Model Description

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May 2020

1 Introduction

Malaria is an infectious disease spread though the bite of mosquitoes. The main challenges on Malaria modelling arise from the complicate nature of Malaria parasites lifecycle. It is difficult to capture this complexity using current biological technologies. It leads less accuracy on the mathematical classic SIRS model. This project aims to build an agent based model which is more flexible and given us more options to embed a more detailed within-host model.

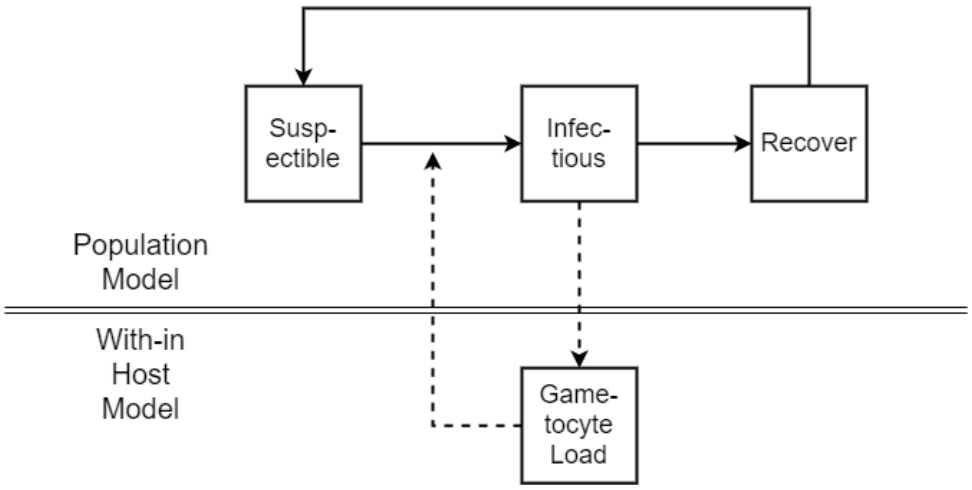

Figure 1: Description of architecture of the model. The top half is population model which is a typical SIR model. The bottom half is with-in host model which monitor gametocyte load in patients' body. The gametocyte load is gathered from infectious individuals, and then influence the probability of infected.

This implementation is a agent based model simulating the malaria epidemic population, by embedded with with-in host model that manifests the level of malaria parasite in body. The human part is agent based model with probabilities, while the mosquito part is deterministic. Because the main task focuses on epidemic in human population, mosquito is the middle layer in transmission, we build it as simple as possible. Figure 1 and Figure 2 shows the processes.

2 Mosquitoes

The project focuses on the human, and due to the dramatically heavy computational complexity, mosquitoes are regarded as an entire group. It is assumed the mosquito can bite any individual in the same time, and can have some chance to be partly infected from any individual.

This particular species mosquito as malaria vector is Anopheles that has a life expectancy of 10 days. So in the model each day ten percent of infected mosquito will die, replaced by new born susceptible mosquito to maintain the size [2][3][1].

For each day of the simulation ...

1. Mosquito updates.
2. With-in host Model: Calculate new global gametocytes level.
3. For each susceptible individual:
   (a) Calculate new λ (the force of infection), and apply to all susceptible individual. If not passing, become infectious.
4. For each infectious individual human:
   (a) Calculate new r (rate at which individuals recover from being infectious), and apply to all individual individual. If not passing, become recover.
5. For each recovered individual human:
   (a) Calculate new w (rate at which individuals lose immune), and apply to all recovered individual. If not passing, become susceptible.

Figure 2: A cycle processes of simulation in this malaria model.

Other than the generation iteration, a portion of mosquitoes can be infected, and become infectious determined by a global Gametocytes level, $G(t)$, in human population. So the mosquito updated in each day is given by

$$\theta(t) = 1 - (1 - \beta_{HM} * G(t))^b \tag{1}$$

$$I_m(t+1) = I_m(t) + \theta(t) * S_m(t) - \frac{I_m(t)}{l} \tag{2}$$

$\theta(t)$ is the rate at which mosquito get infected at time t. β_{HM} is the probability of transmission of a transmitted infection from a human to a mosquito during one feed. b is the mosquito bite frequency per day, typically once per 3 days[2]. S_m is the proportion of susceptible mosquitoes. I_m is the proportion of infectious mosquitoes. l is the life expectancy of mosquitoes.

3 Human

Human is the main part in this model. It is assumed that there is no death and birth in human, and the size of the population remains in a constant level.

