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# 22MAT121
# DISCRETE MATHEMATICS

# EPIDEMIOLOGY SIMULATION OF DENGUE

## Submitted by

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# DECLARATION

We hereby declare that the project entitled is the record of the "Epidemiology Simulation of Dengue" the work done by our team under the guidance of Dr.Ambika.P.S, **Amrita School of Artificial Intelligence**, Coimbatore. To the best of our knowledge this work has not formed the basis for the award of any degree/ diploma/ associate ship/ fellowship/ or a similar award to any candidate in any University

**Signature of the Faculty**

**(**Dr. Ambika P S**)**

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# ACKNOWLEDGEMENT

We would like to express our sincere gratitude to all those who have contributed to the successful completion of this Discrete Mathematics project. Without their support, dedication, and expertise, this project would not have been possible. I extend our heartfelt thanks to our staff Dr.Ambika P S, for providing valuable guidance and insightful feedback throughout the development process. Your expertise and encouragement were instrumental in shaping the project's direction and ensuring its quality.

Special thanks go to Ms. Vandhana, faculty associate, for his assistance in our Discrete Mathematics project. Your input significantly enriched the project, and I am grateful for the time and effort you dedicated to it.

Lastly, I want to express my gratitude to my friends and family for their understanding, encouragement, and patience throughout the project. Your unwavering support has been a constant source of motivation.

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# LIST OF ABBREVIATIONS:

- CDC – centre for disease control and prevention
- $S_h$ -susceptible human population,
- $I_h$ - infected human population
- $R_h$ - infected human population
- $N_h$ -human population
- p - probability of dominant allele
- q - probability of recessive allele
- $p^2$ - probability/proportion of homozygous dominant genotype AA
- $q^2$ -probability/proportion of homozygous recessive genotype aa
- 2pq - probability/proportion of heterozygous genotype Aa
- γ – recovery rate of human beings
- c - birth rate of human population
- $\mu_h$ - death rate of human population
- $\beta_h$ -probability of transmission of virus from a vector to human
- $I_v$ - infected vector population.
- $S_{AA}$ - susceptible vector population of genotype AA
- $S_{Aa}$ - susceptible vector population of genotype Aa
- $S_{aa}$ - susceptible vector population of genotype aa
- $I_{AA}$ - infected vector population of genotype AA
- $I_{Aa}$ - infected vector population of genotype Aa
- $I_{aa}$ - infected vector population of genotype aa
- $\beta_v$ -probability of transmission of virus from a human to vector
- $N_T$ -total vector population
- $\boldsymbol{\theta}$ - vector oviposition rate
- k -carrying capacity of the vectors.
- $\mu_{aa}$, - total mortality rates for recessive homozygotes
- $\mu_{Aa}$ - total mortality rates for recessive heterozygote
- $\mu_{AA}$ - total mortality rates for recessive dominant homozygotes

# ABSTRACT


- This report exhibits the mathematical epidemiology simulation of the dengue virus.
- The simulation is done with the software MATLAB.
- We consider an epidemiological SIRSI compartmental model here, where the SIR compartments are dedicated for the human population dynamics and the SI compartments are dedicated for the vector population dynamics.
- For the vectors, we consider a pair of alleles with dominance trait determined by the rate of mortality induced by the insecticides.
- Differential equations are developed for the compartmental model following the assumptions that we make, and the equations are solved by Euler's numerical method, And the solution obtained is simulated. We do three simulations here.
- The first simulation considers vectors with no resistant-strain and the second and third simulations exhibit the insecticide-resistant evolution of vectors through natural selection. This model developed actually integrates the epidemiology and population genetics of vector population. This report also verifies if the dominance of an insecticide-resistance gene influences the epidemic dynamics.

# INTRODUCTION

## PROBLEM STATEMENT:

Simulate the spread of a disease using graph based models like the SIR model and analyse the impact of different factors.

## OBJECTIVES:

1. To simulate the spreading of dengue virus using the SIRSI compartmental model
2. Integrating the epidemiology model with the population genetics of mosquitoes, considering two alleles with the dominant trait determined by the mortality rate of mosquitoes induced by the insecticides
3. To investigate whether the dominance of an insecticide resistance gene influences the epidemic dynamics

# BACKGROUND

## VECTOR-BORNE DISEASES AND DENGUE:

Vector-borne diseases account for more than 17% of all infectious diseases, causing more than 7,00,000 deaths annually. One of the most common vector-born disease is dengue. According to the CDC, upto 400 million of people are infected with dengue each year. Out of that about 100 million people get sick from the infection and 40,000 die from severe dengue.

Dengue is an infectious disease caused by a virus of the family *Flaviridae* which has four distinct serotypes: DEN1, DEN2, and DEN3 DEN4. The virus has different types, and it spreads through mosquito bites, particularly from a type of mosquito called Aedes aegypti. This mosquito is commonly found in urban areas, and the disease tends to become more common when cities grow quickly and without proper planning.

The problem is that this type of mosquito doesn't just spread Dengue – it can also transmit other viruses like Zika and Chikungunya. In some places, these three diseases exist together.

Even though people are trying hard to control these diseases, it's still tough. Developing new methods and making the current strategies better is very important, but it's a challenging task. So, there's a need for ongoing efforts to find

more effective ways to deal with Dengue and similar diseases. It would be beneficial if we could simulate epidemiology through mathematical models because we can gain a lot of insights from it.

## SIRSI COMPARTMENTAL MODEL FOR EPIDEMILOGY SIMULATION:

An epidemiology model or an epidemic model is a mathematical model that is created to replicate the spreading of a disease over a locality. It is designed to explain the rate at which disease is spreading. Once the model is created, we can use it to analyze how various factors affect the spreading of a disease. We can use it to predict the spreading rate. It also comes in handy when we need to discover antibiotics or vaccine for the disease.

In this report we use the SIRSI model. It is a compartmental model – it means that the model compartmentalizes humans into different compartments: S - Susceptible, I - Infected and R - Recovered groups. It compartmentalizes vectors into two compartments S - Susceptible and I - Infected.

The susceptible group involves all those individuals who are not infected yet. They are susceptible to get infected if they come into contact with the infected hosts. Infected group involves all those individuals who are infected by the disease at a certain point of time.Recovered group involves those people who were in the infected group earlier and then got recovered. Susceptible vectors includes all the vectors

which are not carrying the virus. Infected vectors are those which carry the pathogen.

## VECTOR POPULATION GENETICS:

Population genetics is the branch of biology that investigates the frequencies of alleles and genotypes in a population. A gene is a pair of alleles. Different varieties of gene are called genotypes. Genotype is the genetic makeup of an organism. For our report, we focus on the studies regarding the selection of insecticide-resistant strains of vectors. Resistant strains of vectors are those that resist and survive the effects of insecticides, and usually have their origin in genetic causes. Positive selection of particular phenotypes, such as insecticide resistance, occur because they confer a long-term survival or reproduction rate (*i.e.*, a greater fitness to the environment), and therefore individuals that express them have more chance of transmitting their genes to the next generation. Subsequently, the frequency of the allele which determines resistance increases over time, and so does the proportion of individuals that portray this gene.

In our study we consider only two alleles – A and a. The allele with a lesser mortality rate is naturally selected in the evolution.

If the frequency/probability of dominant allele is p and recessive allele is q then

$p + q = 1$

Hence, $p^2 + 2pq + q^2 = 1$

Where $p^2$ is the probability/proportion of homozygous dominant genotype AA

$q^2$ is the probability/proportion of homozygous recessive genotype aa

2pq is the probability/proportion of heterozygous genotype Aa

When the mortality rate of all the genotypes AA, Aa and aa are equal (all are equally fit and equally resistant to insecticide), then the frequency of these alleles does not change over time. This is the case with Hardy Wienberg equilibrium. If the mortality rate of genotypes is not the same, then the frequency of alleles will change over time. The genotype with the less mortality rate will be naturally selected through evolution and its proportion with respect to the population will increase. The importance of understanding the genetics of vector insecticide resistance is emphasized in the Global Plan for Insecticide Resistance Management from the World Health Organization, in which the relevance of theoretical modelling is also highlighted.

