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PRELIMINARY ANALYSIS OF AN AGENT-BASED MODEL FOR A TICK-BORNE DISEASE

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Abstract. Ticks have a unique life history including a distinct set of life stages and a single blood meal per life stage. This makes tick-host interactions more complex from a mathematical perspective. In addition, any model of these interactions must involve a significant degree of stochasticity on the individual tick level. In an attempt to quantify these relationships, I have developed an individual-based model of the interactions between ticks and their hosts as well as the transmission of tick-borne disease between the two populations. The results from this model are compared with those from previously published differential equation based population models. The findings show that the agent-based model produces significantly lower prevalence of disease in both the ticks and their hosts than what is predicted by a similar differential equation model.

1. **Introduction.** According to the US Centers for Disease Control and Prevention, incidences of tick-borne diseases have risen dramatically in the past decade. In 2006, there were 578 confirmed cases of human monocytic ehrlichiosis (*Ehrlichia chaffeensis*), 19,931 confirmed cases of Lyme disease (*Borrelia burgdorferi*) and 2,288 cases of Rocky Mountain spotted fever (*Rickettsia rickettsii*) [1]. In order to understand these diseases, we must come to understand the underlying dynamics of the tick populations themselves [2]. Mathematical models can play an integral role in this critically important area of research. The challenge with any attempt to create a mathematical model is to identify the most appropriate model structure.

A number of models have been created to look at tick-borne diseases. Gaff, Schaefer and Gross have developed a differential equation based model for ehrlichiosis [3, 4, 5]. Mount and Haile and others formulated a series of computer simulations using age-structured difference equations [6, 7, 8, 9, 10, 11]. Awerbach, Sandberg and others also used matrix-based models to investigate seasonally varying population densities of ticks [12, 13]. Remote sensing and GIS approaches have also been applied to exploring the dynamics of tick-borne diseases [14, 15, 16, 17]. Spatial resolution has been added to vector-borne models using partial differential equation models [18, 19, 20]. Basic ecological modeling approaches have been used to study overarching dynamics such as the relationship between tick-borne diseases and host diversity [21, 22]. Recently hybrid mathematical techniques such as semi-discrete systems have been used to study tick-borne diseases [23, 24].

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While each of these models were helpful to investigate the dynamics of tick and tick-borne diseases, they all use a population approach with generalized mass-action interactions between ticks and their hosts. While this relationship may be applicable, the unique life history of a tick may preclude these models from producing the most appropriate results. This is not as much of a concern to explore the overarching dynamics, but as models are being used to identify areas of risk and fine tune intervention options to reduce these risks, we need to understand when these population-level assumptions are appropriate and when they break down.

Agent-based models, also called individual-based models, are computer-based models that simulate the actions and interactions of autonomous agents that represent the individuals of the population [25, 33]. These models are powerful simulations that can capture the emergent phenomena of a natural system. These types of models have been applied to many different areas of research such as ecology, e.g., white-tailed deer and panther populations in South Florida [26], and epidemiology, e.g., human disease outbreaks in a realistic urban area [27].

As mentioned previously, ticks have a rather unusual life history. In general, hard-bodied (Ixodid) ticks have a two-year life cycle. After hatching from an egg, ticks have three distinct life stages: larval, nymph and adult, and the number and distribution of blood meals required in each life stage varies between tick species. Most tick species in the United States have one blood meal per life stage with a resting period between meals. Population models that allow for continuous mass-action interaction at least over some time ignore this single host-vector interaction per life stage. The preferred host, or hosts, are also species-dependent and can be different for each life stage, adding complexity to the study of tick-borne diseases. Rodents have often been implicated as one of the important hosts for many species of ticks at the nymph stage of life, while deer or other large mammals are preferred at the adult stage [28]. Various tick species differ in their levels of competency for spreading different diseases [29]. To be a competent vector for a disease, the tick must be able to pass the disease transstadially, i.e., from one life stage to the next, or transovarially, i.e., from mother to offspring. The preferred host or hosts vary widely in reservoir competence, the probability that a vector feeding on an infected host will become infected, so the community composition, the variety of species present, of an area can greatly impact the disease prevalence [21], [30].

This paper looks at the initial development of an agent-based model (TICKSIM) for a simple tick-borne disease. The development of the model itself was instructive to clearly delineate the tick-host-pathogen system. The results of the model are presented and compared with those from a population-based model, and the conclusions include many potential future directions for this model.

2. **Methods.**

2.1. **The model.**

The model description follows the ODD (Overview, Design concepts and Details) protocol for describing individual- and agent-based models developed by Grimm [31], [33] and consists of seven elements. The first three elements provide an overview, the fourth element explains general concepts underlying the model's design, and the remaining three elements provide details.

