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DEPARTMENT OF APPLIED MATHEMATICS

Mathematical Modeling and Simulation of Chagas Disease

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Contents

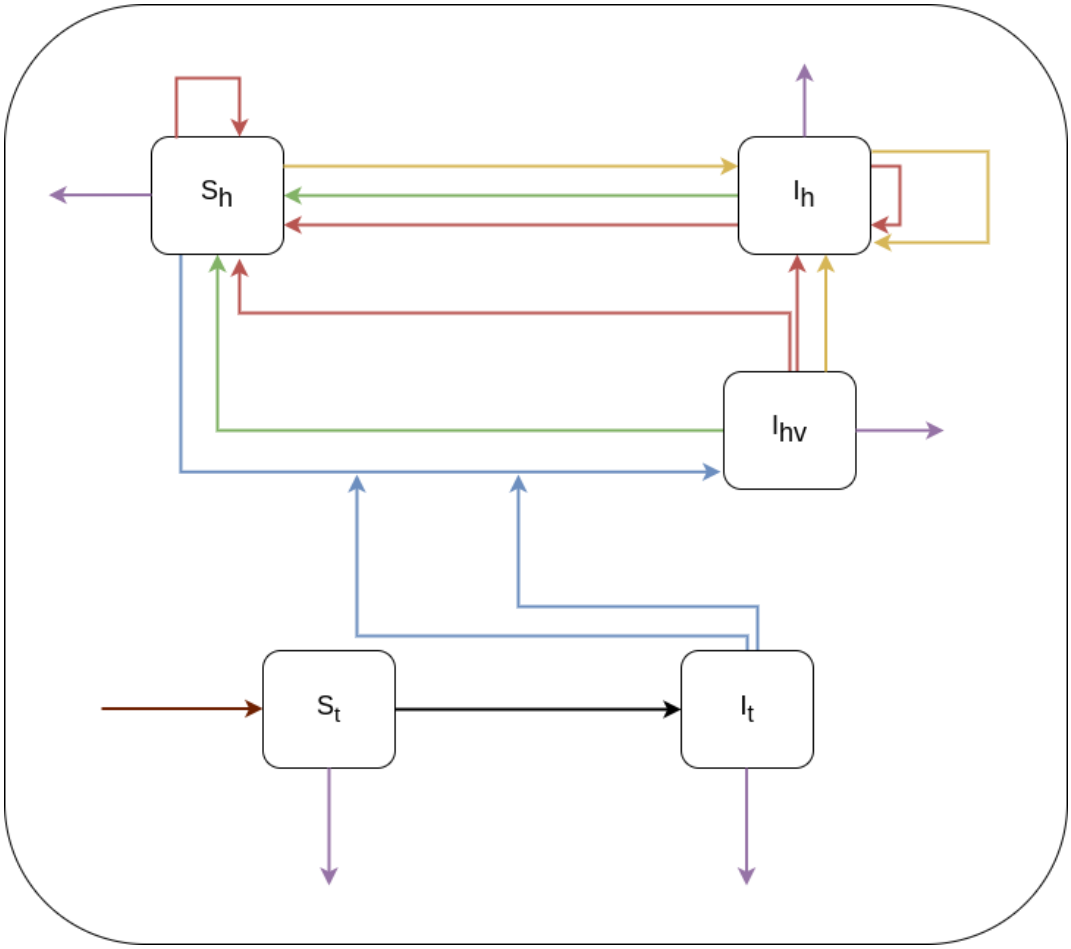
1 Abstract

Chagas Disease is a neglected tropical disease caused by the protozoan parasite *Trypanosoma Cruzi*, afflicting about 6–7 million people worldwide this disease has significant importance in Latin American countries. Chagas Disease main form of transmission is by insect vectors feces, the *Triatomine*, these reside mostly in rural areas, affecting particularly low income housing. Other transmission routes are: congenital transmission, blood transfusion, organ transplantation from infected individuals, by laboratory accident, and by consumption of contaminated food or drinks.

The model displayed in the present work compartmentalizes Humans into infected by insect vectors compartment and infected by other infected humans. Such model refers to a system of differential equations integrated numerically using computational software. The simulations performed show that the model has a expected behavior, reaching stability.