3.1 Within Host Model: Gametocyte Model

Gametocytes is a form of parasite that produced in the ending of malaria lifecycle in human, and it is the most important form can infect mosquitoes from human in transmission. So we focus on the level of gametocytes parasite in human, which guides the disease developing in epidemic.

The gametocyte model is a phenomenological model of gametocyte dynamics that aims to capture the observed change in gametocyte levels over time. As shown in Figure 3, it is supposed to imitate the realistic epidemic data presented by Pengxing [5]. We expects its performances are similar. Variables including n, k and o have no biological interpretation.

Each infectious individual has an attribute recording the level of gametocytes corresponding with its duration of infection. To simplify the model, patients are assumed have identical

development which means at the same time after a succeed inoculation there are same amount of Malaria parasites in the patients' body. Under such assumption, the model we used to describe gametocytes dynamics is identical to every patient.

This model manipulates the quantity rather in the number of parasite, but a proportion of parasites. It has a range between 0 and 1 indicating the level of concentration in an individual. This is mainly because that the amount of parasites vary in different patients. Under our assumption there is no difference on performances between these two expressions. The universal equation for gametocyte level in a human individual is given as following:

$$g(t) = (\frac{t^n}{t^n + k^n} - \frac{o}{1+o})(1+o) \tag{3}$$

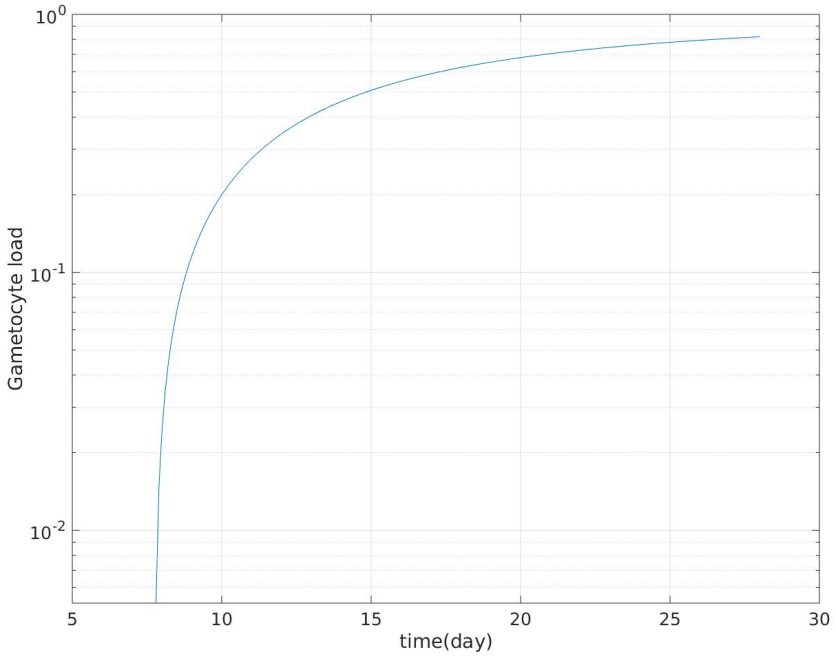

Figure 3: Logarithmic plot of gametocyte curve

Figure 3 shows the gametocyte load against time. o is an offset to cut off curve when time post inoculation is less than 8, and correspondingly resize the rest plot. Because biologically gametocytes are only produced in the latest stage in in-human lifecycle. It usually can be detected after day 8, and will keep grow in later twenty days. Since death is not considered in this model, after 30 days the most patients are recovered, and a small portion of patients who still sick keep carry a high level gametocyte load until recovered.

Moreover we define a global gametocyte level as the mean of individual gametocyte level over all human individuals, as Equation 4. In this case, the model that has a small number of population is more sensitive to the parameter than the model that has large number of population. But it a large simulation with enough turns, we expect the estimate approaches to true mean.

$$G(t) = \frac{\sum_i^I g_i(t)}{N} \tag{4}$$

3.2 Susceptible period (S)

Our mosquito model is simplified as mosquito can bite every human in the same unit time. It means the reproduction number for mosquito is same as the size of human population N. However in the perspective of human, they contribute one global gametocyte load G. So the influence from each individual to the mosquito is reduced by N times. After those two parts are counteracted, it is equivalent to that the reproduction numbers for both mosquito and human are 1.

