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Math 5131

Final Project

A Susceptible-Infected Model of Lyme Disease Incidence on Nantucket Island

Introduction

Lyme Disease is the 5th most common report disease in the United States, and the 1st most common vector borne disease with approximately over 300,000 cases reported each year[1]. The majority of cases in the United States are reported in the Northeast. Lyme disease is a vector-borne disease, spread in the US by Ixodes scapularis ticks (deer ticks)[2].

One of the highest rates of Lyme disease in the United States is on Nantucket Island, Massachusetts[2]. Nantucket Island is an interesting case study for the relationship between deer population and Lyme disease incidence because it is a relatively closed population. Ticks are parasites which feed on deer. Deer have no competitors except for human hunters, which is encouraged to keep the population manageable. The susceptible population (humans) is estimated using a combination or census data and tourism data, as the population doubles in the summer. The infected population is more of a challenge given the semi-transient susceptible population, as many cases are likely reported off the island, and will be recorded by the location or the report, not necessarily the location of the infection.

In 2009 the Nantucket Board of Selectmen assembled a tick-borne disease committee to assess the current state of ticks and deer on the island and provide recommendations. The main recommendation of the committee was to reduce the deer population through increased hunting. This is an unpopular idea which has also been disputed by scientists. Another suggestion has been to introduce genetically modified mice, which will reduce the number of infected mice, which should then reduce the number of infected ticks, and thus the number of infections in humans. This is also an unpopular idea[3].

Since research has shown that reducing the deer population, unless to extinction, is not effective in reducing the tick population (more ticks just crowd on to fewer deer)[4], this analysis seeks to model the dynamic relationship between ticks, mice, and incidence of disease in humans. After modeling the relationship, simulations targeting the mouse population size and mouse Lyme disease burden will be investigated to determine the effect on human cases of disease. The model is ultimately a Susceptible-Infected (SI) model, as the recovered population becomes susceptible again. An unpublished analysis looked at a similar SI model for ticks, deer, and mice. Some parameter estimates such as birth, death, and transmission rates will be adapted from this work[5]. Nantucket-specific parameters will be used where available. The current model will build upon previous work by including the impact on infection incidence in humans.

Model Parameters and Estimates

Susceptible Population

Anyone who visits Nantucket Island has a chance of encountering an infected deer tick on the island, and will be considered susceptible to Lyme disease infection. US Census data is available for the county of Nantucket, which only consists of the Island of Nantucket[6]. The Census data for Nantucket however is considered to be an underestimate of the total population. There are a number of undocumented residents, children, as well as semi-permanent residents who come for work and may not be registered on the street listings used for the census. There is also a large influx of seasonal workers and visitors to take into account. The Nantucket Data Project (NDP) is a project that compiled data from a number of different sources to estimate the total island population, including children and visitors, for 2017. The NDP concluded that with adults, children and semi-permanent residents, the year round population was 17,163[7]

compared to the US Census estimate of 11,229. Seasonal workers, seasonal residents and visitors were estimated by month, making it a little challenging to get a yearly number, as seasonal workers and residents may persist for more than one month, and visitors may visit multiple times. For the purposes of this model, I assumed roughly 90% of seasonal workers, 80% of seasonal residents, and 5% of visitors persisted month after month, for an additional 74,594 unique people. This estimate of 8.2 additional people for every 1 person reported on the census was used to extrapolate population numbers based on census data for 2001-2017. Anecdotal evidence was used to develop the assumptions, as a thorough analysis of population estimates is beyond the scope of this paper. It is noted that a temporary visitor will have less opportunity to encounter and be bitten by an infected tick than a year-round resident, but for the purposes of this paper, time spent on the island will not be factored in. More anecdotal evidence presented in the report of the Nantucket Tick-Borne Disease Committee and in other media argues that visitors may be more susceptible due to less awareness, so this may make up for some of the time-based opportunity.

