{dt}x_1(\tilde{t}) = [a(h^{-1}(t))x_1(t) - \mu_1(0)x_1(h^{-1}(t))]\frac{1}{1 - A'_n(h^{-1}(t))}.$$

That is, the number of newly generated egg-laying females per unit time at time t is given by $y(t) = c(t)x_1(t)$ with

$$c(t) := a(h^{-1}(t))/(1 - A'_n(h^{-1}(t))).$$

Multiplying $x_1(t) = \int_{-\infty}^t e^{-\mu_1(0)(t-s)}a(s)x_1(s - A_n(s))ds$ by $c(t)$ gives

$$\begin{aligned} y(t) &= c(t) \int_{-\infty}^t e^{-\mu_1(0)(t-s)} \frac{a(s)}{c(s - A_n(s))} y(s - A_n(s)) ds \\ &= \int_{A_n(t)}^{\infty} c(t) e^{-\mu_1(0)(t-h^{-1}(t-r))} y(t-r) dr \\ &= \int_0^{\infty} \mathcal{H}(t, r) y(t-r) dr \end{aligned}$$

with

$$\mathcal{H}(t, r) = \begin{cases} b'(0)\hat{\alpha}_n(h^{-1}(t))e^{-\mu_1(0)(t-h^{-1}(t-r))}, & r \geq A_n(t), \\ 0, & r < A_n(t). \end{cases}$$

Note that $\mathcal{H}(t, r)$ is a periodic function with respect to time t , i.e., $\mathcal{H}(t, r) = \mathcal{H}(t + \omega, r)$. Biologically, this means that at time t , only the cohort of egg-laying females who are still alive before time $t - A_n(t)$ is capable of reproducing eggs which will mature to new generation of egg-laying females.

It is now natural to introduce

$$\mathcal{C}_\omega := \{u : R \rightarrow R \text{ is continuous}, u(t + \omega) = u(t)\},$$

equipped with maximum norm $\|\cdot\|$, and let $\mathcal{L} : C_\omega \rightarrow C_\omega$ be defined by

$$(\mathcal{L}u)(t) = \int_0^{\infty} \mathcal{H}(t, r)u(t-r) dr.$$

One can then show that \mathcal{L} is strongly positive, continuous and compact on \mathcal{C}_ω . This is called the *next generation operator* [7]. The basic reproductive number is defined as the spectral radius of the linear integral operator

$$\mathcal{R}_0 = \rho(\mathcal{L}).$$

In [39], it was proved that when $\mathcal{R}_0 < 1$, the zero solution is locally asymptotically stable; when $\mathcal{R}_0 > 1$, the zero solution is unstable. The proof is based on an application of the Krein–Rutman Theorem.¹ We refer to [17, 33] for some earlier results about the threshold R_0 in our setting. The approach of [39] follows more of [1, 2, 36].

5.3.3 Numerical Calculation of the Threshold: The Mathematics Behind a Lyme Tick Risk Map

Not only the size of R_0 relative to the unity is important to evaluate whether the vector population can establish in the region, but also the value of this R_0 is important to estimate the initial growth rate of population since near the zero equilibrium the solution from a non-trivial initial value grows exponentially with the rate $\ln R_0$ if $R_0 > 1$. Therefore, if we are to apply the above theory in a practical context, it is important to develop algorithms for calculating R_0 .

One such algorithm was developed in [39] using the most intuitive discretization and integration. This algorithm links the calculation of \mathcal{R}_0 to the calculation of the spectral radius of a Leslie matrix in a periodic environment. In particular, to compute \mathcal{R}_0 numerically, we partition the interval $[0, \omega]$ into N (a large integer) subintervals of equal length. Set $t_i = (i - 1)\omega/N$ for $i = 1, 2, \dots, N$ and let $W_i = u(t_i)$. Then the problem of estimating \mathcal{R}_0 reduces to the calculation of the spectral radius of a Leslie matrix. Namely, we have the matrix eigenvalue problem of the form $\tilde{R}_0 W = XW$, where $W = (W_1, W_2, \dots, W_N)^T$, and \tilde{R}_0 is the spectral radius of a $N \times N$ positive matrix X . In this matrix, the (i, j) element is given explicitly and with a clear biological interpretation for each metric element.

