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Original Research Article

# Tick seeking assumptions and their implications for Lyme disease predictions

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ABSTRACT

In vector-borne disease modeling, a key assumption is the host–vector interaction pattern encapsulated in the host seeking rate. Here, a model for Lyme disease dynamics with different host seeking rates is used to investigate how different patterns of tick–host interaction affect the model predictions in the context of tick-borne disease control. Three different host seeking behaviors (the frequency-dependent rate, the density-dependent rate and the Holling type 2 rate) are compared. The comparison of results illustrates not only variable relationships between rodents and tick abundance but also different implications for disease control: (i) for the model with the frequency-dependent rate, reducing rodents is always bad for containing the disease; (ii) for density-dependent or the Holling type 2 rate, reducing or increasing rodent population should be carefully considered, since large host population may facilitate the development of immature ticks, resulting in the immature tick population level so low to sustain the transmission cycle. Furthermore, we distinguish different mechanisms of dilution effects (pathogen reduction with the increasing of the host biodiversity) from different tick–host interaction patterns.


## 1. Introduction

Prevention and control of tick-borne diseases is important to human health, animal welfare and economics. Tick-borne encephalitis virus causes thousands of human cases of encephalitis in Europe and Asia every year (Mansfield et al., 2009; Nonaka et al., 2010), and Lyme disease remains the world's most frequently recorded vector-borne diseases in the temperate zone. More than 20,000 cases are reported in the United States each year (Kurtenbach et al., 2006; CDC, 2007), and the number of known endemic areas of Lyme disease in Canada is predicted to be acceleratingly increasing with climate change (Ogden et al., 2009). Though a variety of models have been proposed (see, for example, Caraco et al., 1998; Schmidt and Ostfeld, 2001; Ogden et al., 2005; Ostfeld, 2011; Wu et al., 2013), little has been done to describe the relationship between the model structure and predictions for Lyme disease.

In eastern and central North America, Lyme disease is caused by spirochete bacterium *Borrelia burgdorferi* and transmitted by the tick vector *Ixodes scapularis*. The transmission process of Lyme disease as a zoonotic vector-borne disease is largely affected by the interaction between the vector and its hosts. The tick vector has a wide range of hosts, adult ticks always feed on white-tailed deers while immature ticks normally feed on small mammals, with white-footed mouse as the most efficient reservoir. Thus it is naturally proposed that Lyme disease is closely tied to two host species: deers which determine tick numbers, and rodents (particularly white-footed mice) which determine tick infection (Ostfeld, 2011). Two relationships are important in the ecology and epidemiology of this complex ecological and epidemiological system. The first is the relationship between deer and tick abundance. This relationship seems to be variable, sometimes strong and sometimes weak or nonexistent (Ostfeld, 2011). Another is the relationship between the disease risk and host community diversity. Dilution effect, defined when disease frequency decreases with increasing biodiversity, and the opposite-amplification effect have been discussed in the literature (see Ostfeld, 2011; Keesing et al., 2006; Rudolf and Antonovics, 2005; Schmidt and Ostfeld, 2001, 2001; Mitchell et al., 2002; LoGiudice et al., 2003; Ostfeld and Keesing, 2000; Ostfeld and LoGiudice, 2003; Van Buskirk and Ostfeld, 1995; Ogden and Tsao, 2009). In particular, different possible mechanisms responsible for dilution effects were classified in Keesing et al. (2006). These mechanisms include encounter reduction, transmission reduction, susceptible host regulation, infected host mortality, recovery augmentation

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and vector regulation. Three of these mechanisms seem to be popular and important for the tick-borne disease transmission: encounter reduction, host regulation and vector regulation (Ostfeld, 2011). Here, we employ a mathematical dynamical modeling approach to explore how tick–host interaction patterns affect disease transmission, with Lyme disease as a case study.

As noted in Wonham et al. (2006), a model's mathematical structure should be determined by its underlying biological assumptions, and the model-based prediction is strongly influenced by the model structure. For vector-borne disease modeling, a key assumption is the host–vector interaction represented by the transmission term. Epidemiologists increasingly appreciate that the disease-transmission term may greatly affect the predicted disease transmission pattern and disease control strategies (Wonham et al., 2006). In tick-borne interaction modeling, density-dependent (Caraco et al., 1998) and frequency-dependent (Gaff and Gross, 2007) functions have been widely used. Some other more complicated functional responses, such as the one in Ogden et al. (2005), are also used. These complicated responses, as will be shown, can be considered as intermediate scenarios between the density-dependent and frequency-dependent cases and these responses can be expanded as a combination of the density-dependent and frequency-dependent forces. In dynamic modeling, prediction of long-term disease transmission dynamics and evaluation of disease control strategies are closely related to the calculation of a few indices summarizing the collective impact of model parameters and initial conditions. One important predictive index is the basic reproduction number (Hartemink et al., 2008) which, for tick population is the total number of female adult ticks produced by a single female tick during her entire reproduction period; and for Lyme disease is defined as the average number of secondary cases caused by one infectious individual placed in a population consisting entirely of susceptibles. These indices should be evaluated under different assumptions of tick–host interactions. Also important for determining the human risk of exposure to Lyme disease, as emphasized by Ostfeld (2011), is the number of nymphs responsible for the majority of Lyme disease cases, and three temporally varying measures: nymphal infection prevalence (NIP: which is the proportion of nymphs infected with *B. burgdorferi*), the density of infected nymphs (DIN) and the density of nymphs (DON). In this study, we examine how the choice of different transmission terms qualitatively and quantitatively alters the basic reproduction numbers, the time-evolution of nymphs, NIP, DIN and DON, therefore alters predicted disease transmission patterns and control implications. We hope this modeling approach can contribute to addressing the question "why the relationship between deer and tick abundance be so variable" (Ostfeld, 2011). We also show that while an excessively large rodent population size has positive effects on disease control, the conceptual mechanisms underlying various tick–host seeking patterns are different. We clarify this idea in the context of dilution and/or amplification effect. Moreover, in the case of density-dependent and Holling type 2 transmission terms, we observe both the dilution effect and amplification effect of the host community may take place. Thus, we encounter the dilemma with respect to the disease control: to reduce or to increase rodent population. Solving this dilemma relies on and thus calls for accurate formulation of the transmission patterns of the disease under consideration.