2 Methodology

The Model developed in this work consists of 5 compartments, Susceptible insects (S_t), Infected Insects (I_t), Susceptible Humans (S_h), Infected Humans by non vectors (I_h) and Infected humans by vectors, through the form of infected insect feces or ingestion of contaminated food. N_h is the constant of the total human population: $N_h = S_h + I_h + I_{hv}$.



The arrows are grouped in colours, *Red* represents the birth of individuals, Infected humans can have healthy or infected babies whilst healthy humans only have healthy babies, $Yellow$ represents infections by blood transfu-

sion, organ transplantation and by laboratory accident. $Green$ arrows refer to the Recovery of infected individuals, $Blue$ refers to the infection directly from the insect vectors: by $Triatominae$ feces or by oral ingestion, $Purple$ arrows refer to death of each compartment and finally $Black$ refers to infection of healthy insects by infected humans.

$$\begin{aligned}
\frac{\mathrm{d}S_h(t)}{\mathrm{d}t} &= \alpha_h S_h + \alpha_h(1-\beta_h+\rho_h\beta_h)(I_h+I_{hv}) + C_h I_h + C_h I_{hv} - \delta_h S_h - \tau_h(1-\epsilon_h)S_h I_h(1/N_h) - m_h\frac{S_h I_t}{N_h};\\
\frac{\mathrm{d}I_h(t)}{\mathrm{d}t} &= \alpha_h\beta_h(I_h+I_{hv})(1-\rho_h) - (\gamma_h+C_h)I_h + \tau_h(1-\epsilon_h)S_h(1/N_h);\\
\frac{\mathrm{d}I_{hv}(t)}{\mathrm{d}t} &= -(\gamma_h+C_h)I_{hv} + m_h\frac{S_h I_t}{N_h};\\
\frac{\mathrm{d}S_t(t)}{\mathrm{d}t} &= \beta_t N_t - b_t S_t I_h - \mu_t S_t;\\
\frac{\mathrm{d}I_t(t)}{\mathrm{d}t} &= b_t S_t I_h - \mu_t I_t;
\end{aligned} \tag{1}$$

The parameters correspondent to the model are explained below:
α_h = Birth rate of humans
β_h = probability of a infected mother infecting her child
ρ_h = percent of infected newborn who receive treatment
C_h = Recovery rate C where c = $e * d$, e being treatment effectiveness and d the yearly percentage d of infected individuals that receive treatment
γ_h = Infected Death
δ_h = Mortality rate of healthy humans
τ_h = Blood donation rate
ϵ_h = Effective surveillance
- $1-\epsilon_h$ = Blood not detected
- $\tau p_i(1-\epsilon)$ = proportion as to which a person becomes infected with a parasite from an infected person

m_h = Infection of human by insect $Triatominae$, where m1 = n + m where n is the infection by ingestion and m is the infection by direct contact with the living insect
β_t = Birth rate of insect
b_t = Infection of insect by human (Oral and direct contact with insect)
μ_t = mortality rate of insect

As for $\tau_h = \tau * p_i = 0.0177 * 0.0010$, τ is the donation rate per year and p_i is the proportion of potentially infected blood samples.

For m_h we have: m_h = n + m where n is 255/(5*1532902) = 0.00003327022 (oral infection or ACD []) and m is 34/(5*1532902) = 0.00000443603 (infection by vector), so m equals to 0.00003770625

The region of biological interest is: $\Omega = \{S_h, I_h, I_{hv}, S_t, I_t \in \mathbb{R}^5_+ | N_h = S_h + I_h + I_{hv}, S_t + I_t = N_t\}$
The parameters values are evaluated below in Table 1:

Table 1: Parameters

Parameter	Meaning	Real Value	Source
α_h	Birth rate (year^{-1})	0.016	[1]
β_h	Probability of mother infecting child	0.005	[2]
δ_h	Mortality rate	0.006	[3]
γ_h	Mortality rate due disease	0.00142857142	[4]
τ_h	Rate of infection by infected blood	0.0000177	[5, 6]
C_h	Cure rate	C = 7.5% · 0.1% = 0.0075	[7, 8]
ρ_h	Proportion of new born treated	0.05	Assumed
ϵ_h	Probability of a efficient surveillance	0.05	Assumed
m_h	Infection of human by vector	0.00003770625	[9]
β_t	Birth rate of vector	0.8	Assumed
b_t	Infection of vector by human	0.096	Assumed
μ_t	Natural death of vector	0.05	[10]

