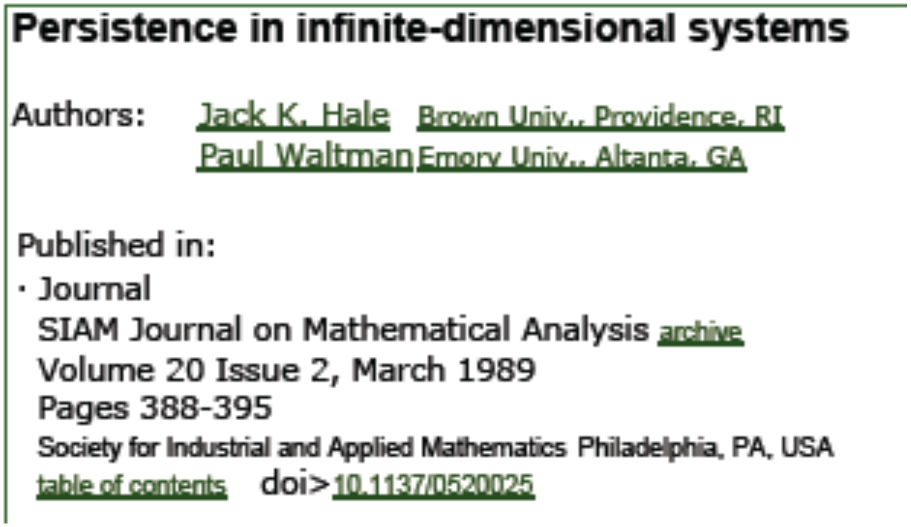
Hale-Waltman’s persistence theory applied to avian influenza spread



Persistence in infinite-dimensional systems

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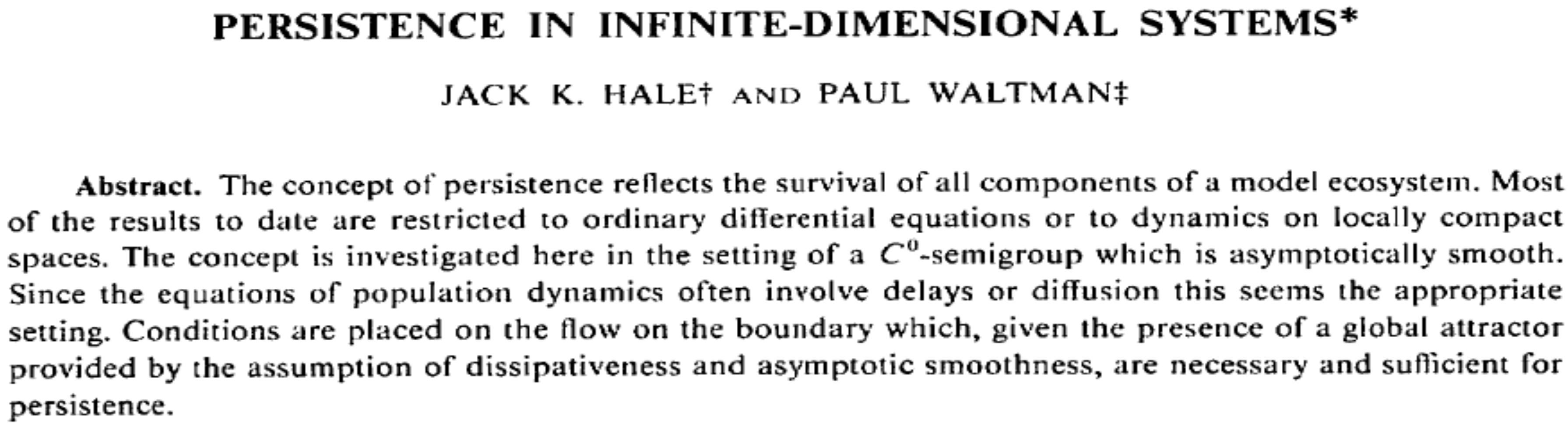
- Hale-Waltman’s theory on persistence of infinite dimensional dynamical systems provides a general geometric framework to address an important issue in biology;
- This theory, when applied to any specific biological system, often provides the sharpest condition for extinction/persistence, which coincides with the threshold phenomena observed in epidemiology;
- We use a delay differential system with periodic coefficients arising from bird immigration and avian influenza spread to demonstrate the effectiveness of Hale-Waltman’s theory.
- We also discuss remaining challenges relevant to more delicate issues of persistent infection, specially the issue of predictability of inter-epidemic duration.



PERSISTENCE IN INFINITE-DIMENSIONAL SYSTEMS*

JACK K. HALE† AND PAUL WALTMAN‡

Abstract. The concept of persistence reflects the survival of all components of a model ecosystem. Most of the results to date are restricted to ordinary differential equations or to dynamics on locally compact spaces. The concept is investigated here in the setting of a C^0-semigroup which is asymptotically smooth. Since the equations of population dynamics often involve delays or diffusion this seems the appropriate setting. Conditions are placed on the flow on the boundary which, given the presence of a global attractor provided by the assumption of dissipativeness and asymptotic smoothness, are necessary and sufficient for persistence.

The concept of persistence reflects the survival of all components of a model ecosystem. Most of the results to date are restricted to ODEs or to dynamics on locally compact spaces. The concept is investigated here in the setting of a C^0-semigroup which is asymptotically smooth. Since the equations of population dynamics often involve delays or diffusion this seems the appropriate setting. Conditions are placed on the flow on the boundary which, given the presence of a global attractor provided by the assumption of dissipativeness and asymptotic smoothness, are necessary and sufficient for persistence.

see, for example, Samanta [26] for a nonautonomous epidemic model. Let a metric space Y be the closure of an open set Y^0, so that $Y = Y^0 \cup \partial Y^0$, where ∂Y^0 is the boundary of Y^0. Let $T(t)$ be a C^0-semigroup on Y satisfying

$$T(t) : Y^0 \to Y^0, \quad T(t) : \partial Y^0 \to \partial Y^0. \tag{5.2}$$

Assume that the restricted semiflow has the global attractor A_∂, and assume that

$$\tilde{A}_\partial = \bigcup_{x \in A_\partial} \omega(x),$$

where $\omega(x)$ is the ω-limit set of x. Then we have the following result from Hale and Waltman [15].

THEOREM 5.1 (Hale and Waltman). *Suppose that* $T(t)$ *satisfies* (5.2) *and that*

(i) *there is a* $t_0 \geq 0$ *such that* $T(t)$ *is compact for* $t > t_0$;

(ii) $T(t)$ *is point dissipative in* Y;

(iii) $\tilde{A}_\partial$ *is isolated and has an acyclic covering* M.