Infection Rate

The CDC collects data on reported cases of Lyme disease as part of its National Notifiable Diseases Surveillance System (NNDSS) [2]. Data is available by year at the county level. Nantucket County numbers reflect only cases reported on the island, by residents of the island. In The Nantucket Tick-Borne Disease Committee report cites one year of reliable hospital data from the one hospital on the island. In 2008 the CDC recorded 44 cases of Lyme disease from Nantucket County residents[2]. That same year, the hospital reported seeing 325 cases[3]. The hospital estimate is still an underestimate, as infected visitors may leave before noticing and reporting symptoms, an additional 10% was added to that number to account for visitors who may not notice or otherwise seek medical care until leaving the island. Assuming this 8.1:1 estimated cases:CDC report ratio would be consistent over time, an estimated number of yearly cases was derived for 2000-2015. CDC data after 2015 appears abnormally low, assuming there may be a reason outside a true decline in incidence, only data up to 2015 was considered for modeling.

An infection rate calculated using just the CDC and census numbers from 2000-2015 would estimate 4.3 infections per 1000 population. Using the estimated population and hospital case incidence results in 3.8 infections per 1000 population. Considering the census number may be an underestimate, the infection rate of 3.8 per 1000 was chosen for this model.

Lyme disease very rarely transmitted from human to human, only through exchange of bodily fluids, and will not be considered in this model.

Ticks

Deer ticks are the carriers of Lyme disease, humans acquire the disease when bitten by an infected tick. Ticks are parasites that rely on deer and other mammals for sustenance. Deer are the primary host. Deer however do not carry Lyme disease. Instead, ticks acquire the infection from mice. In the Jastresbki, et al. SI model study, 36% of ticks carried Lyme disease. Estimates of the tick population on Nantucket were not available, but were extrapolated using the deer:tick ratio of 1:5,100 observed by Jastresbki, et al[5]. It is estimated that there are about 2500 deer on Nantucket, which gives 12,750,000 ticks for Nantucket.

Mice

Mice carry Lyme disease and infect ticks that feed on them. In the Jastresbki, et al. study, 30% of mice were infected[5]. Scientists proposing mouse-based interventions for Nantucket estimate the island has a population of about 500,000 mice.

Table 1. Initial conditions for modeling the SI relationship

Parameter	Description	Value
$T_m(0)$	Total population, mice	500,000
$T_t(0)$	Total population, ticks	12,750,000
$T_h(0)$	Total population, humans	99,357
$S_m(0)$	Susceptible mice	350,000
$S_t(0)$	Susceptible ticks	8,160,000
$S_h(0)$	Susceptible humans	98,894
$I_m(0)$	Infected mice	150000
$I_t(0)$	Infected ticks	4590000
$I_h(0)$	Infected humans	463

Modeling

Basic Assumptions for all models

- Susceptible populations cannot have negative values (S_m, S_t, S_h all ≥ 0).
- Infected populations cannot have negative values (I_m, I_t, I_h all ≥ 0).
- Large numbers of mice, ticks, and humans allow us to ignore individual characteristics
- The death rate for ticks and mice includes death due to competition, otherwise the populations would grow exponentially
- Ticks and mice do not recover from, nor do they die from, Lyme disease
- Humans may die from Lyme disease complications, but this is rare and will not be considered.
- Human Lyme disease recovery is approximately the same rate as the infection rate.
- When humans recover they become susceptible again.

Table 2. SI Model Parameters

Parameter	Description	Value
b_m	Birth rate, mice	0.054
b_t	Birth rate, ticks	0.026
b_h	Birth rate, humans	0.012
β_{mt}	Transmission, mice to ticks	0.0045
β_{tm}	Transmission, ticks to mice	0.0075
β_{th}	Transmission, ticks to humans	0.00036
d_m	Death rate, mice	0.050
d_t	Death rate, ticks	0.025
d_h	Death rate, humans	0.0082

Dynamic Systems Model, Tick and Mouse SI Relationship

Susceptible Mice: $\frac{dS_m}{dt} = b_m(S_m + I_m) - d_m S_t - \beta_{tm} S_t (I_m/(S_m + I_m)$