## 2. Effects of host seeking patterns on disease dynamics

### 2.1. The core model and ecological/epidemiological reproduction numbers

There are many mathematical models developed for tick-borne disease transmission dynamics, such as those in Bolzoni et al. (2012), Tagliapietra et al. (2011), Pugliese and Rosà (2008), Rosà and Pugliese (2007). Here, we adapt the simple model structure of Caraco et al. (1998) to capture some important features of the complex epidemiology of Lyme disease. Namely, we use the system

$$\begin{aligned}\frac{dL(t)}{dt} &= \left(bF_A - \frac{1}{K}A(t)\right)A(t) - (F_L+\mu_L)L(t),\\ \frac{dN(t)}{dt} &= F_L L(t) - (\mu_N+F_N)N(t),\\ \frac{dA(t)}{dt} &= F_N N(t) - \mu_A A(t)\end{aligned} \tag{1}$$

to describe the tick population dynamics, and formulate the system

$$\begin{aligned}\frac{dM_I(t)}{dt} &= \beta_M F_N \frac{M-M_I(t)}{M}N_I(t) - \mu_M M_I(t),\\ \frac{dN_I(t)}{dt} &= \beta_L F_L \frac{M_I(t)}{M}L(t) - (F_N+\mu_N)N_I(t),\\ \frac{dA_I(t)}{dt} &= F_N N_I(t) + \beta_N F_N (N(t)-N_I(t))\frac{M_I(t)}{M} - \mu_A A_I(t)\end{aligned} \tag{2}$$

for the disease transmission dynamics. All of the variables and parameters are presented in Tables 1 and 2. We will also adopt the parameter set from Caraco et al. (1998). Ticks can feed on various vertebrates as hosts (Mannelli et al., 2012). To illustrate our findings, we assume that the immature ticks mainly feed on rodents, while adults feed on deer. We further assume that the total rodent population and the deer population are in their demographic equilibria, fixed at the equilibrium values $M$ and $D$ respectively, but we assume that rodents may change epidemiological status from susceptible to infected through infection by infectious ticks. We should emphasize that the ticks host feeding rates $F_L$, $F_N$, $F_A$ are supposed to have various forms (as detailed in Section 2.2 later). This is different from the model in Caraco et al. (1998), where only density-dependent tick seeking rate is used. Since the pathogen is maintained among the immature ticks and their hosts, the last equation of system (2) can be decoupled from the system.

Since one adult tick, with average life span $1/\mu_A$, can produce an average of $bF_A$ larvae per unit time which will survive to the nymphal stage with the probability of $F_L/(F_L+\mu_L)$, and $F_N/(F_N+\mu_N)$ gives the nymph survival probability to adults, an adult tick can reproduce $bF_AF_L/(F_L+\mu_L)F_N/(\mu_N+F_N)/\mu_A$ adults in its life time, we naturally define the (ecological) reproduction number for the tick population as

$$R_{Tick} = bF_A\frac{F_L}{F_L+\mu_L}\frac{F_N}{\mu_N+F_N}\frac{1}{\mu_A}.$$

The tick subsystem (1) has always a tick-free equilibrium (0, 0, 0). If the reproduction number for ticks is greater than unity, then there exists a positive equilibrium, denoted by $(L^*, N^*, A^*)$, with

$$A^* = K\left(bF_A - \frac{\mu_N+F_N}{F_L}\frac{\mu_A}{F_N}(F_L+\mu_L)\right) = KbF_A\left(1-\frac{1}{R_{Tick}}\right),$$

**Table 1**
Variables for the model system (1) and (2).

| | |
|---|---|
| $L$ | The total number of larval ticks |
| $N$ | The total number of tick nymphs |
| $A$ | The total number of adult ticks |
| $M_I$ | The number of infectious rodents |
| $N_I$ | The number of infectious nymphs |
| $A_I$ | The number of infectious adult ticks |

**Table 2**
Parameters of the model system (1) and (2).

| | |
|---|---|
| $M$ | The total number of rodents |
| $D$ | The total number of the deers |
| $F_A$ | The rate at which adult ticks attack deers, this is a function of $D$ |
| $F_L$ | The rate at which larval ticks attach on rodents, this is a function of $M$ |
| $F_N$ | The rate at which nymphal ticks bite rodents, this is a function of $M$ |
| $b$ | The larvae hatching per adult tick–deer interaction, in the absence of tick self-regulation |
| $1/K$ | The scales self-regulation in tick reproduction |
| $\mu_L$ | The larvae death rate |
| $\mu_N$ | The death rate for tick nymphs |
| $\mu_A$ | The death rate for adult ticks |
| $\beta_M$ | Transmission coefficient of spirochete infection to rodents |
| $\beta_L$ | Transmission coefficient of spirochete infection to larval ticks |
| $\beta_N$ | Transmission coefficient of spirochete infection to nymphal ticks |

where $L^* = (\mu_N + F_N)/F_L(\mu_A/F_N A^*)$ and $N^* = \mu_A/F_N A^*$. In Caraco et al. (1998), it was proved that if $\mathcal{R}_{Tick} \le 1$, then $(0, 0, 0)$ is locally stable. Using the following Lyapunov function, which has been widely used in the mathematical biology literature (see, e.g., Guo and Li, 2004; Ma et al., 2003; Korobeinikov and Maini, 2004 and references therein)