Then $T(t)$ *is uniformly persistent (i.e., there exists* $\eta > 0$ *such that, for any* $y \in Y^0$, $\liminf_{t\to\infty} d(T(t)y, \partial Y^0) \geq \eta$*) if and only if, for each* $M_i \in M$,

$$W^s(M_i) \cap Y^0 = \Phi. \tag{5.3}$$

Persistent Irregular Spatiotemporal Patterns of Vector-borne Disease Spread

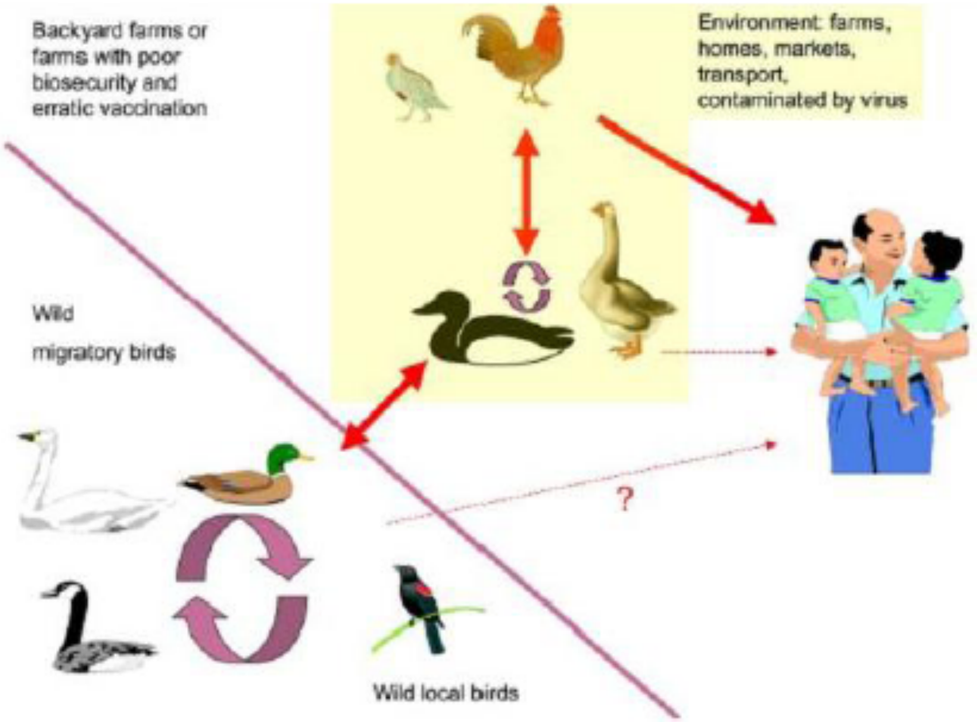
Avian influenza as an example (other applications include Lyme disease, West Nile virus, dengue and possibly Zika);

- Interplay between modeling informed insights of ecological and epidemiological processes and application driven mathematics;
- Simple models can capture essential biological details; and simple biological consideration may lead to complicated models;
- Modeling benefits from surveillance(satellite tracking and GIS technologies); and modeling may contributing to surveillance design;
- Issues: seasonality (Fourier analysis), spatial dispersal (patch models or PDEs), development and transition time (delays);
- Multi scales in changing environment/climate: from global scale of migration to the in-host level of cross-immunity;

The Ecology and Epidemiology of H5N1

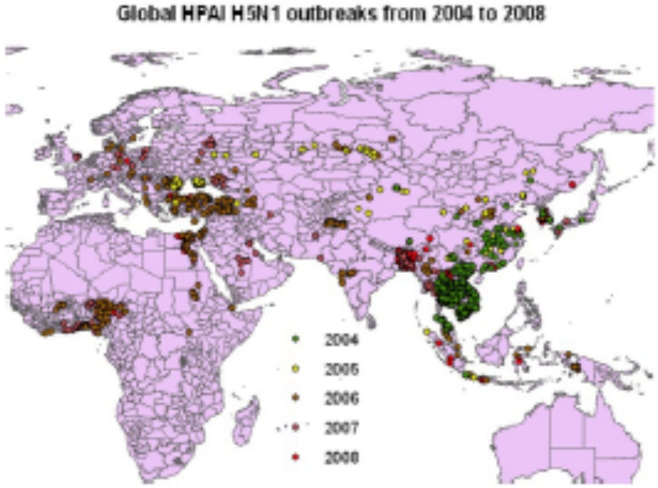
- Influenza viruses are isolated from a wide range of hosts. Types (A, B, C) are based on antigenic differences of gene products.
- Avian influenza was identified first in Italy (E. Perroncito, 1878) (caused by type A strain).
- Avian influenza viruses are (based on pathogenicity) categorized into two distinct groups: Highly Pathogenic Avian Influenza (HPAI) and LPAI.
- H5N1 strains was primarily isolated from a poultry farm of Scotland, UK during 1959. Rapid assortment ability boosted the continuous evolution, leading to spread to different continents since 1996-Asian outbreak.
- The HPAI H5N1 strain poses high risk for wild and domesticated animals, and could pose a threat to humans (WHO,CIDRP 2009).

