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Mathematical Model of Malaria Lifecycle

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Abstract

On April 12, 2018 Dr. Ana-Maria Croica gave a presentation as NSF-Target Infusion Program Seminar Series. Her topic is “An Optimal Control Model to Reduce and Eradicate Anthrax Disease in Herbivorous Animals. This research is based on Saad-Roy’s Mathematical Model of Anthrax Transmission in Animal Population. I was impressed by her mathematical model. Therefore, I would like to apply her process to construct a mathematical model for the Malaria lifecycle. Malaria lifecycle includes two major parts: Human host and Infected Mosquitos. At this research we first created two sub-models: Human Host Sub-Model and Mosquitos Sub-model. The combined these two sub-models into one Malaria Lifecycle model. We also considered the seasonal effect on mosquito’s birth and the effects by immunization and quarantine human host of malaria.

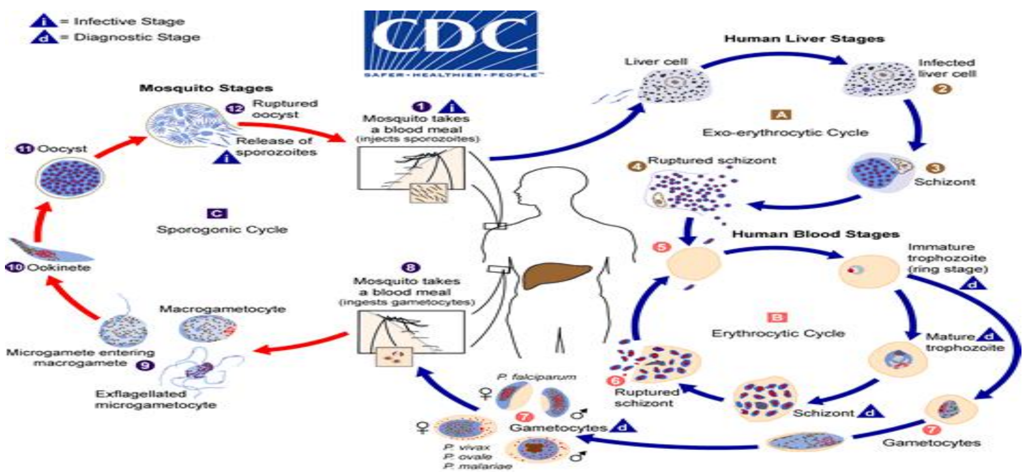
KeyWords: Life Cycle, Malaria, SIR model, Vensim

Introduction

According to CDC report that the natural history of malaria involves cyclical infection of humans and female ***Anopheles*** mosquitoes. In humans, the parasites grow and multiply first in the liver cells and then in the red cells of the blood. In the blood, successive broods of parasites grow inside the red cells and destroy them, releasing daughter parasites ("merozoites") that continue the cycle by invading other red cells.

The blood stage parasites are those that cause the symptoms of malaria. When certain forms of blood stage parasites (gametocytes, which occur in male and female forms) are ingested during blood feeding by a female ***Anopheles***mosquito, they mate in the gut of the mosquito and begin a cycle of growth and multiplication in the mosquito. After 10-18 days, a form of the parasite called a sporozoite migrates to the mosquito's salivary glands. When the ***Anopheles***mosquito takes a blood meal on another human, anticoagulant saliva is injected together with the sporozoites, which migrate to the liver, thereby beginning a new cycle.

Thus the infected mosquito carries the disease from one human to another (acting as a "vector"), while infected humans transmit the parasite to the mosquito, in contrast to the human host, the mosquito vector does not suffer from the presence of the parasites. The following picture is the picture from CDC that shows the Malaria Lifecycle.



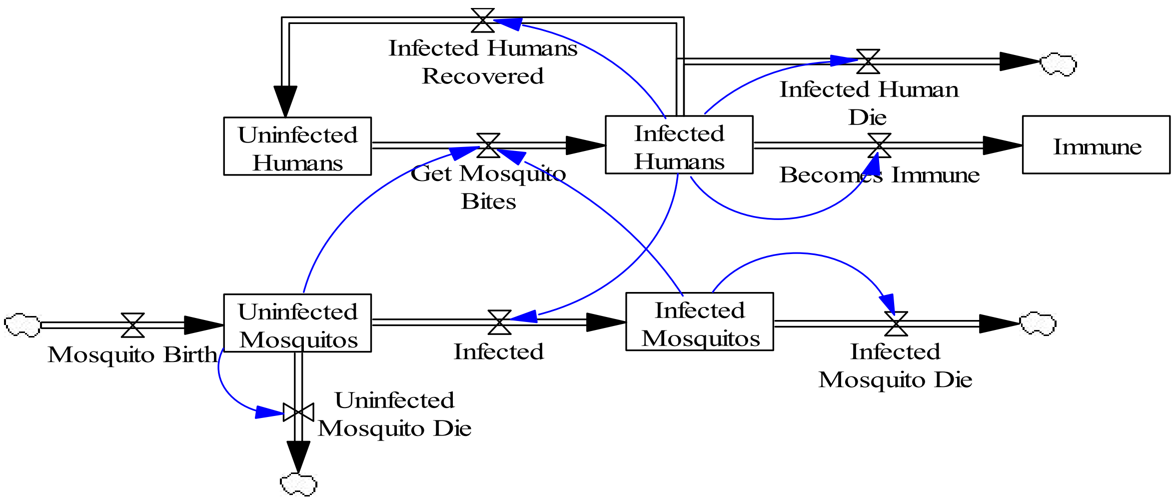
Steps of Modeling Process:

Through the CDC''s documentation, we know malaria lifecycle. We can identify the life cycle has two major sub-model which are human host model and mosquitos' model. Human host model is a modified SIR model and mosquitos' model is a SI model. However, these two models affect each other. Infected mosquitos bite Uninfected humans change uninfected humans into infected humans, and uninfected mosquitos bite infected humans will become infected mosquitos. This interaction can be show at our initial diagram for Malaria Life cycle below.