$$V_1(t) = F_L L(t) + (F_L + \mu_L)N(t) + \frac{(F_L + \mu_L)(\mu_N + F_N)}{F_N}A(t),$$

we can show that every solution of (1) converges to (0, 0, 0) if $\mathcal{R}_{Tick} \le 1$. On the other hand, if $\mathcal{R}_{Tick} > 1$, then (0, 0, 0) is unstable and a unique positive equilibrium $(L^*, N^*, A^*)$ exists. At this positive equilibrium, the transmission dynamics subsystem (2) is reduced to

$$\begin{aligned} \frac{dM_I(t)}{dt} &= \beta_M F_N \frac{M - M_I(t)}{M} N_I(t) - \mu_M M_I(t), \\ \frac{dN_I(t)}{dt} &= \beta_L F_L L^* \frac{M_I(t)}{M} - (F_N + \mu_N)N_I(t). \end{aligned} \tag{3}$$

Note that the equation for $A_I(t)$ is decoupled from the above subsystem. Note also that biologically, infectious nymphs deserve more attention: nymphs transmit the disease more efficiently, and the bacteria is maintained between hosts and immature ticks (Ostfeld, 2011). For the limiting system (3), we can compute the (epidemiological) basic reproduction number using the next generation matrix method (see Diekmann and Heesterbeek, 2000; van den Driessche and Watmough, 2002). In particular, we set the disease transmission matrix

$$F = \begin{pmatrix} 0 & \beta_M F_N \\ \beta_L F_L \dfrac{L^*}{M} & 0 \end{pmatrix}$$

and the transition matrix

$$V = \begin{pmatrix} \mu_M & 0 \\ 0 & F_N + \mu_N \end{pmatrix}.$$

Then the next generation matrix is

$$FV^{-1} = \begin{pmatrix} 0 & \dfrac{\beta_M F_N}{F_N + \mu_N} \\ \beta_L F_L \dfrac{L^*}{M}\dfrac{1}{\mu_M} & 0 \end{pmatrix},$$

and the basic reproduction number is calculated as

$$\mathcal{R}_0 = \sqrt{\frac{\beta_M F_N}{F_N + \mu_N}\frac{\beta_L F_L L^*}{\mu_M M}} = \sqrt{\frac{\beta_M \beta_L \mu_A A^*}{\mu_M M}}.$$

In the case where $\mathcal{R}_0 > 1$, we have a unique positive endemic equilibrium $(M_I^*, N_I^*)$, given by

$$M_I^* = M - \frac{\mu_M M^2(F_N + \mu_N)}{\beta_L F_L L^* \beta_M F_N} = M\left(1 - \frac{1}{\mathcal{R}_0^2}\right),$$
$$N_I^* = \frac{\beta_L F_L L^*}{F_N + \mu_N}\left(1 - \frac{1}{\mathcal{R}_0^2}\right) = \beta_L N^*\left(1 - \frac{1}{\mathcal{R}_0^2}\right).$$

Since system (3) is of the Ross-Macdonald type, we have

**Theorem 2.1.** *If $\mathcal{R}_0 \le 1$, the disease free equilibrium is globally asymptotically stable; if $\mathcal{R}_0 > 1$, there exists a positive disease endemic equilibrium and it is globally asymptotically stable with respect to all nontrivial solutions.*

This result can be obtained by using the Lyapunov function $V_2(t) = M_I(t) + \mu_M M N_I(t)/(\beta_L F_L L^*)$ for the case where $\mathcal{R}_0 \le 1$, and the Lyapunov function

$$V_3(t) = \left(M_I(t) - M_I^* - M_I^* \ln\frac{M_I}{M_I^*}\right) + \frac{\mu_M M}{\beta_L F_L L^*}\left(N_I(t) - N_I^* - N_I^* \ln\frac{N_I}{N_I^*}\right)$$

in the case where $\mathcal{R}_0 > 1$.

Therefore, the dynamics of the model system (Eqs. (1) and (2)) can be determined by the two threshold parameters: the reproduction number for ticks ($\mathcal{R}_{Tick}$) and the basic reproduction number for the Lyme disease ($\mathcal{R}_0$).

### 2.2. Three scenarios

In this section, we discuss the results with respect to different host seeking rates.

#### 2.2.1. Frequency dependent seeking rate

One commonly used vector seeking rate is frequency dependent following Anderson and May (1991) and Wonham et al. (2006) by assuming that the vector seeking rate is saturated and thus not limited by the host density. Thus in the frequency-dependent seeking process, the host searching time of ticks is independent of the host's density, and we have $F_L = p_1$, $F_N = p_2$ and $F_A = p_3$, with constants $p_1$, $p_2$ and $p_3$. In this case, $\mathcal{R}_{Tick}$, $L^*$, $N^*$ and $A^*$ are independent of the rodent and deer populations. Therefore, increasing or decreasing the rodent and deer populations has no effect on tick control. However, increasing the rodent population $M$ implies that $\mathcal{R}_0$ and $N_I^*$ are decreased. So, reducing rodents is always not good for disease control. To control the disease, we should increase the rodent population and set the rodent population size large enough such that $\mathcal{R}_0 \le 1$. To achieve $\mathcal{R}_0 \le 1$, the rodent population should satisfy

$$M \ge \frac{\beta_M \beta_L \mu_A}{\mu_M} K\left(bp_3 - (p_1 + \mu_L)\frac{\mu_N + p_2}{p_1}\frac{\mu_A}{p_2}\right).$$

If more rodents are introduced into the habitat, infectious tick bites may be wasted such that $\mathcal{R}_0 < 1$. We illustrate the above arguments by the numerical simulations (see Fig. 1). In particular, we observe that increasing rodents may decrease disease risk, whether that risk is measured by DIN or by NIP.