Infected Mice: $\frac{dI_m}{dt} = \beta_{tm} S_m (I_t/(S_t + I_t)) \ - d_m I_m$

Susceptible Ticks: $\frac{dS_t}{dt} = b_t(S_t + I_t) - d_t S_t - \beta_{mt} S_t (I_m/(S_m + I_m)$

Infected Ticks: $\frac{dI_m}{dt} = \beta_{mt} S_t (I_m/(S_m + I_m)) - d_t I_t$

Susceptible Humans: $\frac{dS_h}{dt} = b_h(S_h + I_h) - d_h S_h - \beta_{th} S_t (I_m/(S_m + I_m) + \beta_{th} I_h$

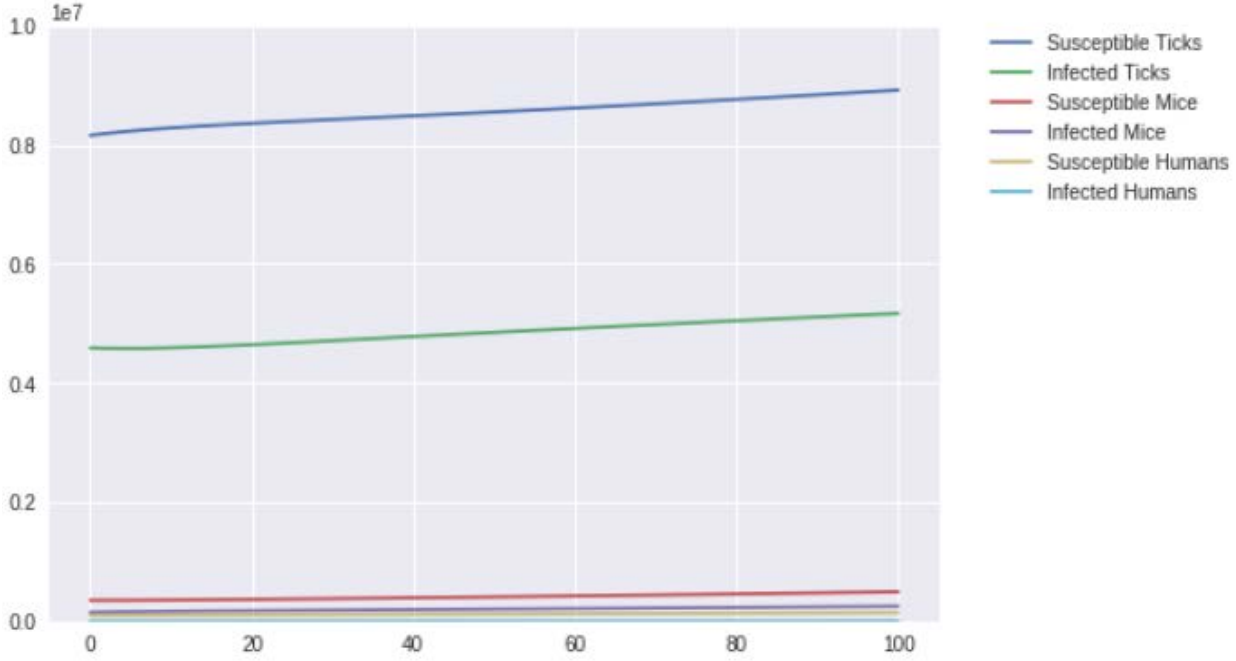
Infected Humans: $\frac{dI_{mh}}{dt} = \beta_{th} S_h (I_t/(S_t + I_t)) - d_h I_h - \beta_{th} I_h$

The above formulas outline the existing relationship of susceptible mouse, tick, and human populations. Mice and ticks may infect each other, but not their own species. The rate of infection depends on the transmission rate from one to another, as well as the proportion of infected members of the transmitting species. Neither mice nor ticks recover from the infection. Humans only become infected from infected ticks. Humans recover at the same rate they become ill, and are again susceptible. In the current state the susceptible and infected populations are rising steadily, although the rise in mice is steepest. Since the transmission rate between species is not changing, and the species do not infect their own, the relationship between susceptible populations and infected populations is nearly linear in the short term. As time extends, these lines diverge more.