First, we formulate the malaria lifecycle as the following Vensim diagram:

Initial Diagram for Malaria Lifecycle Model

Since life expectancy of human is much longer than mosquito's, we ignored the new birth of human. However, the new birth of mosquitos is significant and cannot be ignored. Later we will consider the impact of rain season to the new mosquito birth.



Our main objective is to investigate the progress of malaria. In particular, the relationships between human and *Anopheles* mosquito populations. In this research we only concentrate on mathematics of malaria lifecycle. We ignore the data on malaria, climate effect of malaria, and other malaria biology.

In this research, we need to make some assumptions. As we mentioned before, we ignored the birth of human since human life expectancy is much longer than that of mosquito. We also assume there are no immigration, and human death except the death due to malaria, and the incubation period is short enough to be negligible. The variables of this research are Uninfected Humans, Infected Humans, Immune, Uninfected Mosquitos, and Infected Mosquito. We want to know how many health people will be there after the Malaria epidemic.

Notations we used in this research:

S: Uninfected Humans, who are susceptible to the disease

I: Infected Humans, who have malaria and spread disease to mosquito that bite them

Im: Immune, who are recover from malaria and become immune.

Um: Uninfected Mosquito that do not carry Plasmodium

Iv: Infected mosquitos that carry Plasmodium.