#### 2.2.2. Density dependent seeking rate

Another commonly used vector seeking rate is density dependent, which is termed as mass action (e.g., Wonham et al., 2006). In the density-dependent seeking process, the host searching time of ticks is proportional to the reciprocal of the host density. Hence, we have $F_L = q_1 M$, $F_N = q_2 M$ and $F_A = q_3 D$, where $q_1$, $q_2$ and $q_3$ are constants. Since in this case

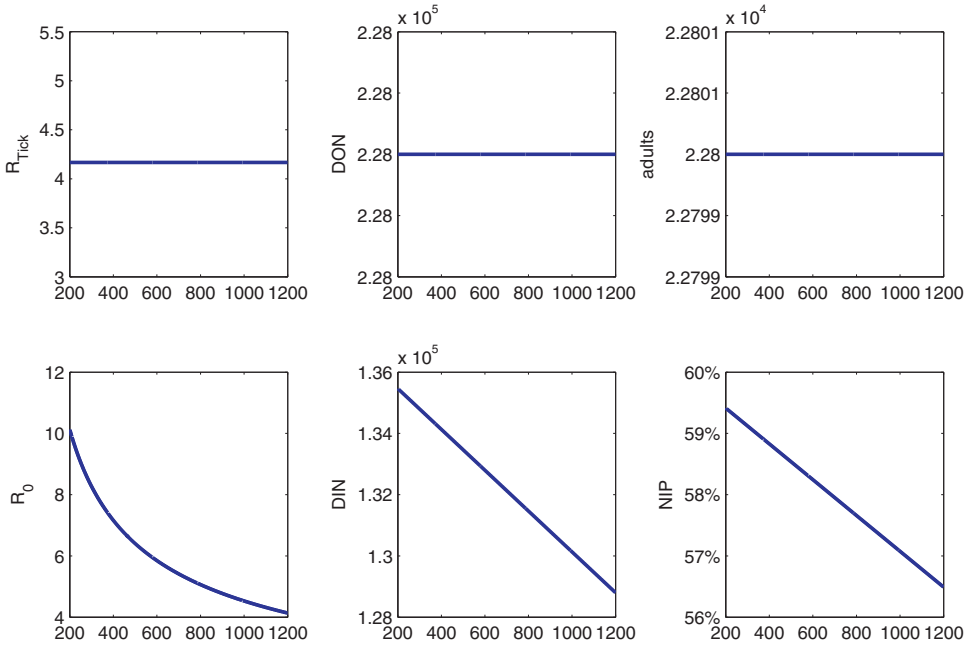


**Fig. 1.** The relationship between a given index and the population of the rodents with frequency-dependent seeking rate: the horizontal $x$-axis is the rodent population size. In this case, the number of infectious nymphs is a linearly decreasing function of the rodent population. Parameter values are: $b = 600$, $K = 100$, $\mu_L = 0.7$, $\mu_N = 0.8$, $\mu_A = 1$, $\mu_M = 0.2$, $\beta_M = 0.3$, $\beta_L = 0.6$, $\beta_N = 0.6$, $D = 50$, $p_1 = 0.1$, $p_2 = 0.1$ and $p_3 = 0.5$. DON: density of nymphs; DIN: density of infected nymphs; NIP: infected nymphal prevalence.

$$\mathcal{R}_{Tick} = bq_3D\frac{q_1M}{q_1M+\mu_L}\frac{q_2M}{q_2M+\mu_N}\frac{1}{\mu_A},$$

is always an increasing function of $D$ and $M$. Set $\mathcal{R}_{Tick} = 1$, we have the following equation

$$\frac{\mu_L\mu_N}{q_1q_2}\left(\frac{1}{M}\right)^2 + \frac{1}{M}\left(\frac{\mu_L}{q_1}+\frac{\mu_N}{q_2}\right) + 1 - bq_3D\frac{1}{\mu_A} = 0. \tag{4}$$

Therefore, if $bq_3D/\mu_A \le 1$ then Eq. (4) for $M$ has no positive root. This means $\mathcal{R}_{Tick} < 1$ for all rodent population sizes, and ticks cannot establish. On the other hand, if $bq_3D/\mu_A > 1$, Eq. (4) has a unique positive root. In this case, the positive root of Eq. $\mathcal{R}_{Tick} = 1$ (Eq. (4)) is

$$M = \frac{2\mu_L\mu_N/(q_1q_2)}{-(\mu_L/q_1+\mu_N/q_2)+\sqrt{\begin{array}{c}(\mu_L/q_1+\mu_N/q_2)^2\\ +4(\mu_L\mu_N)/(q_1q_2)(bq_3D/\mu_A-1)\end{array}}} := M_c.$$

This root $M$ is a decreasing function of $D$. Hence, if the deer population $D \le \mu_A/(bq_3) := D_c$, the tick cannot establish because of insufficient foods for adult ticks. When the deer population exceeds the critical size $\mu_A/(bq_3)$, there is a corresponding critical size $M_c = M_c(D)$ of the rodent population above which tick establishment is possible. This critical value $M_c$ of the rodent population is a decreasing function of the deer population size.

