How does the Zika virus spread when introduced to a closed population, depending on the bite rate of mosquitoes?

Introduction

The recent outbreak of the Zika virus has become an extremely controversial topic, especially after the WHO declared it a public health emergency. This virus typically gives mild symptoms of fever, muscular pain, and rashes for a time period of approximately two to seven days, and is spread by mosquitoes through their saliva. The *Aedes aegypti* mosquito is the main vector of the disease. Because of the suspected, yet unconfirmed ties of the Zika virus with microcephaly and the Guillain-Barré syndrome, it is important for the authorities to take preventative measures and to support efforts to further study the disease and its effects. One of the reasons that has motivated me to study the issue is the fact that it affects the population of my home country, Panama. Furthermore, I have also taken this opportunity to approach the issue from a more computational perspective, considering that I have developed a strong background in programming for some years.

In this investigation, I will create a model that will simulate the spreading of the Zika vi between a closed population of humans and mosquitoes using the Python pro___ming language. I will specifically analyze how modifying the average human bite rate (i.e. how m humans does a single mosquito bite over its lifetime) changes the results of the simulation. Besides than simply understanding the nature of how the disease spreads according to the initial conditions, this question is relevant because of several reasons. The bite rate is a very difficult factor to estimate accurately from experiments; this quantity changes according to many differen ecological, climatic, and spatial factors. In fact, several scientific studies have shown that this quantity varies between different communities (Churcher et al.) and that even within communities, the quantity evolves and fluctuates greatly (Roitberg et al.). Thus, understanding which bite rates produce scenarios closer to real life can give information about which bite rates are those found in nature. Furthermore, understanding their effect on the human and mosquito populations can also give relevant information about how the Zika virus may affect particular populations, such as the risk of suffering an epidemic, the recovery time of the population, etc. This is especially important because Zika is an emergent issue and preventative measures must be taken despite the lack of data.

Theoretical background

Because creating a spatial model would be extremely complex, I decided to use a simple SIR model. This model divides the human population into three different groups: susceptible, infected, and recovered (hence the abbreviation). The assumptions of this model are that all humans are susceptible, and once they are infected through a mosquito bite, they recover in a.. average amount of time. Furthermore, once they recover, they are no longer susceptible. To model the mosquito population, I am using an SI model that takes into account their birth and death rates: any newborn mosquito immediately falls into the S group, and any mosquito that bites an infected human moves to the I group. The death rate of the mosquitoes is assumed to be uniform within both groups since we are dealing with very large numbers of mosquitoes, and the birth rate is assumed to be the same as the death rate for simplicity, so the mosquito population remains constant. All the mosquitoes on the simulation will be assumed to be female, since the male population will not interact with humans because they do not feed on blood.

Since there is no treatment or vaccine for Zika and it is strongly believed that infected people become immune after they recover from the disease, the previously mentioned assumptions make the model a strong fit to describe the spread of this particular disease. Other vector-transmitted diseases may not necessarily fit the model; for example, any disease in which immunity is not acquired, or any disease that is contagious directly between humans. I designed a system of five differential equations, each describing the change of each of the groups with respect to time. We will let the human groups be S, I, and R; the mosquito groups be S_M and I_M; the birth and death rate of the mosquitoes be r; the recovery time for humans be a; the average bites of a single mosquito per day be b; and the average lifetime of a mosquito be l.

We can compute the number of people that move to from the I group to the R group with

$$\frac{\mathrm{d}R}{\mathrm{d}t} = \frac{I}{a}$$

Then, it follows that we can describe how the I group changes by subtracting that same quantity, but also taking into account the people that move from the S group to the I group:

$$\frac{\mathrm{d}I}{\mathrm{d}t} = -\frac{I}{a} + \frac{bSI_M}{I_S + I_M}$$

This follows because we have to take into account the mosquito bites exclusively for the S group, and also because we have to take into account the probability of the mosquito being infected. We can now describe the change of the S group by subtracting the exact term we added previously:

$$\frac{\mathrm{d}S}{\mathrm{d}t} = -\frac{bSI_M}{S_M + I_M}$$

Computing the change for the mosquito groups is almost analogous. We only need to take into account their births and deaths, which depend on the current populations. I will assume these are homogeneous because the simulation will model a very large number of mosquitoes.