Global spread and disease epideiology: transmission cycle

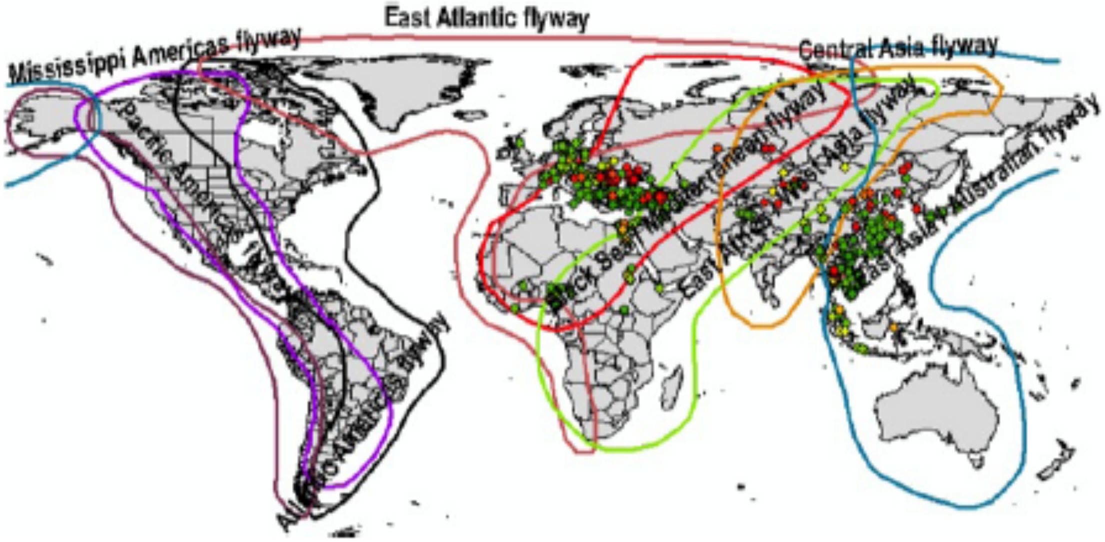


The spread of H5N1 combines interactions between local and long-range dynamics. The local dynamics involve interactions/ cross-contamination of domesticated birds, local poultry industry, and temporary migratory birds. The **nonlocal dynamics** involve the long-range transportation of industrial material and poultry, and the long-range bird migrations.

Migratory Route and H5N1 Global Spread

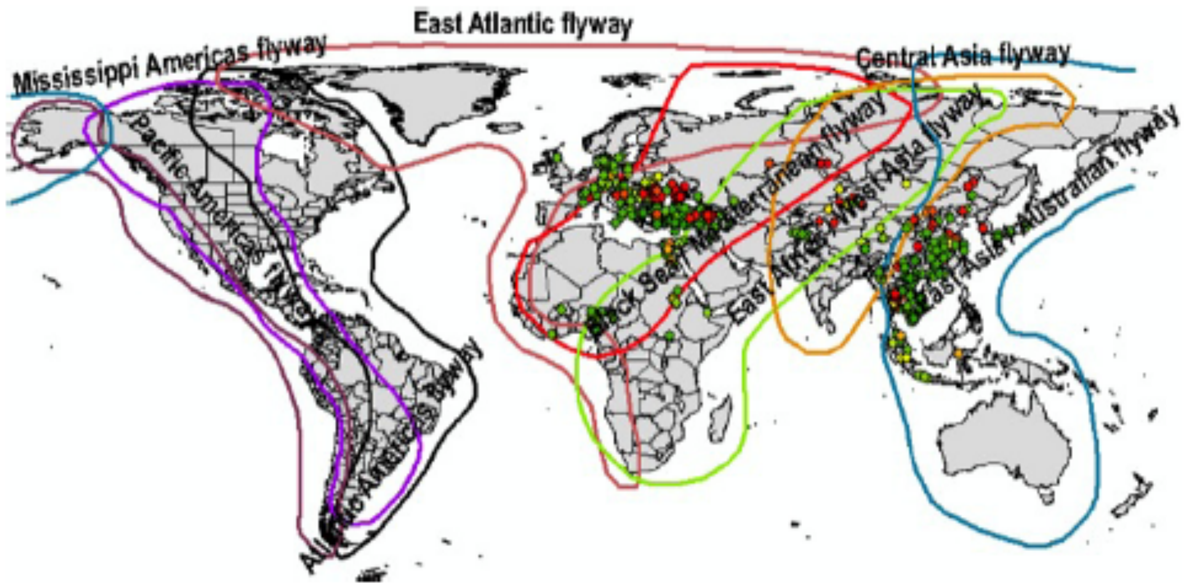


(a)



(b) Migration Route

Spatiotemporal Patterns of Migratory Birds



- Bird migration: a major biological phenomenon with billions of birds extending over distances from the Arctic to Antarctic using 8 broad overlaing corridors during annual cycles.
- A typical migration cycle involves different phases of biological activities and seasonality: **wintering, spring migration, breeding, maturation and autumn migration**.
- Migration routes are "interrupted" by stopovers, which provide the resting locations between the fights for refueling and for recovering from climatic and physiologic stress.

Surveillance Data of Migratory Birds: Satellites Tracking

Using satellites tracking, the U.S. Geological Survey recorded the migration path of a dozen Bar-headed geese.

- The migratory routes follow elongated closed curved routes.
- The birds breed in the summer in the northern part of their path (e.g., Mongolia).
- In the fall, they initiate their southward migration route, until reaching their wintering grounds (e.g., India).
- In the spring, they initiate a northward migration returning to their breeding location.
- Despite variable trajectories, the major stopover locations are common to most tracked flocks.

Model for Spatiotemporal Distributions of Migratory Birds

Assume that migration occurs along a one dimensional continuum, which could be a curve. Let $S_i(t)$ be the number of birds in patch i.

$$
\begin{cases}
S_1'(t) &= b(S_1(t),t) + \alpha_{2,1} d_{2,1}(t-\tau_1) S_2(t-\tau_1) \\
&\quad - d_{1,2}(t) S_1(t) - \mu_1(t) S_1(t), \\
&\vdots \\
S_i'(t) &= \alpha_{i-1,i} d_{i-1,i}(t-\tau_{i-1}) S_{i-1}(t-\tau_{i-1}) - d_{i,i+1}(t) S_i(t) \\
&\quad + \alpha_{i+1,i} d_{i+1,i}(t-\tau_i) S_{i+1}(t-\tau_i) - d_{i,i-1}(t) S_i(t) - \mu_i(t) S_i(t), \\
&\vdots \\
S_n'(t) &= \alpha_{n-1,n} d_{n-1,n}(t-\tau_{n-1}) S_{n-1}(t-\tau_{n-1}) \\
&\quad - d_{n,n-1}(t) S_n(t) - \mu_n(t) S_n(t).
\end{cases}
$$

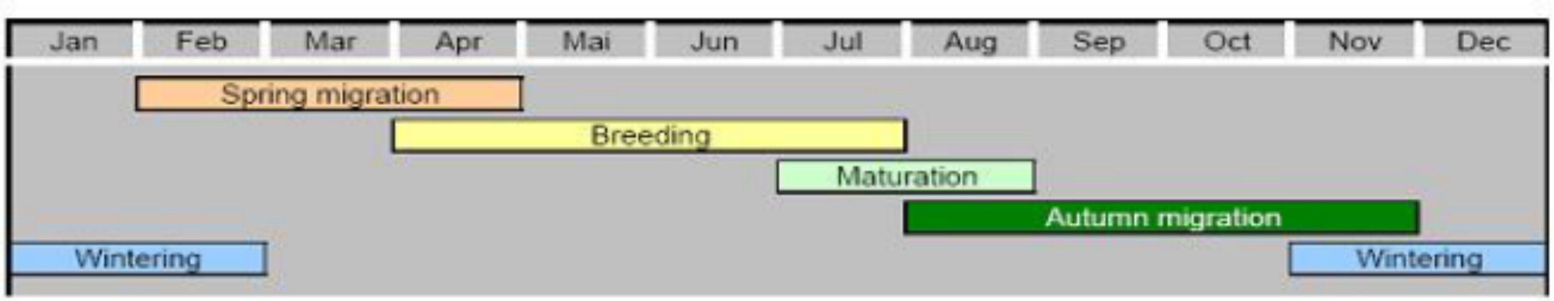
Nonnegativeness, boundedness and point dissipativeness and existence of global attractor all straightforward.