If the reproduction number for ticks $\mathcal{R}_{Tick} > 1$, ticks can establish in the habitat and the equilibrium abundances are

$$A^* = K\left(bq_3D - (F_L+\mu_L)\frac{\mu_N+F_N}{F_L}\frac{\mu_A}{F_N}\right),\ L^* = \frac{\mu_N+F_N}{F_L}\frac{\mu_A}{F_N}A^*,$$
$$N^* = \frac{\mu_A}{F_N}A^*,$$

which are all increasing functions of $D$. Hence, reducing the deer is always beneficial for tick control. In this case, the adult tick population size $A^* = K(bq_3D - \mu_A(1+(\mu_L/(q_1M)))(1+(\mu_N/(q_2M))))$ is an increasing function of $M$. Note that the adult tick population is saturated at the state $K(bq_3D - \mu_A)$ if the deer population is fixed. The population sizes for larvae and nymphs, $L^*$ and $N^*$, can be either increasing or decreasing while $M$ is increased.

Note that $\mathcal{R}_0^2 = (\beta_M\beta_L\mu_AK)/\mu_M[(bq_3D/M) - (\mu_A/M)(1+(\mu_L/(q_1M)))\ (1+(\mu_N/(q_2M)))]$. Therefore, $\mathcal{R}_0$ is an increasing function of $D$, so reducing deers is beneficial for controlling the disease. Using this formula for $\mathcal{R}_0$, we can derive from $(\partial\mathcal{R}_0^2)/\partial M = 0$ the following equation:

$$3\frac{\mu_L}{q_1}\frac{\mu_N}{q_2}\left(\frac{1}{M}\right)^2 + \left(2\frac{\mu_N}{q_2}+2\frac{\mu_L}{q_1}\right)\frac{1}{M} + 1 - \frac{bq_3D}{\mu_A} = 0.$$

When $D > D_c$, that is, the deer host is abundant, the above equation has one positive root $M_0$. Then, $\mathcal{R}_0 = \mathcal{R}_0(M)$ as a function of $M$ increases for $M \le M_0$ ($(\partial\mathcal{R}_0^2)/\partial M > 0$ when $M < M_0$) and then decreases for $M > M_0$ ($(\partial\mathcal{R}_0^2)/\partial M < 0$ when $M > M_0$). Consequently, reducing rodents does not necessarily contribute to the disease control. Setting $\mathcal{R}_0 = 1$, we get

$$\frac{\beta_M\beta_L\mu_A}{\mu_MM}K\left(bq_3D - \mu_A\left(1+\frac{\mu_L}{q_1M}\right)\left(1+\frac{\mu_N}{q_2M}\right)\right) = 1.$$

This equation has two positive roots for $M$ for the fixed deer population $D$. These two positive roots indicate two critical values of rodents size for pathogen maintenance: one corresponds to the case where the tick population size is too small (due to small rodent size) to sustain the transmission cycle. The other to the case where the host population size is so large that immature ticks develop too fast, resulting in a low immature tick population level that no longer sustains the transmission cycle. In this case, large rodent population size will also waste effective infectious bites, leads to the dilution effect due to encounter reduction. This is

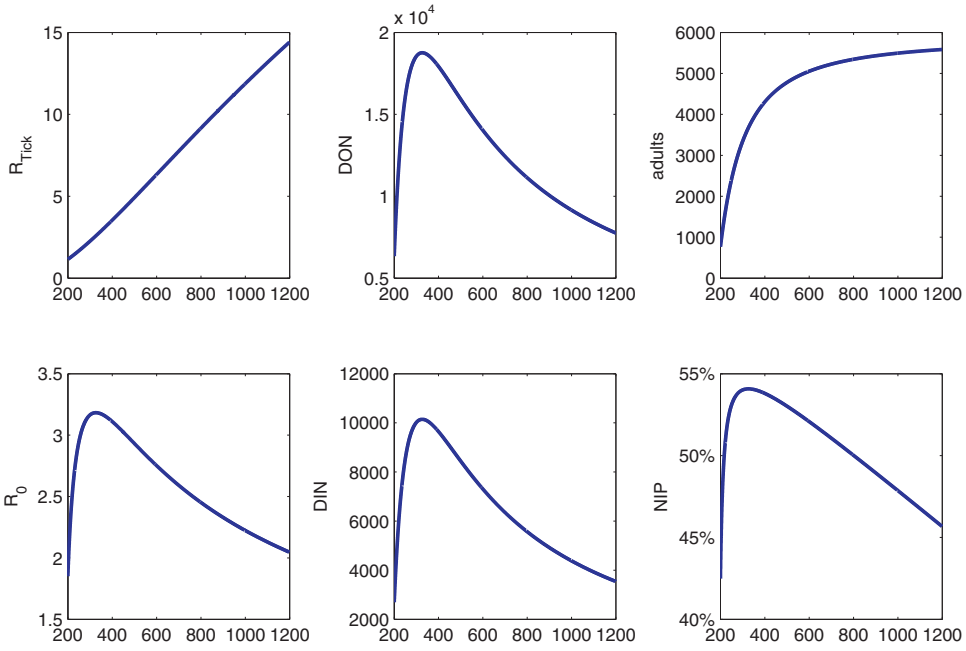


**Fig. 2.** The relationship between a given index and the rodent population size with density-dependent seeking rate: the horizontal $x$-axis is the rodent population size. Parameter values are: $b = 600$, $K = 100$, $\mu_L = 0.7$, $\mu_N = 0.8$, $\mu_A = 1$, $\mu_M = 0.2$, $\beta_M = 0.3$, $\beta_L = 0.6$, $\beta_N = 0.6$, $D = 50$, $q_1 = 0.0006$, $q_2 = 0.0006$ and $q_3 = 0.002$. DON: density of nymphs; DIN: density of infected nymphs; NIP: infected nymphal prevalence.