2.1 Jacobian and Stability

Calculating the Jacobian Matrix [11], we have:

$$J = \begin{bmatrix} \alpha_h - \delta_h - \frac{I_t m_h}{N_h} - \frac{\tau_h(1-\epsilon_h)}{N_h} & \alpha_h(\beta_h\rho_h - \beta_h + 1) + C_h & \alpha_h(\beta_h\rho_h - \beta_h + 1) + C_h & 0 & -\frac{m_h S_h}{N_h} \\ \frac{\tau_h(1-\epsilon)}{N_h} & \alpha_h\beta_h I_h(1-\rho_h)(-C_h-\gamma_h) + \alpha_h\beta_h(1-\rho_h)(-C_h-\gamma_h)(I_h + I_h\upsilon) & \alpha_h\beta_h I_h(1-\rho_h)(-C_h-\gamma_h) & 0 & 0 \\ \frac{I_t m_h}{N_h} & 0 & -C_h - \gamma_h & 0 & \frac{m_h S_h}{N_h} \\ 0 & -\frac{b_t S_t}{N_t} & 0 & -\frac{b_t I_h}{N_t} - \mu_t & 0 \\ 0 & \frac{b_t S_t}{N_t} & 0 & \frac{b_t I_h}{N_t} & -\mu_t \end{bmatrix}$$

- Assuming $I_h = 0$, $I_h\upsilon = 0, I_t = 0$:

$$J(0) = \begin{bmatrix} 0 & \alpha_h(\beta_h\rho_h - \beta_h + 1) + C_h & \alpha_h(\beta_h\rho_h - \beta_h + 1) + C_h & 0 & -\frac{m_h S_h}{N_h} \\ \frac{\tau_h(1-\epsilon)}{N_h} & 0 & 0 & 0 & 0 \\ 0 & 0 & -C_h - \gamma_h & 0 & \frac{m_h S_h}{N_h} \\ 0 & -\frac{b_t S_t}{N_t} & 0 & -\mu_t & 0 \\ 0 & \frac{b_t S_t}{N_t} & 0 & 0 & -\mu_t \end{bmatrix}$$

- $\det(J - \lambda I)$:

$$det(J - \lambda I) = \begin{bmatrix} -\lambda & \alpha_h(\beta_h\rho_h - \beta_h + 1) + C_h & \alpha_h(\beta_h\rho_h - \beta_h + 1) + C_h & 0 & -\frac{m_h S_h}{N_h} \\ \frac{\tau_h(1-\epsilon)}{N_h} & -\lambda & 0 & 0 & 0 \\ 0 & 0 & -C_h - \gamma_h - \lambda & 0 & \frac{m_h S_h}{N_h} \\ 0 & -\frac{b_t S_t}{N_t} & 0 & -\mu_t - \lambda & 0 \\ 0 & \frac{b_t S_t}{N_t} & 0 & 0 & -\mu_t - \lambda \end{bmatrix}$$

Eigenvalues are: $\lambda = 0, \lambda = -C_h - \gamma_h$ and $\lambda = -\mu_t$. Since all eigenvalues have negative real part, the equilibrium is stable!

2.2 Next Generation Matrix

From the Next Generation Matrix method presented in [12] we have: X = $[I_h, I_{hv}, I_t]$ and Y = $[S_h, S_t]$, finally:

- For appearance of new infections in compartments in X we have:

$$\mathscr{F} = \begin{bmatrix} \alpha_h \beta_h (I_h + I_{hv})(1-\rho_h) + \tau_h (1-\epsilon_h) S_h (1/N_h) \\ m_h \frac{S_h I_t}{N_h} \\ b_t S_t I_h \end{bmatrix}$$

$$F = \begin{bmatrix} \alpha_h \beta_h (1-\rho_h) & \alpha_h \beta_h (1-\rho_h) & 0 \\ 0 & 0 & m_h \\ b_t & 0 & 0 \end{bmatrix}$$

