A Numerical Study to Predict the Evolution of Yellow Fever Diseases using fourth order Runge-Kutta Method

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Abstract: Mathematical Modeling has emerged as a vital tool for understanding the dynamics of the spread of many infectious diseases, one amongst is Yellow Fever. The main focus of this paper is to model mathematically the transmission dynamics of Yellow Fever. For this purpose we tend to use basic SIR model of Yellow Fever to predict the outbreak of the diseases. As we cannot fully solve the 3 basic equations of SIR model with a certain formula solution, we introduce fourth order Runge Kutta Method. This strategy is quite efficient and practically well suited for solving initial value problem (IVP) for ordinary differential equations (ODE).We discuss the performance of Runge Kutta method with the actual data. The population that we used for this model had roughly a similar number of individuals as the number was living in Angola during 2016.

Keywords: Evolution of Yellow Fever, Mathematical Modeling of Yellow Fever, Numerical study of Yellow Fever, RK Method, Yellow Fever, YF Outbreak.

1. Introduction

Mathematical models are powerful tools for investigating human infectious diseases such as Yellow Fever (YF), contributing to the understanding of the dynamics of disease and providing useful predictions about the potential transmission of a disease and the effectiveness of possible control measures, which can provide valuable information for public health policy makers. Yellow fever, caused by yellow fever virus, is a mosquito-borne flavivirus disease; it is found in sub-Saharan Africa and tropical South America, where approximately 1 billion people in 46 countries are at risk for it.

The World Health Organization is reporting a yellow fever outbreak in Angola that began in late 2015. The first cases in this outbreak were identified on 5 December 2015 in Viana, Luanda Province, Angola [1]. Mathematical model of the outbreaks of YF can be helpful as it is a platform for understanding the behavior of a dynamical system. The objectives are to apply SIR model to predict the outbreaks of Yellow Fever, determine the effect of the initial number of infectives of the population, comparison with real life data and if necessary fit the model data with real data.

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2. Methodology

2.1 Formulation of SIR model

The SIR model is used to illustrate the transfer of the epidemic through the interaction of the following three different variables:

S = Number of people that are susceptible to YF
I = Number of people infected with YF
R = Number of people recovered from Yellow Fever with total immunity

It makes sense to assume that a fixed population of N people, whereby there are no births and deaths by natural cause i.e.

$$N = S + I + R \quad [2]$$

This is because the population is fixed and therefore, there are only three compartments in which the population may fit into. Thus, the total of the number of people susceptible infected and recovered in equivalent to the total population. The assumption that N is fixed, with no births or deaths, makes sense given 60 days, although it is a simplification.

These variables change over time, so we will define the variable $t =$ time in days. We will set $t = 0$ at the start of May 2016.
The model uses two parameters β and γ with $\beta, \gamma > 0$.
Given these parameters, the model uses 3 differential equations.

The rate of change of the number of people susceptible to the disease over time

$$\frac{dS}{dt} = -\beta IS \qquad (1)$$

The rate of change of the number of people recovered over time

$$\frac{dR}{dt} = \gamma I \qquad (2)$$

The rate of change of the number of people infected.

$$\frac{dI}{dt} = \beta IS - \gamma I \qquad (3)$$

Parameterization of the model

In order to calculate β (the rate of infection) and γ (the rate of recovery), it helps to define two more parameters.

$D =$ Duration of disease for those recovered

$M =$ Mortality rate for those who die per day

This leads to two further equations.
The rate at which the disease is spread

$$\gamma = \frac{1}{D} \quad [3] \qquad (4)$$

The infection rate of the disease

$$\beta = \frac{M}{S} \quad [4] \qquad (5)$$

2.2 Transformation of Runge-Kutta Equations for SIR modeling

RK4 is one of the classic methods for numerical integration of ODE models.

Consider the following initial problem of ODE

$$\frac{dy}{dt} = f(t, y)$$

$$y(t_o) = y_o$$

Where $y(t)$ is the unknown function (scalar or vector) which I would like to approximate.

The Iterative formula of RK4 method for solving ODE is as follows

$$k_1 = hf(t_n, y_n)$$

$$k_2 = hf\left(t_n + \frac{1}{2}h, y_n + \frac{1}{2}k_1\right)$$

$$k_3 = hf\left(t_n + \frac{1}{2}h, y_n + \frac{1}{2}k_2\right)$$

$$k_4 = hf(t_n + h, y_n + k_3)$$

$$y_{n+1} = y_n + \frac{1}{6}(k_1 + 2k_2 + 2k_3 + k_4)$$

For simplicity, here we use the simplest SIR model to examine whether the **RK4** method has been implemented correctly. The SIR model is defined as follows

$$\frac{dS}{dt} = -\beta IS$$

$$\frac{dI}{dt} = \beta IS - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

where $S(t)$ is the number of susceptible people in the population at time t, $I(t)$ is the number of infectious people at time t, $R(t)$ is the number of recovered people at time t, β is the transmission rate, γ represents the recovery rate, and

$N = S(t) + I(t) + R(t)$ is the fixed population.