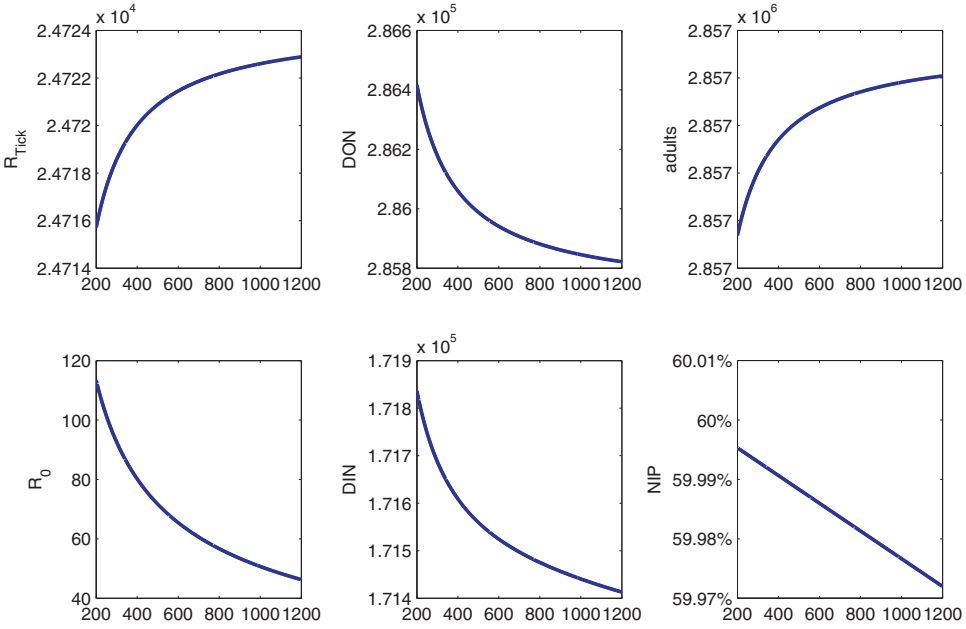


**Fig. 3.** The relationship between a given index and the rodent population size with Holling-type seeking rate: the horizontal $x$-axis is the rodent population size. Parameter values are: $b = 600$, $K = 100$, $\mu_L = 0.7$, $\mu_N = 0.8$, $\mu_A = 1$, $\mu_M = 0.2$, $\beta_M = 0.3$, $\beta_L = 0.6$, $\beta_N = 0.6$, $D = 50$, $a_1 = a_2 = a_3 = 0.1$, $b_1 = b_2 = 0.2$, $b_3 = 0.04$ and $c_1 = c_2 = c_3 = 2$. DON: density of nymphs; DIN: density of infected nymphs; NIP: infected nymphal prevalence.

illustrated in Fig. 2. In particular, increasing rodents may increase or disease risk.

### 2.2.3. Holling type 2 seeking rate

For the Holling type 2 functional response (Holling, 1959), we have $F_L = c_1M/(a_1 + b_1M)$, $F_N = c_2M/(a_2 + b_2M)$ and $F_A = c_3D/(a_3 + b_3D)$, where $a_i$, $b_i$ and $c_i$ are constants for $i = 1, 2, 3$. Because the Holling type 2 response is a mediate situation between the frequency dependent seeking rate and density dependent seeking rate, we can reproduce the results in the first two cases using this host–vector interaction pattern by changing a few parameters in this transmission term. Figs. 3 and 4, with two different sets of parameters for the interaction term, illustrate this mediate situation.

## 3. Discussion

In this paper we investigate the impact of tick seeking assumptions on the Lyme disease prediction. Three different tick seeking assumptions are considered: (i) the average number of bites made by a tick in per unit time is saturated at a constant, and independent of the host density (frequency-dependent rate); (ii)

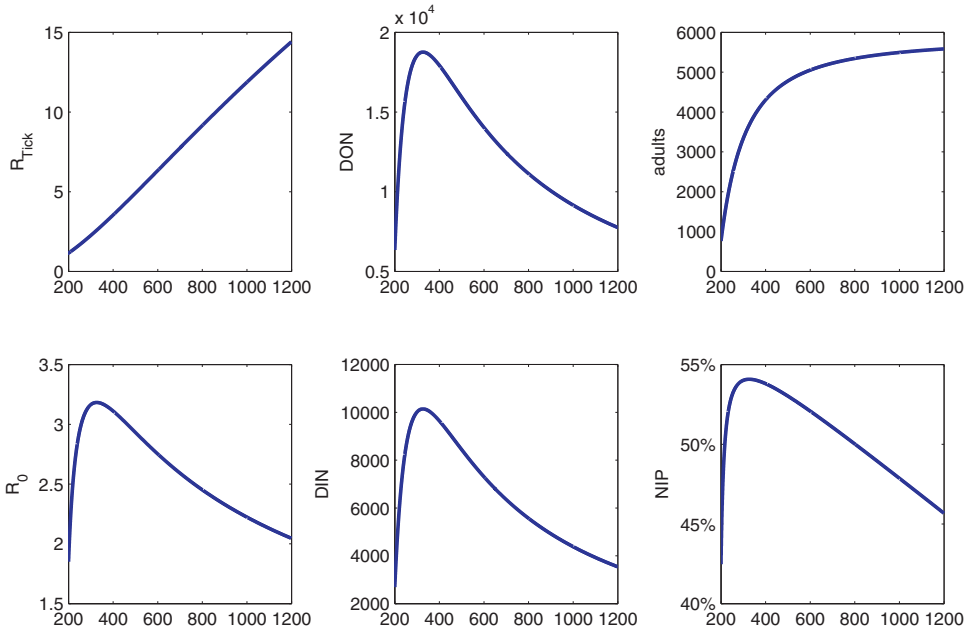


**Fig. 4.** The relationship between a given index and the rodent population size with Holling-type seeking rate: the horizontal $x$-axis is the rodent population size. Parameter values are: $b = 600$, $K = 100$, $\mu_L = 0.7$, $\mu_N = 0.8$, $\mu_A = 1$, $\mu_M = 0.2$, $\beta_M = 0.3$, $\beta_L = 0.6$, $\beta_N = 0.6$, $D = 50$, $a_1 = a_2 = 10{,}000$, $a_3 = 1000$, $b_1 = b_2 = b_3 = 0.001$, $c_1 = c_2 = 6$ and $c_3 = 2$. DON: density of nymphs; DIN: density of infected nymphs; NIP: infected nymphal prevalence.