α: Mosquito bite rate

β: Immunity rate

ϒ: Death rate from malaria

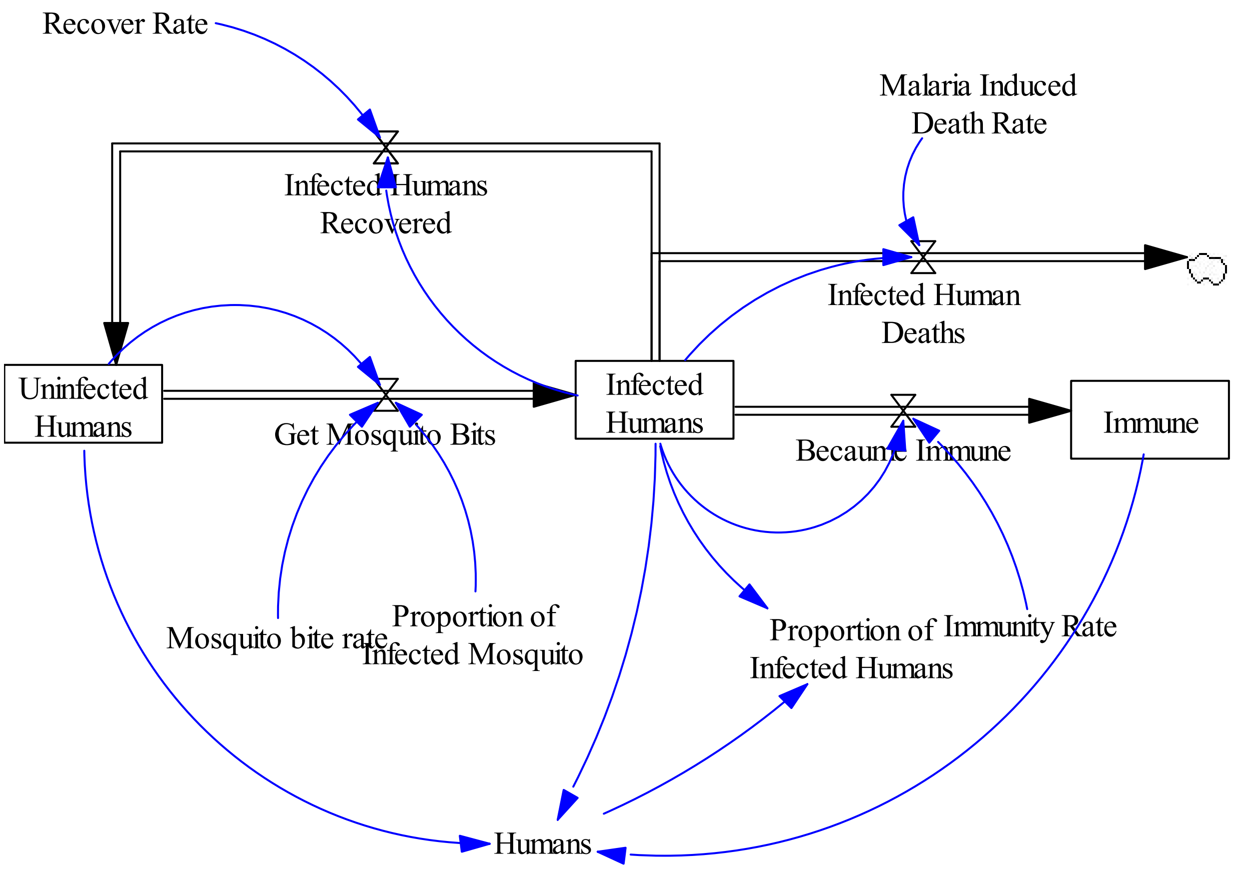
δ: Recovery rate

ε: Mosquito birth rate

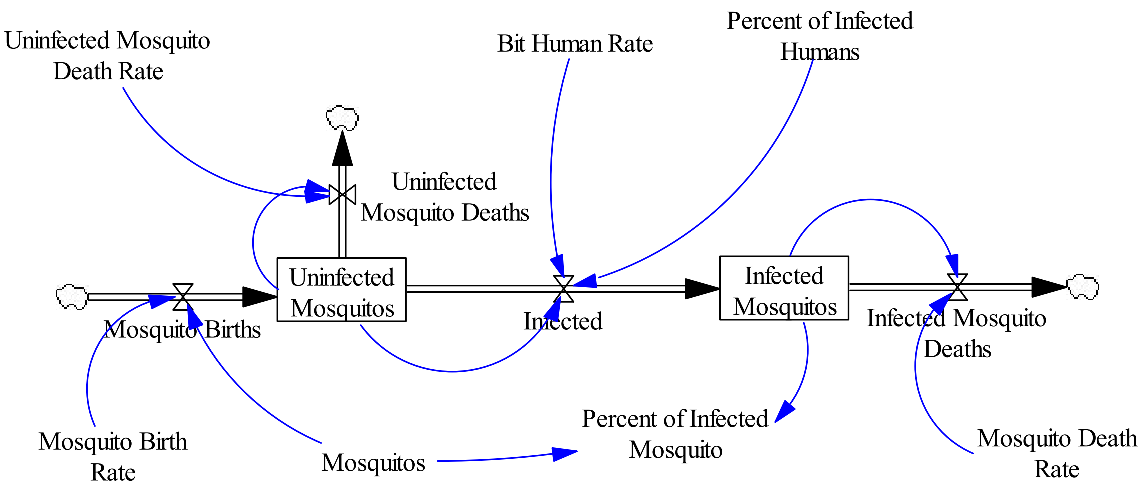
λ: Mosquito death rate

From the malaria lifecycle diagram, we refine our model to a detail Human Sub-Model and a detail Mosquito Sub-Model.

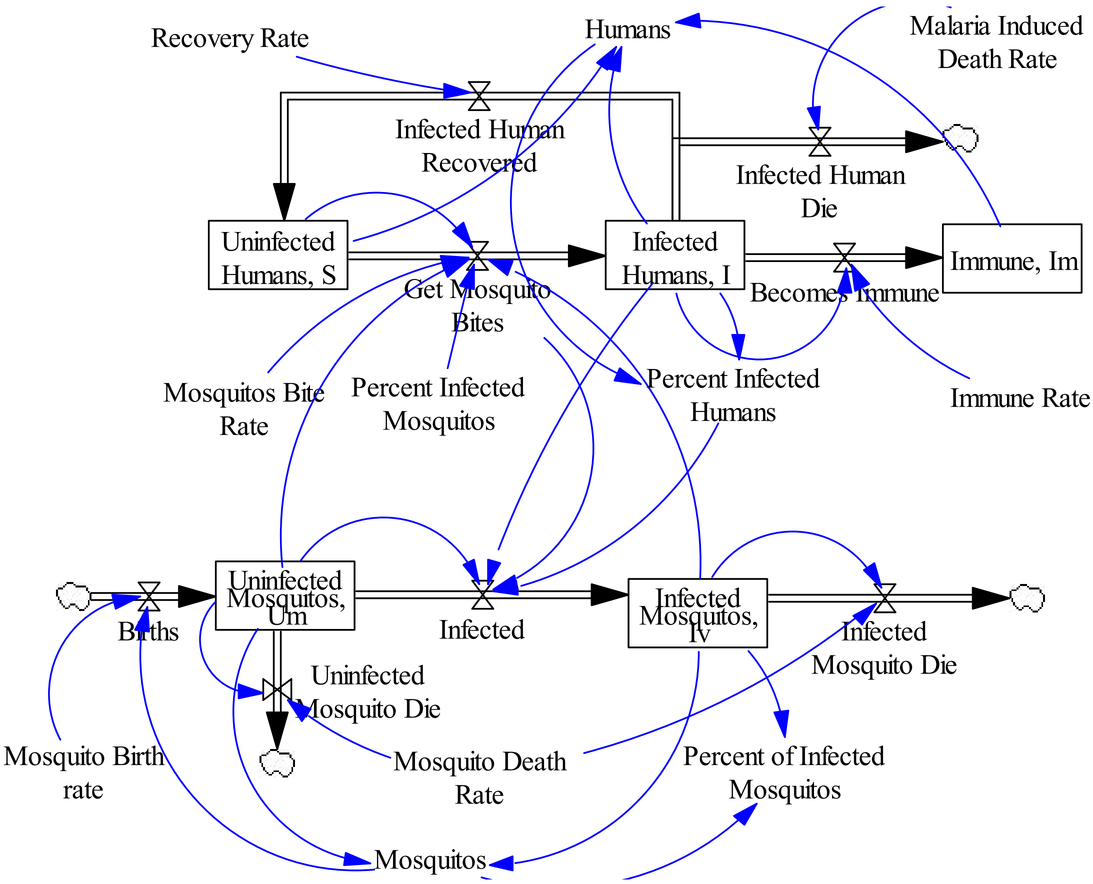
Detail Human Sub-Model



Detail Mosquito Sub-Model



Finally, we combine Human sub-model and Mosquito Sub-Model, we have a combined Malaria lifecycle model:



Relationships Among Variables

At Human Sub-Model, we observe that the rate of change of three variables are

$$\frac{dS}{dt} = -\alpha * \frac{Iv}{Um + Iv} * S + \delta * I$$

$$\frac{dI}{dt} = \alpha * \frac{Iv}{Um + Iv} * S - \delta * I - \beta * I - \Upsilon * I$$

$$\frac{dIm}{dt} = \beta * I$$

At Mosquito Sub-Model, we observe that the rate of change of two variables are

$$\frac{dUm}{dt} = \varepsilon * (Um + Iv) - \lambda * Um - \alpha * Um * (\frac{I}{S + I + Im})$$

$$\frac{dIv}{dt} = \alpha * Um * \frac{I}{S + I + Im} - \lambda * Iv$$

$$Humans = S + I + Im$$

$$Mosquitos = Um + Iv$$

Healthy Humans = $S + Im$

Here, we have a system of five linear differential equations. Certainly, it is very tedious and time consuming to solve for algebraic solutions. With help of computer software, we can get numerical and graphic solutions. We only use Vensim to draw the relationship diagram and use Excel to find numerical and graphic approximation solutions.

The approximation formulas we enter Excel Worksheet that correspond to previous five differential equations respectively are as following:

$$S(t + \Delta t) = S(t) + \Delta t * (-\ \alpha * \frac{Iv}{Um + Iv} * S(t) + \delta * I(t))$$

$$I(t + \Delta t) = I(t) + \Delta t * (\ \alpha * \frac{Iv}{Um + Iv} * S(t) - \delta * I(t) - \beta * I(t) - \Upsilon * I(t))$$

$$Im(t + \Delta t) = Im(t) + \Delta t *\ \beta * I(t)$$

$$Um(t + \Delta t) = Um(t) + \Delta t * (\ \varepsilon * (Um(t) + Iv(t)) - \lambda * Um(t) - \alpha * Um(t) * \left(\frac{I}{S + I + Im}\right))$$

$$Iv(t + \Delta t) = Iv(t) + \Delta t * (\ \alpha * Um(t) * \frac{I}{S + I + Im} - \lambda * Iv(t))$$

$$Humans = S + I + Im$$

$$Mosquito = Um + Iv$$

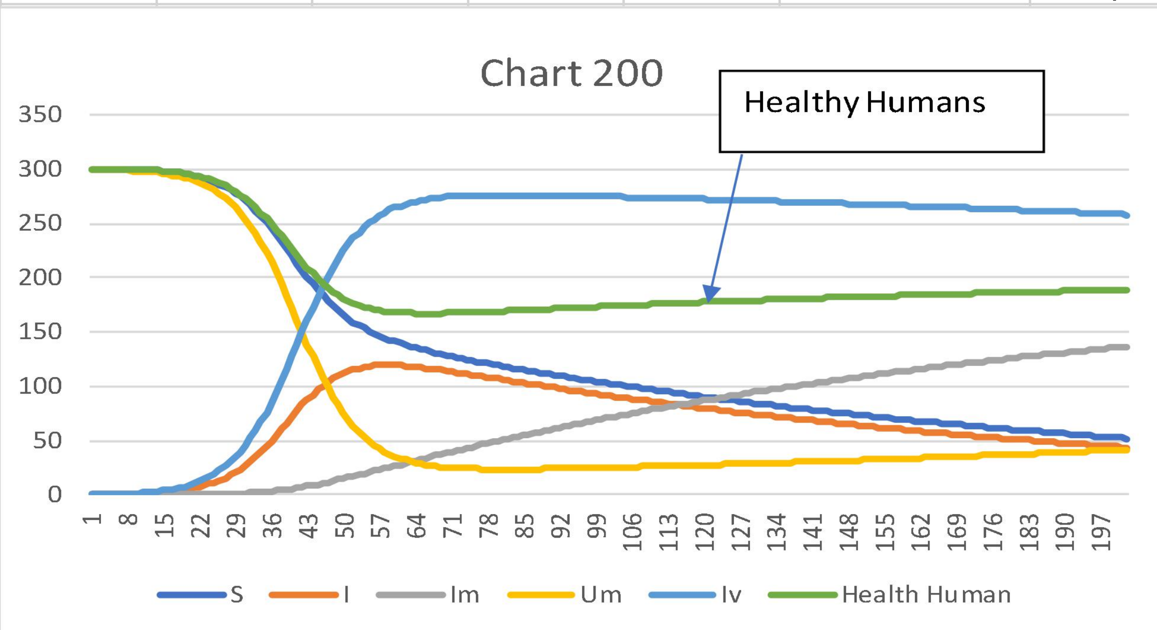
$$Healthy\ Humans = S + Im$$

Now assume initially we have Uninfected Humans, S = 300. Infected Humans, I = 1, Immune, Im = 0. Mosquito bite rate, $\alpha = 0.3$, Recovery rate, δ = 0.3, Immunity rate, β= 0.01, Death rate due to malaria, ϒ = 0.005, Mosquitos birth rate, ε = 0.01, Mosquitos death rate, λ = 0.01, Infected mosquitos, Iv = 0, and Uninfected mosquitos Um = 300.

