Disperse to the North: Climate Impact on Tick Expansion and Lyme Disease Spread

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Collaborators

- Based on the current work with Yijun Lou (The Hong Kong Polytechnic University) and Xiaotian Wu (CDM/York and Western);
- Part of an on-going project in collaboration with
  - Nick Ogden and Yann Pelcat, Public Health Agency of Canada;
  - Milka Radojevic, Environment Canada;
  - Venkata Duvvuri, CDM.
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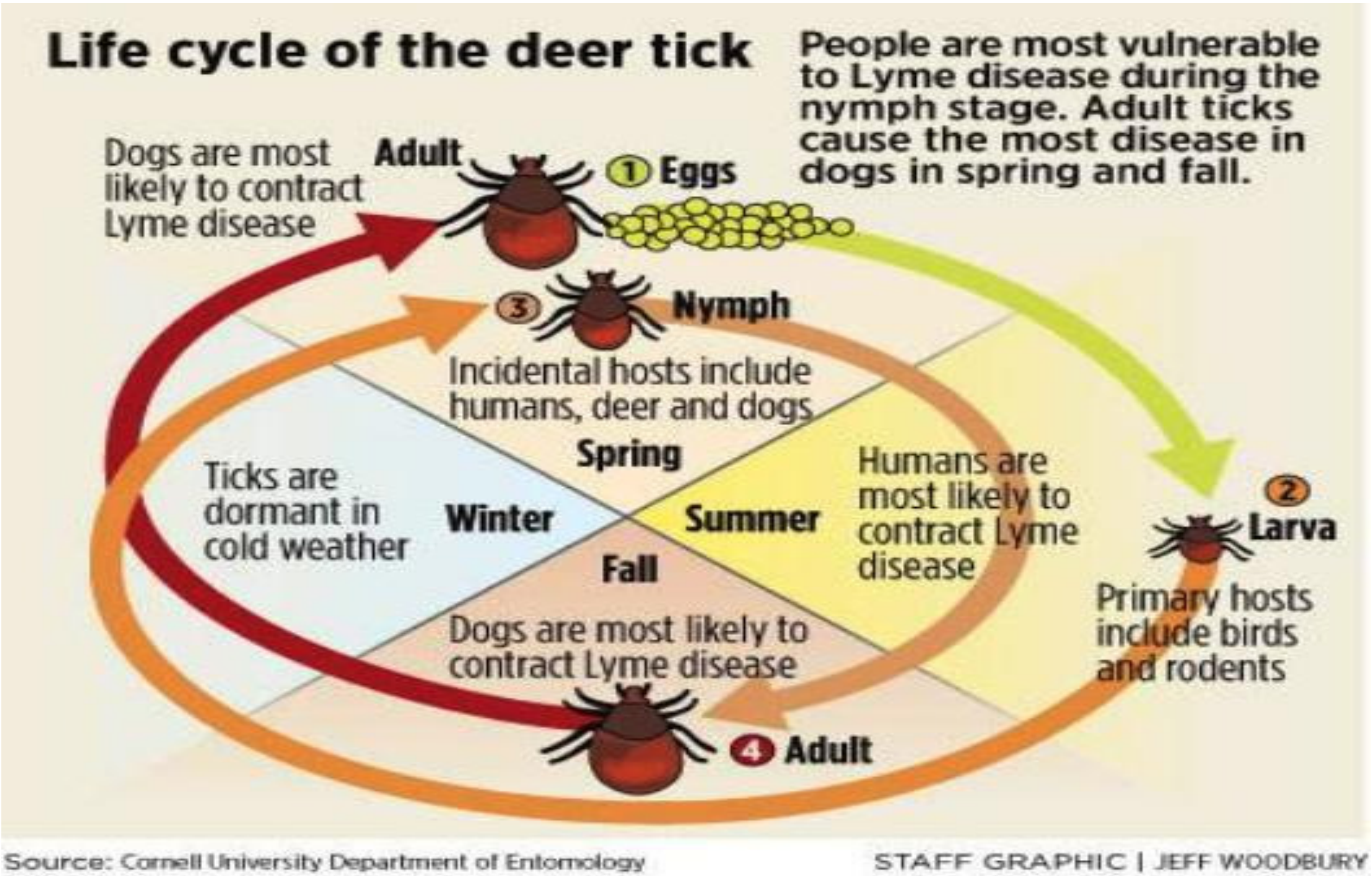
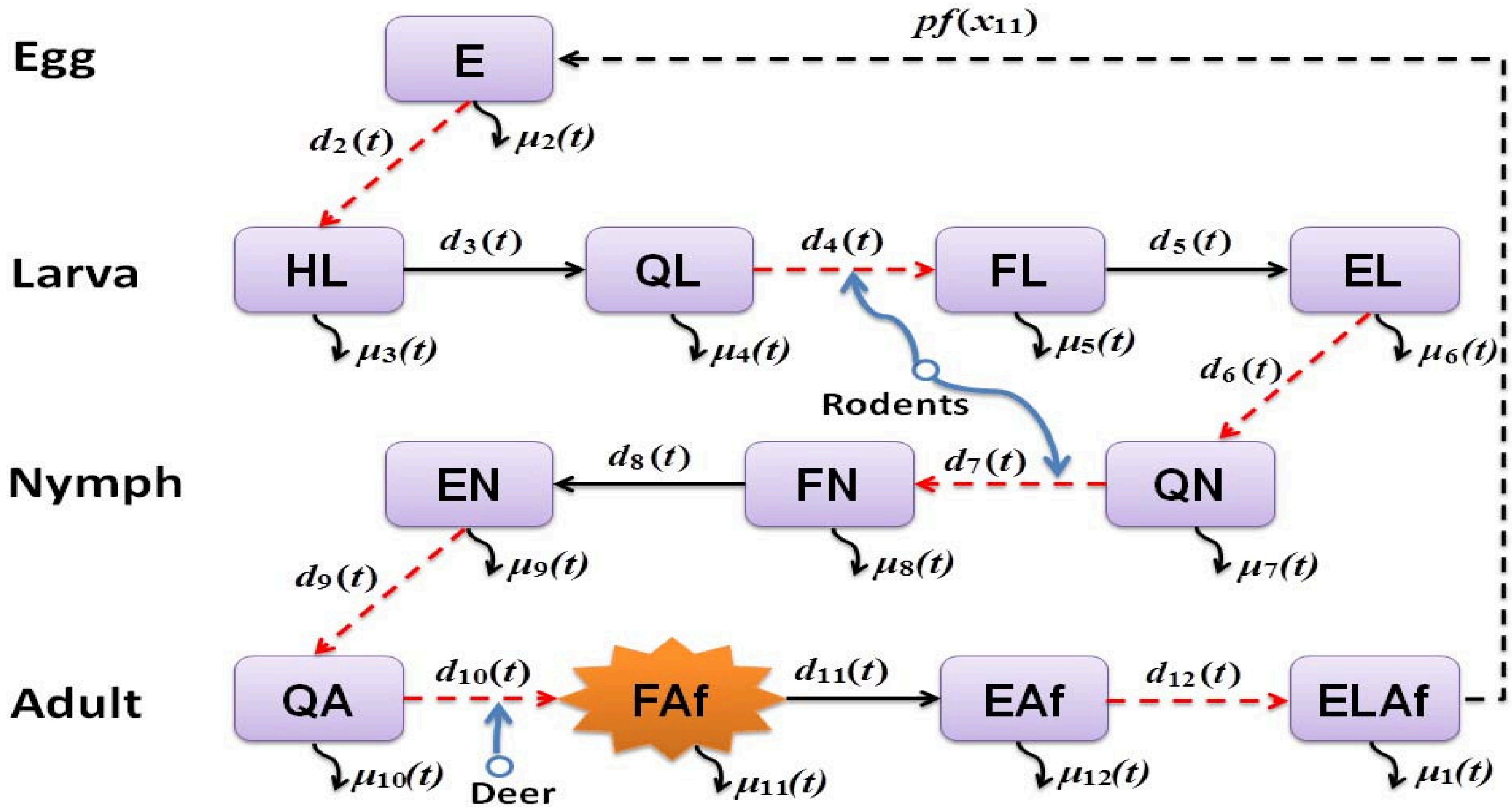
Lyme disease spread

