IDENTIFYING REQUIREMENTS FOR THE INVASION
OF A TICK SPECIES AND TICK-BORNE
PATHOGEN THROUGH TICKSIM

Holly Gaff and Robyn Nadolny

Department of Biological Sciences, Old Dominion University
110 MGB, Norfolk, Virginia 23529, USA

Abstract. Ticks and tick-borne diseases have been on the move throughout the United State over the past twenty years. We use an agent-based model, TICKSIM, to identify the key parameters that determine the success of invasion of the tick and if that is successful, the succees of the tick-borne pathogen. We find that if an area has competent hosts, an initial population of ten ticks is predicted to always establish a new population. The establishment of the tick-borne pathogen depends on three parameters: the initial prevalence in the ten founding ticks, the probability that a tick infects the longer-lived hosts and the probability that a tick infects the shorter-lived hosts. These results indicate that the transmission rates to hosts in the newly established area can be used to predict the potential risk of disease to humans.

1. **Introduction.** Tick-borne diseases have been on the rise in the United States for the past twenty years [2]. New diseases are emerging, and old diseases are being found in new areas. As tick populations that carry the pathogens that cause these diseases expand their natural range, it is critically important to understand the factors that affect the prevalence of pathogens in the new areas and thus the risk of human disease. The animal hosts and humans in these regions are frequently naive to the invading pathogen, and thus the risk of disease may be significantly higher in these newly established populations. Mathematical models provide an invaluable tool in assessing the requirements of an area to allow for successful establishment of a new tick species and the tick-borne pathogen assuming the tick species is successful. Here we explore the expansion of a previously published model, TICKSIM [7], to identify these requirements. TICKSIM was orignially designed to study the lone star tick (*Amblyomma americanum*) and the tick-borne pathogen, *Ehrlichia chaffeensis*.

Human monocytic ehrlichiosis (HME) is an emerging tick-borne disease caused by the bacteria, *E. chaffeensis*, and spread by the lone star tick (LST), *A. americanum* [1] HME can cause severe to fatal illness and is of increasing concern in the southeast and south-central regions of the US, where incidence is on the rise [4, 3]. The majority of reported cases of HME coincide with the highest reported densities of the LST not surprisingly also in the southern and southeastern US. Severe HME primarily impacts the immuno-compromised and those over 60, but has been lethal even to young, healthy individuals [9, 6].

Historically, LSTs were primarily known as a nuisance tick because of their aggression toward humans and their generalist feeding habits on a wide range of avian and mammal hosts. Since the 1980s, LSTs have been recognized as a vector of significant human pathogens including *E. chaffeensis* [3]. LSTs are by far the most abundant tick in the southern US, making up more than 90% of ticks encountered and often exceeding encounter rates of 500 nymphs per hour in heavily infested areas [10, 14]. The success of the LST is partially because their preferred habitat of young second-growth forest is abundant and has recently expanded through suburbanization [13, 12]. LSTs are generalist feeders and are known to parasitize white-tailed deer (*Odocoileus virginianus*), raccoons (*Procyon lotor*), red foxes (*Vulpes vulpes*), coyotes (*Canis latrans*), white-footed mice (*Peromyscus leucopus*), and Virginia opossums (*Didelphis virginianus*) [3, 12, 5, 11], all of which are also well adapted to suburban areas. All of these host species and particularly white-tailed deer have been shown to be competent reservoirs for the pathogen, *E. chaffeensis* [11]. The abundance of ticks, suitable habitat and competent hosts has resulted in increased risk to humans of LST tick encounter and thus exposure to *E. chaffeensis* [12, 3].

Modeling ticks and tick-borne infections is challenging because of the complex ecology and life history of ticks. Tick life history consists of four discrete life stages: egg, larva, nymph and adult. Ticks only feed once during each of the three latter life stages and generally live for a total of two to three years. Ticks will spend several days or weeks searching for a suitable host, known as questing, and then a few days to a week attached and feeding from a host. Larva and nymphs will then be dormant for months to a year while digesting the blood and molting to the next life stage. Adult male LSTs take smaller blood meals and seek females on the host while the LST females take large blood meals and then lay an egg mass. LSTs are nonspecific feeders and will aggressively seek out hosts at all three questing life stages rather than the sit and wait strategy used by many other species. Hosts have varying levels of susceptibility to tick-borne pathogens, so the success of a pathogen is dependent on the suitability of the hosts on which the tick feeds.