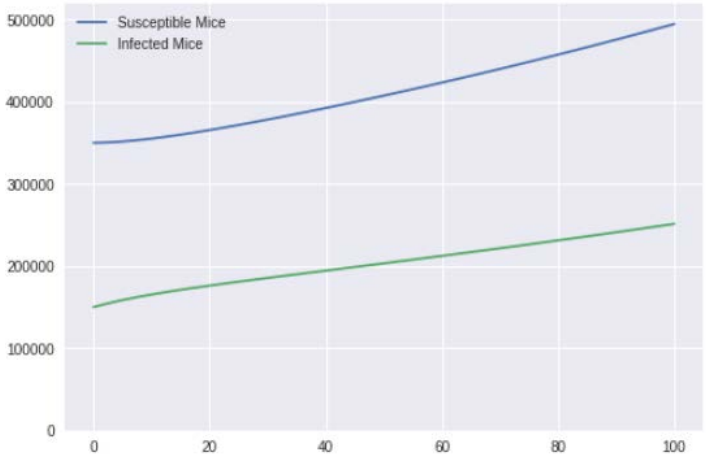
Figure 1 outlines the full system. The difference in scale makes it hard to see anything but ticks, so each species is also plotted separately.

Figure 1.

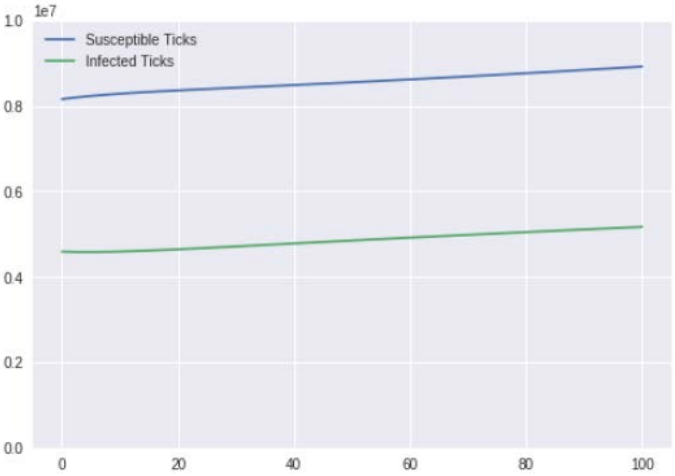
Panel a. Full SI model



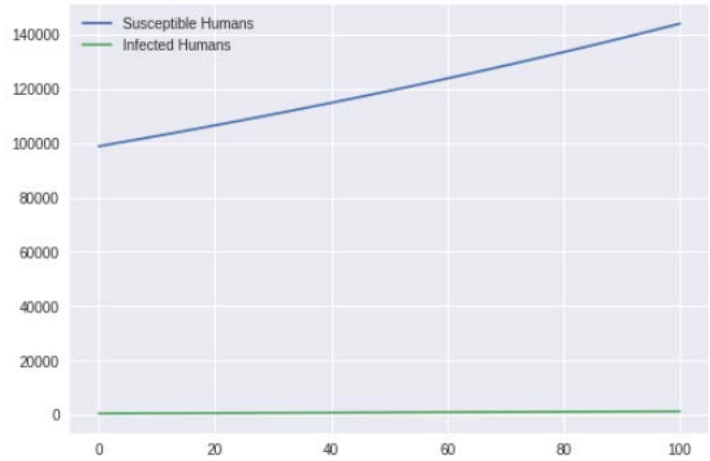
Panel B. Mouse parameters: $S_m(t)$ and $I_m(t)$