# WHAT IS OUR STUDY ABOUT:

We do three simulations in this. We divide the vector population into three genotypes – Aa, AA and aa. The first one considers the Hardy-Weinberg equilibrium condition – we consider all the genotypes to have same mortality rates due to insecticides. In the second simulation we consider the genotype AA and Aa to have more mortality rate than aa. In the third simulation we consider aa to have a higher mortality rate than AA or Aa. Since A is the dominant allele over a, the genotype Aa and AA will have the same mortality rate.

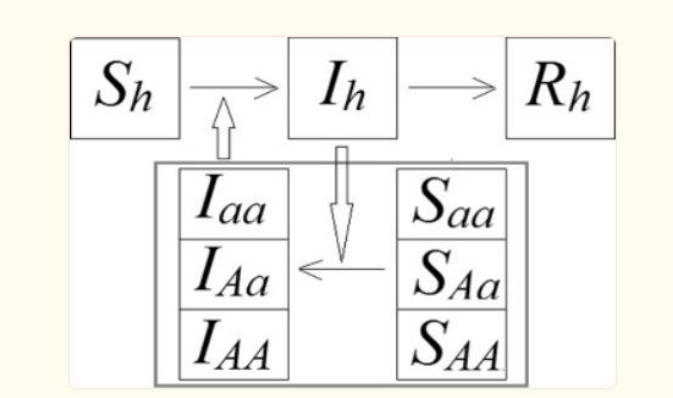
# METHODOLOGY:

## Assumptions of the model:

1. All the individuals have the same chance of reproduction, and they mate with any other individual in the population with the same probability.
2. The disease is transmitted only horizontally. Vertical transmission occurs in real situations, but we disregarded it in order to present a clearer model.
3. There are no evolutionary factors except for the biological selection (we disregard genetic drift and mutation, for instance) to avoid a very complex model
4. The lifetime span of the vectors is not long enough for the recovery of an infected insect.
5. The recovered humans do not get infected again – they will not be susceptible to infection.
6. There are no immigrants or emigrants in the populations considered, since considering human mobility would imply additional features, such as separation of population into patches which is not the focus of this investigation.

# Development of the model:

Following the assumptions that we made above, we get the following picture of the model:




**Explanation for the human compartments:**

- $S_h$ is the susceptible human population, $I_h$ is the infected human population and $R_h$ is the infected human population. $N_h$ is the total human population
- The susceptible individuals will become infected when any infected vector bites the susceptible humans
- The infected individuals will recover at the rate of γ and become the recovered individuals. The recovered individuals will not become susceptible following our assumption.
- If c is the birth rate of human population, all the new individuals born will directly get introduced into the susceptible compartment since we have assumed no vertical transmission. $\mu_h$ is the death rate of human population.

- If $\beta_h$ is the probability of transmission of virus from a vector to human, then the rate of infection is given by $\beta_h*(I_v / N_h)$ where $I_v$ is the infected vector population.

**Explanation for the vector compartments:**

- As we said earlier, we divide the entire vector population into 3 genotypes – AA, Aa and aa. Hence there are in total 3 genotypes * 2 compartments for each which is equal to 6 compartments.
- $S_{AA}$, $S_{Aa}$ and $S_{aa}$ are the susceptible vector population of genotypes AA, Aa and aa respectively.
- $I_{AA}$, $I_{Aa}$ and $I_{aa}$ are the infected vector population of genotypes AA, Aa and aa respectively.
- The susceptible vectors are those that do not carry infection. When susceptible vectors bite the infected human population, those vectors become infected.
- If $\beta_v$ is the probability of transmission of virus from a human to vector, then the rate at which vectors go from susceptible compartment to infected is given by $\beta_v*(I_h/N_h)$
- We express the dominant allele by A and recessive one by a. let the frequency of the dominant allele be p and the recessive be q.
  $f(A) = p = (2*N_{AA} + N_{Aa})/2*N_T$
  $f(a) = q = (2*N_{aa} + N_{Aa})/2*N_T$
  where $N_{AA}$ is the total population of vectors of genotype AA,

$N_{Aa}$ is the total population of vectors of genotype Aa,

$N_{aa}$ is the total population of vectors of genotype Aa,

And $N_T$ is the total vector population.

- Hence $p^2$ is the probability/proportion of homozygous dominant genotype AA, $q^2$ is the probability/proportion of homozygous recessive genotype aa, 2pq is the probability/proportion of heterozygous genotype Aa
- Let $\boldsymbol{\theta}$ be the vector oviposition rate and k be the carrying capacity of the vectors.
- The total mortality rate of vectors has two components – the natural mortality rate and the insecticide induced mortality rate. They add up to give the total mortality rate. The natural mortality will be the same for all the vectors.
- We considered $\mu_{aa}$, $\mu_{Aa}$ and $\mu_{AA}$ as the total mortality rates for recessive homozygotes, heterozygotes and dominant homozygotes, respectively. As allele *A* is dominant over *a* and we consider a complete dominance interaction, $\mu_{AA}$ and $\mu_{AA}$ will always have the same value.
- The frequency of AA genotype is $N_{AA}/N_T$
- The frequency of Aa genotype is $N_{Aa}/N_T$
- The frequency of AA genotype is $N_{aa}/N_T$

# The Set of Differential equations:

We developed the set of ordinary differential equations following the model that we developed:

These equations are first order ordinary differential equations. These can be solved using the Euler's numerical method and solution set can be obtained.

$$\frac{dS_h}{dt} = cN_h - \left(\frac{\beta_h I_v}{N_h} + \mu_h\right) S_h$$

$$\frac{dI_h}{dt} = \frac{\beta_h I_v}{N_h} S_h - (\gamma + \mu_h) I_h$$

$$\frac{dR_h}{dt} = \gamma I_h - \mu_h R_h$$

$$\frac{dS_{aa}}{dt} = q^2 \theta N_v \left(1 - \frac{N_v}{K}\right) - \left(\frac{\beta_v I_h}{N_h} + \mu_{aa}\right) S_{aa}$$

$$\frac{dI_{aa}}{dt} = \frac{\beta_v I_h}{N_h} S_{aa} - \mu_{aa} I_{aa}$$

$$\frac{dS_{Aa}}{dt} = 2\mathrm{pq}\theta N_v \left(1 - \frac{N_v}{K}\right) - \left(\frac{\beta_v I_h}{N_h} + \mu_{Aa}\right) S_{Aa}$$

$$\frac{dI_{Aa}}{dt} = \frac{\beta_v I_h}{N_h} S_{Aa} - \mu_{Aa} I_{Aa}$$

$$\frac{dS_{AA}}{dt} = p^2 \theta N_v \left(1 - \frac{N_v}{K}\right) - \left(\frac{\beta_v I_h}{N_h} + \mu_{AA}\right) S_{AA}$$

$$\frac{dI_{AA}}{dt} = \frac{\beta_v I_h}{N_h} S_{AA} - \mu_{AA} I_{AA}$$

# DATASET DESCRIPTION:

The parametric and initial data for our model was collected from the research paper that we referred to (link is present in the reference).