2.1.1. *Purpose.* The main purpose of this initial model is to explore population dynamics of a model that includes the specific life history characteristics of ticks at an individual level. The results of the agent-based model will be compared with

the results from other population-based approach models. The results will highlight when population-based models are appropriate for tick-borne disease studies and when more detail is required such as that available from an agent-based model.

2.1.2. *State variables and scales.* In the agent-based model, two populations are considered: ticks and hosts. Each tick and each host along with their respective traits are followed over successive time intervals. This simple initial model uses a generic version of each of these agents, but the parameter values are based loosely on those for the lone star tick, *Amblyomma americanum*, and the white-tailed deer, *Odocoileus virginianus*. The environment is set up as 25x25 patches of equal quality with wrapping boundaries.

Each tick agent has a unique identification number, sex, age, location, life stage (egg, larva, nymph, adult), time in current stage, infection status (susceptible, infectious), current activity (resting, questing, feeding, laying eggs (females) and hosts (list of all hosts used for blood meals). Similarly, host agents have a unique identification number, age, list of all ticks current on the host, list of all ticks ever on the host and infection status (susceptible, infectious, immune).

2.1.3. *Process overview and scheduling.* The model follows the same steps every day of the simulation as shown in Figure 1. The mortality of ticks is based on the time of the year with higher probabilities of death in the winter and summer. If a host dies, all ticks on that host are also assumed to die. The host is also immediately replaced to maintain a constant population.

2.1.4. *Design concepts.* The agents in the simulation interact as the ticks find hosts to use for blood meals. The ticks can only sense hosts within their patch, and there is still only a small probability of actually successfully attaching to that host. The density dependence is only indirectly implemented by giving a maximum number of ticks per host. All processes are stochastic for all runs, and currently there are no fitness differences between agents. Host movement between patches is currently simply a random process, but this will be changed to reflect foraging value of that patch in future versions.

2.1.5. *Input.* Each simulation is initiated in a uniform 25x25 patch grid with an initial 100 hosts randomly spread across the grid. The probability that a given deer will start the simulation infected is 0.1. Additionally, 1000 ticks are randomly spread across the grid. The probability that a given tick will be infected is also 0.1. The simulations are assumed to begin on June 1, at which time larval stages would not be present, and thus the initial ticks are split into adults and nymphs with approximately 100 adults and 900 nymphs. All other parameters are given in Table 1. These parameters are taken from Gaff and Gross (2007) to allow for comparison between this model and the differential equation model analyzed in that paper.

2.2. **Simulation experiments.** Two experiments were conducted for this initial analysis. The first experiment ran the basic model 100 times using the same initial values. The results were averaged in an attempt to identify population trends and to avoid stochastic anomalies. Counts of the number of ticks in each age class, number of deer, number of infected ticks, number of infected deer and number of questing ticks was recorded for each day of the 10 year simulation. The second experiment looked at the time to extinction. Given that the disease prevalence dropped to very low values at certain times of the year, the stochastic nature of the

simulation guarantees that the disease will eventually die out. 100 simulations were allowed to run until no infected ticks remained, and that time was recorded.

The model was coded using the programmable modeling environment, NetLogo. This software was authored by Uri Wilensky in 1999 and is freely available (http://ccl.northwestern.edu/netlogo/).

3. **Results.** The average results of the first experiment are shown in Figures 2 and 3. The average number of ticks remains fairly stable of the ten years of the scenario, but the percent infected for ticks and deer decline over time. This decline is partially because some scenarios lose the disease through stochastic die-out, but it also simply reflects that the initial conditions of 10% infected are much higher than the final values. Figure 4 shows a single run of TICKSIM that stabilizes with approximately 5% of the hosts infected and 3% of the ticks infected. These values are significantly lower than those from the differential equation model shown in Figure 5, which had hosts infected at nearly 40% and ticks infected between 5-15%.

The second experiment shows that the average time until the disease would die out in a completely isolated population would be about 20 years. There is wide variation in this time to extinction as shown in Figure 6 with some runs losing the disease in less than 10 years while others keep the disease over 50 years. There is no equivalent to this metric in a differential equation model as that class of models allows for a very small percentage of infected ticks.