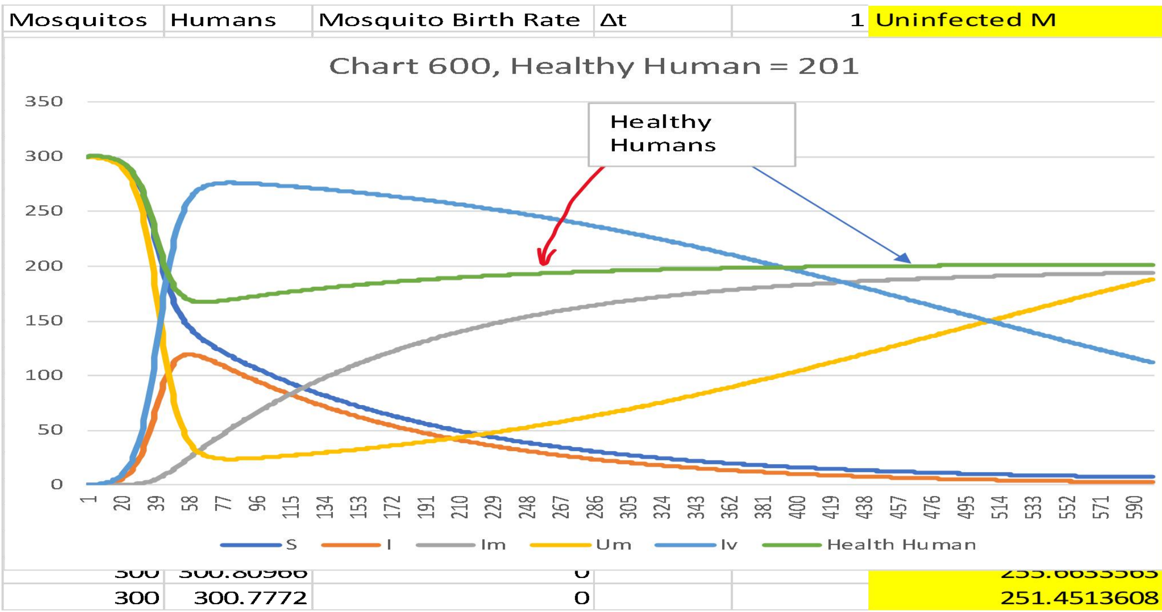
Excel Worksheet show the graph solution as following:

We ran Excel for 200 days; the graphic solution shows healthy human is about 189. The population of uninfected humans is going down to 53 and immune population is going up to 156.

S	I	Im	Um	Iv	Health Human	Mosquitos
						300
						300
						300
						300
						300
						300
						300
						300
						300
						300
						300
						300
						300
						300
298.2344	2.545951	0.146448	295.8542	4.145818	298.3808255	300



We ran Excel for 600 days; the healthy humans went down to 201, the uninfected humans were down to 7 and immune humans went up to 194. From the graph 201 looks like the horizontal asymptote for healthy humans.



Immunization and Quarantine

Ultimately, the purpose of models are to find measures that can reduce the effects of infection and hence improve healthy human population. Immunization and quarantine can reduce human infection rate, and reducing mosquito population can be another way to reduce human infection rate.

If we immunize a% (50%) of uninfected humans, then the first equation becomes

$$\frac{dS}{dt} = -\alpha * \frac{Iv}{Um + Iv} * S * (1 - a\%) + \delta * I$$

And second equation becomes

$$\frac{dI}{dt} = \alpha * \frac{Iv}{Um + Iv} * S * (1 - a\%) - \delta * I - \beta * I - \Upsilon * I$$

Suppose we also quarantine b% (60%) of infected humans, then

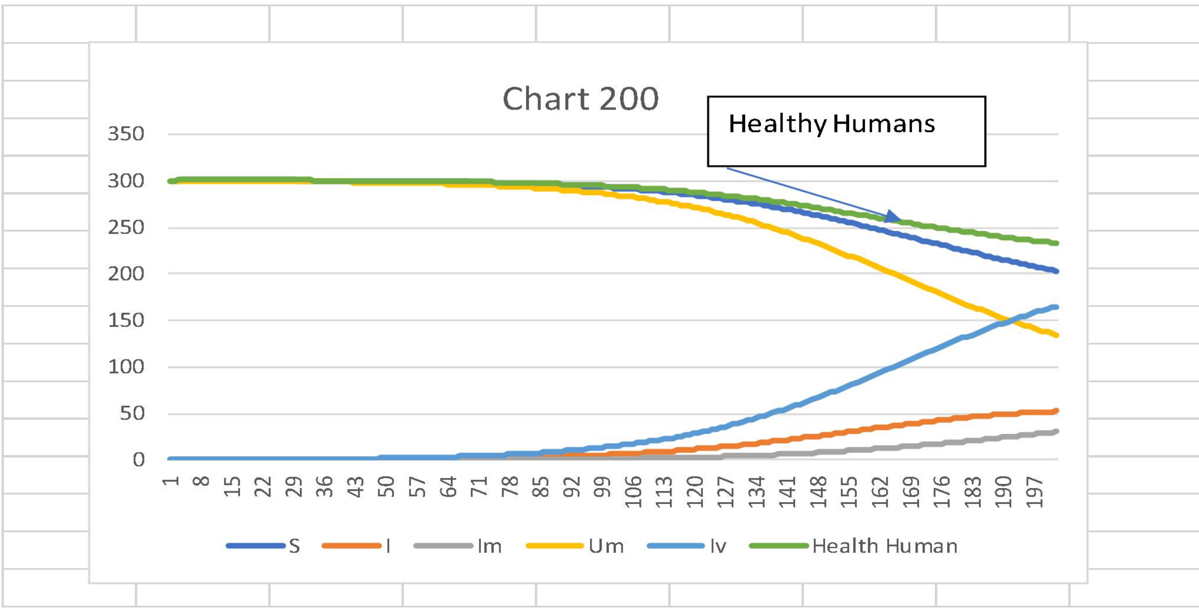
$$\frac{dUm}{dt} = \varepsilon * (Um + Iv) - \lambda * Um - \alpha * Um * (\frac{I * (1 - b\%)}{S + I + Im})$$