Table 2

Biological parameter values and meanings

| Parameter | Meaning | Value | Parameter | Meaning | Value |
|---|---|---|---|---|---|
| $C$ | Human birth rate | $0.457 \cdot 10^{-4}$ | $\mu_{aa}$ | Recessive homozygote vector mortality rate | Table 4 |
| $\mu_h$ | Human mortality rate | $0.457 \cdot 10^{-4}$ | $\mu_{Aa}$ | Heterozygote vector mortality rate | Table 4 |
| $\beta_h$ | Probability of vector-human transmission | 0.4 | $\mu_{AA}$ | Dominant homozygote vector mortality rate | Table 4 |
| $\gamma$ | Human recovery rate | 0.121 | $\beta_v$ | Probability of human-vector transmission | 0.4 |
| $\theta$ | Vector oviposition rate | 6.353 | $K$ | Carrying capacity | $2 \cdot 10^5$ |

Table 3

Variable values and meanings

| Variable | Meaning | Initial value | Variable | Meaning | Initial value |
|---|---|---|---|---|---|
| $S_h$ | Human susceptible population | $9 \cdot 10^3$ | $S_{aa}$ | Recessive homozygote vector susceptible population | $4.75 \cdot 10^3$ |
| $I_h$ | Human infected population | $2 \cdot 10^2$ | $I_{aa}$ | Recessive homozygote vector infected population | $4.75 \cdot 10^3$ |
| $R_h$ | Human recovered population | $3 \cdot 10^2$ | $N_{aa}$ | Recessive homozygote vector total population | $9.5 \cdot 10^3$ |
| $N_h$ | Human total population | $9.5 \cdot 10^3$ | $S_{AA}$ | Dominant homozygote vector susceptible population | $2.375 \cdot 10^3$ |
| $S_{Aa}$ | Heterozygote vector susceptible population | $2.375 \cdot 10^3$ | $I_{AA}$ | Dominant homozygote vector infected population | $2.375 \cdot 10^3$ |
| $I_{Aa}$ | Heterozygote vector infected population | $2.375 \cdot 10^3$ | $N_{AA}$ | Dominant homozygote vector total population | $4.75 \cdot 10^3$ |
| $N_{Aa}$ | Heterozygote vector total population | $4.75 \cdot 10^3$ | $N_v$ | Vector total population | $1.9 \cdot 10^4$ |
| $I_v$ | Infected vector population | $3 \cdot 10^4$ | $f_{aa}$ | Frequency of recessive homozygotes | $\frac{N_{aa}}{N_v}$ |
| $f_{Aa}$ | Frequency of heterozygotes | $\frac{N_{aa}}{N_v}$ | $f_{AA}$ | Frequency of dominant homozygotes | $\frac{N_{aa}}{N_v}$ |
| $q$ | Frequency of recessive allele | Eq. 2 | $p$ | Frequency of dominant allele | Eq. 3 |

Table 4

Values of mortality rates for the three simulations

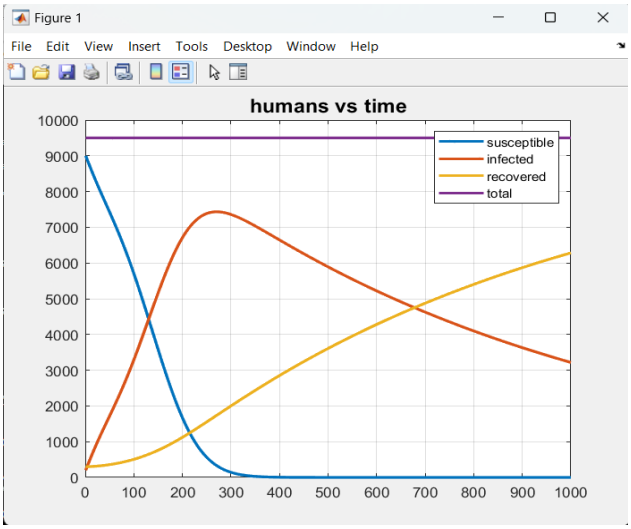
| Allele | Genotypes in which the allele expresses | Mortality rate ($day^{-1}$) | | |
|---|---|---|---|---|
| | | Simulation 1 | Simulation 2 | Simulation 3 |
| Recessive ($a$) | $aa$ | 0.25 | 0.01 | 0.25 |
| Dominant ($A$) | $A\,a$,$A\,A$ | 0.25 | 0.25 | 0.01 |

# RESULTS AND DISCUSSION:

## Simulation 1:

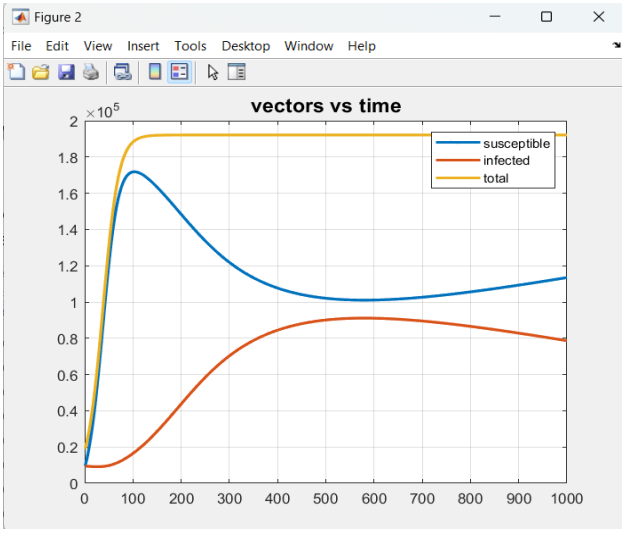
Here we consider the case when the mortality of all the genotypes are equal. It is the case of Hardy Weinberg equilibrium.

**Figure 1 is the plot containing the susceptible, infected, recovered and total human population:**




We see that susceptible population comes down very quickly at the beginning and the infected population for the same time interval increases very steeply until it reaches the peak value between 250-300 days. The recovered humans proportion is almost increasing linearly

**Figure 2 is the plot containing the susceptible, infected and total vector population:**




We see that the infected vector and susceptible vector population are increasing for a while and decreasing.

The total vector population increases for initial hundred days and remains stable later on.