The calculated R_0 values for different regions and under different observed and predicted environmental conditions can then be used to depict the tick reproduction map for *I. scapularis*, see [38, 39]. This can then be used to estimate the impact of predicted climate change on tick population dynamics [25], as illustrated in Fig. 5.4. We should mention a recent study [5] that shows how remote sensing data can be further used to increase the spatial detail for this Lyme disease risk mapping. This

¹In functional analysis, the Krein–Rutman theorem is a generalization of the Perron–Frobenius theorem to infinite-dimensional Banach spaces. It was proved by Krein and Rutman in 1948. The Krein–Rutman Theorem states that: Let X be a Banach space, and let $K \subset X$ be a convex cone such that $K - K$ is dense in X . Let $T : X \rightarrow X$ be a non-zero compact operator which is positive, meaning that $T(K) \subset K$, and assume that its spectral radius $\rho(T)$ is strictly positive. Then $\rho(T)$ is an eigenvalue of T with positive eigenvector, meaning that there exists $u \in K \setminus \{0\}$ such that $T(u) = \rho(T)u$.

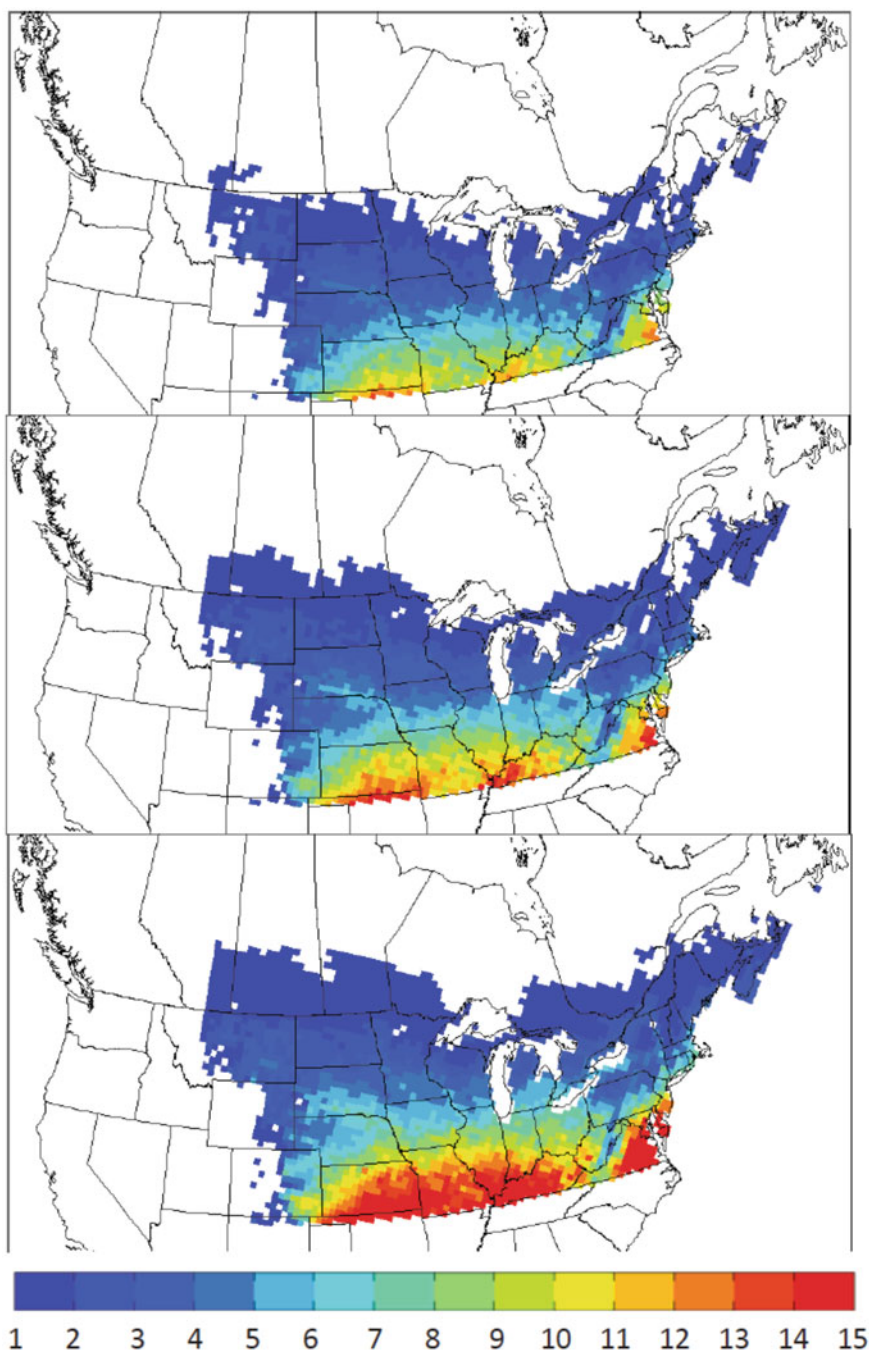


Fig. 5.4 Maps of values of R_0 in North America, estimated from climate observations (1971–2000: upper panel), and projected climate for 2011 to 2040 (middle panel) and for 2041 to 2070 (bottom panel). The color scale indicates R_0 values. Figure is taken from [25], and shows the northward expansion of the tick establishment due to climate warming. See [10] for a recent modelling study about the epidemic propagation speed and patterns in a wave-like environment as illustrated in the above maps

study also shows how well the risk map coincides with the number of ticks submitted to the Public Health Ontario, in the study area.

As another remark, we note that the equation for x_1 is de-coupled from the rest due to the use of the delay. However, for the purpose of Lyme disease risk projection, it is important to describe the density and variation of feeding nymphs and ticks in other stages since ticks in these stages are more involved in sharing the host for the Lyme pathogen transmission, and for human to get infection from the infected ticks. These densities can be described, using the formulation derived from Eq. (5.2), for $i = 2, \dots, n$, given below:

$$\begin{aligned} x'_i &= \alpha_{i-1}(t, t - A_{i-1}(t))b(x_1(t - A_{i-1}(t)))(1 - A'_{i-1}(t)) \\ &\quad - \alpha_i(t, t - A_i(t))b(x_1(t - A_i(t)))(1 - A'_i(t)) - \mu_i(x_i(t))x_i(t). \end{aligned}$$