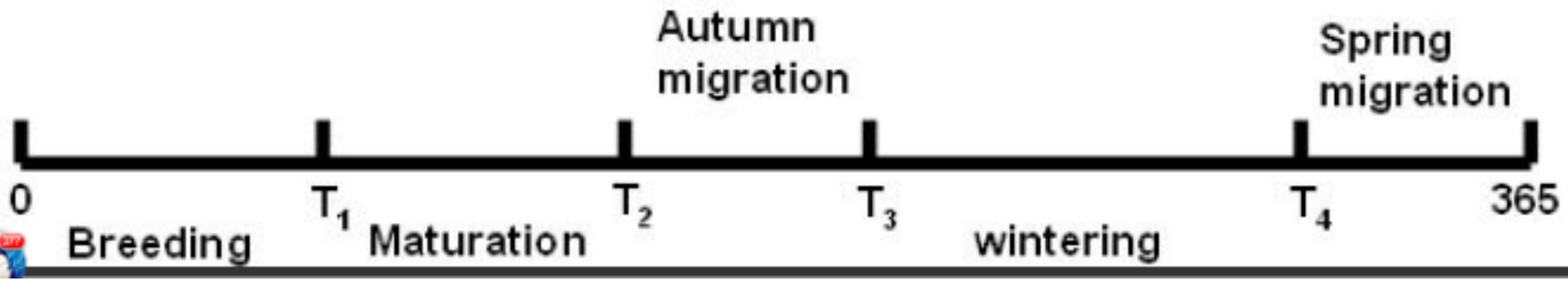
Challenge for Studying the Global Dynamics: Seasonality

- The model generates an order-preserving periodic process. This process however is NOT strongly order-preserving.

$$
\begin{aligned}
S_i'(t) \quad = \quad & \alpha_{i-1,i} d_{i-1,i}(t-\tau_{i-1}) S_{i-1}(t-\tau_{i-1}) - d_{i,i+1}(t) S_i(t) \\
& + \alpha_{i+1,i} d_{i+1,i}(t-\tau_i) S_{i+1}(t-\tau_i) - d_{i,i-1}(t) S_i(t) - \mu_i(t) S_i(t)
\end{aligned}
$$

Seasonal migrations





Seasonal Migration Null Space

Need to remove the subspace

$$\begin{aligned} M := \{\phi \in Y; \phi_i(0) = 0, 1 \leq i \leq n; \\ d_{i,i+1}(\theta_i)\phi_i(\theta_i) = 0 \text{ for } 1 \leq i \leq n-1, \theta_i \in [-\tau_i, 0]; \\ d_{i,i-1}(\theta_i)\phi_i(\theta_i) = 0 \text{ for } 2 \leq i \leq n, \theta_i \in [-\tau_{i-1}, 0]\}. \end{aligned}$$

- This, determined by the migration patterns, is a closed subspace of Y.
- Nontrivial initial data from M will give rise to a solution identically to zero for all future time.
- A natural phase space is Y/M.
- The model gives a periodic process in this quotient space.

Threshold Dynamics Theorem

Theorem: Suppose that $\lambda b(S_1, t) < b(\lambda S_1, t)$ when $\lambda \in (0, 1)$ and $S_1 > 0$. Then either

(i) every solution tends to zero as $t \to \infty$, or

(ii) the system has a T-periodic solution which is strictly positive (componentwise) at all times, and this solution attracts all solutions with initial data not in the subspace M;

(iii) conclusion (i) (resp. (ii)) holds if the spectral radius of $DF(0)$ is strictly less (resp. larger) than 1, where F is the Poincare operator which maps the initial datum to the state at time T.

Validation: Long-term Pattern

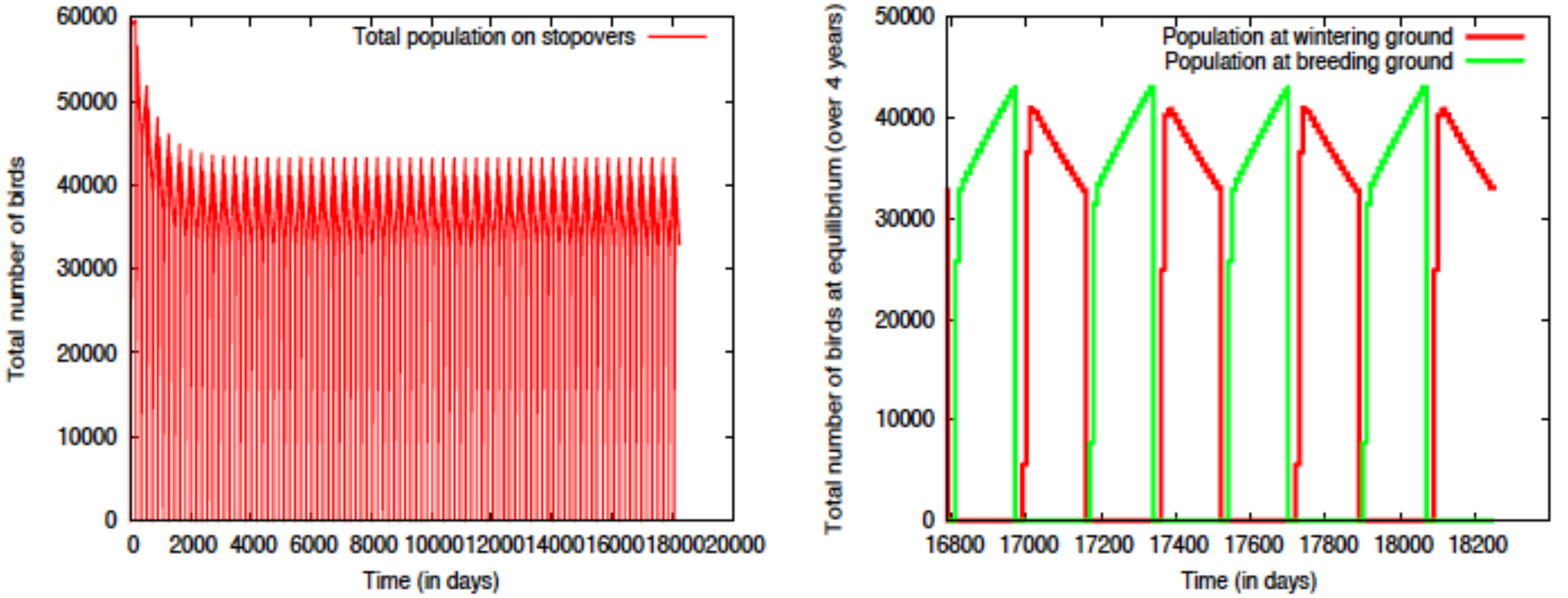


Figure: Simulation with satellite track data of the U.S. Geological Survey on Bar-headed geese.