$$\frac{\mathrm{d}I_M}{\mathrm{d}t} = \frac{bS_M I}{S + I + R} - \frac{I_M}{l}$$
$$\frac{\mathrm{d}S_M}{\mathrm{d}t} = -\frac{bS_M I}{S + I + R} + \frac{S_M + I_M}{l} - \frac{S_M}{l}$$

Method

Since the methodology of this investigation revolves around a simulation I have created using th Python programming language, safety issues are not a concern. The simulation will produce the necessary numerical output and their plots. To address the research question, the bite rate will b the only independent variable. This quantity consists of the constant 3/14 multiplied by a variable factor between 0 and 1. The number has to be at most 3/14 bites per day and mosquito, since female mosquitoes lay their eggs after a blood meal and can do so at most three times before they die. However, it can be reduced because of several reasons, including the fact that mosquitoes may bite less than three times during their lifetime, but more importantly, that they do not feed solely on humans.

I will now discuss the controlled variables. First, all humans will be assumed to not have contracted the disease, and the initial amount of infected mosquitoes will be fixed to 1000, as this will model what occurs as the disease is introduced to the population. Assuming less mosquitoes are infected is not realistic because their effect will be almost negligible, and they always reproduce in (and live in) large numbers. It is also unrealistic to assume that a large percentage of the mosquito population is infected when no humans within the same population are. The size of the human population that we will use will be 3.9 million, which is approximately the population of Panama (2013 est.), and the population of mosquitoes will be fixed to 100 million for it to be greater than the human population. Not only will both populations be initially fixed; we will also assume they will remain constant for the entire simulation for simplicity. Since the simulation will only model the effect of the virus for a fixed maximum of 10 years, human births and deaths will not have any significant impact. Mosquito births and deaths, on the other hand, are taken into consideration within the model. The recovery time of humans will also be fixed to 4.5 days, considering that the average time of the symptoms estimated by the WHO is between 2-7 days. The mosquito lifetime will be fixed to 2 weeks: while some sources estimate that the *Aedes aegypti* female mosquito has an average lifespan ranging from two weeks to a month, others estimate that it is only two weeks. We will use the two weeks estimate because these averages were taken under the assumption that the mosquitoes are in a natural habitat, when in reality, mosquitoes can die from many other causes besides aging.

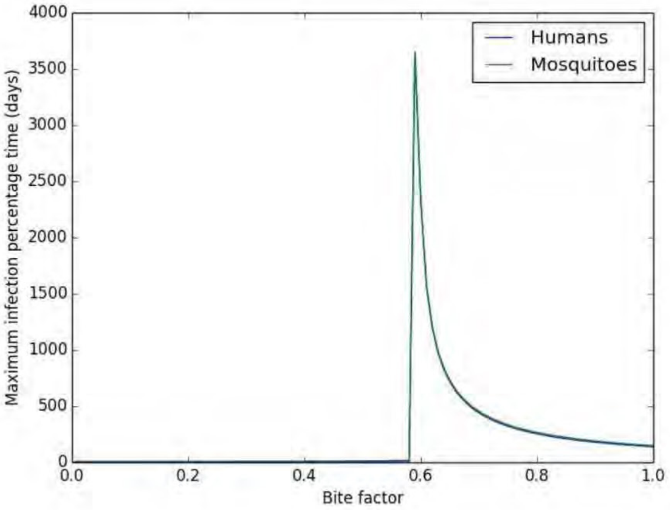
As for dependent variables, I will first use the maximum percentage of infection (of both humans and mosquitoes). This "peak" gives very useful information about each simulation. For instance, how severe was the spread of the disease, and how long does the spread last (when we measure the time of occurrence of this peak implies that the spread will decline afterwards). I will determine patterns and anomalies here to then examine the actual simulations for particular values. In these, I will also use the percentage of the recovered human population as a dependent variable, as it gives information about the total number of people affected, which is useful to compare the simulation with real life scenarios.