- 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, where $> 23,000$ Lyme disease cases occur annually.
- Northward invasive spread of the tick vectors from United States endemic foci to non-endemic Canadian habitats is currently a public health concern;
- Lyme disease risk is changing rapidly in Canada. A decade ago *I. scapularis populations* were geographically restricted to specific locations on the north shores of Lake Erie and Lake Ontario, one location in southeast Manitoba and one location in Nova Scotia. However, more recently *I. scapularis tick* populations have been identified in multiple locations in southern Manitoba, New Brunswick and Nova Scotia and is spreading widely in some areas of southern Ontario and Quebec.

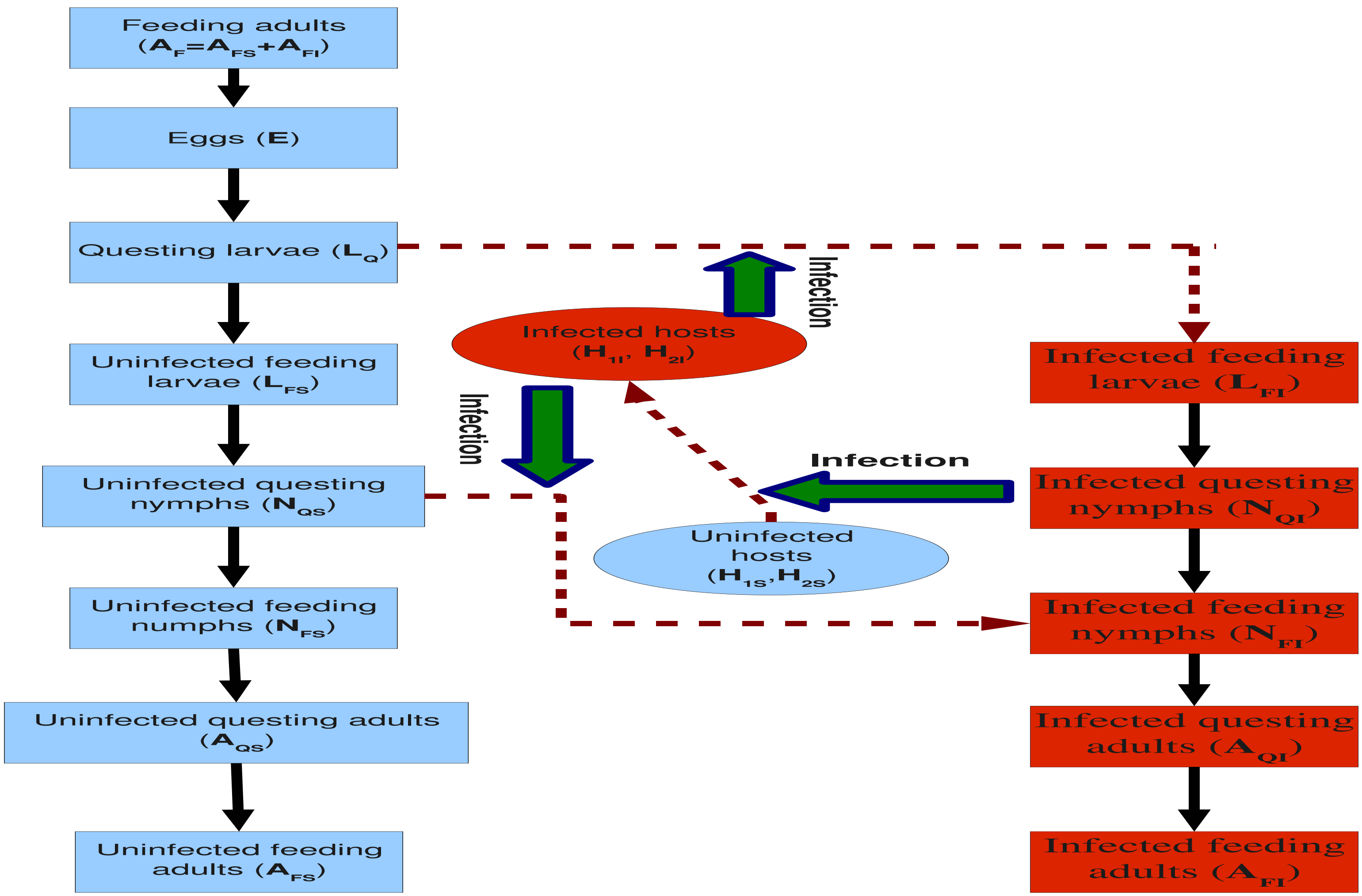
Life Cycle of Ixodes Species



Life Cycle and Tick Population Ecology



Lyme Disease Epidemiology



Lyme Disease Transmission Model (with Two Hosts)

$$
\begin{aligned}
E' &= b(A_{FS}+A_{FI}) - \mu_E E - d_E E,\\
L'_Q &= d_E E - \mu_{QL} L_Q - F_L L_Q,\\
L'_{FS} &= (1-(\beta_{H1L}\frac{H_{1I}}{H_1+p_1H_2} + \beta_{H2L}\frac{p_1H_{2I}}{H_1+p_1H_2}))F_L L_Q\\
&\quad -\mu_{FL}(t)L_{FS}(t) - D_L(t)(L_{FS}(t)+L_{FI}(t))L_{FS}(t) - d_L(t)L_{FS},\\
L'_{FI} &= (\beta_{H1L}\frac{H_{1I}}{H_1+p_1H_2} + \beta_{H2L}\frac{p_1H_{2I}}{H_1+p_1H_2})F_L L_Q\\
&\quad -\mu_{FL}(t)L_{FI}(t) - D_L(t)(L_{FS}(t)+L_{FI}(t))L_{FI}(t) - d_L(t)L_{FI},\\
N'_{QS} &= d_L L_{FS} - \mu_{QN} N_{QS} - F_N N_{QS},\\
N'_{QI} &= d_L L_{FI} - \mu_{QN}(t) N_{QI} - F_N N_{QI},\\
N'_{FS} &= (1-(\beta_{H1N}\frac{H_{1I}}{H_1+p_2H_2} + \beta_{H2N}\frac{p_2H_{2I}}{H_1+p_2H_2}))F_N N_{QS}\\
&\quad -\mu_{FN}N_{FS} - D_N(N_{FS}+N_{FI})N_{FS} - d_N N_{FS},\\
N'_{FI} &= F_N N_{QI} + (\beta_{H1N}\frac{H_{1I}(t)}{H_1+p_2H_2} + \beta_{H2N}\frac{p_2H_{2I}}{H_1+p_2H_2})F_N N_{QS}\\
&\quad -\mu_{FN}N_{FI} - D_N(N_{FS}+N_{FI})N_{FI} - d_N N_{FI},\\
A'_{QS} &= d_N N_{FS} - \mu_{QA} A_{QS} - F_A A_{QS},\\
A'_{QI} &= d_N(t) N_{FI} - \mu_{QA} A_{QI} - F_A A_{QI},\\
A'_{FS} &= F_A A_{QS} - \mu_{FA} A_{FS} - D_A(A_{FS}+A_{FI})A_{FS},\\
A'_{FI} &= F_A A_{QI} - \mu_{FA} A_{FI} - D_A(A_{FS}+A_{FI})A_{FI},\\
H'_{1I} &= F_N \beta_{NH1} N_{QI}\frac{H_1-H_{1I}}{H_1+p_2H_2} - \mu_{H1}H_{1I},\\
H'_{2I} &= F_N \beta_{NH2} N_{QI}\frac{p_2(H_2-H_{2I})}{H_1+p_2H_2} - \mu_{H2}H_{2I}.
\end{aligned}
$$

Term-by-Term change rate: Compartment for Infected Feeding Larvae

$$\frac{dL_{FI}}{dt} = \underbrace{(\beta_{H1L}\frac{H_{1I}(t)}{H_1+p_1H_2}+\beta_{H2L}\frac{p_1H_{2I}(t)}{H_1+p_1H_2})F_L(t)L_Q(t)}_{\text{infection}}$$

$$-\underbrace{d_L(t)L_{FI}(t)}_{\text{development}}$$

$$-\underbrace{\mu_{FL}(t)L_{FI}(t)}_{\text{natural death}},$$

$$-\underbrace{D_L(t)(L_{FS}(t)+L_{FI}(t))L_{FI}(t)}_{\text{host-resistance death}}$$