The force of infection $\lambda(t)$ is updated each unit time. It indicates the rate at which susceptible individuals become infected at time t. It is proportional to the mosquito bite rate b, effective contact probability from mosquito to human β_{MH}, and the proportion of infectious mosquitoes $I_M(t)$:

$$\lambda(t) = I_M(t) * b * \beta_{MH} \tag{5}$$

In each day each susceptible individual draws an number from an uniform distribution. If the random number is below the force of infection, then the individual turns to be infectious.

3.3 Infectious period (I)

WHO reported that the typical period range from the time of malaria infection to the time of initial symptoms occurring is about 8-14 days [4]. It is also the time gametocyte about produced. Details are mentioned in With-in Host section.

Therapy and medicine will taken by patients after their symptoms appeared and be noticed. However the time gap between medical diagnosis and treatment applied is various and the efficacy of treatment is very individually dependent. We assume that the average time between symptoms appearing and patient taking treatment is 30 days, and the efficacy of this treatment is 100% effective which eliminates all malaria parasites in body immediately. The patients are recovered and get immune immediately.

The rate of recovery is denoted by a Poisson distribution with $\lambda = 20$, we expects patients will have medical therapy averagely in 20 days, as Equation 6. The number is drawn from the Poisson distribution once an individual be infected. After that each day each infected individual draws an number from an uniform distribution. If the random number is below the force of infection, then the individual turns to be infectious.

$$r(t) = Pois(20) \tag{6}$$

3.4 Recovery

The immune of recovered patients wanes as the time goes on. At some stage a recovered individual can become fully susceptible to infection again. We assume the period of time is 50 days[1]. The rate at which individuals lose immune shows in Equation 7.

$$w(t) = Pois(50) \tag{7}$$

[1] requiring source

4 Parameters[2]

Symbol	Definition	Value
β_{HM}	The probability of transmission of a transmitted infection from a human to a mosquito during one feed.	0.3
β_{MH}	The probability of transmission of a transmitted infection from a mosquito to a human during one feed.	0.8
d_I	The average days for patients recovering.	30 days
d_R	The average days for immune waning.	50 days
b	Bite rate of mosquitoes.	1/3
l	Life expectancy of mosquitoes.	10 days[1][2][3]
d_R	The average time taken for immune waning.	50 days

Model parameters

Symbol	Definition	Value
n		2
k		10
o	Offset.	0.6
g_{max}	Maximum amount of gametocytes level.	1

Gametocytes Model parameters

Symbol	Definition	Value
N	(Initial) size of human population.	100000
S	(Initial) number of susceptible individuals.	90000
I	(Initial) number of infectious individuals.	10000
R	(Initial) number of recovered individuals.	0
I_m	(Initial) proportion of infectious mosquitoes.	0