Agent based models (ABM) also called individual based models have previously been shown to be effective for simulating tick-borne diseases [7]. This model builds on the model described in Gaff's 2011 paper by adding a secondary host and through the performance of a sensitivity analysis on ten parameters to determine the importance of different variables in the tick-host-pathogen system. Climate change resulting in warmer winters and the abundance of disturbed woodland habitat because of suburbanization could contribute to in populations of LSTs becoming established outside of their usual range, particularly in the northeast and central US [12]. In addition, the aging US population represents a demographic at increased risk of HME. Our model describes the parameters that most impact the likelihood of *E. chaffeensis* becoming established if an infected population of LSTs was to invade an area with suitable habitat and competent hosts.

2. **Methods.**

2.1. **Model description.** This model description follows the ODD (Overview, Design concept and Details) protocol for describing individual and agent-based models developed by Grimm [8] and consists of five elements. The first three elements provide an overview, the fourth element explains general concepts underlying the model design, and the last element provides details.

1. Purpose

    The purpose of this model is to simulate an invasion of a new population of infected ticks in a multi-host community and to determine which parameters are responsible for the success or extinction of the invading pathogen. The model will be run using "base level" parameters derived from the literature, and then ten disease related parameters will be varied to determine the effect of each on the model predictions. The results of these simulations will help determine which parameters influence the probability that an initial population of infected ticks will not just establish a new population but also spread the agent of the disease.

2. Entities, state variables and scales

    This agent-based model considers the interactions among three populations: ticks, deer, and other hosts. Other hosts are a generic category of all other competent hosts such as raccoons and white-footed mice, and these agents are assumed to have shorter lifespans than deer. In this generalized model, the parameter values are loosely based on the LST, the white-tailed deer and an average of values for raccoons and rodents. This mix of hosts represents a typical environment in the eastern US that could easily be the site of an introduction of a new population of infected LSTs. The environment is set up as a grid of 25x25 uniform patches of equal quality with wrapping boundaries and assumed to represent approximately 100m by 100m. Each time step represents one day.

    Each of the tick agents has the following characteristics: a unique identification number; life stage: egg, larva, nymph, adult; infection status: susceptible, infectious; list of hosts ever used for blood meals; location; and current activity: resting, questing, feeding, laying eggs. Adult ticks are able to reproduce after feeding, so the tick population does not remain constant. Each of the deer and host agents also has an identity number; infection status: susceptible, infectious, immune; list of ticks ever attached; list of all ticks currently attached; current location; and age.

3. Process Overview and Scheduling

    This model follows the same steps every day of the simulation, as outlined in Figure 1 [7]. Tick mortality is dependent on the season of the year, with higher mortalities in the winter and summer because of the potential for desiccation during these time periods. If a deer or host dies, all ticks on that host are assumed to also die. The populations of hosts remain constant so that if one animal dies it is automatically and instantly replaced with another of the same species. This allows us to simulate a population of individuals using a simplified host life history and is useful for a simple model of disease.

4. Design Concepts

    i Basic Principles. The underlying principle of this model is that independent agents interact with one another and simulate the interactions that parasites would have with their hosts in the wild. Ticks interact with both deer and hosts by using them as sources of blood meals. Deer and hosts do not interact with each other but simply move randomly across the uniform landscape. As infected ticks feed on an uninfected host, there is a probability of transmission from that tick to that host. Similarly, if an uninfected tick feeds on an infected host, that host will transmit that

pathogen back to the tick at a given probability. Through these inter-
actions, an infection will either become established in the tick and host
populations, or the pathogen will go extinct.

ii Emergence. While the movement of the hosts is simple, with ticks and
hosts moving randomly from patch to patch, the tick feeding behavior, and
hence the possible disease transmission, is established through a series of
probabilities. If ticks and hosts are in the same patch, ticks sense the host
and then have a probability of successfully attaching. Once attached, there
is a probability of successful pathogen transmission between host and tick,
and an associated probability of mortality. By varying these probabilities
and through the use of stochasticity, the parameters that most impact the
emergence of a persistent infection will be determined.