**Figure 3 is the plot containing the susceptible, infected and total vector population of aa**

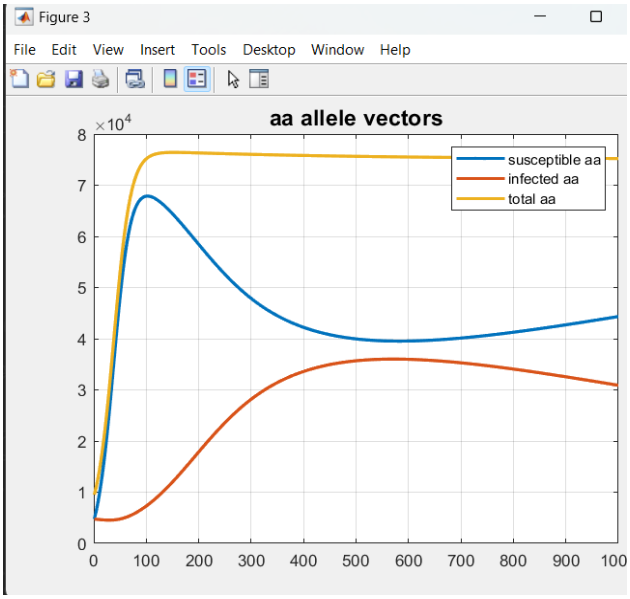



**Figure 4 is the plot containing the susceptible, infected and total vector population of Aa genotype:**

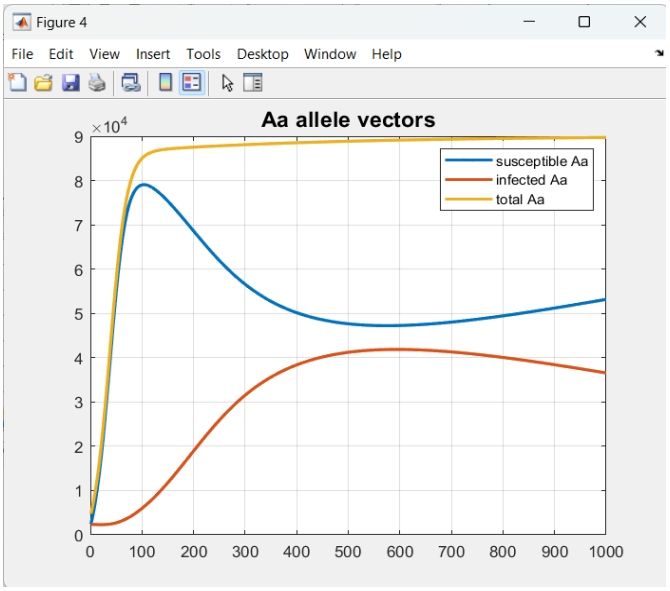



**Figure 5 is the plot containing the susceptible, infected and total vector population of AA genotype**

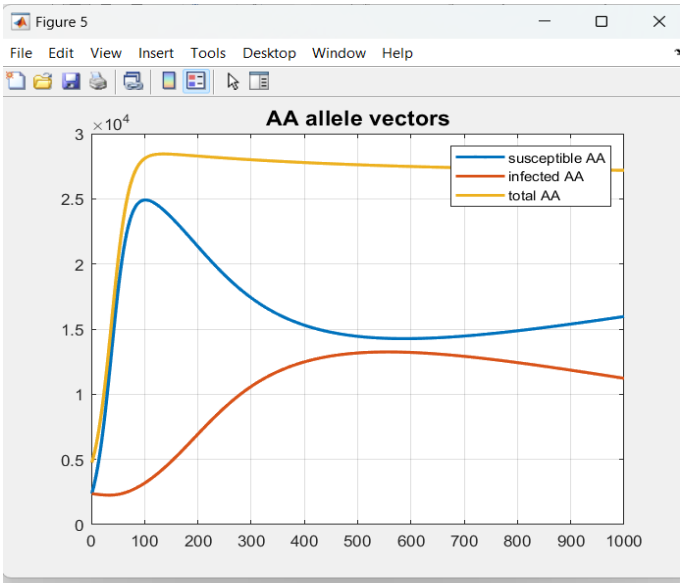


**Figure 6 is the plot containing the susceptible vectors of different genotypes:**

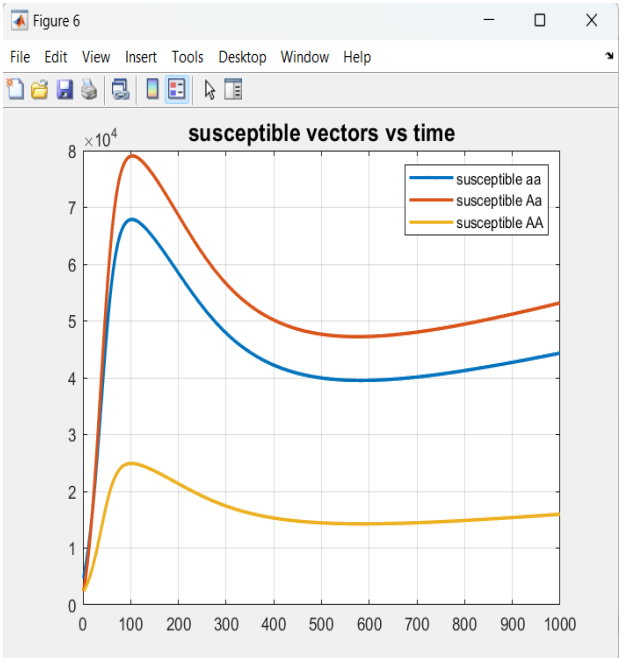



**Figure 7 is the plot containing the infected vectors of different genotypes:**

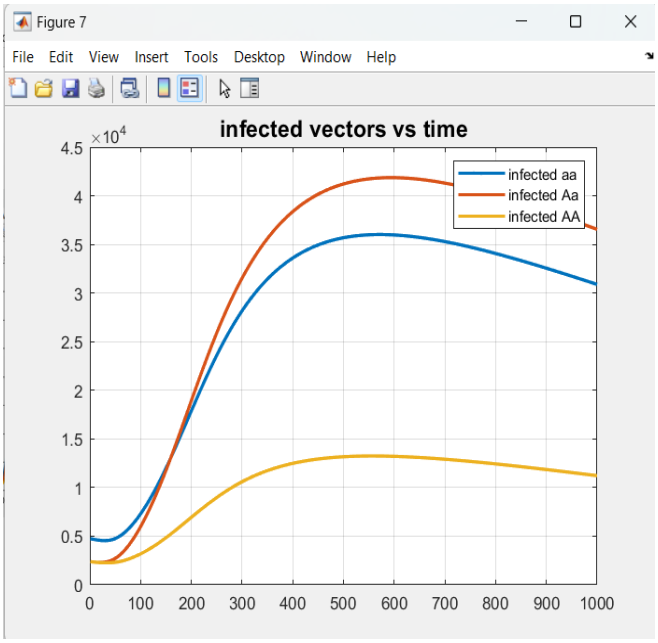



**Figure 8 is the plot containing the frequencies of different genotypes:**

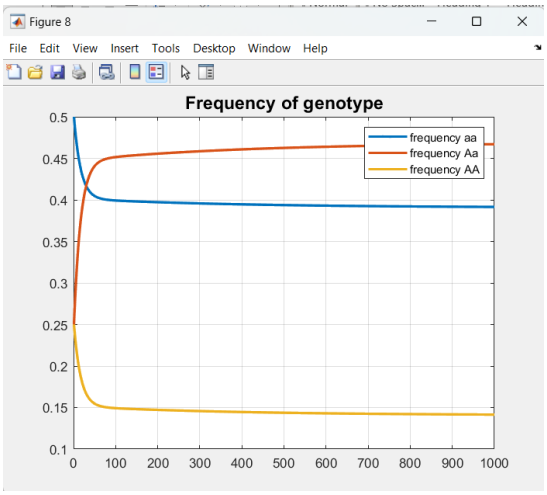
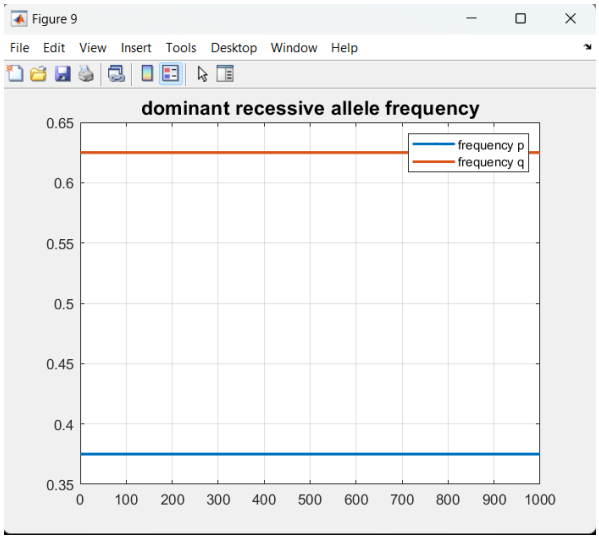


**Figure 9 is the plot containing the frequencies of allele A and allele a:**




We see that the frequency of the allele A and allele a remain constant throughout as it is the case of Hardy-Weinberg equilibrium

## Simulation 2:

Here we consider the homozygous recessive genotype to have lower mortality rate compared to the other two and hence this genotype will be naturally selected through evolution.