Panel C. Tick parameters: $S_t(t)$ and $I_t(t)$



Panel D. Human parameters: $S_h(t)$ and $I_h(t)$



Disease Free Equilibria

In a disease free state, all individuals would be in the susceptible population, and none in the infected. Since humans do not pass the disease on, we only need to set I_m and I_t equal to 0. Following a similar method as used by Jastresbki, et al.[5], we set up the following matrices,

$$X=\begin{pmatrix} I_m \\ I_t \end{pmatrix}, \qquad Y=\begin{pmatrix} S_m \\ S_t \end{pmatrix}$$

The system of equations is rewritten as

$$\frac{\partial X}{\partial t} = F(X,Y) - V(X,Y)$$

$$F = \begin{pmatrix} \beta_{tm} S_m (I_t/(S_t + I_t)) \\ \beta_{mt} S_t (I_m/(S_m + I_m)) \end{pmatrix} \qquad V = \begin{pmatrix} d_m S_m \\ d_t S_t \end{pmatrix},$$

Next, we define F=J(F) and V=J(F) where J is the Jacobian, and compute the eigenvalues of the matrix FV^{-1}. Taking the largest eigenvalue gives us the following formula for the reproduction number,

$$R_0 = \sqrt{\frac{\beta_{mt}\beta_{tm}}{d_m d_t}}$$

When $R_0 < 1$, our disease free equilibrium will be stable. If $R_0 > 1$ then the equilibrium is unstable.

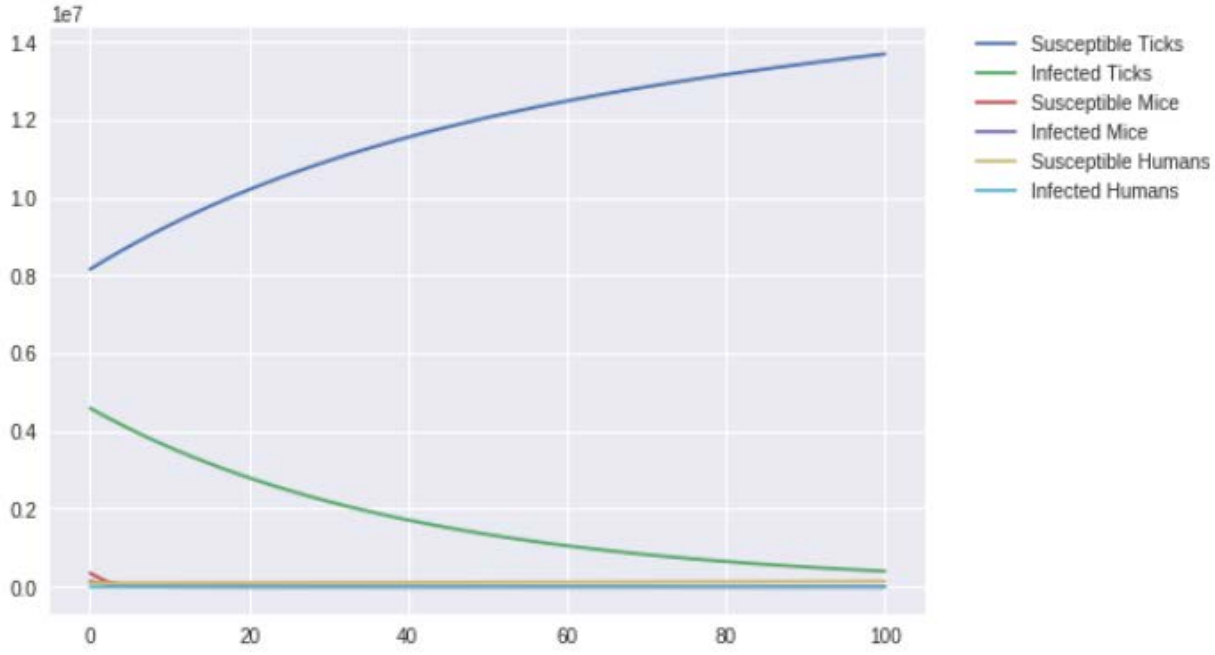
Therfore, for an stable disease free state, we need to have $d_m d_t > \beta_{mt}\beta_{tm}$.