The simulation will solve the differential equations using the Forward Euler method, which simply computes the change in each variable for a given amount of time steps. This step size will be fixed to 0.1 days. This size is sufficiently accurate because the Forward Euler Method's error range is proportional to the step size, and any errors of ±0.1 days will not have any major significance on conclusions about long-term impact on human populations. The reader may access the simulation here: https://gist.github.com/djwatt5/ae8f295d66256c3c6d91

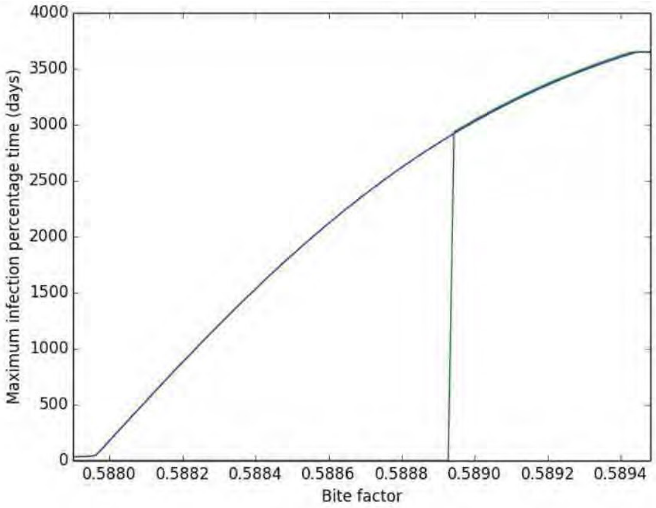
My hypothesis is that for lower bite rates, the infection will not have enough capacity to spread, resulting in relatively low infections for a short period of time. For extremely high bite rates, an unrealistic scenario will occur in which a huge portion of the population will be infected, but the disease will stop spreading quickly because humans will develop herd immunity very quickly. Thus, for values in between the very small and very large, we should expect a realistic model of the spread of Zika within the given population. I also expect humans and mosquitoes to "behave" similarly, as to how one population changes in response to the other (e.g. if the mosquito infection percentage begins to drop, the human population will respond similarly and begin decreasing shortly afterwards).

Results

The first test, which measured the occurrence of the maximum percentage of infection, in both humans and mosquitoes, is given by the following graph:

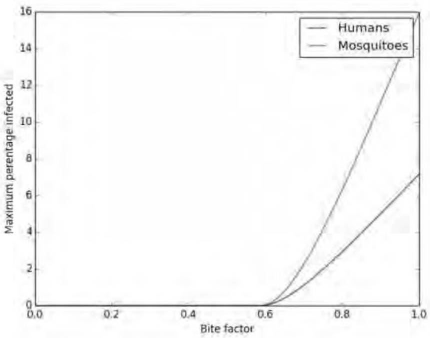


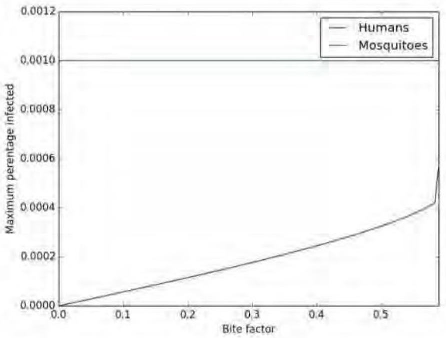
The simulation was run for 100 values for the bite factor (0.01, 0.02, etc. until 1), using the command `` `plot_bite_factor('time', 0., 1.)` ``. Because the raw output indicates a sudden spike, I used `` `plot_bite_factor('time', .5879, .589481, show_legend=False)` `` to examine how the y-axis behaves near the spike:



This shows that the observed "spike" in the human maximum occurrence is actually due to inaccuracy, as it grows very quickly but still smoothly. The fact that the spike still occurs for mosquitoes is not an error or due to further inaccuracy, but due to the fact that the maximum percentage has a positive value at the beginning of the simulation. Thus, this "spike" is a point of interest in which the mosquito population reaches a higher infection than what it started with. The raw data from `plot_bite_factor('time', .58892, .58898, show_legend=False)` suggests that this point is at $b = .5889386$. Also notice the fact that the maximum value of the first graph is 10 years, which is the duration of the simulation. Thus, when the graph marks this point in time, it implies that the maximum may occur at any point in time afterwards (the infection rate may continue increasing if we let the simulation run for a longer time). The raw data from `plot_bite_factor('time', .58943357, .59288, show_legend=False)` suggests that this occurs at bite rates within the range $[.5894680343, .5928110714]$.