Tick Population Dynamics (Simplified)–in the absence of Lyme disease

$$
\begin{aligned}
\frac{dE}{dt} &= b(t)A_F(t) - (\mu_E(t) + d_E(t))E(t), \\
\frac{dL_Q}{dt} &= d_E(t)E(t) - (\mu_{QL}(t) + F_L(t))L_Q(t), \\
\frac{dL_F}{dt} &= F_L(t)L_Q(t) - D_L(t)L_F^2(t) - (\mu_{FL}(t) + d_L(t))L_F(t), \\
\frac{dN_Q}{dt} &= d_L(t)L_F(t) - (\mu_{QN}(t) + F_N(t))N_Q(t), \\
\frac{dN_F}{dt} &= F_N(t)N_Q(t) - D_N(t)N_F^2(t) - (\mu_{FN}(t) + d_N(t))N_F(t), \\
\frac{dA_Q}{dt} &= d_N(t)N_F(t) - (\mu_{QA}(t) + F_A(t))A_Q(t), \\
\frac{dA_F}{dt} &= F_A(t)A_Q(t) - \mu_{FA}(t)A_F(t) - D_A(t)A_F^2(t).
\end{aligned}
$$

Define Tick Population Dynamics Threshold $\mathcal{R}_v$ (no claim for originality)

Rewrite the linearization at zero as $\frac{dx(t)}{dt} = (F(t) - V(t))x(t)$, and let $Y(t,s)$, $t \geq s$, be the evolution operator of the linear periodic system $\frac{dy}{dt} = -V(t)y$.

If ϕ is the initial distribution of ticks, then $F(s)\phi(s)$ is the rate of new ticks, and $Y(t,s)F(s)\phi(s)$ is the distribution of those ticks alive at time t for $t \geq s$. Hence,

$$\psi(t) = \int_{-\infty}^{t} Y(t,s)F(s)\phi(s)ds = \int_{0}^{\infty} Y(t,t-a)F(t-a)\phi(t-a)da$$

is the distribution of accumulative ticks at time t produced by all those ticks $\phi(s)$ introduced at the previous time. Define the next generation operator $G : C_T \to C_T$ by

$$(G\phi)(t) = \int_{0}^{\infty} Y(t,t-a)F(t-a)\phi(t-a)da \quad \forall t \in \mathbb{R}, \quad \phi \in C_T.$$

Then the basic reproduction ratio for ticks is $\mathcal{R}_v := \rho(G)$, the spectral radius of G.

Tick Population Dynamics

Theorem 1. *The following statements are valid:*

- *If* $\mathcal{R}_v \leq 1$*, then zero is globally asymptotically stable;*
- *If* $\mathcal{R}_v > 1$*, then system admits a unique* T*-positive periodic solution*

$$(E^*(t), L_Q^*(t), L_F^*(t), N_Q^*(t), N_F^*(t), A_Q^*(t), A_F^*(t)),$$

  and it is globally asymptotically stable.

Ingredients of proof:

- Local stability by using Theorem 2.2, Wang and Zhao 2008.
- Strongly monotone of 6T-periodic operator (idea from Smith 1987).
- Apply Theorem 2.3.4, Zhao 2003 to 6T-map.
- 6T-periodic solutions are T-periodic solutions.

Applications of the Tick Ecology Model and Analysis

- Developing a temperature-driven map of the basic reproductive number of the emerging tick vector of Lyme disease *Ixodes scapularis* in Canada, 2012, Xiaotian Wu, Venkata R. Duvvuri, Yijun Lou, Nicholas H. Ogden, Yann Pelca, Jianhong Wu, JTB on line now.

- Using lab. data and temperature normals smoothed by Fourier analysis, we generated seasonal temperature-driven development rates and host biting rates to parametrize the model;

- We used the model to obtain values for the basic reproduction number for *I. scapularis* at locations in southern Canada where the tick is established and emerging;

- The $\mathcal{R}_v$ at Long Point, Point Pelee and Chatham sites where *I.scapularis* are established, was estimated at 1.5, 3.19 and 3.65 respectively;

- The threshold temperature conditions for tick population survival ($\mathcal{R}_0 = 1$) were shown to be the same as those identified using the mechanistic model (2800-3100 cumulative annual degree days $> 0°\mathrm{C}$);

- A map of $\mathcal{R}_v$ for *I. scapularis*, the first such map for an arthropod vector, was drawn for Canada east of the Rocky Mountains. This map supports current risk assessments for Lyme disease risk emergence in Canada;

- Sensitivity analysis identified host abundance, tick development rates and summer temperatures as highly influential variables in the model, which is consistent with our current knowledge of the biology of this tick.

- The development of a deterministic model for *I. scapularis* that is capable of providing values for $\mathcal{R}_v$ is a key step in our evolving ability to develop tools for assessment of Lyme disease risk emergence and for development of public health policies on surveillance, prevention and control.

Figure 1: Development rates and host-attaching rates of *I. scapularis* ticks using the mean monthly normal temperature data of Delhi CDA for 1971-2000 periods.