Simulating Disease Free Scenarios

Assuming the mouse population is easier to target for interventions than the tick population, we can look for ways to make $d_m > \beta_{mt}$, by either increasing the death rate of mice, or decreasing the transmission rate to ticks.

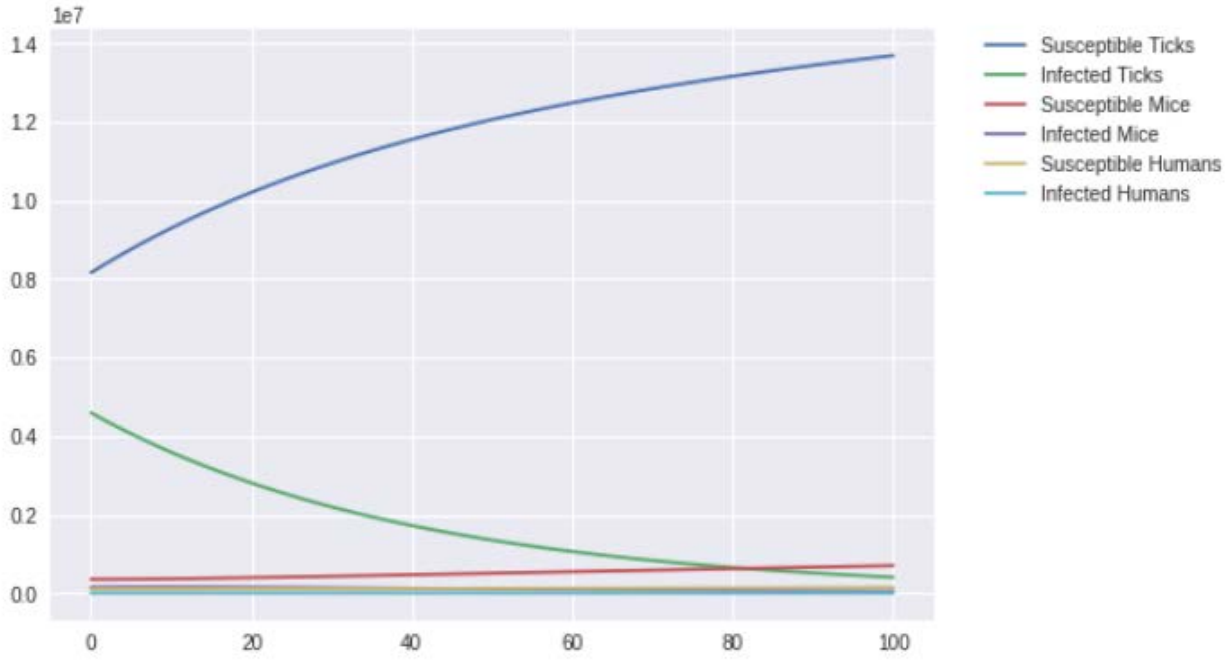
Option 1: Increase the rate of mouse death. This will force the mouse population into extinction.

Figure 2. The death rate of mice is $d_m$is multiplied by 10



Option 2: Decrease the transmission rate from mice to ticks. In this scenario, the mouse population survives.

Figure 3, β_{mt}, the transmission rate from mice to ticks is reduced by 10%.



Limitations of the Current Study

The relationship between ticks, mice, and humans, has been greatly simplified for the purposes of this analysis. A more in-depth analysis would take into account other factors such as the fact that tick life cycles determine transmission rates and contact with mice. A more advanced model may also take into account the seasonality of Lyme disease. Transmission rates are much higher in the warmer months when humans are outdoors more and wearing less clothing, making contact with ticks more likely. Lastly, many of the numbers in this analysis were simulated due to lack of availability of better data. A more accurate relationship might be obtained with numbers from studies of the exact population of interest.