5.4 Bird Migration Dynamics: Spatial Heterogeneity and Transition Delay

Structured population dynamics arises not only from temporally structured populations, but also spatially segregated populations. We illustrate this here with a model for bird migration. The model described is taken from a series of studies [3, 4, 12, 34] on avian influenza spread modelling. The central issue of this series of studies is seasonal bird migration dynamics and spatial-temporal distribution, and its implications for avian influenza spread patterns.

This series of studies has been guided by some satellite tracking data from the U.S. Geological Survey which recorded the migration path of a dozen bar-headed geese (from Mongolia to India). The data also shows that migration routes are often one-dimensional, as they tend to be funnelled into narrow pathways, often following coastlines or mountain ranges.

It is therefore natural that we start with the spatially explicit bird migration model using advection equations. Let x be the arc length along the continuum. Let $x_1 = 0$ be the summer breeding site, x_n be the winter feeding location and $x_i, i = 2, 3, \dots, n - 1$ be the stopover locations where birds stop for short periods to feed. Let l_i be the distance between the locations x_i and x_{i+1} and U_i be the mean flight velocity between these two locations, so that the time taken to fly between x_i and x_{i+1} will be

$$\tau_i = l_i / U_i.$$

The density $s(t, x)$ obeys the advection equation

$$\left(\frac{\partial}{\partial t} + U_i \frac{\partial}{\partial x} \right) s(t, x) = -\mu_i s(t, x).$$

Let $S_i(t)$ be the number of birds at location x_i . Then at time t , the rate of birds leaving patch x_i is $d_i(t)S_i(t)$, with $d_i(t)$ being the rate of outward migration from patch i . The rate of birds arriving into patch x_{i+1} is

$$U_i s(t, x_{i+1}) = d_i(t - \tau_i)S_i(t - \tau_i)\alpha_i(t).$$

Using integration along characteristics, one can obtain the following bird migration patchy model:

$$\begin{cases} S'_1(t) = p(t)b(S_1(t)) + \alpha_n d_n(t - \tau_n)S_n(t - \tau_n) - d_1(t)S_1(t) - \mu_1(t)S_1(t), \\ \quad \vdots \\ S'_i(t) = \alpha_{i-1}d_{i-1}(t - \tau_{i-1})S_{i-1}(t - \tau_{i-1}) - d_i(t)S_i(t) - \mu_i(t)S_i(t), 2 \leq i \leq n. \end{cases}$$

It is natural to choose the phase space $C := \Pi_{i=1}^n C([- \tau_i, 0])$.