4. **Conclusions.** TICKSIM is a successful implementation of tick-borne disease system using an agent-based model. The model is based on the life history of ticks and a simplistic host species. The overall results show that this agent-based model produces results significantly lower than was found with the differential equation model using similar parameter values. The dynamics are similar with the annual fluctuations found in tick populations. Unlike the differential equation based model, the disease can be truly eliminated from the agent-based model making comparisons of long-term results more challenging. While some of the continuing predicted decline of prevalence of disease can be attributed to the effects of stochastic die out, no single simulation run could produce results similar to those from the population model.

This difference between the results of the TICKSIM and the differential equation based model demonstrates the importance of understanding the transmission rate and interaction patterns. Mathematically, every tick and every host interact in the differential equation model, while in the agent- based model, each tick only interacts with three specific hosts. This difference can explain the large gap in the resulting percent infected. The estimates for the transmission rates were calculated for the differential equation based model assuming continuous mixing of ticks and hosts. Transmission rate is a challenging parameter to estimate for all diseases as there are so many factors influencing it. The results of the model are very sensitive to this parameter, and further research to better identify this would be helpful.

Tick-borne disease data is highly variable by the nature of the tick's life history. Validating a tick-borne disease model with data is challenging because the data is scarce and at varying scales. The results of these simulation experiments are certainly within the range of data values that exist in the literature [34, 35, 36]. The important finding here is that the differential equation models may overestimate the actual prevalence of disease. Similar findings have been shown in comparisons between agent-based models and differential equation models in immunology [32].

The process of creating both the agent-based and differential equation models has highlighted a number of key parameters that need to be better quantified from data. Additionally, the process of translating the differential equation based parameter values to an agent-based system isn't a standard procedure, and so refinement of the parameter might account for improved reliability of model results. Similarly, including host dynamics such as foraging and more realistic survival and reproduction may change the results. Identification of a specific tick species and its hosts would allow for a more specialized application.

The results of this model have been used to help shape a current coastal Virginia field study. The data from this study will then be used for improved parameter estimates, verification and validation of this model. Once either the agent-based or the differential equation based model has been shown to be appropriate for a given tick-borne disease system, that model can be used to explore various control strategies to help minimize disease risk to humans.

TABLE 1. Parameter values. These parameter values are used for all runs of TICKSIM. From [3]

Parameter	Value
Initial tick population	1000 (10% adults, 90 %nymphs, 10% of each infected)
Initial host population	100 (10% 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
Host mortality	0.002 (500 day average lifespan)
Maximum questing time	42 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	0.0
Prob of deer infecting tick	0.05
Prob of tick infecting host	0.05
Prob of tick infecting deer	0.1

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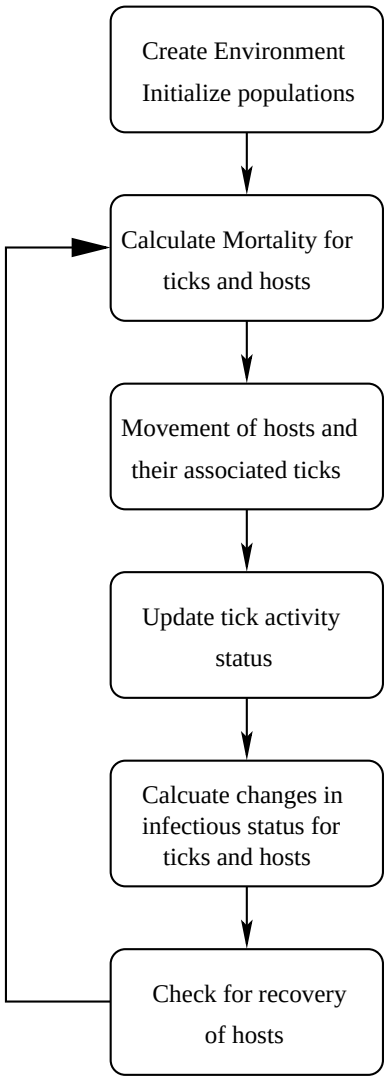