and

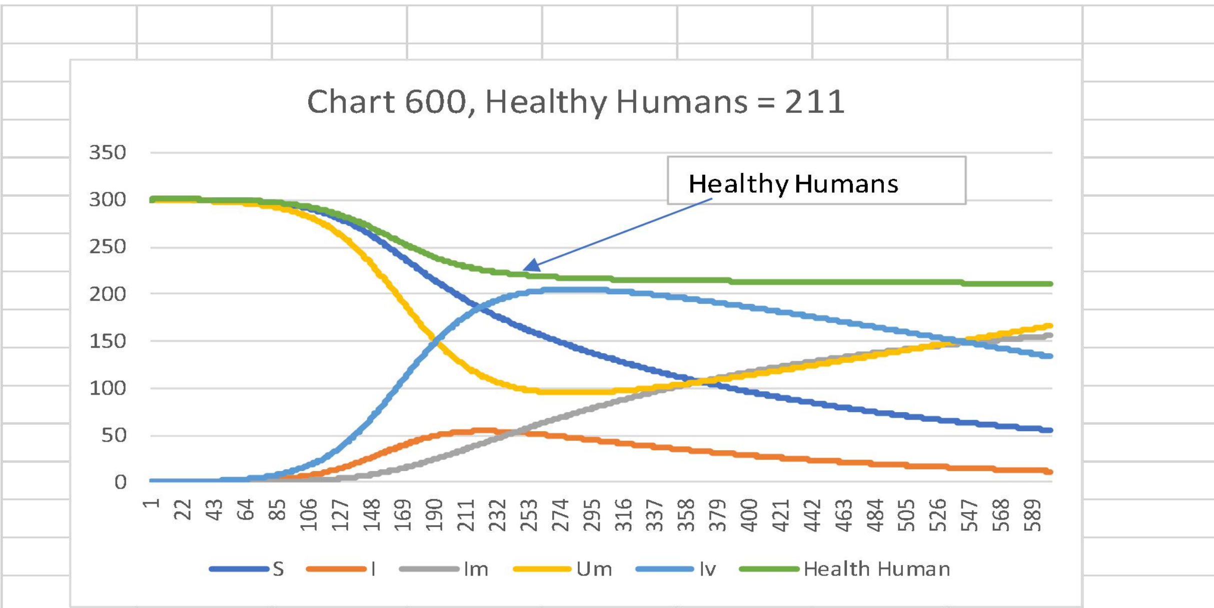
$$\frac{dIv}{dt} = \alpha * Um * \frac{I * (1 - b\%)}{S + I + Im} - \lambda * Iv$$

Now our graphic solutions are as following:

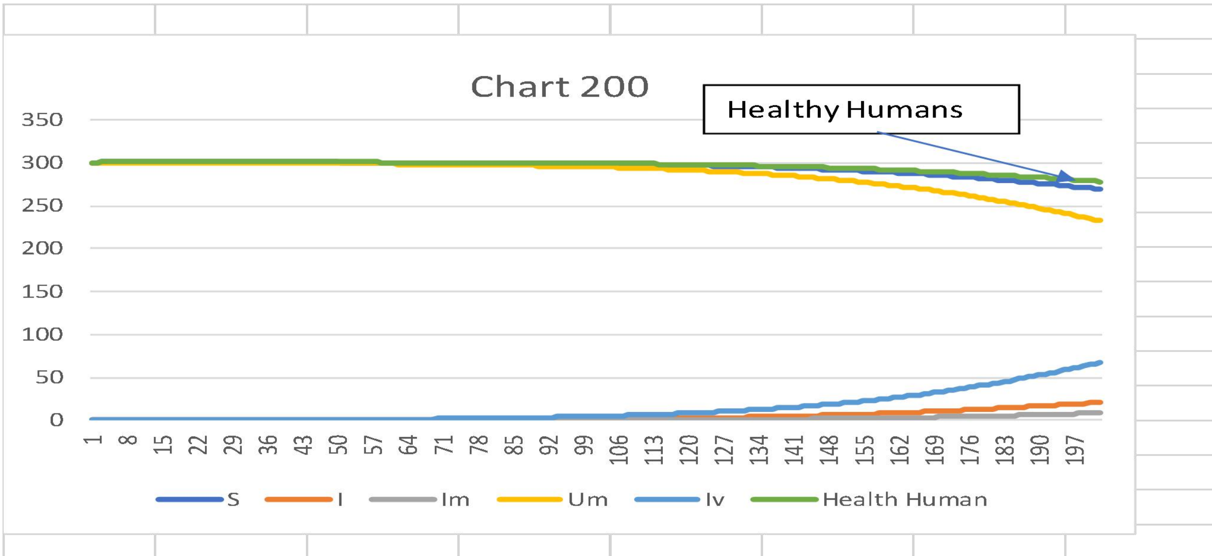
We ran Excel for 200 days; the graphic solution shows healthy human is about 233. The population of uninfected humans is going down to around 203 and immune population is going up slowly to about 30. The healthy human population is significantly improved from 185 to 233.