the number of bites made by a tick per unit time increases linearly with host population size (the density-dependent rate); and (iii) the number of bites made by a tick per unit time increases with host density when the density is small, but becomes saturated with large host population size (the Holling type 2 rate). Conflicting outbreak predictions are generated by different assumptions: The frequency-dependent assumption predicts that reducing the rodent population will always reduce Lyme disease outbreaks, whereas the density-dependent and Holling type 2 seeking assumptions predict that this will reduce or exacerbate infection risk.

A host species that is a competent reservoir for *B. burgdorferi* can cause infection in a high proportion of the ticks that feed on it in nature. In our model, we first consider rodents as the sole host species for immature ticks. Ecologically, rodent is a competent reservoir, which is efficient in feeding and infecting ticks. In reality, the host community of ticks is very complicated and shows high level of diversity (Mannelli et al., 2012; Ostfeld, 2011). If we add another host species to the model, whereas the added species shares the similar growth and reservoir competence with the existing rodent population, then increasing the rodent population size in the model can be considered as adding this species to the existing host community, which in turn enhancing the biodiversity in the habitat with an additional similar host species. Then we can use the model to study the effect of increasing biodiversity on pathogen transmission and disease risk. We emphasize that a multi-host model will be needed if different rodent species behaves differently with respect to the disease and/or have different life history parameters. Adding disease incompetent reservoirs into the existing community was shown to dilute the Lyme disease transmission (Ostfeld and Keesing, 2000). However, increasing the community diversity with a disease competent reservoir species (increasing the rodent population size in our model) can also reduce the disease transmission, as our analysis suggested. We addressed this dilution effect for different host seeking patterns. For the frequency-dependent seeking rate, the infectious nymph population size and the epidemiological basic reproduction number are decreased with increasing rodent population because the infectious bites of nymphs are wasted in superfluous susceptible rodents, i.e., the number of infectious ticks per rodent would be very low such that the pathogen can not be transmitted to new ticks. This phenomenon occurs when lots of infectious bites are wasted on the host population, making the per capita transmission rates actually fall. This mechanism can be termed as encounter reduction (Keesing et al., 2006), which is also similar to the study about West Nile virus transmission (Wonham et al., 2006), where it was noted that increasing the bird population might decrease the pathogen risk for the frequency-dependent contact process. However, for the density-dependent case, both the amplification effect and dilution effect were observed. With low level of biodiversity, increasing biodiversity provides more food supply for immature ticks and thus increases tick survival and abundance, which in turn enhancing the disease risk. However, with high level of biodiversity, increasing the biodiversity may induce a decrease in pathogen transmission, yielding the dilution effect. The infectious nymph population and the epidemiological basic reproduction number are decreased while the rodent population is increased because of the fast development of the larvae to the adult stage thanks to the sufficient food (rodents) supply. However, since the adult tick population may be saturated at a level limited by its food supply (deers), the nymph population can only survive at a low abundance. Since the pathogen transmission cycle is maintained between rodents and immature ticks, and the population of infectious nymphs is directly regulated by the population of larvae and nymphs (as shown in the limiting system (3)), the total number of immature ticks regulates the disease risk. Thus, large rodent populations promote the development of immature ticks and the abundance of immature ticks becomes low, reducing the probability for ticks to infect the rodents and the probability for ticks to get infected. The mechanism under this dilution effect can be termed as vector regulation (Keesing et al., 2006). However, this development related dilution shows the decrease of disease incidence as the result of the large development rate with a small size of immature ticks to sustain the transmission cycle. Note that, whether the seeking rate is density-dependent or frequency-dependent, our model suggests that high host diversity is more likely to decrease rather than to increase disease risk, which is consistent with the other studies such as Keesing et al. (2006).

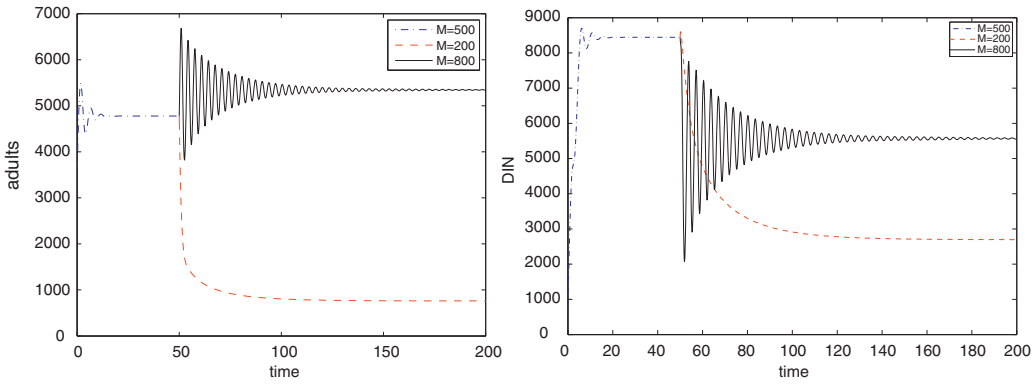


**Fig. 5.** Impact of rodent removal and rodent increase in the context of Lyme disease control, in the case of the density-dependent interaction rate. Rodent removal and increase occurs at $t = 50$. The parameters are same as those in Fig. 2 with the rodent population $M = 500$ at first, and increased to $M = 800$ or decreased to $M = 200$ after $t > 50$. DIN: density of infected nymphs.