To describe the qualitative behaviors of the model equation, we will need the following section on discrete dynamical systems.

5.4.1 Monotone Maps and Threshold Dynamics

We start with introducing a few concepts:

- Let E be an ordered Banach space with positive cone P such that $\text{int}(P) \neq \emptyset$. For $x, y \in E$, we write $x \geq y$ if $x - y \in P$; $x > y$ if $x - y \in P \setminus \{0\}$ and $x \gg y$ if $x - y \in \text{int}P$.
- Let $U \subset E$ and $f : U \rightarrow U$ be a given continuous map. We say that f is monotone if $x \geq y$ implies $f(x) \geq f(y)$; strongly monotone if $x > y$ implies $f(x) \gg f(y)$.
- $f : U \rightarrow U$ is said to be strictly subhomogeneous if $f(\lambda x) > \lambda f(x)$ for any $x \in U$ with $x \gg 0$ and $\lambda \in (0, 1)$.

In terms of the bird migration model, we define $f : \Pi_{i=1}^n C([- \tau_i, 0]) \rightarrow \Pi_{i=1}^n C([- \tau_i, 0])$ by $f(\phi) = (S_i(\phi)_\omega)_{i=1}^n$ for the period (ω) -operator of the model. We also define $P = \Pi_{i=1}^n C([- \tau_i, 0]; \mathbb{R}^+)$. Then we have

- E is an ordered Banach space with positive cone P ;
- $f : P \rightarrow P$ is monotone; S^m is strongly monotone when $m\omega \geq \max \tau_i$;
- Assume all $p(t)$ and $d_i(t)$ are positive and ω -periodic and positive (this assumption can be weakened), and $b(0) = 0$ and $b : [0, \infty) \rightarrow [0, \infty)$ being C^1 and strictly monotone. Therefore for any integer m such that $m\omega > \tau$, $S^m : U \rightarrow U$ is strongly monotone and precompact (i.e., the image of a bounded set in U under S^m is contained in a compact set).

We then have the following general result on threshold dynamics of monotone maps [41]:

Theorem 5.1 (Threshold Dynamics Theorem) *Let $f : P \rightarrow P$ be given such that*

- (H1) *f is strongly monotone and strictly subhomogeneous;*
- (H2) *f^m is precompact for some positive integer m , and every positive orbit $\{f^n(x); n = 1, 2, \dots\}$ is bounded;*
- (H3) *$f(0) = 0$ and $Df(0)$ is compact and strongly positive.*

Then the following threshold dynamics holds:

- (TD1) *if $\rho(Df(0)) \leq 1$, then every positive orbit in P converges to 0;*
- (TD2) *if $\rho(Df(0)) > 1$, then there exists a unique fixed point $u^* \gg 0$ in P such that every positive orbit in $P \setminus \{0\}$ converges to u^* .*

To apply this for the bird migration model, we define R_0 as $\rho(Df(0))$ with f defined as above, then we conclude that if $R_0 \leq 1$, then $S_i(\phi) \rightarrow 0$ as $t \rightarrow \infty$ for all $\phi \in P$; if $R_0 > 1$, then the system has a unique positive ω -periodic solution such that every solution of the system starting from $P \setminus \{0\}$ converges to this positive periodic solution. Calculation of R_0 was performed in [35].

Despite this straightforward application of a general threshold dynamics theorem, the established global asymptotical stability of a unique positive solution is significant for the purpose of modelling bird influenza infection dynamics since this global stability result gives us the theoretical foundation to estimate the initial condition for bird influenza epidemic models. Namely, the theoretical result ensures that starting from an arbitrary initial condition, the solution is eventually stabilized at a unique positive periodic solution (assuming the threshold is larger than 1). This unique periodic solution, easily obtained through numerically simulating the bird migration model with an arbitrarily given initial data of birds for a sufficient period of time, gives the initial susceptible birds at the onset of a bird influenza outbreak. The long-term *Limiting* behaviors of an ecological model (bird migration dynamics) give the *Initial Condition* of the epidemic model for a considered bird flu outbreak.