iii Sensing. Deer and hosts move around the environment independently of
one another, and do not sense each other or interact in this simple model.
Ticks sense deer and hosts only within their own patch, and then have a
given probability of successful attachment to that deer or host.

iv Interaction. As mentioned, the two host species do not interact. The ticks
sense hosts on their patch and attach to a host in an attempt to successfully
obtain a blood meal. Each host species has a maximum number of ticks
that can be on a host at one time to account for density dependence. Ticks
do not interact with each other, only with hosts. Through the interactions
of ticks and hosts, the pathogen is transmitted and can spread throughout
agent populations over time.

v Stochasticity: Probabilities are given for parameters as described in Ta-
ble 1. Hosts and deer can move randomly to any adjacent patch and take
along any ticks currently feeding on them. The tick has a probability of at-
taching, a probability of mortality, and a probability of becoming infected
or transmitting infection. Deer and hosts have a probability of infecting
the tick, and a probability of mortality. The processes are stochastic for
each run, and each agent has equivalent fitness.

vi Collectives. While deer and hosts have social behaviors in the wild, i.e.,
herding or living with family groups in defined territories, we have omitted
these behaviors in this simple model. The simulated environment that the
model represents is small enough so that we believe there would be no sig-
nificant impact of social behavior on the emergence of the pathogen. More
complex models will take animal behavior into account. Ticks are known
to aggregate based on chemical cues, i.e. more ticks will be attracted to
a host that already has ticks on it, but this occurs at a very small spatial
scale and could be addressed in future models.

vii Observation. The number of tick, deer, and raccoon agents is monitored,
and data is collected on the daily prevalence of the pathogen in the tick,
deer and host agent populations, defined as the number infected divided
by the total number of agents.

5. Initialization

We initialized the static landscape of 25 by 25 patches of equal value with
wrapping boundaries, with an initial population of 10 adult ticks, 50 deer
and 500 hosts. The tick population has purposefully been set to a very low
number to simulate a new population of ticks entering an ecosystem, i.e., from
a migrating animal that had 10 nymphs feed to repletion the previous year

and survive to adulthood. The deer and hosts are randomly spread across the patch landscape, but the ticks are all placed into a single patch in the middle of the landscape. The parameters are listed in Table 1 and were based on those used by Gaff [7].

2.2. **Simulations.** In order to identify which factors contribute to the probability of establishment of a tick-borne pathogen such as *E. chaffeensis*, we chose to vary ten parameters one at a time as shown in Table 2 while keeping all other parameters as shown in Table 1. Each of the variants of these parameters was run 25 times until the extinction of the disease, defined as no remaining infected ticks or hosts, or 10,000 time steps. For each parameter variation, the average number of time steps to disease extinction and average maximum infection rates for deer, ticks, and other hosts were taken over the 25 runs.

The model was programmed using NetLogo version 5.0. This software was programmed by Uri Wilensky in 1999 and is freely available (http://ccl.northwestern.edu/netlogo/).

3. **Results.** The overall results demonstrate that while the tick population was able to become established for every simulation, the pathogen was far less likely to become established and typically remained in the system for less than two years. Three of the ten simulated parameters were found to have significant impacts on the time to disease extinction or infection prevalence (see Figure 2, Tables 3, 4, 5). Varying the initial prevalence of disease in the tick population had by far the most serious impact on time to disease extinction, as well as impacting the average maximum infection rates in deer, raccoons, and ticks (see Table 3). There was a significant positive correlation between initial prevalence and average time to extinction ($r = 0.81, p = 0.005$), average maximum tick infection rate ($r = .99, p < 0.0001$), average maximum deer infection rate ($r = .8, p = 0.005$), and average maximum host infection rate ($r = .94, p = 0.0001$).

Second, varying the probability that a tick would infect a deer when attached also produced a significant positive correlation (see Table 4). There was a significant positive correlation with the average maximum deer infection prevalence ($r = 0.73, p = 0.0125$).

Finally, varying the probability that a tick would infect a host when attached produced a significant positive correlation with the average maximum host infection prevalence (Table 4, $r = 0.81, p = 0.003$). None of the other parameters varied resulted in significant positive or negative correlations.