Important: gives the Initial Condition of bird species population of the considered H5N1 Outbreak.

Disease Epidemiology: Dynamics and Spread

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.

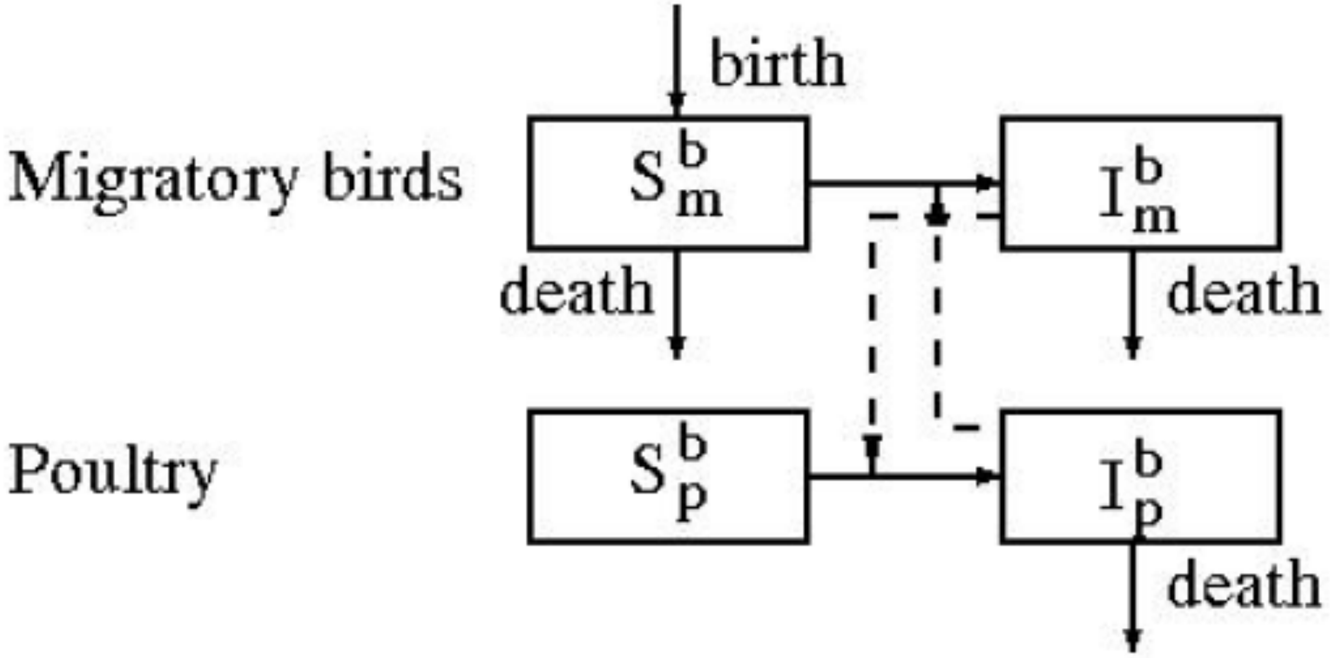
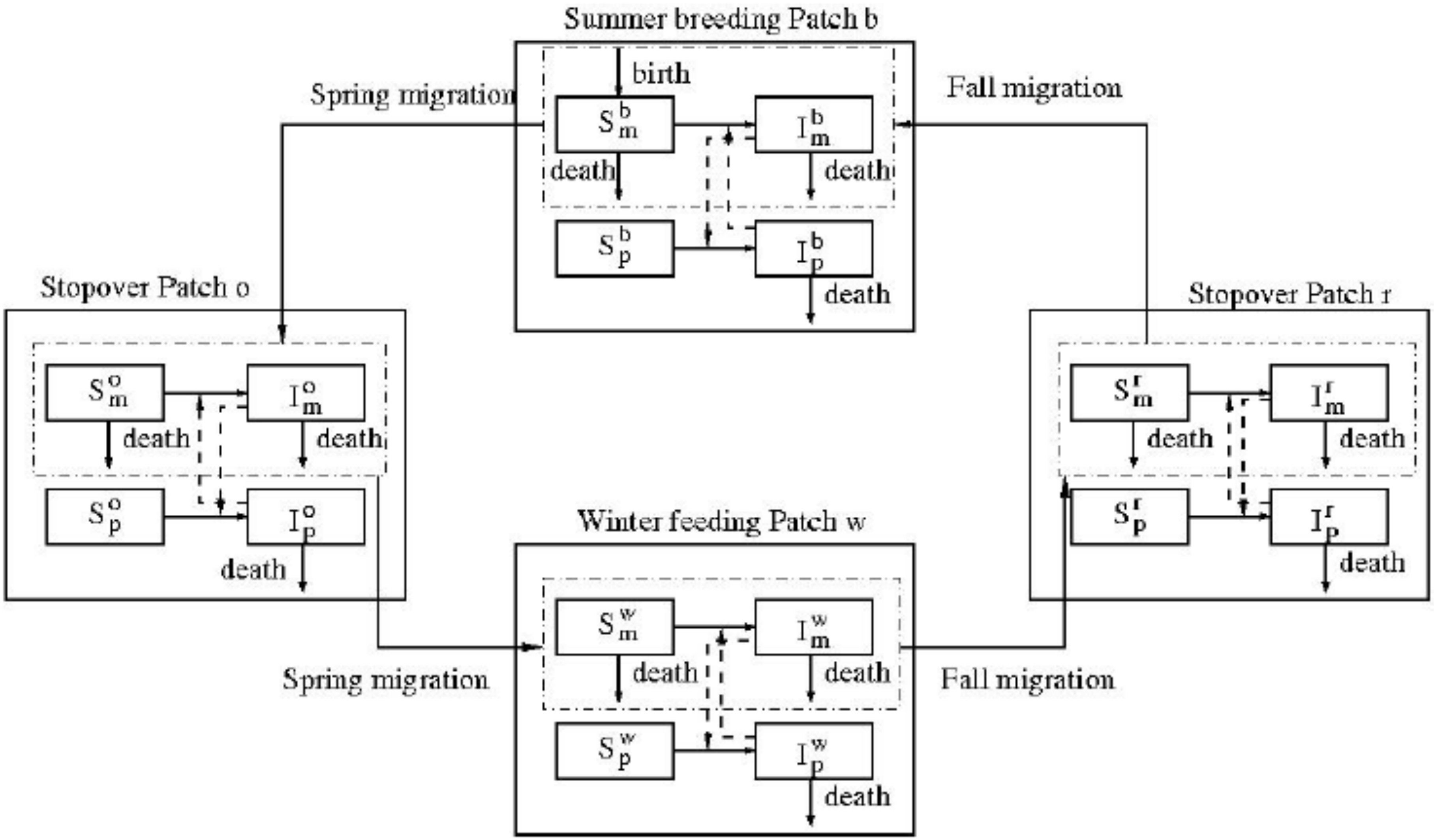