- For the transfer of individuals out of compartments in X:

$$\mathscr{V} = \begin{bmatrix} (\gamma_h + C_h) I_h \\ (\gamma_h + C_h) I_{hv} \\ \mu_t I_t \end{bmatrix}$$

$$V = \begin{bmatrix} (\gamma_h + C_h) & 0 & 0 \\ 0 & (\gamma_h + C_h) & 0 \\ 0 & 0 & \mu_t \end{bmatrix}$$

- As for the NGM:

$$NGM = FV^{-1} = \begin{bmatrix} \alpha_h \beta_h (1-\rho_h) & \alpha_h \beta_h (1-\rho_h) & 0 \\ 0 & 0 & m_h \\ b_t & 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{(\gamma_h + C_h)} & 0 & 0 \\ 0 & \frac{1}{(\gamma_h + C_h)} & 0 \\ 0 & 0 & \frac{1}{\mu_t} \end{bmatrix} = \begin{bmatrix} \frac{\alpha_h \beta_h (1-\rho_h)}{\gamma_h + C_h} & \frac{\alpha_h \beta_h (1-\rho_h)}{\gamma_h + C_h} & 0 \\ 0 & 0 & \frac{m_h}{(\mu_t)} \\ \frac{b_t}{\gamma_h + C_h} & 0 & 0 \end{bmatrix}$$

- So the $\det(FV^{-1} - \lambda I) = 0$ gives us:

$$\frac{\alpha_h\, b_t\, \beta_h\, m_h\, (1-\rho_h)}{\mu_t\, (C_h+\gamma_h)^2} + \lambda^2 \left(\frac{\alpha_h \beta_h (1-\rho_h)}{C_h+\gamma_h} - \lambda \right) = 0 \tag{2}$$

- Replacing the parameters with their real values, we have:

$$\lambda^3 - 0.008512 + \lambda^2 0.00006901829 = 0 \tag{3}$$

- Solving with Newton-Raphson we have the solution of the equation above and:

$$R0 = 0.04220 \tag{4}$$

As we can see, R0 is < 1 and considerably small, the smaller the R0, more controlled is the epidemic.

3 Simulations

The model was simulated using python's odeint, a library containing a collection of advanced numerical algorithms, such as RungeKutta, to solve initial-value problems of ordinary differential equations.
The values referent to the model are shown in Table 2.

Table 2: Simulations

Parameter	Simulation 1	Simulation 2
α_h	0.7	1
β_h	0.8	1
δ_h	0.7	1
γ_h	0.857142	1
τ_h	0.00000177	10
C_h	1.95	0.5
ρ_h	0.0005	0.05
ϵ_h	0.0005	0.05
m_h	0.0000003770625	10
β_t	0.8	1
b_t	0.0000096	10
μ_t	0.8	5
S_{h0}	10000	10000
I_{h0}	10000	10000
$I_h \upsilon_0$	10000	10000
S_{t0}	2000	2000
I_{t0}	10000	10000

Table 3: Simulation Parameters of the Model

The first simulation is shown in Figure 1, in such simulation you can observe the disease reaches a disease free equilibrium.