Model Settings

5 Result

[2]requiring source

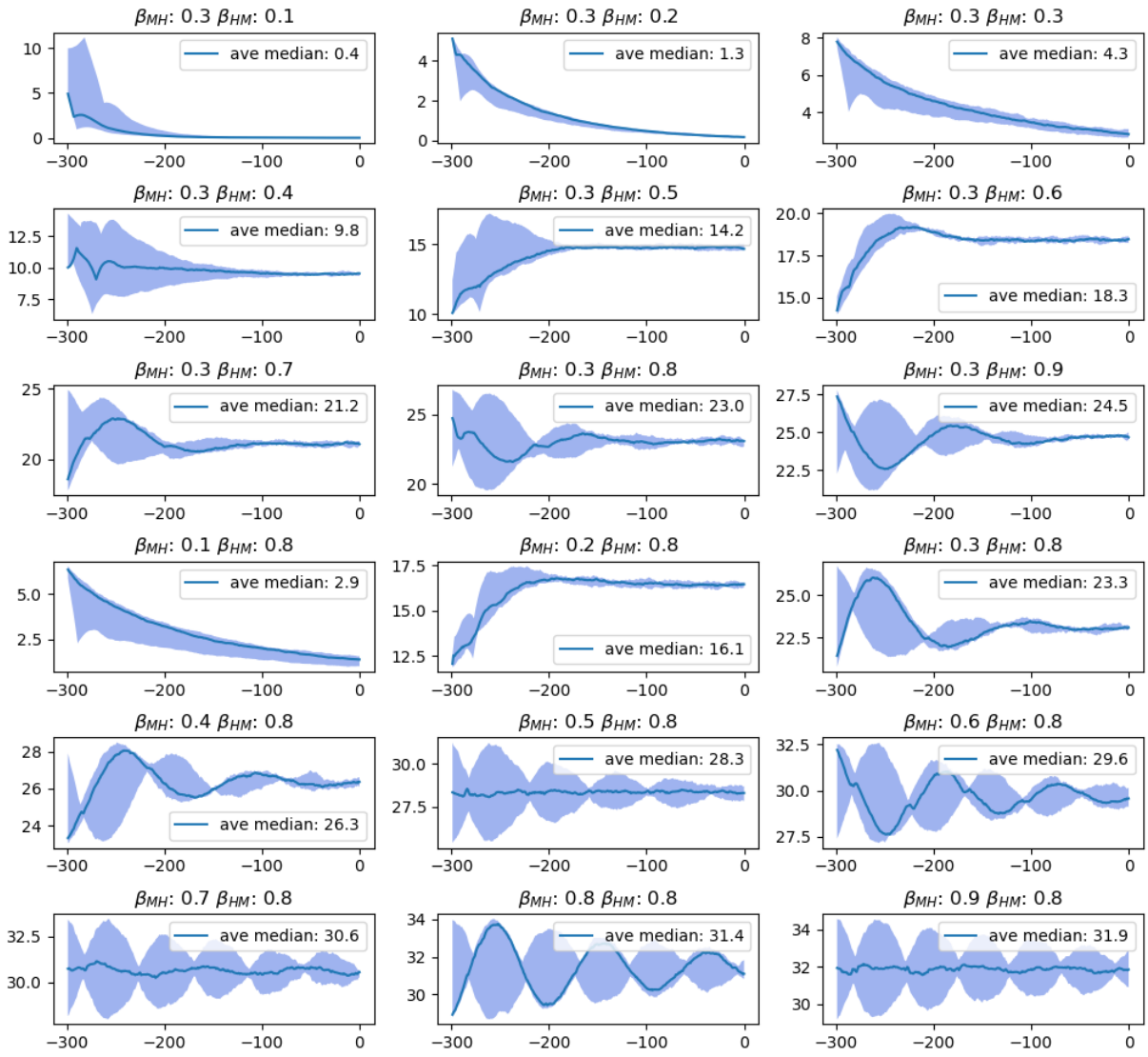

Figure 4:

References

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[3] Michael T White et al. "Modelling the contribution of the hypnozoite reservoir to Plasmodium vivax transmission". In: *Elife* 3 (2014), e04692.

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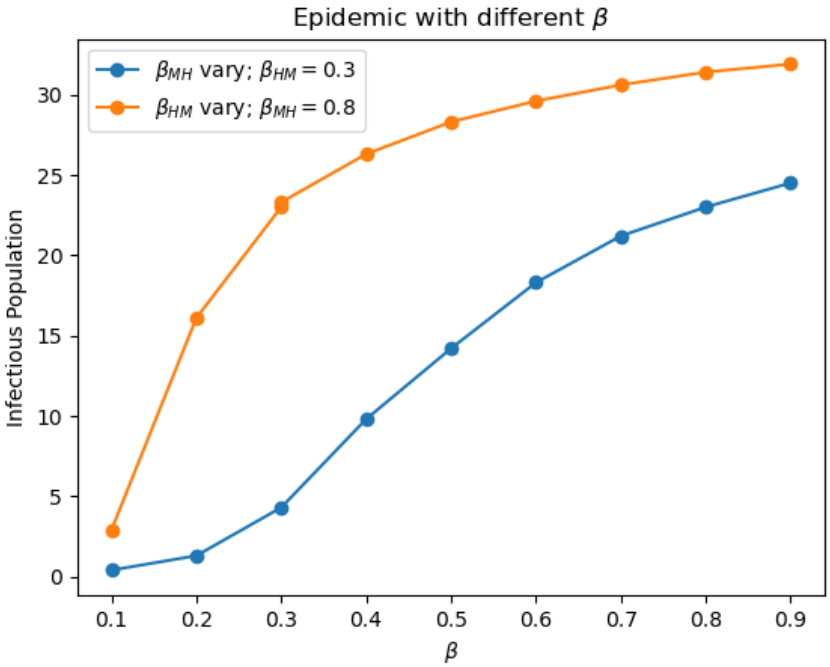

Figure 5:

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[5] Pengxing Cao et al. "Modelling the population dynamics of Plasmodium falciparum gametocytes in humans during malaria infection". In: *bioRxiv* (2019). DOI: 10.1101/641472. eprint: https://www.biorxiv.org/content/early/2019/05/21/641472.full.pdf. URL: https://www.biorxiv.org/content/early/2019/05/21/641472.