Figure: A schematic illustration of the local transmission cycle

Integration: global seasonal migration and local transmission via a meta-population



The Meta-Population Model

Migratory bird dynamics

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

Poultry population dynamics:

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

Disease Extinction and Persistence of the Full Model

Global Threshold Theorem: 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 a disease free equilibrium, can be theoretically derived, a close form in terms of the model parameters being possible.

- The nontrivial disease free equilibrium is global 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 $c = b, o, w, r$,

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

see, for example, Samanta [26] for a nonautonomous epidemic model. Let a metric space Y be the closure of an open set Y^0, so that $Y = Y^0 \cup \partial Y^0$, where ∂Y^0 is the boundary of Y^0. Let $T(t)$ be a C^0-semigroup on Y satisfying

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$$W^s(M_i) \cap Y^0 = \Phi. \tag{5.3}$$

Persistent non-periodic oscillation

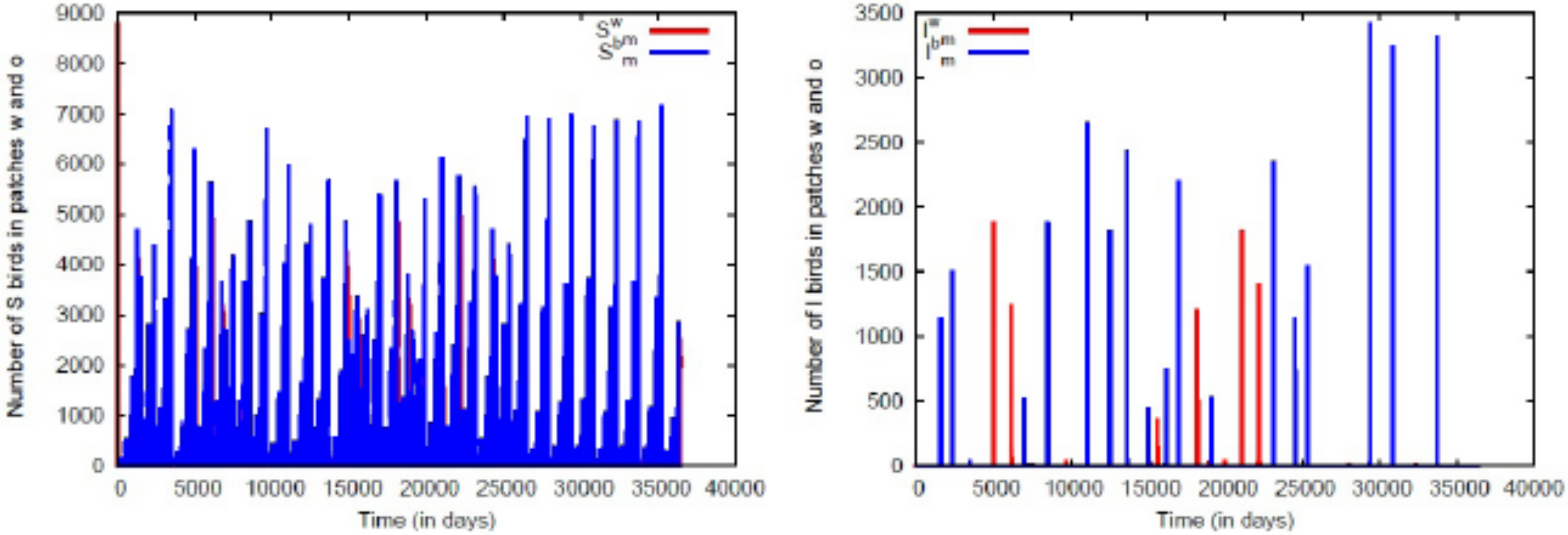

Figure: Number of (left) susceptible and (right) infected migratory birds over 100 years in the absence of poultry showing disease persistence and appearance of non-periodic oscillation of the number of migratory birds.

How to determine inter-epidemic intervals from the historical surveillance data?

References and other remarks

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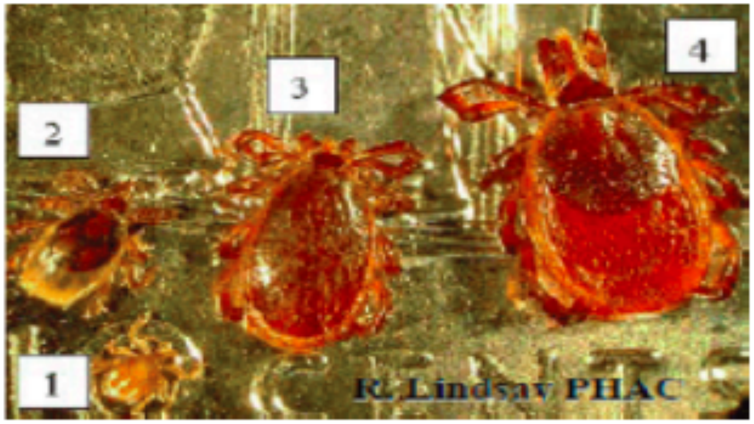
Lyme tick/disease in North American

Lyme disease spread involves complex interaction of a spirochete, multiple vertebrate hosts, and a vector with a two-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 is currently a public health concern.