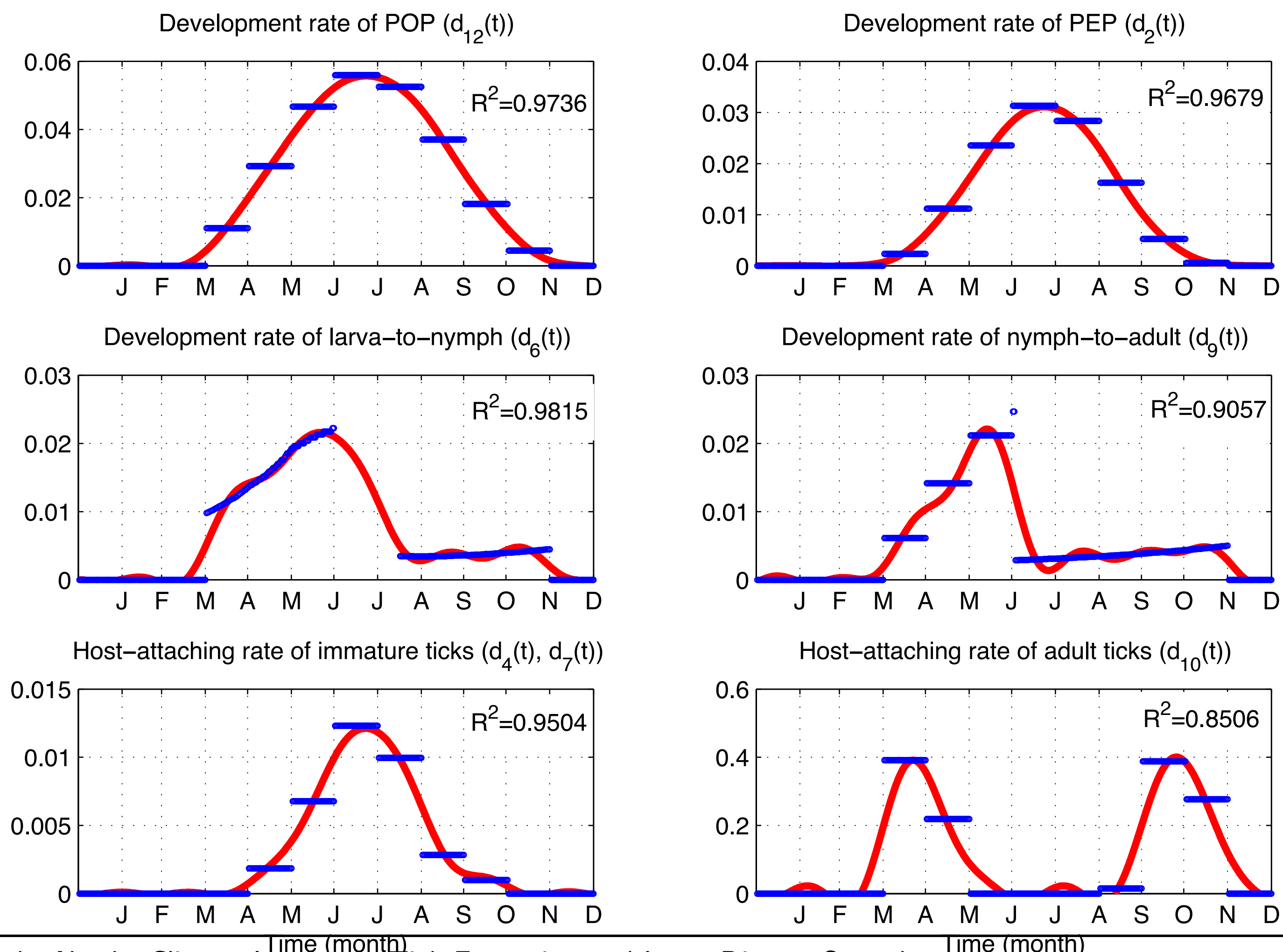


Figure 2: $\mathcal{R}_v$ and the maximum numbers of feeding adult ticks at equilibrium, plotted against the mean annual number of degree-days $> 0°\mathrm{C}$ ($DD > 0°\mathrm{C}$) for the meteorological stations in Ontario.