4. **Conclusions.** Initial disease prevalence and probability that a tick will infect a host are shown to be the most influential parameters for the establishment of *E. chaffeensis* in our agent-based model. Even within these results, it is clear that establishment of a tick population is nearly guaranteed in a completely isolated environment with competent hosts. In contrast, the pathogen rarely is able to become established in an isolated environment. This would imply that there would need to be connectivity to other areas where the pathogen has already been established to prevent this stochastic die out. Alternatively, a pathogen may be transovarially transmitted from a female tick directly to her eggs to increase likelihood of pathogen establishment, but. *E. chaffeensis* is not thought to be transovarially transmitted. These results also suggest that the reservoir competence of the hosts at the site of a potential tick population invasion is the most important factor in the establishment

of a disease. The initial infection rate of a new population of ticks will be linked to
the host that those ticks dropped off when initially invading. Because white-tailed
deer are considered to be the primary host for LSTs and are abundant across the
eastern US, it is likely that white-tailed deer would serve as the transportation for
LSTs into new environments. White-tailed deer have also been shown to be a highly
competent reservoir for *E. chaffeensis*, which increases the chance of a high initial
infection rate among ticks. Because white-tailed deer, raccoons, and other highly
competent reservoirs such as wild turkeys are abundant in forested and edge habi-
tat, an initial population would have a good chance of finding suitable hosts, but
connectivity to areas of established presence of *E. chaffeensis* would be required to
establish both the ticks and the pathogen. The TICKSIM model will be modified
in the future to explore this connectivity hypothesis and explore the dynamics at
the front of the invasion wave in contrast to this isolated drop off population.

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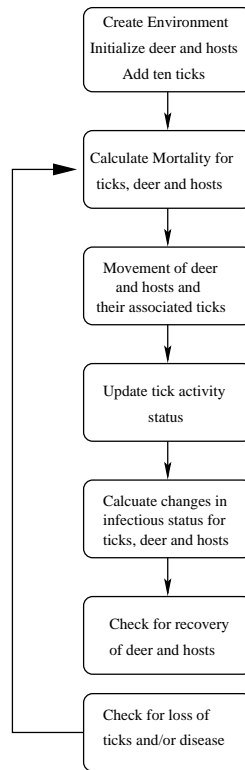of Microbiology, (2005).

FIGURE 1. Flow diagram for agent based model, based on TICK-SIM [12].

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E-mail address: hgaff@odu.edu
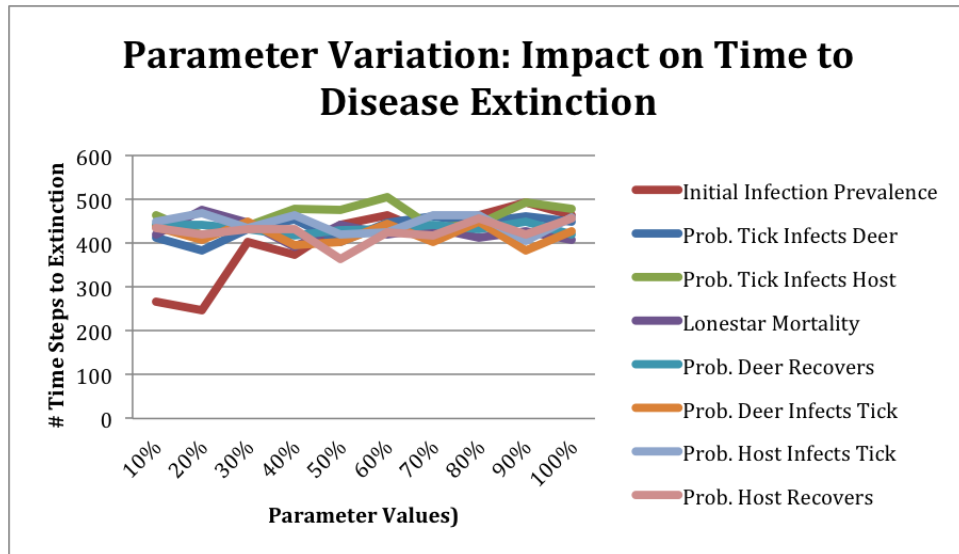*E-mail address*: rnado002@odu.edu

FIGURE 2. Results of the variation of eight parameters (from 10-100%) on the number of time steps to disease extinction. Only the initial infection prevalence of the tick population had a significant effect on number of time steps until the disease was lost from the system.