Life Cycle of Ixodes Species

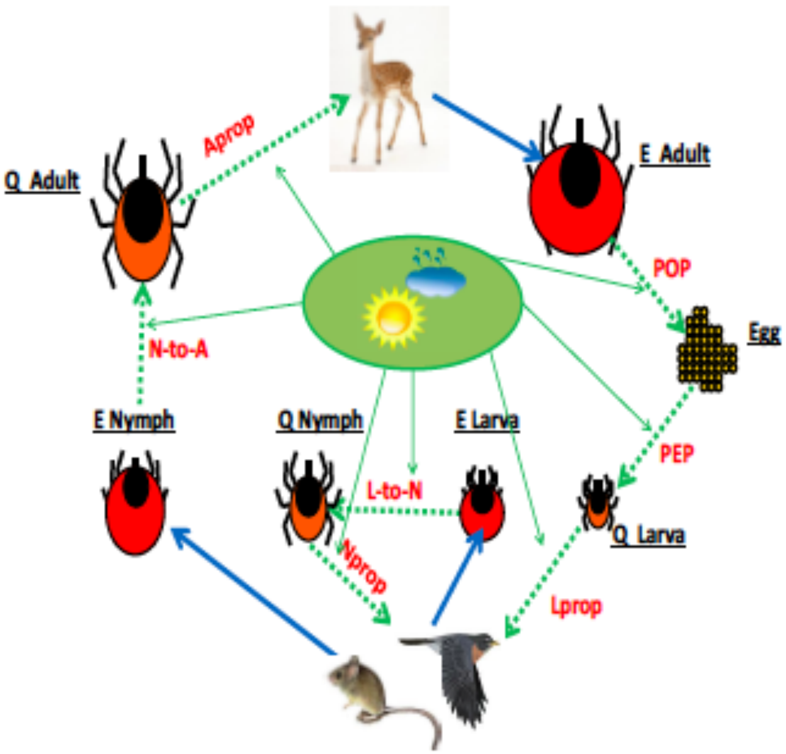


Figure: Tick life cycle, X. Wu, unpublished.

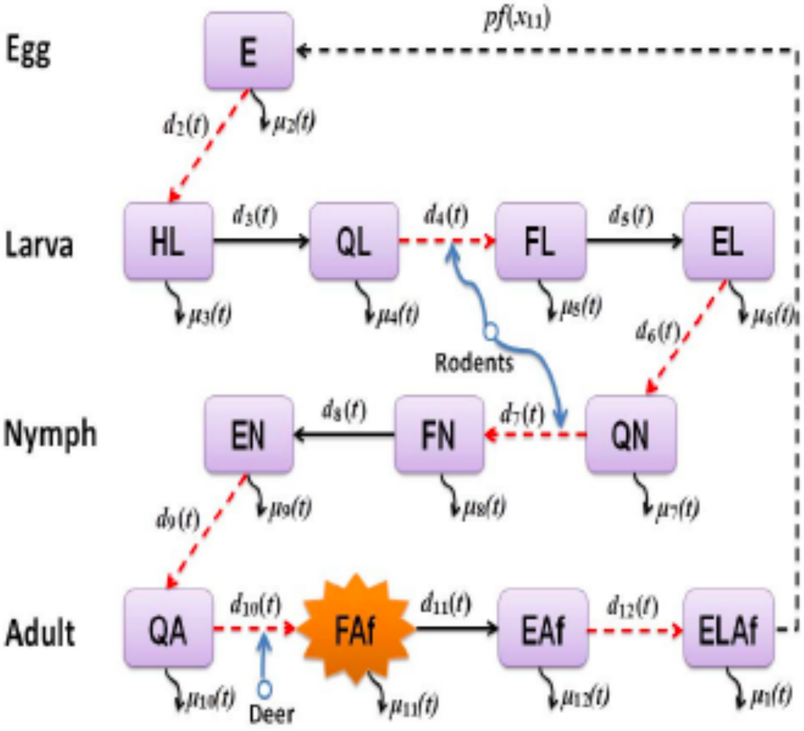
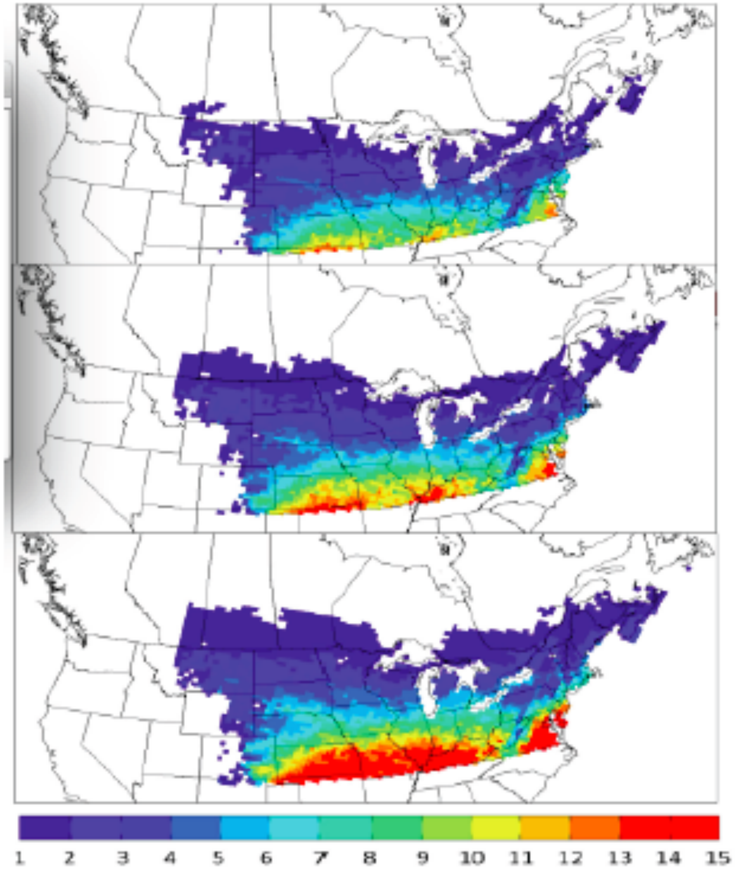


Figure: Stage-structured tick population dynamics diagram, X. Wu et al., JTB, 2013; EHP, 2014

Periodic ODEs or DDEs, parameters from many years of surveillance, lab test and field data, recent development on calculating the Floquet multipliers of periodic systems.

Lyme tick risk index R_0 and range expansion speed

- Left: The R_0 map for *I. scapularis*, X. Wu et al., JTB, 2013; Wu, Magpantay, Wu, Zou, MMAS 2015;
- Right: Maps of values of R_0: (1971-2000: upper panel), 2011-2040 (middle panel), 2041-2070 (bottom panel), Ogden et al., EHP, 2014.