Now, let us examine what are the actual values of the maximum infection percentages as we vary the bite factor. I added an additional plot to better observe the smaller values:



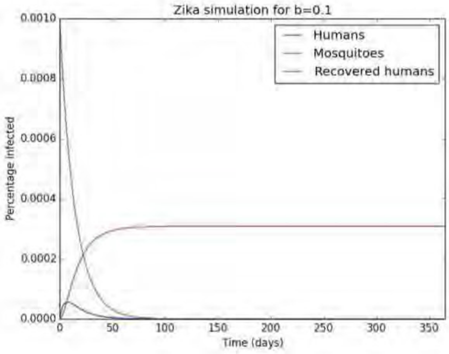


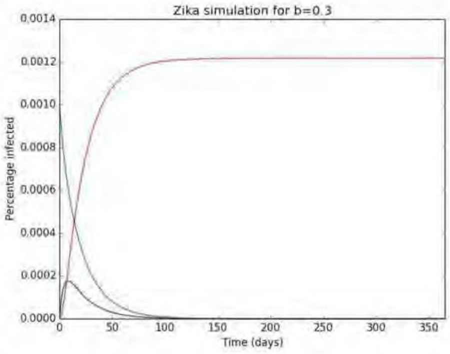
For the plot in the right hand side, the raw output indicated that the maximum percentage of infected mosquitoes remained at 0.001 between $b = 0$ and the last step before $b = .5889386$, which is consistent with the explanation I provided about the mosquito spike.

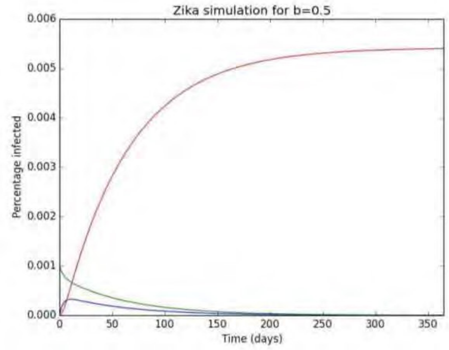
This leads us to consider particular values for closer examination. I will use three b-values below the "critical point" of $b = .5889386$, as well as this b-value, three b-values found within the range at which the maximum is reached at the end of the simulation, and then three b-values after this range. The raw data will be shown in percentages on the following table, and then in plots to show their change with respect to time:

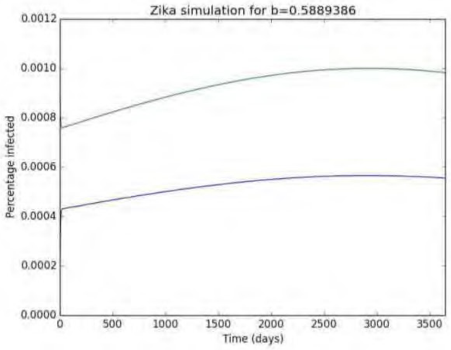
b	$\max_H\%$	$\max_H$ time (days)	$\max_M\%$	$\max_M$ time (days)	$R\%$
0.1	.0000569	7	0.001	0	.0003089
0.3	.0001769	8	0.001	0	.0012167
0.5	.0003251	10	0.001	0	.0054187
0.5889386	.0005660	2912	.0010001	2926	.4265308
0.5894681	.0007511	3650	.0013282	3650	.5082020
0.5911396	.0018064	3650	.0031994	3650	.9061824
0.5928111	.0036770	3650	.0065382	3650	1.615038
0.595	.0071884	3121	.0128285	3135	3.131882
0.6	.0197099	2320	.0354568	2334	7.442759
0.7	1.115708	441	2.251768	454	50.81099