5.5 Global Spread and Disease Epidemiology

The spread of avian flu with a particular strain such as H5N1 combines interactions between local and long-range dynamics. The local dynamics involve interactions/cross-contamination of domesticated birds, local poultry industry and temporary migratory birds. The nonlocal dynamics involve the long-range transportation of industrial material and poultry, and the long-range bird migrations (Fig. 5.5).

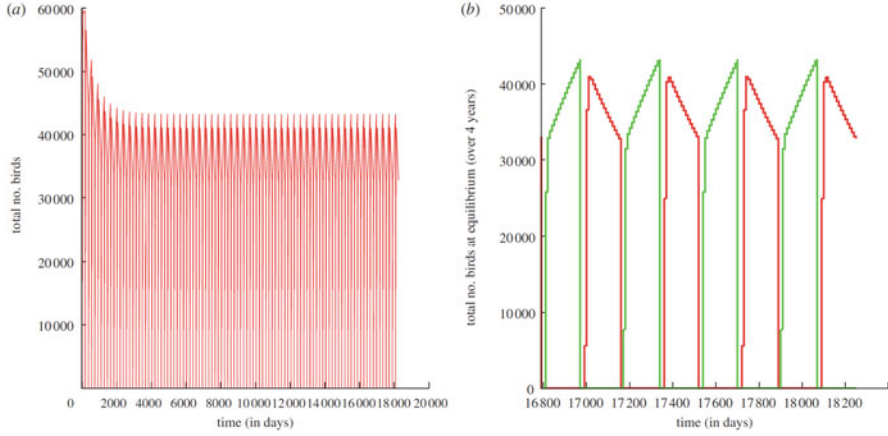


Fig. 5.5 The study [3] chose to focus on bar-headed geese as example species due to their vulnerability to the avian influenza H5N1, as highlighted by the death toll in the 2005 Qinghai Lake outbreak. The study used some satellite tracking data of bar-headed geese to extract the information of arrival, the length of stay and the date and time since deployment, as well as the average distance and time of flight between the current and previous stop sites. This information was then used to parameterize the model and to produce the simulation results showing here. The simulation shows that over a simulation of 50 years, the bird population reaches positive periodic solution. This periodic state is reached for all non-trivial initial conditions, illustrating the theoretically established global asymptotic stability of a unique periodic solution of the model equation

To model the interaction of migratory birds and domestic poultry we must stratify the migratory birds by their disease status and need to add domestic poultry. We use a patch model, where we consider four representative patches: breeding ground (b), wintering ground (w), spring onward migration stop over (o) and fall migration, returning to the wintering ground, patch (r). Within each patch, we need to consider the migratory bird (subindex m) and domestic poultry (subindex p) populations, and both are needed to be stratified by their infection status, susceptible (s) and infected (i). Within each patch, we have the standard mass action for the disease transmission, and between patch we assume migration of the migratory birds. This yields the systems of differential equations for *Migratory Bird Dynamics*:

$$\begin{aligned}
 \dot{S}_m^b &= B_m(t, S_m^b) + \alpha_{rb}^s d_{rb}^s S_m^r(t - \tau_{rb}^s) - \beta_m^b S_m^b I_m^b - \beta_{pm}^b S_m^b I_p^b - d_{bo}^s S_m^b - \mu_{ms}^b S_m^b, \\
 \dot{I}_m^b &= \alpha_{rb}^i d_{rb}^i I_m^r(t - \tau_{rb}^i) + \beta_{pm}^b S_m^b I_p^b - d_{bo}^i I_m^b - \mu_{mi}^b I_m^b, \\
 \dot{S}_m^o &= \alpha_{bo}^s d_{bo}^s S_m^b(t - \tau_{bo}^s) - \beta_m^o S_m^o I_m^o - \beta_{pm}^o S_m^o I_p^o - d_{ow}^s S_m^o - \mu_{ms}^o S_m^o, \\
 \dot{I}_m^o &= \alpha_{bo}^i d_{bo}^i I_m^b(t - \tau_{bo}^i) + \beta_{pm}^o S_m^o I_p^o - d_{ow}^i I_m^o - \mu_{mi}^o I_m^o, \\
 \dot{S}_m^w &= \alpha_{ow}^s d_{ow}^s S_m^o(t - \tau_{ow}^s) - \beta_m^w S_m^w I_m^w - \beta_{pm}^w S_m^w I_p^w - d_{wr}^s S_m^w - \mu_{ms}^w S_m^w, \\
 \dot{I}_m^w &= \alpha_{ow}^i d_{ow}^i I_m^o(t - \tau_{ow}^i) + \beta_{pm}^w S_m^w I_p^w - d_{wr}^i I_m^w - \mu_{mi}^w I_m^w, \\
 \dot{S}_m^r &= \alpha_{wr}^s d_{wr}^s S_m^w(t - \tau_{wr}^s) - \beta_m^r S_m^r I_m^r - \beta_{pm}^r S_m^r I_p^r - d_{rb}^s S_m^r - \mu_{ms}^r S_m^r, \\
 \dot{I}_m^r &= \alpha_{wr}^i d_{wr}^i I_m^w(t - \tau_{wr}^i) + \beta_{pm}^r S_m^r I_p^r - d_{rb}^i I_m^r - \mu_{mi}^r I_m^r
 \end{aligned}$$

coupled with the system for *Poultry Population Dynamics*:

$$\begin{aligned} \dot{I}_p^b &= \beta_p^b(N_p^b - I_p^b)I_p^b + \beta_{mp}^b(N_p^b - I_p^b)I_m^b - \mu_p^b I_p^b, \\ \dot{I}_p^o &= \beta_p^o(N_p^o - I_p^o)I_p^o + \beta_{mp}^o(N_p^o - I_p^o)I_m^o - \mu_p^o I_p^o, \\ \dot{I}_p^w &= \beta_p^w(N_p^w - I_p^w)I_p^w + \beta_{mp}^w(N_p^w - I_p^w)I_m^w - \mu_p^w I_p^w, \\ \dot{I}_p^r &= \beta_p^r(N_p^r - I_p^r)I_p^r + \beta_{mp}^r(N_p^r - I_p^r)I_m^r - \mu_p^r I_p^r. \end{aligned}$$

In [12], a threshold, given in terms of the spectral radius $r(T_I)$ of the time T -solution operator of the linearized periodic system of delay differential equations at the disease-free equilibrium, was theoretically derived. A closed form in terms of the model parameters is possible in some special cases. It was then shown that this threshold determines whether disease persists or not: the non-trivial disease-free equilibrium is globally asymptotically stable once the threshold is below 1; if the threshold is larger than 1, then the disease is uniformly strongly persistent in the sense that there exists some constant $\eta > 0$, which is independent of the initial conditions, such that, for each $c = b, o, w, r$,

$$\liminf_{t \rightarrow \infty} I_m^c(t) \geq \eta, \quad \liminf_{t \rightarrow \infty} I_p^c(t) \geq \eta.$$

This result is based on the persistence theory discussed below: Let X be a complete metric space with the metric d . Let X_0 and ∂X_0 be open and closed subsets of X , respectively, such that $X_0 \cap \partial X_0 = \emptyset$ and $X = X_0 \cup \partial X_0$. Let $S : X \rightarrow X$ be a continuous map with $S(X_0) \subset X_0$. We introduce a few concepts here:

- S is uniformly persistent with respect to $(X_0, \partial X_0)$ if there exists $\eta > 0$ such that for any $x \in X_0$, $\liminf_{n \rightarrow \infty} d(S^n x, \partial X_0) \geq \eta$;
- A nonempty invariant set $M \subset \partial X_0$ is isolated if it is the maximal invariant set in some neighbourhood of itself;
- An isolated set $A \subset \partial X_0$ is chained to an isolated set $B \subset \partial X_0$, written as $A \rightarrow B$, if there exists a full orbit through some $x \notin A \cup B$ such that $\omega(x) \subset B$ and $\alpha(x) \subset A$;
- A finite sequence $\{M_1, \dots, M_k\}$ of invariant sets is called a chain if $M_1 \rightarrow M_2 \rightarrow \dots \rightarrow M_k$. The chain is called a cycle if $M_k = M_1$.