Conclusion

If left in the current state, the number mouse and tick populations on Nantucket will continue to infect each other, and the number of infected ticks will rise. The rising number of infected ticks will lead to an increase in the number of Lyme disease cases reported in humans. A couple of interventions shown to be successful with these models were suggested. The first option, increase the death rate of mice, leading to their extinction on the island. This option is easily accomplished by the use of rodenticides or introducing a competing species. Environmentally, neither are desirable options, and this is also quite inhumane. The second option, decreasing the rate of transmission from mice to ticks may be possible by introducing genetically modified mice, or vaccinating a portion of the existing tick population.

References

1 Shaprio, E. (2014). Lyme Disease. *New England Journal of Medicine*, *370(18)*, 1724-1731

2 CDC , "County-level Lyme disease data from 2000-2017", accessed 18 November 2018 from https://www.cdc.gov/lyme/stats/survfaq.html

3 Nantucket Tick-Borne Disease Committee, Report to The Nantucket Board of Health and Selectmen, 16 November 2009

4 Kugeler, K. J., Jordan, R. A., Schulze, T. L., Griffith, K. S., Mead, P. S. (2015). Will Culling White-Tailed Deer Prevent Lyme Disease? *Zoonoses and Public Health, 63(5)*, 337-345

5 Jastresbki, M., Ponce, J., Burkow, D., Udiani, O., Arriola, L. (2018). Ticks, Deer, Mice, and a Touch of Sensitivity: A Recipe for Controlling Lyme Disease. *Unpublished*, Retreived 18 November 2018 from the arXiv database

6 U.S. Census Bureau, Quick Facts. accessed 18 November 2018

7 Nantucket Data Project, Making It Count; A Data-Driven Look at Nantucket's Dynamic Population. Accessed 18 November 2018

Appendix

Python code for analyses:

Packages used:

```
from scipy.integrate import odeint
import matplotlib.pyplot as plt
import numpy as np
```

Human, Tick, Mouse SI Model:

```
#fixed values
bt=0.026 #tick birth rate
dt=0.025 #tick death rate
Btm=0.075 #transmission rate, ticks to mice

bm=0.054 #mouse birth rate
dm=0.050 #mouse death rate
Bmt=0.045 #transmission rate, mice to ticks

bh=0.012 #human birth rate
dh=0.0082 #human death rate
Bth=0.00036 #transmission rate, ticks to humans

def model(Y,t):
   St,It,Sm,Im,Sh,Ih = Y
   dYdt = [bt*(St+It)-dt*St-Bmt*St*(Im/(Im+Sm)), Bmt*St*(Im/(Im+Sm))-dt*It, bm*(Sm+Im)-dm*Sm-Btm*Sm*(It/(It+St)),
         Btm*Sm*(It/(It+St))-dm*Im, bh*(Sh+Ih)-dh*Sh-Bth*Sh*(It/(It+St))+Bth*Ih, Bth*Sh*(It/(It+St))-dh*Ih-Bth*Ih]
   return dYdt

#initial conditions
#[susceptible ticks, infected ticks, susceptible mice, infected mice, susceptible humans, infected humans]
Y0 = [8160000, 4590000, 350000, 150000, 98894, 463]

t = np.linspace(0,100)

sol = odeint(model,Y0,t)

St_sol = sol[:,0]
It_sol = sol[:,1]
Sm_sol = sol[:,2]
Im_sol = sol[:,3]
Sh_sol = sol[:,4]
Ih_sol = sol[:,5]

plt.plot(t,St_sol, label="Susceptible Ticks")
plt.plot(t,It_sol, label="Infected Ticks")
plt.plot(t,Sm_sol, label="Susceptible Mice")
plt.plot(t,Im_sol, label="Infected Mice")
plt.plot(t,Sh_sol, label="Susceptible Humans")
plt.plot(t,Ih_sol, label="Infected Humans")
plt.ylim(0, 10000000)
plt.legend(bbox_to_anchor=(1.05, 1), loc=2, borderaxespad=0.)
```