General Setting for Epidemic Waves with a Changing Environment

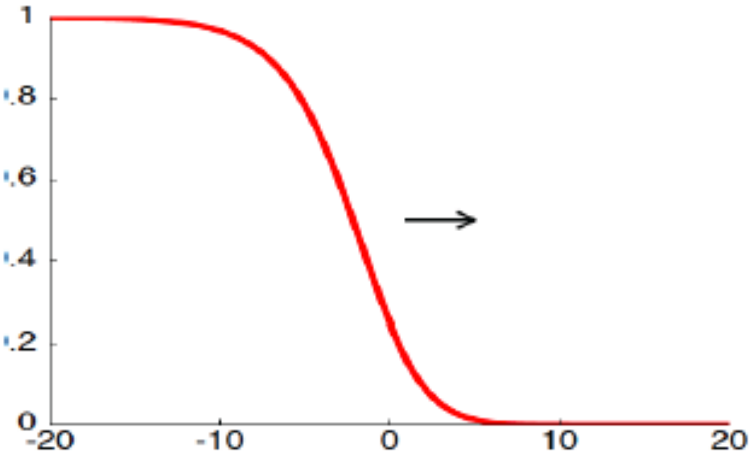


Figure: $u'(t) = ru(t)[1 - u(t)/K]$ and $u_t = Du_{xx} + ru(1 - u/K)$: Wavefronts ($u = \phi(x - ct)$) representing biological invasion and range expansion with constant diffusion, convection, reproduction and death. Traveling wave from the capacity K to zero

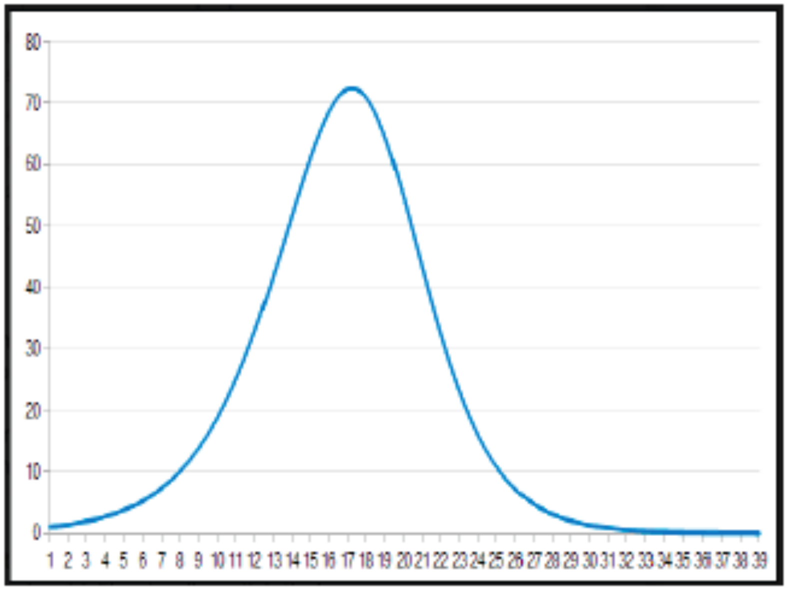


Figure: Disease outbreak: sudden and exponential growth and sudden and exponential death using the SIR model: $S' = -\omega SI, I' = \omega SI - \gamma I$. Outbreak occurs when $R_0 := \omega S(0)/\gamma > 1$, or $\omega > \gamma/S(0)$.

Fang, Lou and Wu, 2016.

Our Framework

$$\begin{aligned} S_t &= DS_{xx} + B(N)N - \mu(N)S - \omega SI + \gamma I, \\ I_t &= DI_{xx} - \mu(N)I + \omega SI - \gamma I. \end{aligned}$$

When $B(N) = b$ and $\mu(N) = d + \frac{N}{K}$, we have the Fisher-KPP equation:

$$N_t = DN_{xx} + (b-d)N\left[1 - \frac{N}{(b-d)K}\right].$$

This has the traveling wavefront with the minimal wave speed

$$c_N^* = 2\sqrt{D(b-d)}$$(Minimal ECOLOGICAL invasion speed).

Replacing $N(t,x)$ and S by $n(x - c_1 t)$ and $n(x - c_1 t) - I$ in I-equation (and rescaling), we obtain

$$v_t = v_{xx} + v[a(x - ct) - v],$$

where α is decreasing function with $a(+\infty) < 0$, and
$\alpha := a(-\infty) > 0$ if and only if $\omega > \omega_1 := \frac{\gamma + b}{(b-d)K}$.

$$
\begin{aligned}
S_t &= DS_{xx} + B(N)N - \mu(N)S - \omega SI + \gamma I,\\
I_t &= DI_{xx} - \mu(N)I + \omega SI - \gamma I.
\end{aligned}
$$

Theroem: Assume that $S_0, I_0 \in C(\mathbb{R}, \mathbb{R}^+)$ with $I_0 \not\equiv 0$ have compact supports. Let $S(t,x), I(t,x)$ be the solution with $S(0,x) = S_0(x)$ and $I(0,x) = I_0(x)$. Then

(1) If $\omega \in (0, \omega_1]$, then $\lim_{t\to\infty} I(t,x) = 0$ uniformly in $x \in \mathbb{R}$.

(2) If $\omega \in (\omega_1, \omega_2)$, then for any $c \in (0, c_\omega)$ there exist $t_0 > 0$ and $\underline{U}, \overline{U} \in C(\mathbb{R}, \mathbb{R}^+)$ with $\underline{U} \not\equiv 0$ such that

$$\underline{U}(x - ct) \le I(t,x) \le \overline{U}(x - c_\omega t), \quad \forall t \ge t_0, x \in \mathbb{R}.$$

(3) If $\omega \in [\omega_2, \infty)$, then for any $c \in (0, c_N^*)$ there exist $t_0 > 0$ and $\underline{U}, \overline{U} \in C(\mathbb{R}, \mathbb{R}^+)$ with $\underline{U} \not\equiv 0$ such that

$$\underline{U}(x - ct) \le I(t,x) \le \overline{U}(x - c_N^* t), \quad \forall t \ge t_0, x \in \mathbb{R}.$$

Epidemiology: Disease propagate with the speed c_I^* and not necessarily as a wave solution

$$
c_I^* = \begin{cases} 0, & \omega \in (0, \omega_1] \\ c_\omega^*, & \omega \in (\omega_1, \omega_2] \\ c_N^*, & \omega \in (\omega_2, \infty]. \end{cases}
$$