We refer to [16, 32, 41] for more systematic treatments of the persistence theory, but the theorem below is what was used in [12]:

Theorem 5.2 *Assume that*

- $S : X \rightarrow X$ has a global attractor;
- Let A_δ be the maximal compactor invariant set of S in ∂X_0 . $\tilde{A}_\delta = \cup_{x \in A_\delta} \omega(x)$ has an isolated and acyclic covering $\cup_{i=1}^k M_i$ in ∂X_0 (that is, $A_\delta \subset \cup_{i=1}^k M_i$, where M_1, M_2, \dots, M_k are pairwise disjoint and compact and isolated invariant sets of S in ∂X_0 such that each M_i is also an isolated invariant set in X , and no subset of the M_i 's forms a cycle for $S_\delta = S|_{A_\delta}$ in A_δ).

Then S is uniformly persistent if and only if for each M_i , we have $W^s(M_i) \cap X_0 = \emptyset$, where $W^s(M_i) = \{x, x \in X, \omega(x) \neq \emptyset, \omega(x) \subset M_i\}$ is the stable set of M_i .

The persistence theory, when applied to the above avian influenza model, concludes that the avian influenza spread persists in the sense that both infected migratory and domestic poultry birds will remain strictly larger than a unspecified constant. Numerical simulations have indicated that the pattern of disease persistence can be quite complicated, and is not necessarily fluctuating regularly as an annual cycle. This raises an issue about the estimation of inter-pandemic and intra-pandemic intervals. There seems to be no theoretical framework that has been applied to address this important practical issue.

Lyme disease dynamics was also considered in the study [20] with standard stratification of tick populations by the infection status and by tick development stages. The first such model is to assume the development rate is exponentially distributed (and time-independent). This leads to an epidemic system of ordinary differential equations with periodic coefficients. This formulation facilitates refined persistence results about the periodicity of persistent disease spread patterns. It remains to see whether the introduction of periodically varying delay will make the model analysis much more complicated. From the public health prospective, it would be desirable to establish not only the Lyme tick risk map, but Lyme disease risk map—in terms of the threshold values of the epidemic models.

5.6 Summary

In this chapter, we consider modelling environment impact on vector-borne infection dynamics using delay differential equations. This is based on a series of sections which introduce a general framework using delay differential equations, and relevant results on global dynamics and persistence about the implication of environment changes for the interplay of vector species ecology and vector-borne disease epidemiology. General results are illustrated by applications to avian influenza and Lyme disease spread.

We first consider spatiotemporal patterns of bird migration and seasonal stage-activities of tick populations with focus on model formulation and parameterization. Here, we derive, from first-order hyperbolic partial differential equations, prototype delay differential equations describing the spatial dynamics of migratory birds and stage-structured tick population dynamics. The periodicity in model coefficients and delays arises due to seasonality. We illustrate how surveillance, laboratory, field study and satellite/remote sensing data can be integrated to parameterize the models.

We then use the model to describe spatiotemporal patterns of bird migration and seasonal stage-activities of tick populations: global dynamics. We describe the phase space and general framework for the qualitative behaviors of delay differential equations with periodic coefficients/delays and examine the global dynamics of

the model systems using the monotone dynamical systems theory. We discuss the impact of climate changes on vector establishment risks.

We finally consider avian influenza spread and Lyme disease epidemics: persistence and irregular infection dynamics. Here we stratify the vector populations in terms of their infection status (susceptible or infectious) and obtain corresponding epidemic models. We introduce the concept and general results of infection persistence and threshold phenomena, and we discuss further challenges depicting the inter-epidemics and intra-epidemic intervals.

There are a number of challenging issues for the modelling, parameterization, dynamic behavior analysis and numerics of structured population models arising from vector-borne disease infection risk assessment consideration. Such a model framework seems to be appropriate given the important role of the physiological or geographical status of the vector species in defining the vector population dynamics and the disease spread. The reduction from the structured population models to delay differential equations is both mandated and facilitated by the fact that surveillance data is normally collected for the vector in a certain physiological stage or a geographic location, and this reduction also renders the well-established dynamical systems theory of delay differential equations applicable to considering some important ecological and epidemiological systems.

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