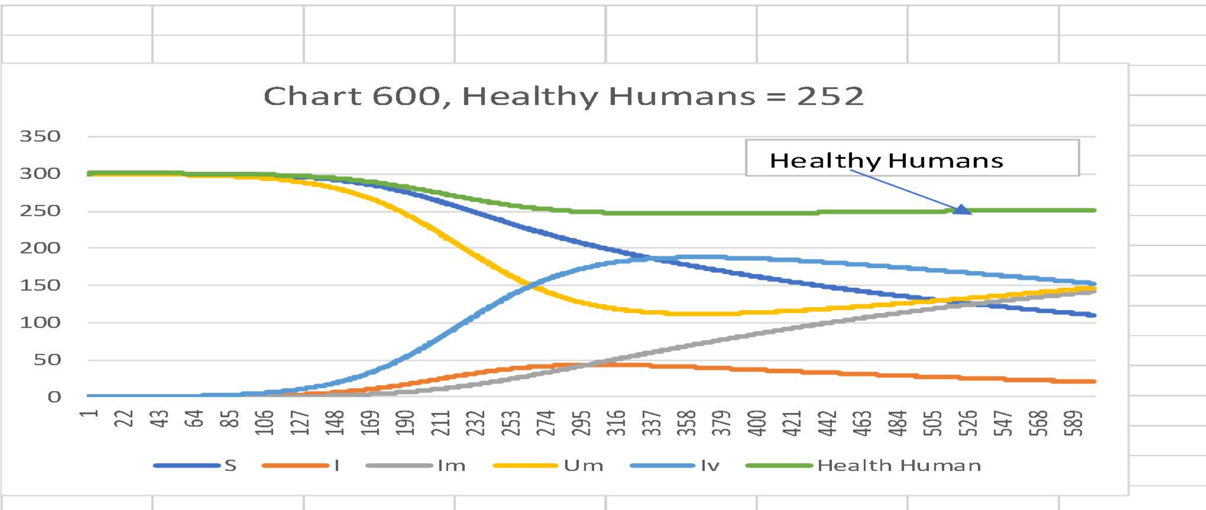
Surprisingly if We ran Excel for 600 days; the graphic solution shows healthy human is about 212. The population of uninfected humans is going down to 56 and immune population is going up to 156. Why does population of healthy human is slightly increase from 201 to 212?



Post infection treatments take effect in two ways. First, treatments reduce the number of deaths. Second, treatments can be used to reduce the amount of time an infection lasts. For this model, we ignore the treatments that reduce the severity of malaria. Treatments that reduce the death take effect by reducing the death rate due to malaria and recovery rate. Let us assume after treatments the death rate reduces from 0.005 to 0.002 and recovery rate increases from 0.3 to 0.4.



We ran Excel for 200 days; the graphic solution shows healthy human is about 278. The population of uninfected humans is going down to around 269 and immune population is going up slowly to about 9. The healthy human population is significantly improved from 185 to 278.

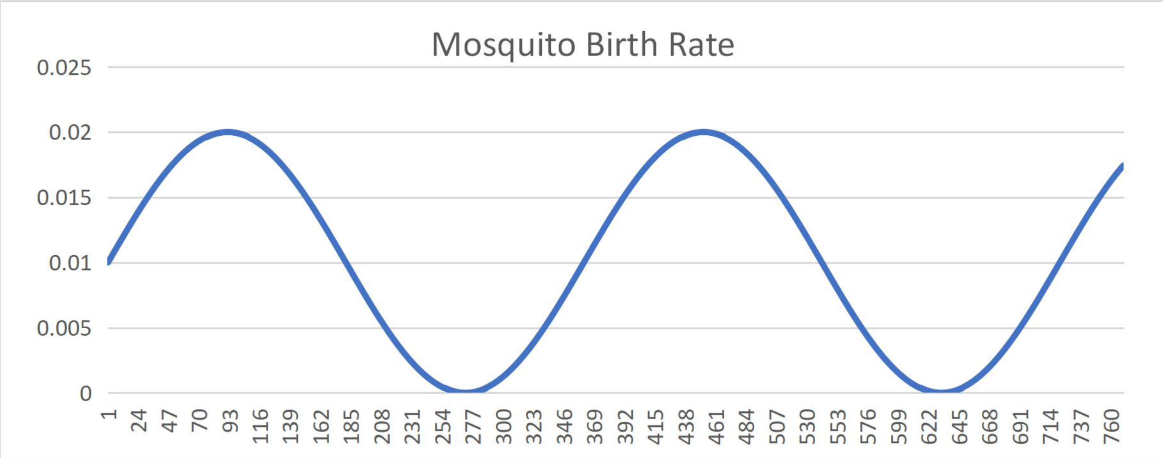


We ran Excel for 600 days; the graphic solution shows healthy human is about 252. The population of uninfected humans is going down to around 210 and immune population is going up slowly to about 142. The healthy human population is slightly improved from 201 to 252.