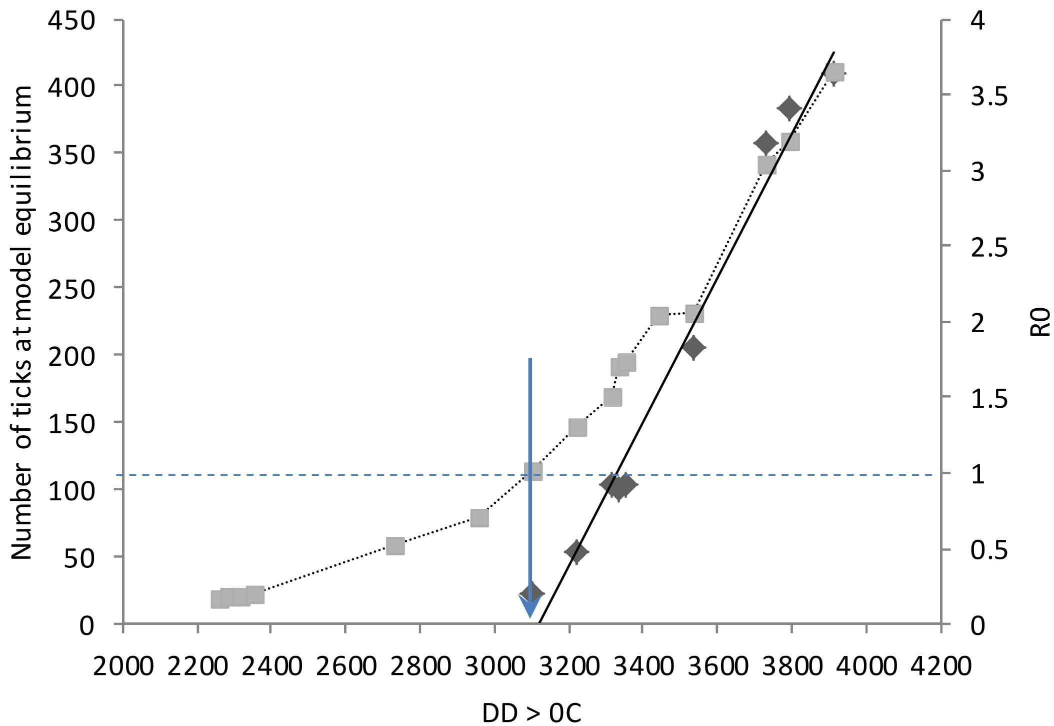
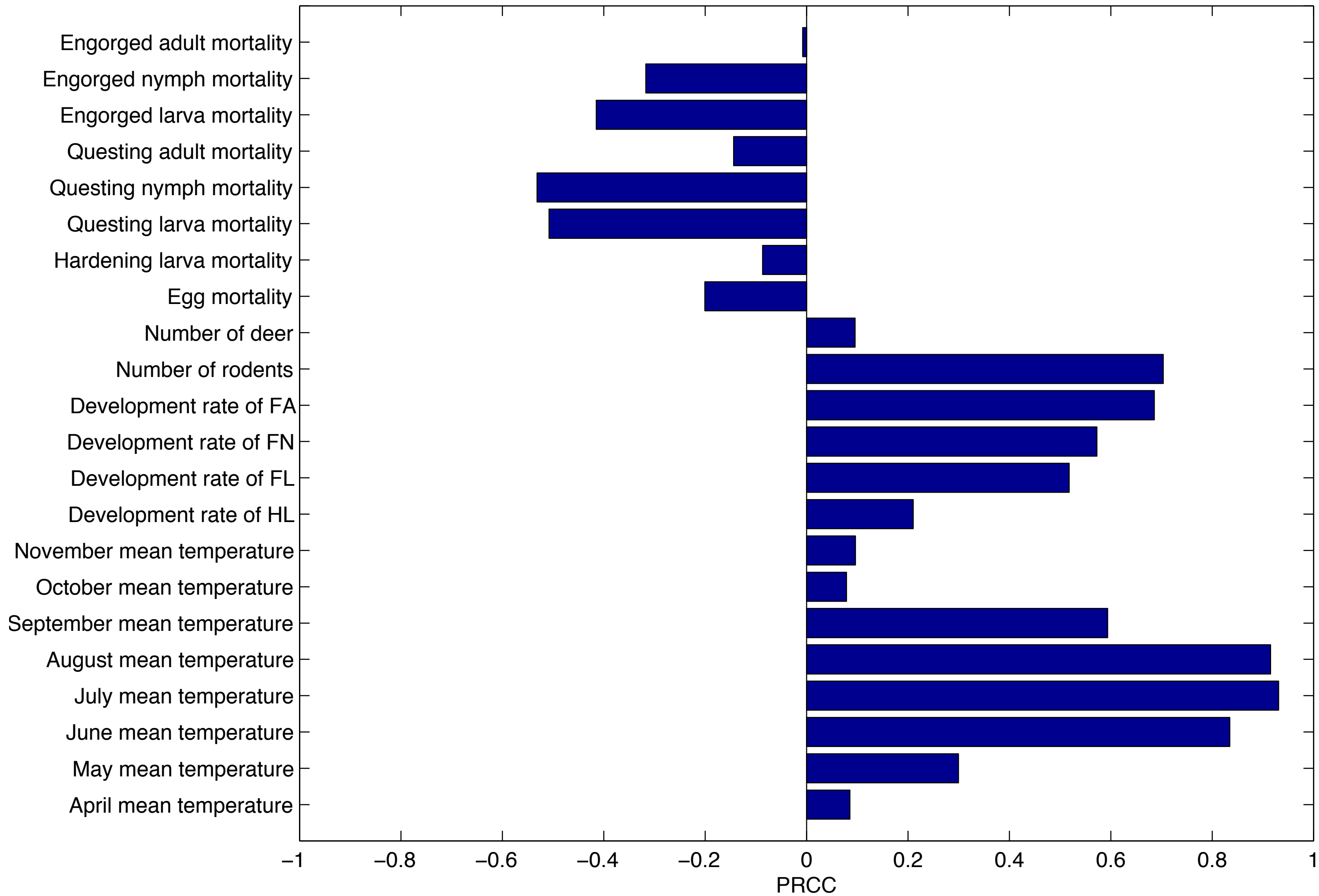


Figure 3: A $\mathcal{R}_v$ map for $I.scapularis$ for Canada east of the Rocky Mountains.

Figure 4: Global sensitivity analysis of $\mathcal{R}_v$.



The Global Dynamics of Lyme Disease Infection if $\mathcal{R}_v > 1$

There exists a positive periodic solution, $(E^*, L_Q^*, L_F^*, N_Q^*, N_F^*, A_Q^*, A_F^*)$ such that

$$\begin{aligned} & \lim_{t\to\infty}(E(t), L_Q(t), L_F(t), N_Q(t), N_F(t), A_Q(t), A_F(t)) \\ = \quad & (E^*(t), L_Q^*(t), L_F^*(t), N_Q^*(t), N_F^*(t), A_Q^*(t), A_F^*(t)). \end{aligned}$$

In this case, equations for the infected populations in system (EM) give rise to the following limiting system:

$$\begin{aligned} \frac{dL_{FI}}{dt} &= (\beta_{H1L}\frac{H_{1I}(t)}{H_1+p_1H_2} + \beta_{H2L}\frac{p_1H_{2I}(t)}{H_1+p_1H_2})F_L(t)L_Q^*(t) \\ &\quad -D_L(t)L_F^*(t)L_{FI}(t) - (d_L(t)+\mu_{FL}(t))L_{FI}(t), \\ \frac{dN_{QI}}{dt} &= d_L(t)L_{FI}(t) - (\mu_{QN}(t)+F_N(t))N_{QI}(t), \\ \frac{dH_{1I}}{dt} &= F_N(t)\beta_{NH1}N_{QI}(t)\frac{H_1-H_{1I}(t)}{H_1+p_2H_2} - \mu_{H1}H_{1I}(t), \\ \frac{dH_{2I}}{dt} &= F_N(t)\beta_{NH2}N_{QI}(t)\frac{p_2(H_2-H_{2I}(t))}{H_1+p_2H_2} - \mu_{H2}H_{2I}(t). \end{aligned} \qquad \text{(LM)}$$

Limiting Equation Dynamics

We can define the next generation operator $\widetilde{G}$ and the threshold value for the $\mathcal{R}_d := \rho(\widetilde{G})$, the spectral radius of $\widetilde{G}$.