Simulation, Increased Mouse Death Rate

```
#fixed values
bt=0.026 #tick birth rate
dt=0.025 #tick death rate
Btm=0.075 #transmission rate, ticks to mice

bm=0.054 #mouse birth rate
dm=0.050*10 #mouse death rate
Bmt=0.045  #transmission rate, mice to ticks

bh=0.012 #human birth rate
dh=0.0082 #human death rate
Bth=0.00036 #transmission rate, ticks to humans

def model(Y,t):
   St,It,Sm,Im,Sh,Ih = Y
   dYdt = [bt*(St+It)-dt*St-Bmt*St*(Im/(Im+Sm)), Bmt*St*(Im/(Im+Sm))-dt*It, bm*(Sm+Im)-dm*Sm-Btm*Sm*(It/(It+St)),
           Btm*Sm*(It/(It+St))-dm*Im, bh*(Sh+Ih)-dh*Sh-Bth*Sh*(It/(It+St))+Bth*Ih, Bth*Sh*(It/(It+St))-dh*Ih-Bth*Ih]
   return dYdt

#initial conditions
#[susceptible ticks, infected ticks, susceptible mice, infected mice, susceptible humans, infected humans]
Y0 = [8160000, 4590000, 350000, 150000, 98894, 463]

t = np.linspace(0,100)

sol = odeint(model,Y0,t)

St_sol = sol[:,0]
It_sol = sol[:,1]
Sm_sol = sol[:,2]
Im_sol = sol[:,3]
Sh_sol = sol[:,4]
Ih_sol = sol[:,5]

plt.plot(t,St_sol, label="Susceptible Ticks")
plt.plot(t,It_sol, label="Infected Ticks")
plt.plot(t,Sm_sol, label="Susceptible Mice")
plt.plot(t,Im_sol, label="Infected Mice")
plt.plot(t,Sh_sol, label="Susceptible Humans")
plt.plot(t,Ih_sol, label="Infected Humans")
#plt.ylim(0, 10000000)
#plt.ylim(0, 520000)
#plt.ylim(0, 100000)
plt.legend(loc='upper left')
plt.legend(bbox_to_anchor=(1.05, 1), loc=2, borderaxespad=0.)
```

Simulation, Reduced Mouse to Tick Infection Transmission Rate

```
#fixed values
bt=0.026 #tick birth rate
dt=0.025 #tick death rate
Btm=0.075 #transmission rate, ticks to mice

bm=0.054 #mouse birth rate
dm=0.050 #mouse death rate
Bmt=0.045*.01 #transmission rate, mice to ticks

bh=0.012 #human birth rate
dh=0.0082 #human death rate
Bth=0.00036 #transmission rate, ticks to humans

def model(Y,t):
   St,It,Sm,Im,Sh,Ih = Y
   dYdt = [bt*(St+It)-dt*St-Bmt*St*(Im/(Im+Sm)), Bmt*St*(Im/(Im+Sm))-dt*It, bm*(Sm+Im)-dm*Sm-Btm*Sm*(It/(It+St)),
         Btm*Sm*(It/(It+St))-dm*Im, bh*(Sh+Ih)-dh*Sh-Bth*Sh*(It/(It+St))+Bth*Ih, Bth*Sh*(It/(It+St))-dh*Ih-Bth*Ih]
   return dYdt

#initial conditions
#[susceptible ticks, infected ticks, susceptible mice, infected mice, susceptible humans, infected humans]
Y0 = [8160000, 4590000, 350000, 150000, 98894, 463]

t = np.linspace(0,100)

sol = odeint(model,Y0,t)

St_sol = sol[:,0]
It_sol = sol[:,1]
Sm_sol = sol[:,2]
Im_sol = sol[:,3]
Sh_sol = sol[:,4]
Ih_sol = sol[:,5]

plt.plot(t,St_sol, label="Susceptible Ticks")
plt.plot(t,It_sol, label="Infected Ticks")
plt.plot(t,Sm_sol, label="Susceptible Mice")
plt.plot(t,Im_sol, label="Infected Mice")
plt.plot(t,Sh_sol, label="Susceptible Humans")
plt.plot(t,Ih_sol, label="Infected Humans")

plt.legend(bbox_to_anchor=(1.05, 1), loc=2, borderaxespad=0.)
```