**Figure 1 is the plot containing the susceptible, infected, recovered and total human population:**

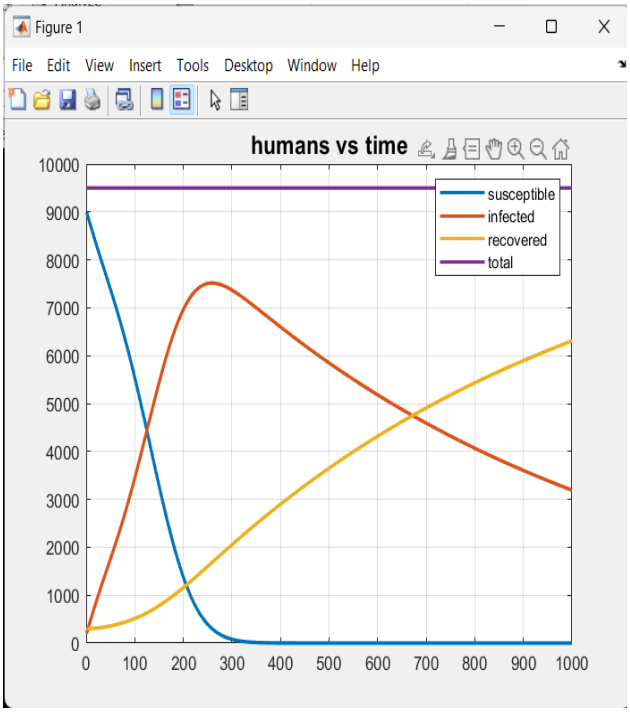
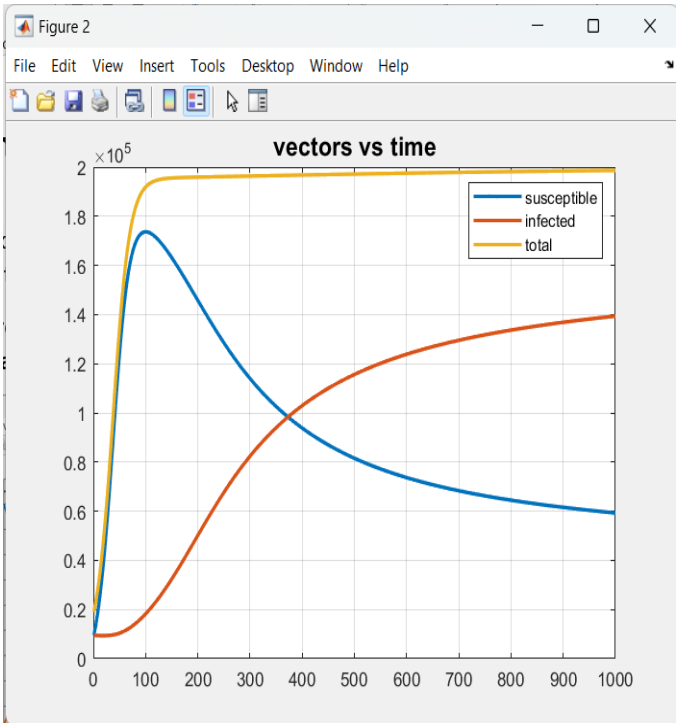
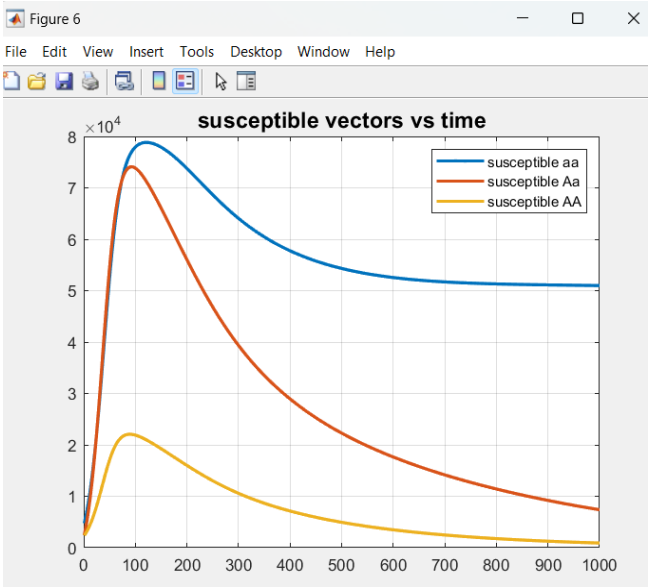



**Figure 2 is the plot containing the susceptible, infected and total vector population:**

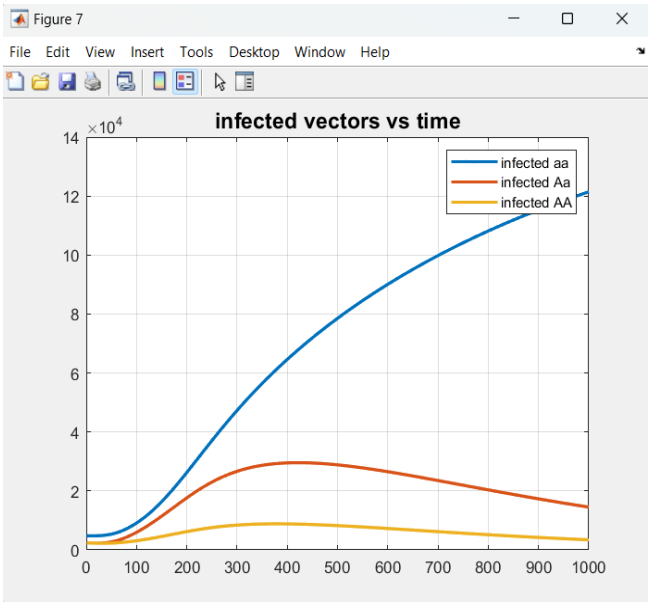


## Figure 6 is the plot containing the susceptible vectors of different genotypes:



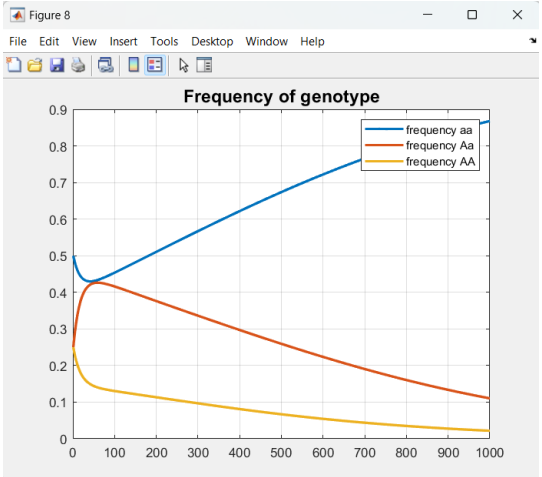

We see that , since the genotype aa is having lower mortality rate – it is resistant strain and hence it is naturally selected. We see that the susceptible vector population of aa genotype does not decrease much

## Figure 7 is the plot containing the infected vectors of different genotypes:



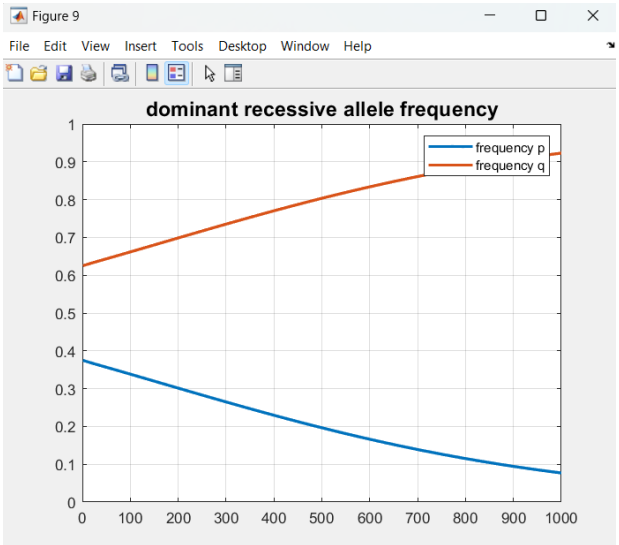

We see that , since the genotype aa is having lower mortality rate – it is resistant strain and hence it is naturally selected. We see that the infected vectors of aa genotype do not die out much if insecticides are used because they are more resistant strain.

# Figure 8 is the plot containing the frequencies of different genotypes:




Overall , the proportion of vector population having aa genotype increases as time passes and the proportion of the other two genotypes decreases very much. This exhibits the natural selection through evolution.

# Figure 9 is the plot containing the frequencies of allele A and allele a:




We see that frequency of recessive allele in the population increases and the dominant allele decreases.

## Simulation 3:

Here we consider the homozygous recessive genotype to have higher mortality rate compared to the other two. Hence the genotypes AA and Aa will be naturally selected through the evolution.