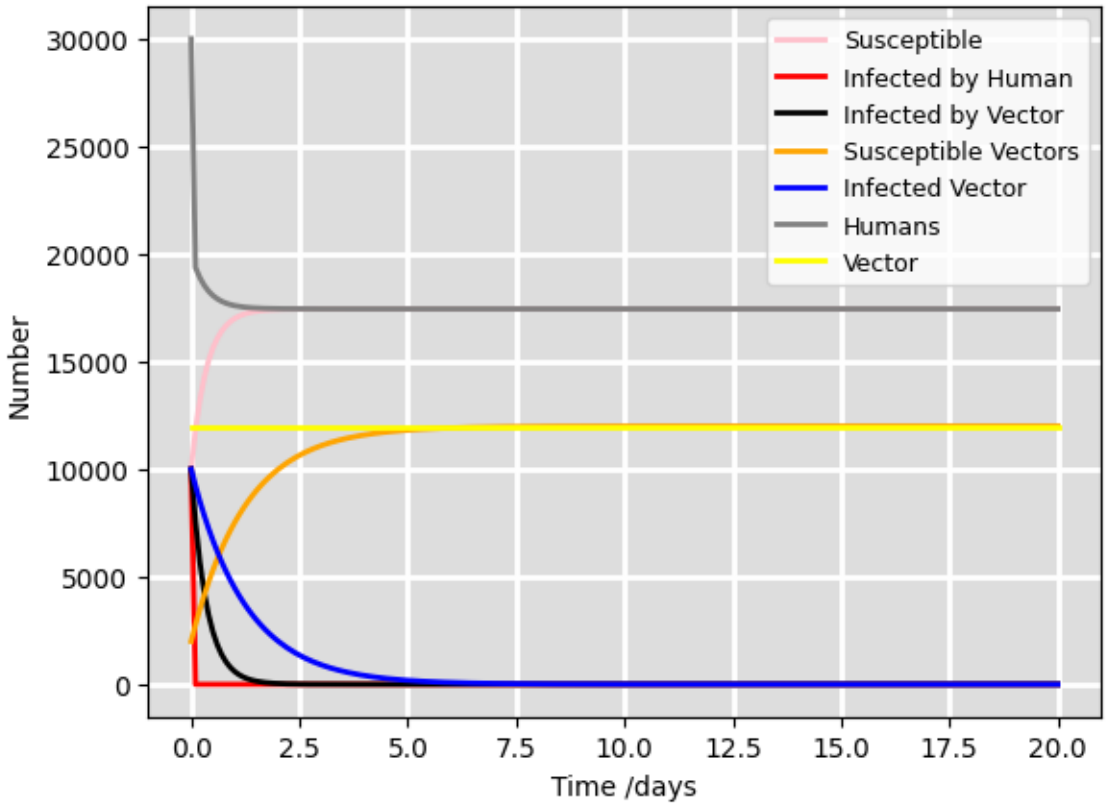


Figure 1: Simulation 1

The second simulation, Figure 2, shows the elimination of all population by raising the parameters that contribute to dead and infectious individuals.