TABLE 1. Parameter values. These parameter values are used for all runs of TICKSIM. See [7] for sources.

Parameter	Value
Initial tick population	10% adults, 50% infected
Initial deer population	50 (0% infected)
Initial host population	500 (0% infected)
Eggs per female	250
Time from egg to questing larval stage	90 days
Time from fed larval to questing nymphal stage	270 days
Time from fed nymphal to questing adult stage	360 days
Tick mortality	0.1 in Jan, Feb, Mar, Jul, Oct, Nov and Dec 0.01 in Apr, May, Jun, Aug, Sep
Deer mortality	0.002 (500 day average lifespan)
Host mortality	0.02 (50 day average lifespan)
Maximum questing time	14 days
Length of blood meal	3 days
Prob of successful attachment on host	0.75
Prob of successful attachment on deer	0.75
Maximum ticks per host	200
Prob of deer recovery	0.05
Prob of host recovery	0.05
Prob of deer infecting tick	0.05
Prob of tick infecting host	0.05
Prob of tick infecting deer	0.1
Prob of tick infecting deer	0.05

TABLE 2. Parameters and ranges for those varied in simulations.

Parameter	Min	Max	Increment
Eggs per female	100	1900	200
Initial infection prevalence in invading ticks	10%	100%	10%
Mortality of LSTs	0%	100%	10%
Prob of deer recovery	0%	100%	10%
Prob of host recovery	0%	100%	10%
Prob of tick infects deer	0%	100%	10%
Prob of deer infects tick	0%	100%	10%
Prob of tick infects host	0%	100%	10%
Prob of host infects tick	0%	100%	10%
Number of days spent questing	5	50	5

TABLE 3. Results from varying initial prevalence of ten invading ticks.

Initial Prevalence	Average time to extinction	Average max tick infection prevalence	Average max deer infection prevalence	Average max host infection prevalence
10%	150.76	0.112	0.0008	0.00032
20%	230.84	0.195142857	0.0016	0.0004
30%	326.88	0.289	0.0016	0.0008
40%	443.08	0.486857143	0.004	0.00072
50%	456.44	0.584	0.0056	0.00152
60%	470.6	0.648666667	0.0032	0.00176
70%	479.68	0.753555556	0.0048	0.00176
80%	493.24	0.837333333	0.0064	0.00216
90%	458.8	0.912	0.0048	0.002
100%	448.68	1	0.0048	0.002

TABLE 4. Results from varying probability that ticks infect deer.

Probability tick infects deer	Average time to extinction	Average max tick infection prevalence	Average max deer infection prevalence	Average max host infection prevalence
0	432.08	0.54	0	0.0016
0.1	458.32	0.553	0.0024	0.00144
0.2	368.8	0.538666667	0.0048	0.00136
0.3	448.92	0.515	0.0088	0.00104
0.4	418.64	0.586285714	0.0048	0.00168
0.5	397.32	0.507666667	0.008	0.00128
0.6	413.32	0.477968254	0.0112	0.00136
0.7	433.4	0.564	0.0088	0.00112
0.8	422.6	0.485333333	0.0072	0.00128
0.9	390.48	0.526	0.0088	0.00112
1	470.36	0.541888889	0.008	0.0016

TABLE 5. Results from varying probability that ticks infect hosts.

Probability tick infects host	Average time to extinction	Average max tick infection prevalence	Average max deer infection prevalence	Average max host infection prevalence
0	428.08	0.52	0.0048	0
0.1	415.96	0.517	0.0024	0.002
0.2	37.28	0.497777778	0.0072	0.00272
0.3	456.92	0.608	0.0024	0.00336
0.4	473.04	0.574857143	0.0032	0.00328
0.5	458.16	0.607285714	0.0032	0.00416
0.6	436.84	0.561	0.0032	0.00376
0.7	463.88	0.57123095	0.0024	0.00424
0.8	432.52	0.522	0.0048	0.00408
0.9	425.08	0.532444444	0.004	0.0036
1	448.2	0.540571429	0.0024	0.00432