Modeling the Dynamics of Lyme Disease in a Tick-Mouse System Subject to Vaccination of Mice Populations

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Abstract

Lyme disease is one of the most prevalent and the fastest growing vector-borne bacterial illness in the United States, with over 25,000 new confirmed cases and 300,000 associated illnesses every year. The Centers for Disease Control and Prevention estimates that those numbers could be significantly underrepresented. Lyme Disease is caused by the bacteria, *Borrelia burgdorferi*, which humans contract through the bite of *Ixodes scapularis*, commonly known as the deer tick or Eastern blacklegged tick. Ticks receive the pathogen through numerous reservoirs, chiefly the white footed mouse *Peromyscus leucopus*. **Our research assesses whether vaccines targeting mice are an effective method to reduce human risk for Lyme Disease**. We do this using a system of nonlinear difference equations to model transmission dynamics and vector demographics in both tick and mice populations.

Background

Lyme disease can cause debilitating symptoms. It is most frequent in the Northeastern United States but nearly every state has a recorded case. On the right is a map of US cases in 2016. Below is an image of ticks in various stages of their lives.

Figure 1: https://www.cdc.gov/lyme/transmission/index.html

- Tick stage/activity depends on season, see Figure 4.
  - Summer year 1: Larvae feed on mice.
  - Spring year 2: Nymphs feed on all sizes of animals (including humans).
  - Fall year 2: Adults feed on large animals (including humans).
- Always two coexistent generations at different life stages, but only one stage is actively biting at a time.
- Ticks have a very sedentary lifestyle and rely mostly on hosts for movement.
- They only feed on blood and require these blood meals in order to make it to the next stage.
- Mice have same activity level until winter.
- Mice thrive in fragmented forest areas, environments of small disconnected patches of forest with low biodiversity.
- Bait boxes are specially designated for white-footed mice. The smell of the food entices the mice to enter the box.
- The vaccine is administered orally in the food.

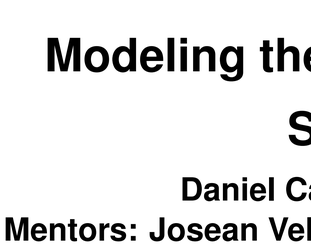

Figure 2: https://www.cdc.gov/lyme/stats/index.html

Figure 3: https://www.cdc.gov/ticknet/ltdps/ltdps_bait.html

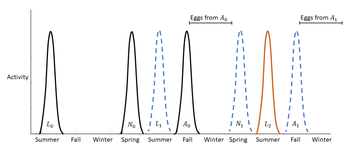

Figure 4: Tick Life Cycle

Model Development

To understand the tick-mouse transmission system we first construct a compartmental diagram. SIV for mice and stage-structured SI for ticks as shown in Figure 5. Parameter defintions can be found in Table 1.

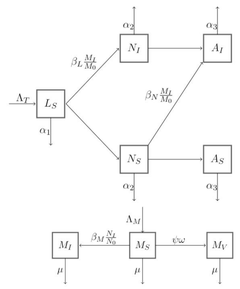

Figure 5: Tick/Mice Flowcharts

Param.	Definition	Value
M	Total mouse population	50
Λ_M	Birth/recruitment of mice	65.02
ψ	Contact between mice and vaccines	Estimated, 1/year
β_M	Transmission constant from nymphs to mice	Estimated, 1/year
ω	Proportion of vaccine effectiveness	0.96/year
μ	Natural death rate of mice	4.38/year
N	Total nymph population	1000
Λ_T	Recruitment of larvae	1.998×10^5
β_L	Transmission constant from mice to larvae	Estimated, 1/year
β_N	Transmission constant from mice to nymphs	Estimated, 1/year
α_1	Egg to larva natural death	11.98/year
α_2	Larva to nymph natural death	3.07/year
α_3	Nymph adult natural death	3.22/year

Table 1

Mathematical Analysis

Model indexed by single years. There are 2 generations that overlap each year, but assume only one stage active at a time. Yearly sampling period is in spring prior to vaccination and any biting season. Only nymphs are active so they are the only tick to appear in the equations.

$$N_I(\tau+1) = \Lambda_T e^{-\frac{(\alpha_1+3\alpha_2)}{4}} \left(1 - e^{-\frac{\beta_L}{4} \frac{M_I(\tau)e^{-\frac{\mu}{4}} + M_S(\tau)e^{-\frac{\mu}{4}}e^{-\frac{\psi\omega}{4}}\left(1-e^{-\frac{\beta_M}{2}\frac{N_I(\tau)}{N(\tau)}}\right)}{e^{-\frac{\mu}{4}}M(\tau)+\frac{\Lambda_M}{4}}} \right), \tag{1}$$

$$N_S(\tau+1) = \Lambda_T e^{-\frac{(\alpha_1+3\alpha_2)}{4}} \left(e^{-\frac{\beta_L}{4} \frac{M_I(\tau)e^{-\frac{\mu}{4}} + M_S(\tau)e^{-\frac{\mu}{4}}e^{-\frac{\psi\omega}{4}}\left(1-e^{-\frac{\beta_M}{2}\frac{N_I(\tau)}{N(\tau)}}\right)}{e^{-\frac{\mu}{4}}M(\tau)+\frac{\Lambda_M}{4}}} \right). \tag{2}$$

$$M_S(\tau+1) = M_S(\tau)e^{-\mu}e^{-\frac{\psi\omega}{4}}e^{-\frac{\beta_M}{2}\frac{N_I(\tau)}{N(\tau)}} + \frac{\Lambda_M}{4}\left(e^{-\frac{3\mu}{4}}+3\right), \tag{3}$$

$$M_I(\tau+1) = M_I(\tau)e^{-\mu} + M_S(\tau)e^{-\mu}e^{-\frac{\psi\omega}{4}}\left(1-e^{-\frac{\beta_M}{2}\frac{N_I(\tau)}{N(\tau)}}\right), \tag{4}$$

$$M_V(\tau+1) = M_V(\tau)e^{-\mu} + M_S(\tau)e^{-\mu}\left(1-e^{-\frac{\psi\omega}{4}}\right). \tag{5}$$