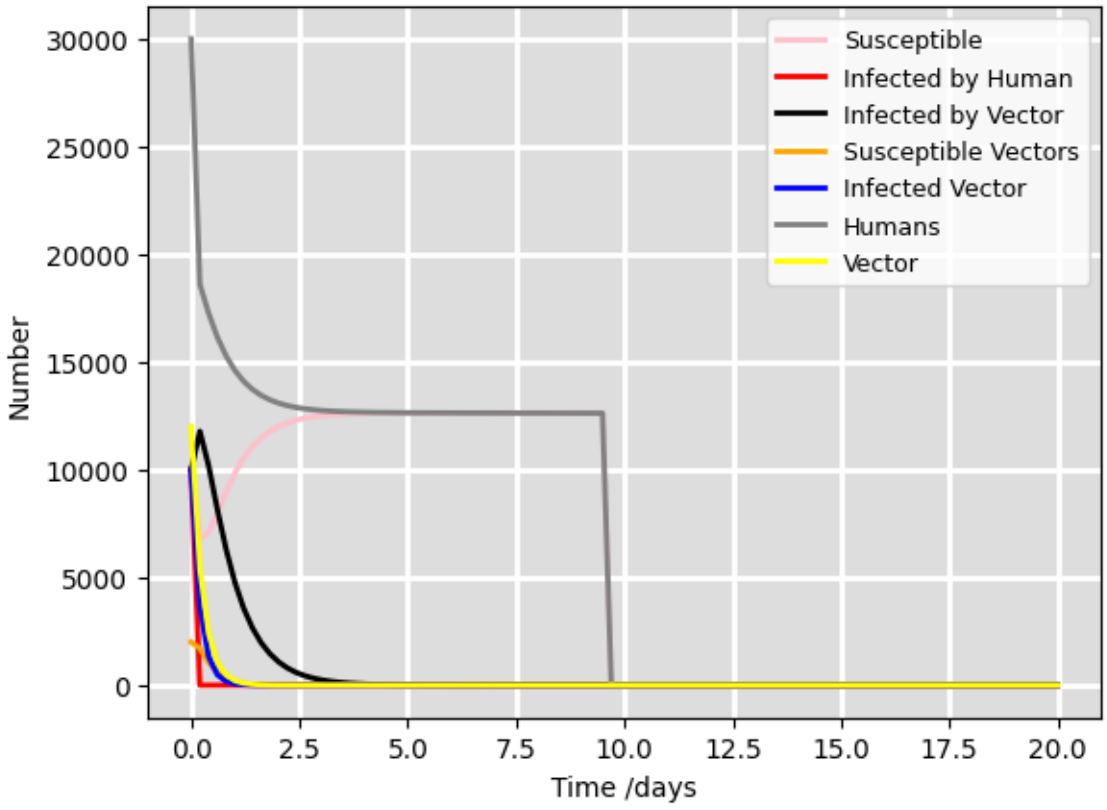


Figure 2: Simulation 2

4 Conclusions

In this report we developed a model for Chagas Disease, such model reflects the dynamic of infection between humans and vectors and between infected humans and susceptible humans. The stability of the model was shown through simulations, as was the effect of the infectious class on the susceptible population.

As we could see the R0 is considerably small, taking in consideration the parameters researched. This means the disease is supposedly under control, this could be due to the improvement of sanitary and living conditions, also a influential aspect can be the urbanization of rural living areas, bringing better sanitation and conditions to block the transmitting vector. This does not mean Chagas disease ceases to be a relevant disease. This disease has frequently grown in it's Oral transmitted form, known as Acute Chagas Disease [13].Furthermore, in many forms, Chagas Disease still continues to affect millions of people, especially in low income communities, hence it's categorization as a neglected disease.

5 Acknowledgments

I would like to thank my advisor and friend João Frederico da Costa de Azevedo Meyer, who has always helped me on the path of becoming a thinker and researcher in the most diverse ways, that transcend the mathematical field.

Additionally, I would like to thank the Drugs for Neglected Diseases Organization (DNDI), for paying mind to the importance of neglected diseases and for being available to the knowledge exchange.

6 Code

The code referent to the simulations was developed in python3.8 and is presented below:

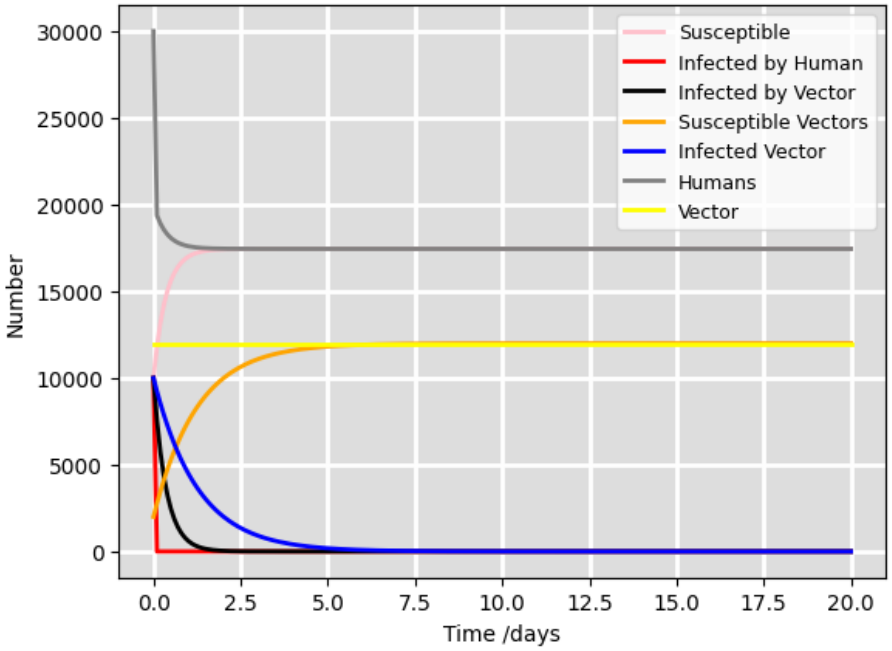
In [ ]:
```
import numpy as np
from scipy.integrate import odeint
import matplotlib.pyplot as plt

#Initial conditions
S_h_0 = 10000
I_h_0 = 10000
I_hv_0 = 10000
S_t_0 = 2000
I_t_0 = 10000

#Parameters:
alpha_h =  0.7
beta_h =  0.8
delta_h =  0.7
gamma_h =  0.857142
tau_h =  0.00000177
C_h =  1.95
rho_h  =  0.0005
epsilon_h =  0.0005
m_h =  0.0000003770625
beta_t =  0.8
b_t =  0.0000096
mu_t =  0.8
c_t= 0.0005

N_h = S_h_0 + I_h_0 + I_hv_0
N_t = S_t_0 + I_t_0

t = np.linspace(0, 20, 200)

print(t)
print(f'{S_h_0}\n{I_h_0}\n{I_hv_0}\n{S_t_0}\n{I_t_0}\n{alpha_h}\n{beta_h}\n{delta_h}\n{gamma_h}\n{tau_h}\n{C
```