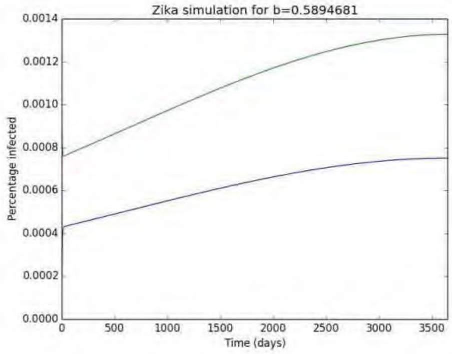
These are the plots of the individual simulations, showing how the I groups change over time. I shrinked the x-axis in some of the graphs so the parts where the values actually change are more visible. I also removed the R group in most of the graphs because it was significantly larger, and plotting would therefore make the y values of the other groups too small to be visible (the final R values are on the table anyway):

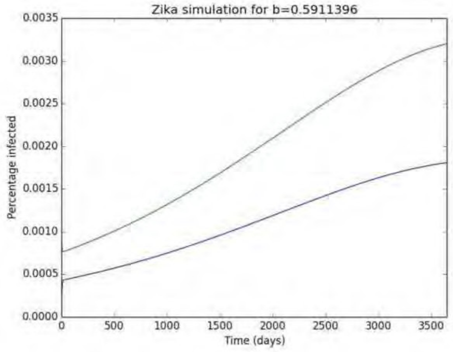


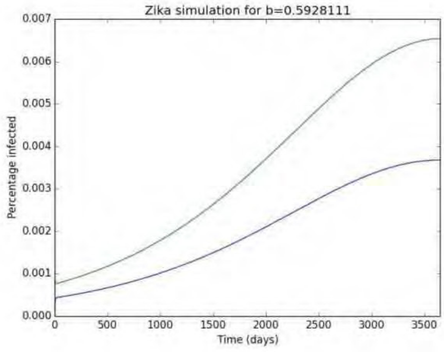


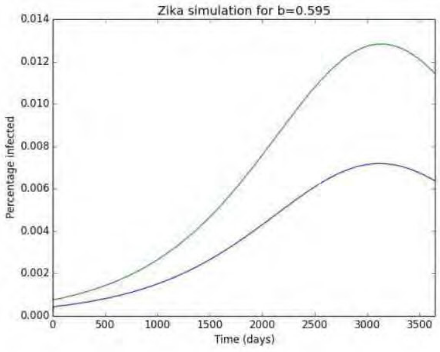

Zika simulation for b=0.5
Percentage infected
0.006
0.005
0.004
0.003
0.002
0.001
0.000
0
50
100
150
200
250
300
350
Time (days)

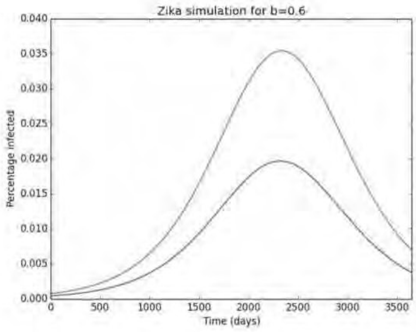

Zika simulation for b=0.5889386
Percentage infected
0.0012
0.0010
0.0008
0.0006
0.0004
0.0002
0.0000
0
500
1000
1500
2000
2500
3000
3500
Time (days)

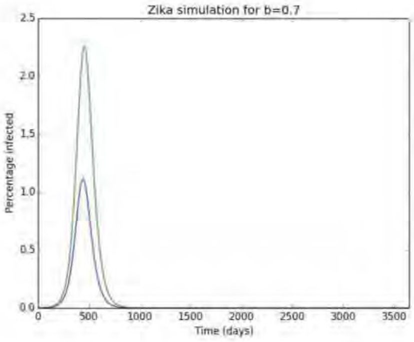

Zika simulation for b=0.5894681
Percentage infected
0.0014
0.0012
0.0010
0.0008
0.0006
0.0004
0.0002
0.0000
0
500
1000
1500
2000
2500
3000
3500
Time (days)