Theorem 2. *The following statements are valid:*

(i) If $\mathcal{R}_d \leq 1$, then zero is globally asymptotically stable for system (LM) in $\mathbb{R}^4_+$;

(ii) If $\mathcal{R}_d > 1$, then system (LM) admits a unique positive periodic solution $(L^*_{FI}(t), N^*_{QI}(t), H^*_{1I}(t), H^*_{2I}(t))$ and it is globally asymptotically stable.

Classification of Global Dynamics of Lyme Disease Model via $\mathcal{R}_v$ and $\mathcal{R}_d$

Theorem 3. *Let $x(t, x^0)$ be the solution of system (EM) through x^0. Then*

(i) If $\mathcal{R}_v \le 1$, then zero is globally attractive for system (EM);

(ii) If $\mathcal{R}_v > 1$ and $\mathcal{R}_d \le 1$, then

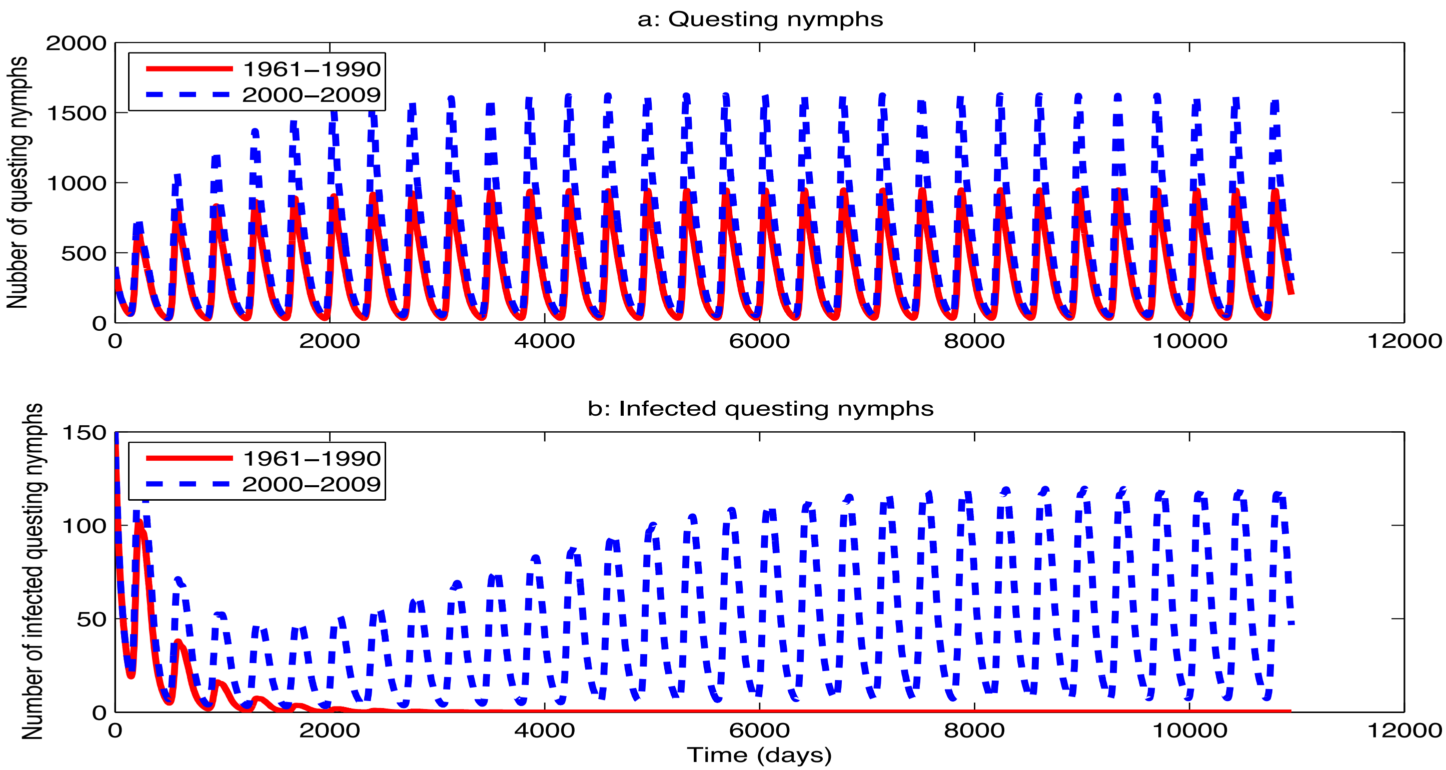
$$\begin{aligned} &\lim_{t\to\infty}(x_1(t), x_2(t), x_3(t), x_4(t), x_5(t), x_6(t), x_7(t)) \\ = \;&(E^*(t), L_Q^*(t), L_F^*(t), N_Q^*(t), N_F^*(t), A_Q^*(t), A_F^*(t)), \end{aligned}$$

and $\lim_{t\to\infty} x_i(t) = 0$ for $i \in [8, 11]$;

(iii) If $\mathcal{R}_v > 1$ and $\mathcal{R}_d > 1$, then there exists a positive periodic solution $x^*(t)$, and this periodic solution is globally attractive for system (EM) with respect to all positive solutions.

Climate impact on questing nymphs: uninfected vs infected

Red: $1961 - 1990$ temperature data ($\mathcal{R}_v = 1.6996$, $\mathcal{R}_d = 0.7585$), Blue: $2000 - 2009$ temperature data ($\mathcal{R}_v = 2.1915$,$\mathcal{R}_d = 1.0867$).