FIGURE 1. Flow diagram for TICKSIM agent-based model

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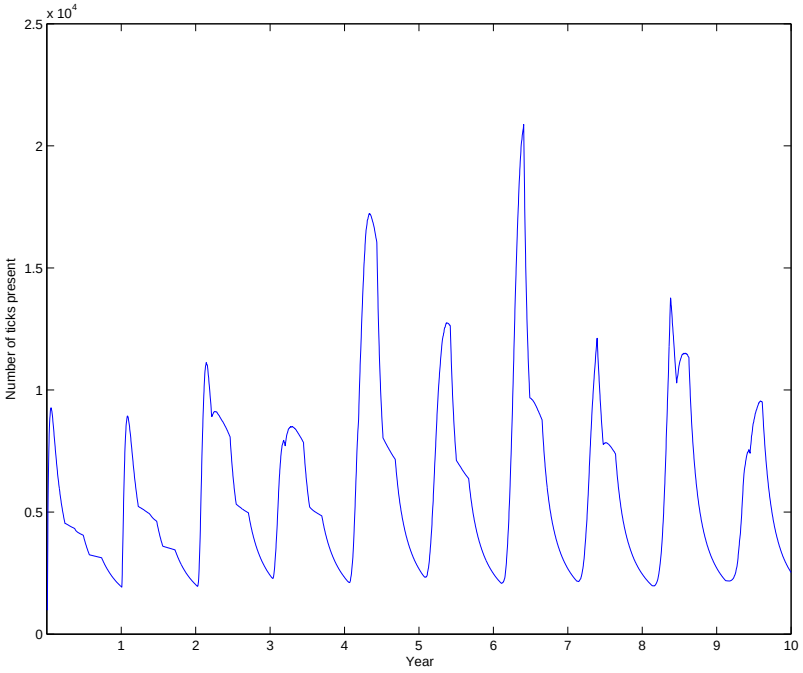

FIGURE 2. Results from Experiment 1. This plot shows the total number of ticks, not including eggs, in all patches for each day of the simulation run. The values are averaged across all 100 runs. The x-axis gives the year, and the y-axis gives the total number of ticks. The number of ticks varies widely over different parts of the year owing to the tick life cycle.

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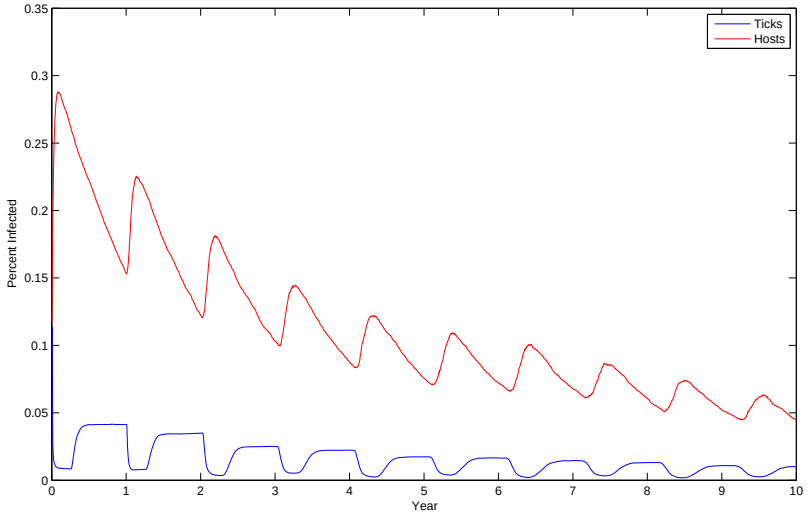

FIGURE 3. Results from Experiment 1. This plot shows the average fraction of ticks and deer that are infected in all patches for each day of the simulation run. The values vary throughout the year as the ticks become active. The peak fraction infected occurs slightly after the peak of number of ticks each year.

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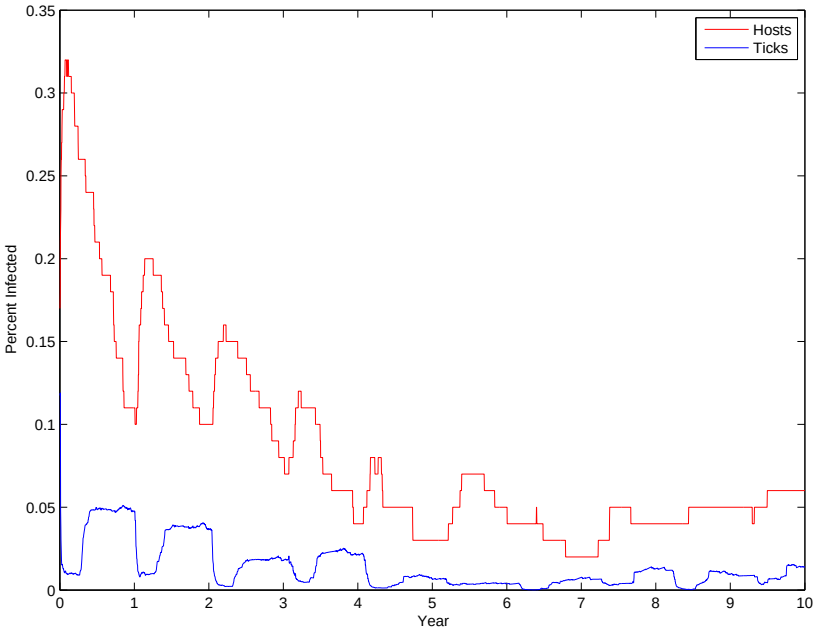

FIGURE 4. Results from Experiment 1. This plot shows the fraction of ticks and deer infected in all patches for each day of the simulation for a single run. This run shows a sustained infection rate of around 5% for deer and 2-3% for ticks.