Zika simulation for b=0.5911396
Percentage infected
0.0035
0.0030
0.0025
0.0020
0.0015
0.0010
0.0005
0.0000
0
500
1000
1500
2000
2500
3000
3500
Time (days)


Zika simulation for b=0.5928111
Percentage infected
0.007
0.006
0.005
0.004
0.003
0.002
0.001
0.000
0
500
1000
1500
2000
2500
3000
3500
Time (days)


Zika simulation for b=0.595
Percentage infected
0.014
0.012
0.010
0.008
0.006
0.004
0.002
0.000
0
500
1000
1500
2000
2500
3000
3500
Time (days)





Conclusion

The hypothesis was proven to be true, but only to a certain extent. For the bite rates lower than the discovered “critical point”, the spread was almost negligible. This can be seen in the time of the maxima lasting only about ten days, and also because the percentage of the infected mosquitoes never increased from its initial value. It was also true that as we drifted away from the critical point, the spread of the disease lasted for a much shorter period of time as the population acquired herd immunity. As for the behavior similarity between humans and mosquitoes, the time occurrence of the maxima was almost the same, except for the encountered “spike”, which was simply due to the difference on their initial conditions. On the other hand, the infection rates themselves differed between humans and mosquitoes (their difference was also variable). The only similarity that matches the hypothesis to a certain extent is the rate of change between the I groups, which can be qualitatively observed in the graphs following the table. However, this similarity is broken at the beginning of the simulation, since the mosquitoes’ I group decreases as the humans’ increases. Nevertheless, it is still true that as one of the I groups changed, the other responds, therefore resulting in similar rates of change over time.

The question of which models are closer to reality, however, can only be answered to a very limited extent. The issue of Zika is still emerging, and there aren’t any case studies that have concluded. Furthermore, the gravity of the issue between different countries has huge variations, all depending on their geographic distribution, the measures that each government has taken to mitigate the disease, the behavior of mosquito populations and habitats with the different ecosystems, the variations in temperature and climatic factors, and more factors that this study does not take into account. This study can conclude, however, that bite rates above $b = 0.6$ are already not realistic– it is very unlikely that 1,000 infected mosquitoes will have an impact on over 10% of the human population (the value of the R group at the end of the simulation shows this), when there are many other species that they can pray on. It is also unrealistic to have integer percentages of the population infected all at once, as shown in the graph of $b = 0.7$. The other bite rates, however, maintain realistic scenarios as to how many people are affected, and suggest a very concerning conclusion: if nothing is done to lower the bite rate, the disease may continue being an issue for decades. By implementing solutions (and thus lowering the bite rate) such as constantly fumigating urban areas, using nets and other protection methods, and disposing of cesspools where mosquitoes can reproduce near human populations, the spread of the disease can be dramatically reduced, both in duration and in number of human victims, as suggested by the data.

Improvements and extensions

There are several limitations on the accuracy of the simulation. The most obvious one is that the population is assumed to be homogeneous, as we are not dealing with a spatial model. In reality, there are huge variations on the densities of human and mosquito populations, and this certainly has an impact over how the Zika virus may spread. The modeling of reproduction also has it limits. For mosquitoes, we just assume that they reproduce and that the total population is constant, when this is obviously not true in real life scenarios. The human population is assumed to be immortal and unchanging, while in reality, there are births, deaths, migration, and movement. Also, some details about the Zika virus itself and its dynamics were omitted. For instance, it was assumed that the virus has no incubation period, and that humans and mosquitoes will infect each other with certainty. In reality, there are probabilities in which these events can occur.

While I was always aware of these factors, it is important to consider that taking more parameters into account on simulations can also have negative implications. For instance, how is it possible to accurately know the probability of the virus spreading on the event of a single bite? Assuming that these parameters have particular values it not a safe idea unless these values are known with certainty. Doing so will limit the impact of the conclusions to very particular cases, as well as adding more assumptions that can drift away from real life scenarios as the model becomes increasingly complex. The more detailed the model is, the more sensitive it is to these new parameters, and therefore more inaccurate and prone to error.

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