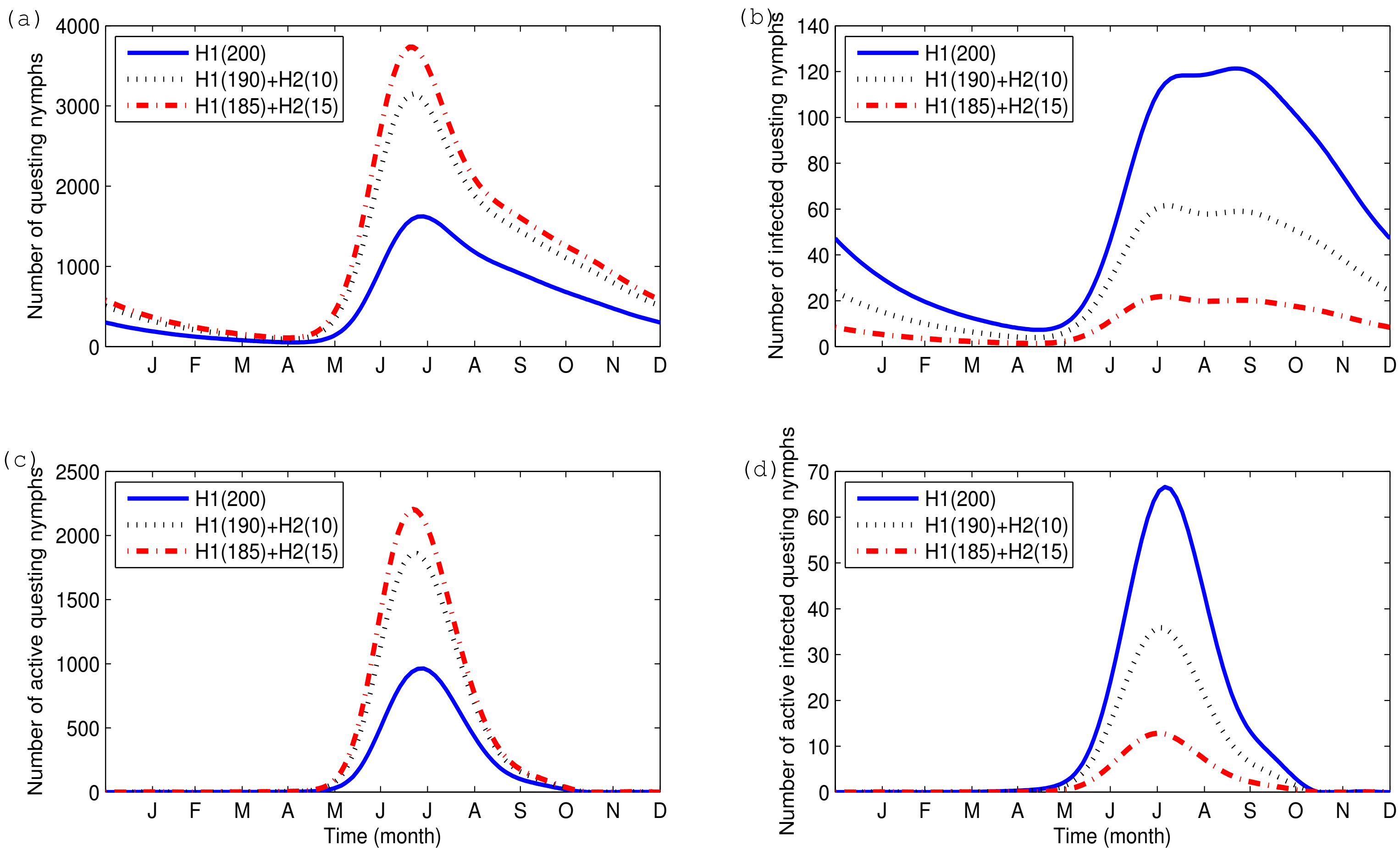


Host Diversity without interspecific competition

Table 1: The effect of adding an alternative host species on the disease risk.

Species	β_{H_2L}	β_{NH_2}	μ_{H_2}	p_1	p_2	Density	AIQN	INP	$\mathcal{R}_v$	$\mathcal{R}_d$
Eastern chipmunk	0.569	0.971	0.00274	0.4	3.5	20	A	A	2.4978	1.2579
Raccoon	0.017	1.0	0.0005	8.5	5.3	20	A	D	3.3775	1.9705
				18.5	5.6	20	A	D	4.0814	2.6701
				1.3	11.1	20	A	D	3.0456	1.3899
Virginia opossum	0.004	0.261	0.0018	8.6	3.9	10	A	D	2.7542	1.1217
				7.6	8.0	10	A	D	2.8775	1.1184
				7.2	36.9	20	D	D	4.7264	1.0601
Striped skunk	0.191	0.530	0.00274	10.9	8.0	10	A	A	3.0230	1.8792
Short-tailed shrew	0.505	0.831	0.001	2^*	1^*	20	A	A	2.4612	1.6240
Sorex shrews	0.537	0.701	0.0018	2^*	1^*	20	A	A	2.4612	1.3724
Red and grey squirrel	0.061	0.831	0.0002	1.8	6.9	10	A	A	2.5475	1.9863
				1.3	4.4	10	A	A	2.4285	1.5788
Resources	(Brunner2008a)	(Brunner2008a)	Animal	(Ogden2009)	(Ogden2009)					

Host Diversity with interspecific competition (adding an alternative host *Virginia opossum*)



Summary

- Multiple models for tick ecology and Lyme disease epidemiology;
- Techniques to derive from lab. data and temperature normals smoothed by Fourier analysis the seasonal temperature-driven development rates and host biting rates;
- Algorithms to calculate the basic reproduction ratios and confirmations that these are powerful and practical indices;
- Risk maps of $\mathcal{R}_0$ supporting risk assessments;
- Sensitivity analysis to identify key surveillance;
- Analysis about the dilution/amlification of host diversity

Projects ahead

- Variations via different climate models;
- Functional connectivity and the dynamics of parasite invasion;
- Modelling temporal variation of development delay.