Disease-free equilibrium given by $(N_S^*, N_I^*, M_S^*, M_I^*, M_V^*)$, where $N_S^* = \Lambda_T e^{-\frac{(\alpha_1+3\alpha_2)}{4}}$, $M_S^* = \frac{\Lambda_M}{4}\frac{(e^{-\frac{3\mu}{4}}+3)}{1-e^{-\mu-\frac{\psi\omega}{4}}}$, $M_V^* = \frac{\Lambda_M}{4}\frac{(e^{-\frac{3\mu}{4}}+3)}{1-e^{-\mu}}\frac{e^{-\mu}(1-e^{-\frac{\psi\omega}{4}})}{1-e^{-\mu-\frac{\psi\omega}{4}}}$ and $N_I^* = 0, M_I^* = 0$.

We found $\mathcal{R}_0$ using next-generation matrix

$$\mathcal{R}_C = \frac{1}{2}\left(\frac{\left(1-e^{-\mu}\right)\left(e^{-\mu}+3e^{-\mu/4}\right)\beta_L\beta_M e^{-\frac{3\mu}{4}-\frac{\psi\omega}{4}}}{8\left(3e^{-\mu}+e^{-3\mu/4}\right)\left(1-e^{-\mu-\frac{\psi\omega}{4}}\right)}\right) + \frac{1}{2}\sqrt{\frac{\left(1-e^{-\mu}\right)^2\left(e^{-\mu}+3e^{-\mu/4}\right)^2\beta_L^2\beta_M^2 e^{-\frac{3\mu}{2}-\frac{\psi\omega}{2}}}{64\left(3e^{-\mu}+e^{-3\mu/4}\right)^2\left(1-e^{-\mu-\frac{\psi\omega}{4}}\right)^2} + \frac{\left(e^{-\mu}+3e^{-\mu/4}\right)\beta_L\beta_M e^{-\frac{7\mu}{4}-\frac{\psi\omega}{4}}}{2\left(3e^{-\mu}+e^{-3\mu/4}\right)\left(1-e^{-\mu-\frac{\psi\omega}{4}}\right)}}$$

If $\mathcal{R}_C < 1$, the D.F.E is stable. Otherwise, it is unstable and there exists an endemic equilibrium. Using the Jacobian of the system, we derive a simpler condition r based on its eigenvalues. $r = \left(\frac{\beta_M\beta_L}{8(1-e^{-\mu-\frac{\psi\omega}{4}})}\right)\left(\frac{e^{-\mu}+3e^{-\frac{\mu}{4}}}{e^{-\frac{3\mu}{4}}+3e^{-\mu}}\right)e^{-\frac{3\mu}{4}-\frac{\psi\omega}{4}}$. If $r < 1$, the D.F.E is stable. Otherwise, it is unstable.

Simulations and Cost-Benefit Analysis

Transmission rates β_N, β_L, and β_M were the most difficult to find and adapt to the model. Graphs of the equilibrium populations over varying values of ψ for two different sets of transmission rates.

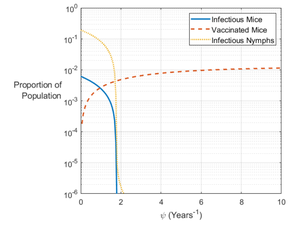

Figure 5: $\beta_N = 0.68$, $\beta_L = 3.41$, $\beta_M = 7.05$

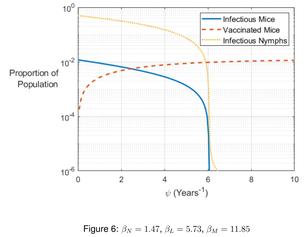

Figure 6: $\beta_N = 1.47$, $\beta_L = 5.73$, $\beta_M = 11.85$

To estimate combined the total cost savings from this intervention, we need a cost function:

$$I(\tau) = \frac{N_I(\tau)}{N} \cdot \rho \cdot \gamma_S,$$
$$C_{total}(\tau) = x \cdot \psi + I(\tau) \cdot \theta$$

Param.	Definition	Value
x	Increase in cost per increase in vaccination rate	$329.29
ψ	Contact between mice and vaccines	Estimated, 1/year
θ	Average cost of Lyme disease treatment	$3537.70/year
ρ	Probability of infection for humans after nymph bite	.031 infections/bites
γ	Biting rate of tick nymph per human per year	Estimated, bites/(human·year)
H_S	Susceptible humans	Estimated

Table 2

Cost analysis of vaccination shows that vaccination can be cost effective in most exposure areas, as shown in figure below. Points mark optimal expenditures on vaccination.

NewGraphs/Cost(MedBeta)New.png

Figure 7: Cost effectiveness of Vaccination at 10 years for $\beta_N = 0.86$, $\beta_L = 4.29$, and $\beta_M = 8.87$

Results and Discussion

- Developed a discrete-time model to describe mouse-tick interaction.
  - Modeled mouse and tick transmission dynamics from year-to-year.
  - Discovered fixed points, disease free equilibrium stability, and R_0 for tick-mouse system.
- Showed that vaccines can feasibly reduce or eliminate infected tick nymphs and can do so while saving money by reducing medical expenditures due to Lyme Disease.
- Future Work: Modeling other intervention strategies such as predator introduction or chemical/ fungal pesticides to compare effectiveness to vaccines.

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