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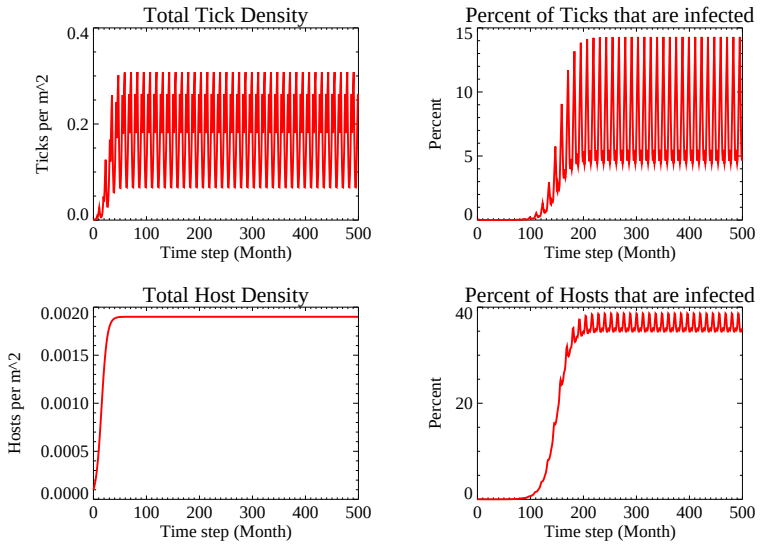

FIGURE 5. Results from a differential equation model. These plots show the results from a single run of a differential equation model using the same parameter values. The top left plot shows the total number of ticks by density, and the bottom left plot shows the total number of hosts. The two right hand plots show the percent of each population that is infected. This model predicts much high prevalence that the results shown in the previous figures.

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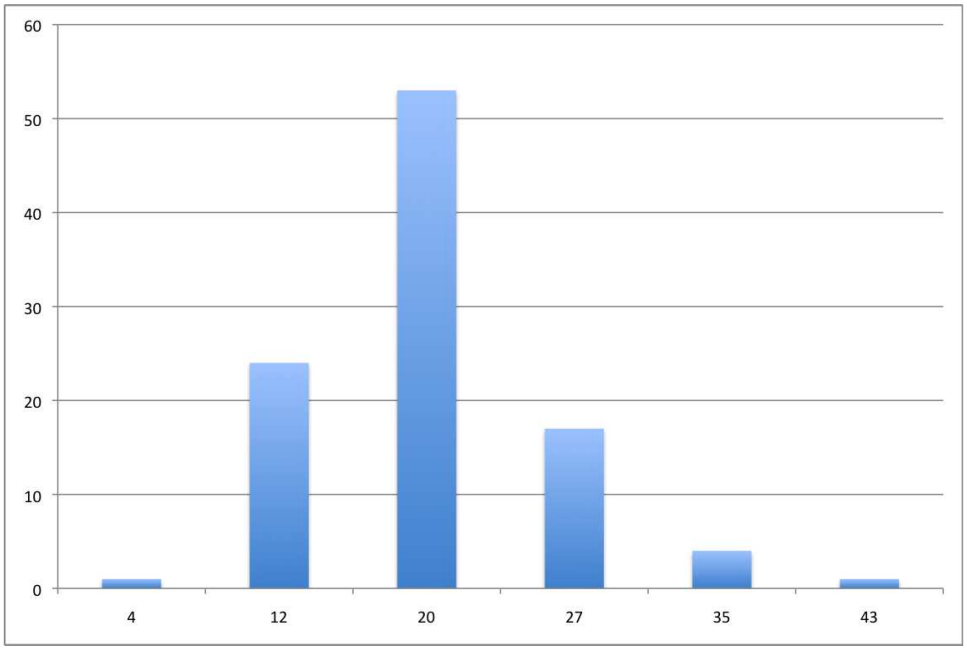

FIGURE 6. Results from Experiment Two. This plot shows a histogram of the time to extinction for each of the 100 simulation runs. The average length of time to disease extinction was 20 years, but there is wide variance with some simulation runs maintaining the disease for over 50 years while others lost the disease after fewer than 10 years.

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