**Figure 1 is the plot containing the susceptible, infected, recovered and total human population:**

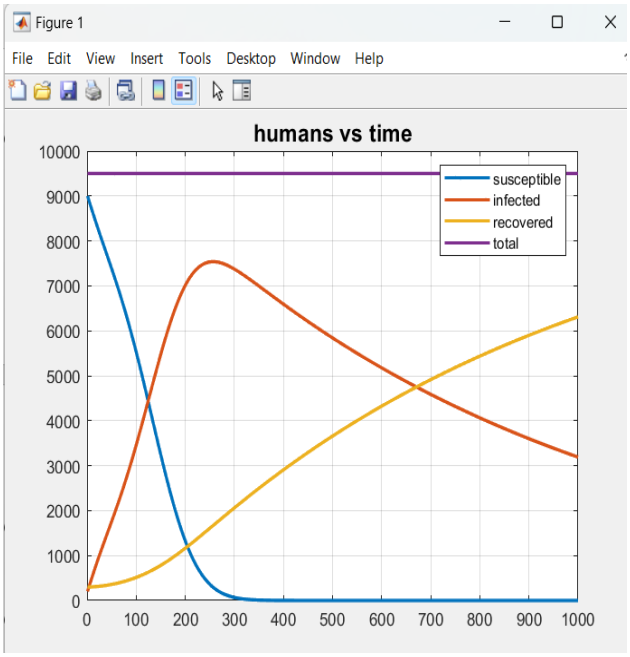
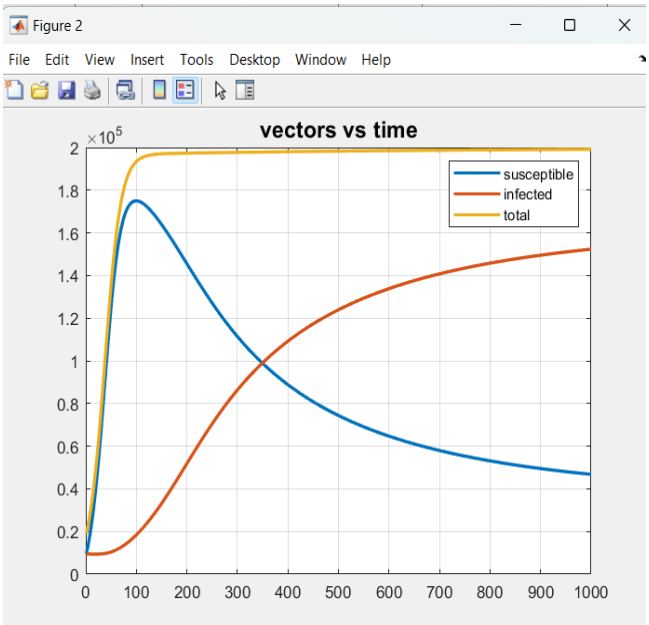
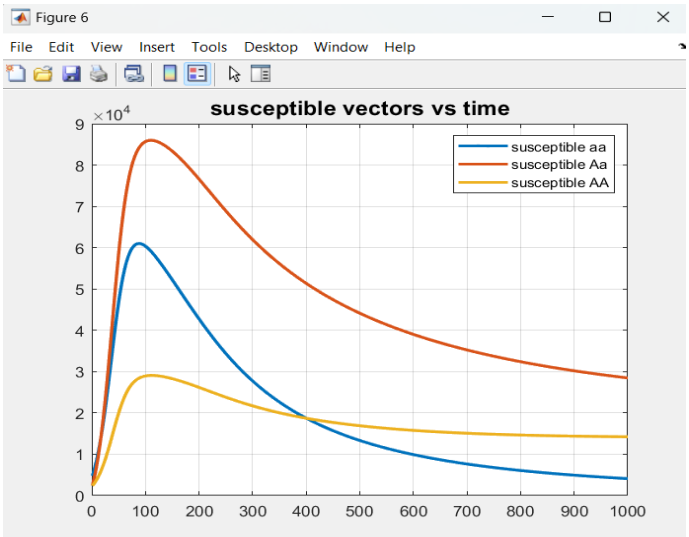



**Figure 2 is the plot containing the susceptible, infected and total vector population:**

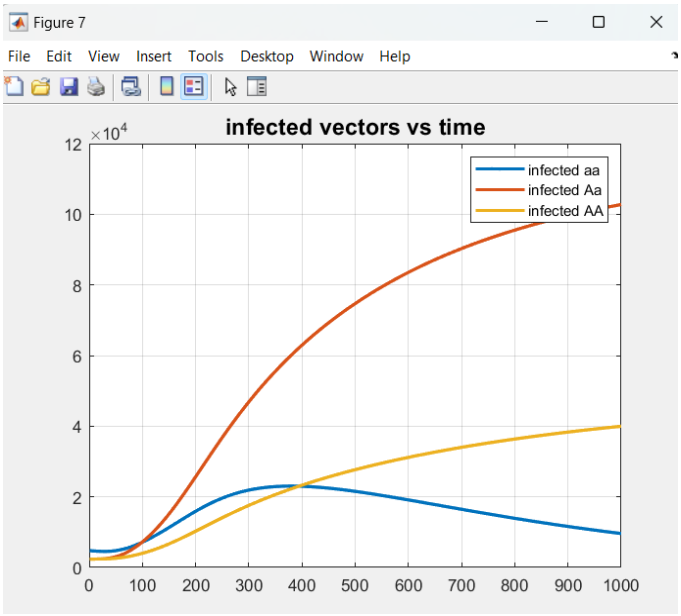


## Figure 6 is the plot containing the susceptible vectors of different genotypes:



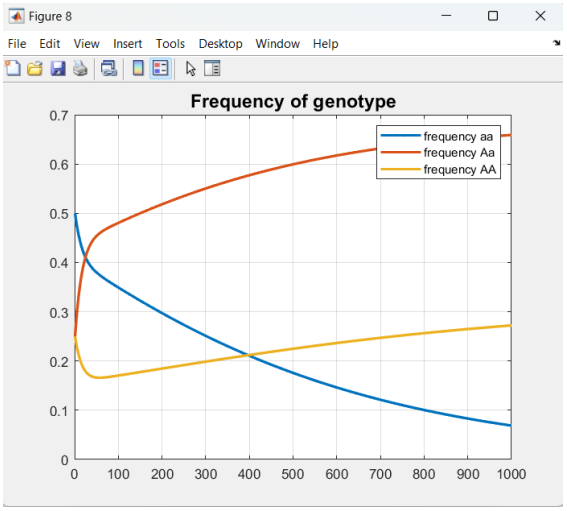

We see that , since the genotype aa is having higher mortality rate – it is not resistant strain. Whereas the AA and Aa are more resistant strain. hence it is naturally selected. We see that the susceptible vector population of AA does not decrease much.

## Figure 7 is the plot containing the infected vectors of different genotypes:



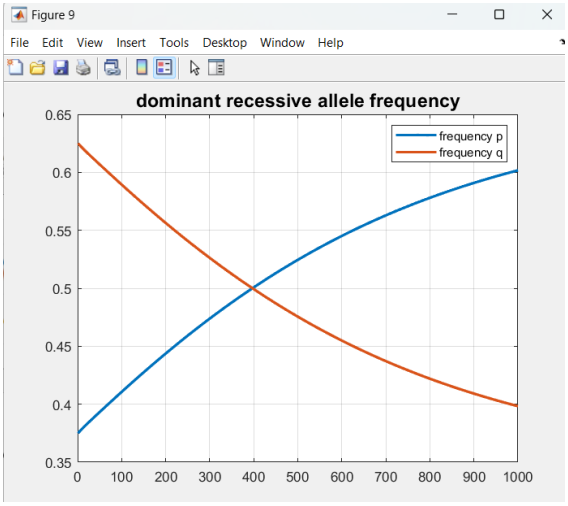

We see that the infected vector population of AA and Aa is not decreasing because they are more resistant strain and hence they do not die out very easily when insecticides are used.

# Figure 8 is the plot containing the frequencies of different genotypes:




Overall , the proportion of vector population having AA and Aa genotypes increases as time passes and the proportion of the aa genotype decreases very much. This exhibits the natural selection through evolution.