In [ ]:
```
def deriv(y, t,alpha_h,beta_h,delta_h,gamma_h,tau_h,C_h,rho_h ,epsilon_h,m_h,beta_t,b_t,mu_t,c_t):
    S_h, I_h, I_hv, S_t, I_t = y
    N_h = S_h + I_h + I_hv
    N_t = S_t + I_t

    dS_hdt = alpha_h * S_h + alpha_h * (1 - beta_h + rho_h * beta_h) * (I_h + I_hv) + C_h * I_h + C_h * I_hv
    dI_hdt = alpha_h * beta_h * (I_h + I_hv)*(1 - rho_h) *  - (gamma_h + C_h) * I_h + tau_h * (1 - epsilon_h
    dI_hvdt =  - (gamma_h + C_h) * I_hv + m_h * S_h * I_t/(N_h)
    dS_tdt = beta_t * N_t - b_t * S_t * I_h/N_t - mu_t * S_t
    dI_tdt = b_t * S_t * I_h/N_t - mu_t * I_t
    (alpha_h * S_h + alpha_h * (1 - beta_h + rho_h * beta_h) * (I_h + I_hv) + C_h * I_h + C_h * I_hv - delta
    (S_h, I_h, I_hv, S_t, I_t )
    return dS_hdt,dI_hdt,dI_hvdt,dS_tdt,dI_tdt
```

In [ ]:
```
# Initial conditions vector
y0 = S_h_0,I_h_0,I_hv_0,S_t_0,I_t_0
# Integrate the model equations over the time grid, t.
ret = odeint(deriv, y0, t, args=(alpha_h,beta_h,delta_h,gamma_h,tau_h,C_h,rho_h ,epsilon_h,m_h,beta_t,b_t,mu
S_h, I_h, I_hv, S_t, I_t = ret.T
N_h_list = S_h + I_h + I_hv
N_t_list = S_t + I_t
```

In [ ]:
```
# Plot the data on three separate curves for S(t), I(t) and R(t)
fig = plt.figure(facecolor='w')
ax = fig.add_subplot(111, facecolor='#dddddd', axisbelow=True)
ax.plot(t, S_h, 'pink', lw=2, label='Susceptible')
ax.plot(t, I_h, 'r', lw=2, label='Infected by Human')
ax.plot(t, I_hv, 'black', lw=2, label='Infected by Vector')
ax.plot(t, S_t, 'orange', lw=2, label='Susceptible Vectors')
ax.plot(t, I_t, 'b', lw=2, label='Infected Vector')
ax.plot(t, N_h_list, 'grey', lw=2, label='Humans')
ax.plot(t, N_t_list, 'yellow', lw=2, label='Vector')

ax.set_xlabel('Time /days')
ax.set_ylabel('Number')
ax.grid(b=True, which='major', c='w', lw=2, ls='-')
legend = ax.legend(prop={'size': 9})
plt.show()
```

```
/tmp/ipykernel_7645/2481677942.py:14: MatplotlibDeprecationWarning: The 'b' parameter of grid() has been re
named 'visible' since Matplotlib 3.5; support for the old name will be dropped two minor releases later.
  ax.grid(b=True, which='major', c='w', lw=2, ls='-')
```


Susceptible
Infected by Human
Infected by Vector
Susceptible Vectors
Infected Vector
Humans
Vector
Number
30000
25000
20000
15000
10000
5000
0
0.0
2.5
5.0
7.5
10.0
12.5
15.0
17.5
20.0
Time /days

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