Seasonal Effect to the Mosquito Population

Mosquito population plays significant role in malaria lifecycle. Mosquito birth rate is higher during the rainy season and lower during dry season. We may assume the birth rate is a sinusoidal curve that is defined by $birth\,rate = c1sin\left(\frac{\pi}{180}t\right) + c2$. The period of this function is 360 which is closed to one year.

We will let c1 = c2 = ε. The curve of birth rate will be



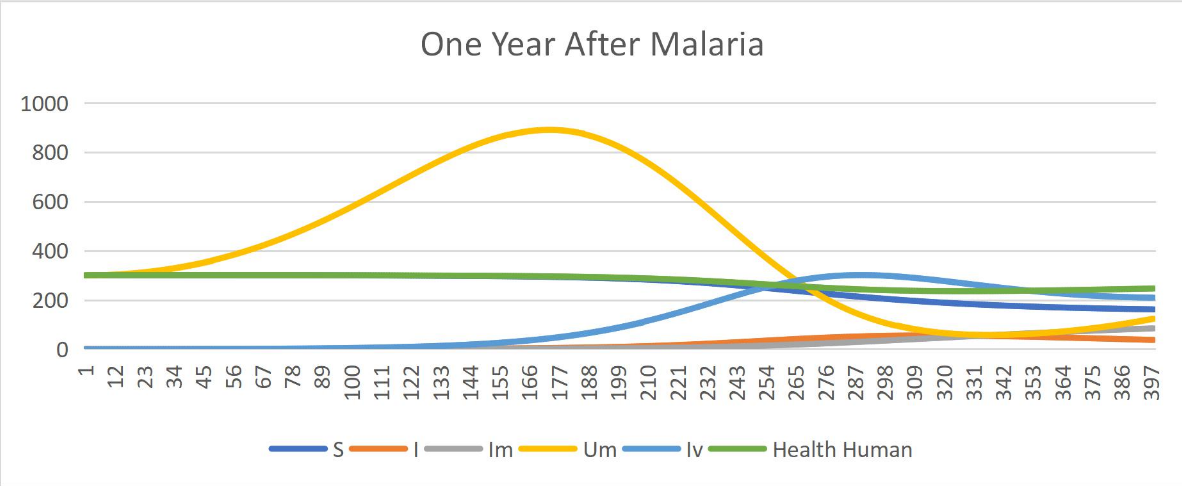
The equation of the change of uninfected mosquito becomes

$$\frac{dUm}{dt} = (\varepsilon * sin\left(\frac{\pi}{180}t\right) + \varepsilon) * (Um + Iv) - \lambda * Um - \alpha * Um * (\frac{I}{S + I + Im})$$

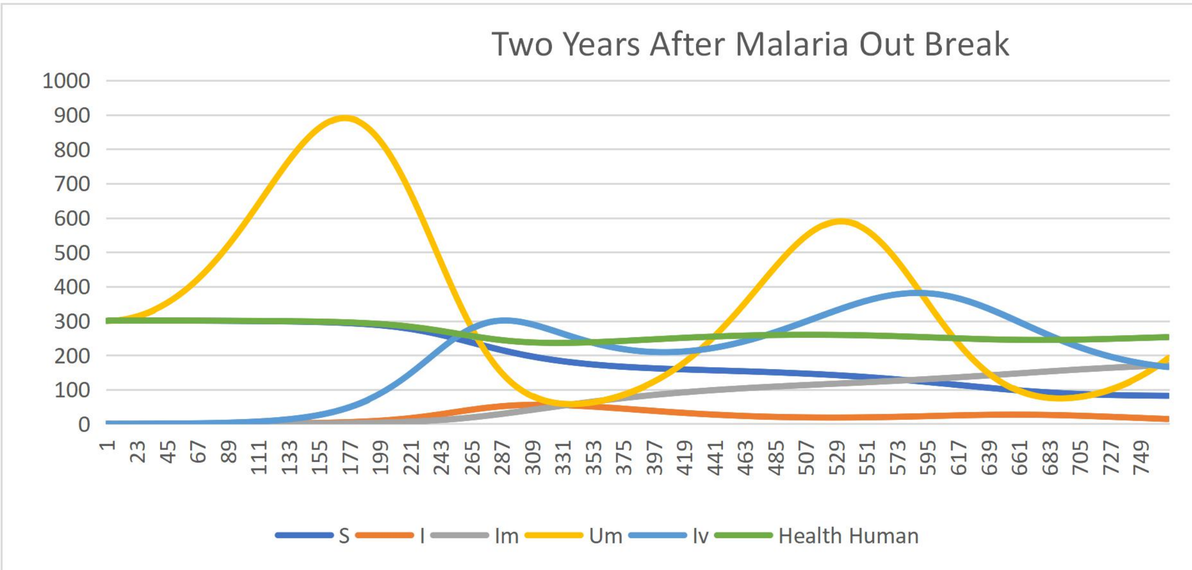
When we put quarantine in consideration the equation becomes

$$\frac{dUm}{dt} = (\varepsilon * sin\left(\frac{\pi}{180}t\right) + \varepsilon) * (Um + Iv) - \lambda * Um - \alpha * Um * (\frac{I * (1 - b\%)}{S + I + Im})$$

The Excel graphic solution when we run 365 days is



If we run Excel for 720 days we get



Both graphs show the seasonal effects.

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