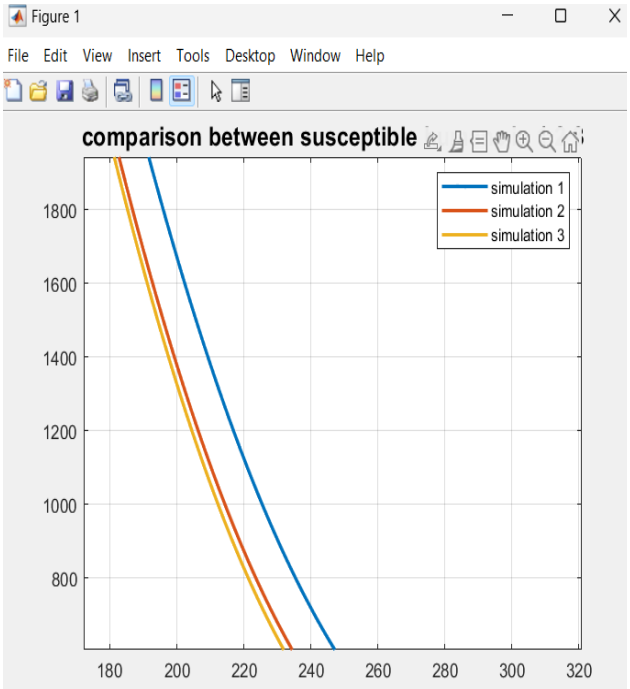
# Figure 9 is the plot containing the frequencies of allele A and allele a:




We see that frequency of the dominant allele increases over time and the frequency of the recessive allele decreases over time

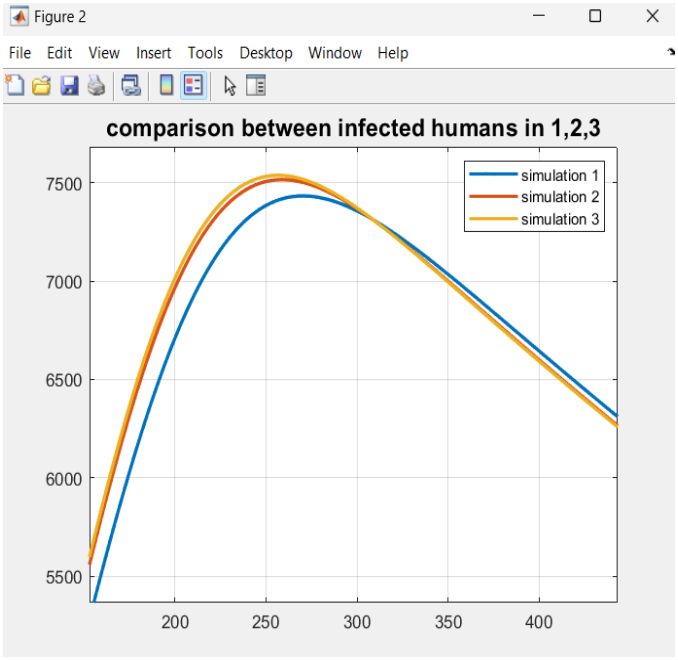
# COMPARING THE THREE SIMULATIONS:

Comparing the susceptible human population in all the three simulations:




Comparing the three simulations of susceptible humans , we see that at a particular instant of time , the susceptible humans is lesser in the case of resistant strain vectors (simulation 3 and 2) than in the case of no-resistant strain (simulation 1).

Comparing the infected human population in all the three simulations:




Comparing the three simulations of infected humans , we see that at a particular instant of time during initial 250 days , the infected humans is more in the case of resistant strain vectors (simulation 3 and 2) than in the case of no-resistant strain (simulation 1).

# CONCLUSION:

- The model exhibited the epidemical dynamics of dengue virus.
- We analyzed the epidemical changed caused by changing the factors affecting population genetics. Hence a successful mathematical model was built that integrates epidemiology simulation and population genetics.
- The computational simulations have shown that the presence of an insecticide resistance gene is related to a bigger number of infected humans and vectors. Thus, they affect the epidemical dynamic

# SCOPE FOR IMPROVEMENTS:

1. The model could be improved by considering other factors like the different life stages of vectors
2. The model can also be upgraded to include different serotypes of the dengue virus.
3. This model considered only one trait – insecticide resistance strain that can affect the epidemics. Practically there could be a lot of other traits which will also affect the epidemiology dynamics. It would be more sophisticated to have a model that considers so many other traits.
4. considering the case of immigrants and emigrants into the population would also be useful as it a realistic scenario.

# REFERENCES:


https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5501426/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6136472/