Our hypothetical model with a density-dependent rate indicates that the tick populations and the density of infected nymphs (DIN) are positively and closely tied to the deer population (as one increases, so does the other). Thus deer abundance threshold is critical for tick survival and disease transmission. Deer control would be considered as a method of reducing the tick population and human risk to exposure to the Lyme disease. However, as reviewed in Ostfeld (2011, p. 32), some studies show that even deers are eliminated, reduced by hunting, or excluded by fencing, the next several years sees an increase in the proportion of immature ticks that are infected with Lyme disease spirochetes, thus the increase in disease risk. The inconsistency of our result and those studies arises from our assumption that deers are the sole host for adult ticks and that rodents are the host for immature ticks. In reality, adult ticks that would have fed on deers will evolve to feed on other hosts, such as rodents in the case when deers are rare (Ostfeld, 2011, p. 32). Incorporating this evolutionary selective behavior of ticks would enrich our understanding of mapping disease risks and controlling disease transmission. However, our model with frequency dependent seeking rate indicates that the tick abundance and disease risk are independent of the deer population, thus there is no threshold of deer abundance, which in turn supporting that reducing deer is not necessarily an efficient way to control the disease sometimes.

In mathematical biology, different contact rates between the vector and hosts are proposed under different assumptions. The frequency dependent seeking rate (the tick seeking rate is independent of the host population size) is suitable for the case when the host population size is very large, while on the contrary, the density-dependent seeking rate (the vector seeking rate is proportional to the host population size) is suitable for the case when the host population size is small. In this sense, the model with Holling type 2 transmission term is more appropriate. Our model with different vector seeking patterns shows why in some cases the deer population abundance is closely related to ticks (as in the density-dependent case), and why the relationship is weak (as in the frequency-dependent case). In response to the question "why might the relationship between deer and tick abundance be so viable, sometimes strong and sometimes weak or nonexistent?" proposed in Ostfeld (2011), we provided an interpretation from our modeling approach: when the deer population size is small, it is more appropriate to use density-dependent seeking pattern to describe tick–host interaction, thus the threshold of deer abundance is important and the deer and tick populations are closely related; while deers are abundant, the tick seeking rate is likely to be fixed, regardless of the deer population density (it is more appropriate to use frequency-dependent seeking rate to model the tick–host interaction), the threshold deer abundance is absent and the relationship between deers and tick abundances is nonexistent.

The host seeking behavior will have implications for control strategies based on the conceptual model. In the frequency-dependent interaction scenario, increasing rodents is always advantageous to contain the disease since more rodents may waste the infectious tick biting. However, for the density-dependent and Holling type 2 interaction scenarios, increasing rodents may increase or decrease the disease risk because of the existence of both the amplification effect and dilution effect. When the rodent population size is low, it is suggestive to reduce rodents to reduce the development of ticks, thus reducing the reproduction number of ticks and eradicating ticks. On the other hand, when the rodent population size is high, increasing the rodents will increase the development rates of immature ticks. Because of the self-regulation of the tick population, we may have saturated adult tick population. Thus, the population size of immature ticks stays at a low level due to the large development rate at the immature stage of ticks. Since the disease pathogen is maintained in the immature stage of ticks, the disease risk is lowered. Fig. 5 shows a special case where both increasing and decreasing the rodent population are beneficial for disease control. Although increasing or decreasing the rodent population may lead to more or less adults ticks, the infectious ticks may become less and the disease risk is lowered.

For tick-borne diseases, such as Lyme disease, we should not directly use some existing results arising from mosquito-borne diseases such as those in Wonham et al. (2006) where the bird reservoirs are not explicitly incorporated as a food supply for mosquitoes. Moreover, for the mosquito-borne disease, the transmission cycle is mainly maintained in the infected adult mosquito-reservoir-susceptible adult mosquito cycle, while the Lyme transmission is maintained in the infected nymphs-reservoir-susceptible larvae cycle, where nymphal and larval tick populations may be regulated by the adult survival probability, involving another host community different from that for immature ticks. In conclusion, our study shows that the tick–juvenile host interaction has to be considered as an important factor when investigating Lyme disease transmission. Our theoretical results advocate the pressing need for empirical studies on the functional form of interspecific transmission process in multihost pathogen system. Moreover, other transmission complications should be considered in the context of disease transmission.

In the Lyme disease transmission, various host species are involved, which makes it a multi-host system. For the disease transmission dynamics, dilution effects (Bolzoni et al., 2012; Tagliapietra et al., 2011; Pugliese and Rosà, 2008; Rosà and

Pugliese, 2007) and amplification effect are observed (Ogden and Tsao, 2009) by mathematical models. For the dynamics of Lyme disease transmission in multi-host system, we refer the reader to a recent review (Mannelli et al., 2012). In our present study, we mainly focus on the effect of tick seeking assumptions on model predictions. Here we use the Lyme disease as a representative of tick-borne diseases, however the model structure is also suitable to describe other tick-borne disease dynamics transmitted by three-host ticks, and the methodologies here can also be used to predict the disease risk of other tick-borne pathogens.

We have interpreted our analysis solely in terms of Lyme disease prevention and control. For example, we concluded that in many cases it is preferable to protect rodents, or even enhance their populations. How the presence of large rodent populations affects the population dynamics for other species and for human health remains a much challenging issue in managing a complex ecosystem with conflicting goals.

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