# MATLAB CODE:

```
clear
clc
clearvars
%constants
Nh0=9.5*power(10,3); %initial total human population
Sh0=9*power(10,3); %initial susceptible human population
Ih0=2*power(10,2); %initial infected human population
Rh0=3*power(10,2); %initial recovered human population

c=0.457*power(10,-4); % birth rate of human
Muh=0.457*power(10,-4); %death rate of human
Bh=0.4; %vector to human transmission probability
Y=0.121; % human recovery rate

theta=6.353; % vector oviposition rate
Bv=0.4; %human to vector transmission probability

Sv0=9.5*power(10,3); %initial susceptible vector population
Iv0=9.5*power(10,3); %initial infected vector population
Nv0=1.9*power(10,4); %initial total vector population

Naa0=9.5*power(10,3); %initial aa genotype population of vectors
NAa0=4.75*power(10,3); %initial Aa genotype population of vectors
NAA0=4.75*power(10,3); %initial AA genotype population of vectors

Saa0=4.75*power(10,3); %initial aa genotype susceptible population of vectors
SAa0=2.375*power(10,3); %initial Aa genotype susceptible population of vectors
SAA0=2.375*power(10,3); %initial AA genotype susceptible population of vectors

Iaa0=4.75*power(10,3); %initial aa genotype infected population of vectors
IAa0=2.375*power(10,3);%initial Aa genotype infected population of vectors
IAA0=2.375*power(10,3);%initial AA genotype infected population of vectors
K=2*power(10,5); %carrying capacity of the vectors

Muaa=0.25;%death rate of aa genotype vectors
MuAa=0.25;%death rate of Aa genotype vectors
MuAA=0.25;%death rate of AA genotype vectors

q=(2*Naa0 + NAa0)/2*Nv0; % recessive allele frequency
p=(2*NAA0 + NAa0)/2*Nv0; % dominant allele frequency
Faa0=Naa0/Nv0; %frequency of aa genotype
FAa0=NAa0/Nv0; %frequency of Aa genotype
FAA0=NAA0/Nv0; %frequency of AA genotype
no_of_days=1000; %no of days for the simulation
```

```
%arrays to store the values
susceptible_Humans=zeros(1,no_of_days);
infected_Humans=zeros(1,no_of_days);
Recovered_Humans=zeros(1,no_of_days);
Saa_population = zeros(1,no_of_days);
SAa_population = zeros(1,no_of_days);
SAA_population = zeros(1,no_of_days);
Iaa_population = zeros(1,no_of_days);
IAa_population = zeros(1,no_of_days);
IAA_population = zeros(1,no_of_days);
Naa_population = zeros(1,no_of_days);
NAa_population = zeros(1,no_of_days);
NAA_population = zeros(1,no_of_days);
total_Susceptible_vectors=zeros(1,no_of_days);
total_Infected_vectors=zeros(1,no_of_days);
total_Human_population=zeros(1,no_of_days);
total_Vector_Population=zeros(1,no_of_days);
frequency_aa=zeros(1,no_of_days);
frequency_Aa=zeros(1,no_of_days);
frequency_AA=zeros(1,no_of_days);
frequency_p=zeros(1,no_of_days);
frequency_q=zeros(1,no_of_days);
Time=zeros(1,no_of_days);
```

```
%Model processing
dt=0.01;        % delta t = 1 day
% y(t)=y(t-1) + dt*(function value at t-1)
for i=1:1:no_of_days
    Sh=Sh0;
    Ih=Ih0;
    Rh=Rh0;
    Nh=Nh0;
    Saa=Saa0;
    SAa=SAa0;
    SAA=SAA0;
    Iaa=Iaa0;
    IAa=IAa0;
    IAA=IAA0;
    Naa=Naa0;
    NAa=NAa0;
    NAA=NAA0;
    Sv=Sv0;
    Iv=Iv0;
    Nv=Nv0;
    q=(2*Naa0 + NAa0)/(2*Nv0);
    p=(2*NAA0 + NAa0)/(2*Nv0);
    Faa=Faa0;
    FAa=FAa0;
    FAA=FAA0;
```

```
susceptible_Humans(1,i)=Sh0;
infected_Humans(1,i)=Ih0;
Recovered_Humans(1,i)=Rh0;
Saa_population(1,i)=Saa0;
SAa_population(1,i)=SAa0;
SAA_population(1,i)=SAA0;
Iaa_population(1,i)=Iaa0;
IAa_population(1,i)=IAa0;
IAA_population(1,i)=IAA0;
Naa_population(1,i)=Naa0;
NAa_population(1,i)=NAa0;
NAA_population(1,i)=NAA0;
total_Susceptible_vectors(1,i)=Sv0;
total_Infected_vectors(1,i)=Iv0;
total_Human_population(1,i)=Nh0;
total_Vector_Population(1,i)=Nv0;
frequency_aa(1,i)=Faa0;
frequency_Aa(1,i)=FAa0;
frequency_AA(1,i)=FAA0;
frequency_p(1,i)=p;
frequency_q(1,i)=q;
Time(1,i)=i;
```

```
    Sh0=Sh + dt*fx(c,Nh,Bh,Iv,Sh,Muh);
    Ih0=Ih + dt*gx(Bh,Iv,Nh,Sh,Muh,Ih,Y);
    Rh0=Rh + dt*hx(Y,Ih,Muh,Rh);
    Saa0=Saa + dt*px(q,theta,Nv,K,Bv,Ih,Nh,Saa,Muaa);
    Iaa0=Iaa + dt*qx(Bv,Ih,Nh,Saa,Muaa,Iaa);
    SAa0=SAa + dt*rx(p,q,theta,Nv,K,Bv,Ih,Nh,SAa,MuAa);
    IAa0=IAa + dt*sx(Bv,Ih,Nh,SAa,MuAa,IAa);
    SAA0=SAA + dt*tx(p,theta,Nv,K,Bv,Ih,Nh,SAA,MuAA);
    IAA0=IAA + dt*ux(Bv,Ih,Nh,SAA,MuAA,IAA);
    Sv0=Saa0+SAa0+SAA0;
    Iv0=Iaa0+IAa0+IAA0;
    Naa0=Saa0+Iaa0;
    NAa0=SAa0+IAa0;
    NAA0=SAA0+IAA0;
    Nh0=Sh0+Ih0+Rh0;
    Nv0=Sv0+Iv0;
    Faa0=Naa0/Nv0;
    FAa0=NAa0/Nv0;
    FAA0=NAA0/Nv0;

end
```

```
% simulation graphs
%simulation 1
figure(1)
clf;
plot(Time,susceptible_Humans,LineWidth=2,DisplayName='susceptible');
hold on
plot(Time,infected_Humans,LineWidth=2,DisplayName='infected');
hold on
plot(Time,Recovered_Humans,LineWidth=2,DisplayName='recovered');
hold on
plot(Time,total_Human_population,LineWidth=2,DisplayName='total');
legend('show')
title('humans vs time',FontSize=14);
grid on
hold off

figure(2)
clf;
plot(Time,total_Susceptible_vectors,LineWidth=2,DisplayName='susceptible');
hold on
plot(Time,total_Infected_vectors,LineWidth=2,DisplayName='infected');
hold on
plot(Time,total_Vector_Population,LineWidth=2,DisplayName='total');
legend('show')
title('vectors vs time',FontSize=14);
grid on

figure(3)
clf;
plot(Time,Saa_population,LineWidth=2,DisplayName='susceptible aa');
hold on
plot(Time,Iaa_population,LineWidth=2,DisplayName='infected aa');
hold on
plot(Time,Naa_population,LineWidth=2,DisplayName='total aa');
legend('show')
title('aa allele vectors',FontSize=14);
grid on
```

```
figure(4)
clf;
plot(Time,SAa_population,LineWidth=2,DisplayName='susceptible Aa');
hold on
plot(Time,IAa_population,LineWidth=2,DisplayName='infected Aa');
hold on
plot(Time,NAa_population,LineWidth=2,DisplayName='total Aa');
legend('show')
title('Aa allele vectors',FontSize=14);
grid on

figure(5)
clf;
plot(Time,SAA_population,LineWidth=2,DisplayName='susceptible AA');
hold on
plot(Time,IAA_population,LineWidth=2,DisplayName='infected AA');
hold on
plot(Time,NAA_population,LineWidth=2,DisplayName='total AA');
legend('show')
title('AA allele vectors',FontSize=14);
grid on

figure(6)
clf;
plot(Time,Saa_population,LineWidth=2,DisplayName='susceptible aa');
hold on
plot(Time,SAa_population,LineWidth=2,DisplayName='susceptible Aa');
hold on
plot(Time,SAA_population,LineWidth=2,DisplayName='susceptible AA');
legend('show')
title('susceptible vectors vs time',FontSize=14);
grid on

figure(7)
clf;
plot(Time,Iaa_population,LineWidth=2,DisplayName='infected aa');
hold on
plot(Time,IAa_population,LineWidth=2,DisplayName='infected Aa');
hold on
plot(Time,IAA_population,LineWidth=2,DisplayName='infected AA');
legend('show')
title('infected vectors vs time',FontSize=14);
grid on
```

```
figure(8)
clf;
plot(Time,frequency_aa,LineWidth=2,DisplayName='frequency aa');
hold on
plot(Time,frequency_Aa,LineWidth=2,DisplayName='frequency Aa');
hold on
plot(Time,frequency_AA,LineWidth=2,DisplayName='frequency AA');
legend('show')
title('Frequency of genotype',FontSize=14);
grid on

figure(9)
clf;
plot(Time,frequency_p,LineWidth=2,DisplayName='frequency p');
hold on
plot(Time,frequency_q,LineWidth=2,DisplayName='frequency q');
legend('show')
title('dominant recessive frequency',FontSize=14);
grid on
```

```
%functions for the model equations
function y1=fx(c,Nh,Bh,Iv,Sh,Muh)
    y1=c*Nh - (Bh*Iv/Nh)*Sh - Muh*Sh;
end

function y2=gx(Bh,Iv,Nh,Sh,Muh,Ih,Y)
    y2=(Bh*Iv/Nh)*Sh - Muh*Ih - Y*Ih;
end

function y3=hx(Y,Ih,Muh,Rh)
    y3=(Y*Ih)-(Muh*Rh);
end

function y4=px(q,theta,Nv,K,Bv,Ih,Nh,Saa,Muaa)
    y4=q*q*theta*Nv*(1 - Nv/K)-(Bv*Ih/Nh)*Saa - Muaa*Saa;
end

function y5=qx(Bv,Ih,Nh,Saa,Muaa,Iaa)
    y5=(Bv*Ih/Nh)*Saa - Muaa*Iaa;
end
function y6=rx(p,q,theta,Nv,K,Bv,Ih,Nh,SAa,MuAa)
    y6=2*p*q*theta*Nv*(1 - Nv/K)-(Bv*Ih/Nh)*SAa - MuAa*SAa;
end
function y7=sx(Bv,Ih,Nh,SAa,MuAa,IAa)
    y7=(Bv*Ih/Nh)*SAa - MuAa*IAa;
end
function y8=tx(p,theta,Nv,K,Bv,Ih,Nh,SAA,MuAA)
    y8=p*p*theta*Nv*(1 - Nv/K)-(Bv*Ih/Nh)*SAA - MuAA*SAA;
end
function y9=ux(Bv,Ih,Nh,SAA,MuAA,IAA)
    y9=(Bv*Ih/Nh)*SAA - MuAA*IAA;
end
```