According to the general iterative formula, the iterative formulas for $S(t), I(t)$ and $R(t)$ of SIR model can be written out

$$S_{n+1} = S_n + \frac{\Delta t}{6}(k_1^S + 2k_2^S + 2k_3^S + k_4^S)$$

$$k_1^S = f(t_n, S_n, I_n) = -\beta S_n I_n$$

$$k_2^S = f\left(t_n + \frac{\Delta t}{2}, S_n + \frac{k_1^S \Delta t}{2}, I_n + \frac{k_1^I \Delta t}{2}\right)$$

$$= -\beta\left(S_n + \frac{k_1^S \Delta t}{2}\right)(I_n + \frac{k_1^I \Delta t}{2})$$

$$k_3^S = f\left(t_n + \frac{\Delta t}{2}, S_n + \frac{k_2^S \Delta t}{2}, I_n + \frac{k_2^I \Delta t}{2}\right)$$

$$= -\beta\left(S_n + \frac{k_2^S \Delta t}{2}\right)(I_n + \frac{k_2^I \Delta t}{2})$$

$$k_4^S = f(t_n + \Delta t, S_n + k_3^S \Delta t, I_n + k_3^I \Delta t)$$

$$= -\beta(S_n + k_3^S \Delta t)(I_n + k_3^I \Delta t)$$

$$I_{n+1} = I_n + \frac{\Delta t}{6}(k_1^I + 2k_2^I + 2k_3^I + k_4^I)$$

$$k_1^I = f(t_n, S_n, I_n) = \beta S_n I_n - \gamma I_n$$

$$k_2^I = f\left(t_n + \frac{\Delta t}{2}, S_n + \frac{k_1^S \Delta t}{2}, I_n + \frac{k_1^I \Delta t}{2}\right)$$

$$= \beta\left(S_n + \frac{k_1^S \Delta t}{2}\right)\left(I_n + \frac{k_1^I \Delta t}{2}\right) - \left(I_n + \frac{k_1^I \Delta t}{2}\right)$$

$$k_3^I = f\left(t_n + \frac{\Delta t}{2}, S_n + \frac{k_2^S \Delta t}{2}, I_n + \frac{k_2^I \Delta t}{2}\right)$$

$$= \beta\left(S_n + \frac{k_2^S \Delta t}{2}\right)\left(I_n + \frac{k_2^I \Delta t}{2}\right) - \left(I_n + \frac{k_2^I \Delta t}{2}\right)$$

$$k_4^I = f(t_n + \Delta t, S_n + k_3^S \Delta t, I_n + k_3^I \Delta t)$$

$$= \beta(S_n + k_3^S \Delta t)(I_n + k_3^I \Delta t) - (I_n + k_3^I \Delta t)$$

$$R_{n+1} = R_n + \frac{\Delta t}{6}(k_1^R + 2k_2^R + 2k_3^R + k_4^R)$$

$$k_1^R = f(t_n, I_n) = \gamma I_n$$

$$k_2^R = f\left(t_n + \frac{\Delta t}{2}, I_n + \frac{k_1^I \Delta t}{2}\right) = \gamma\left(I_n + \frac{k_1^I \Delta t}{2}\right)$$

$$k_3^R = f\left(t_n + \frac{\Delta t}{2}, I_n + \frac{k_2^I \Delta t}{2}\right) = \gamma\left(I_n + \frac{k_2^I \Delta t}{2}\right)$$

$$k_4^R = f(t_n + \Delta t, I_n + k_3^I \Delta t) = \gamma(I_n + k_3^I \Delta t)$$

3. Analysis and Result Discussion

If we now take the example of the Yellow Fever in Angola 2016, we can assign the parameters with the following values. The total population of Angola, N = 25830958 [5], and according to data from WHO, the number of people infected, I =2267[6] and the number of people dead is 293 [6]. Seeing as R includes the number of people who have received permanent immunity, this includes those who have died as they have permanent immunity, in addition to those who have recovered with permanent immunity.

Therefore, number of people recovered $R = 293 + (0.87 \times 2267) \approx 2265$

We will now use this data to provide the parameters with the following values.

$N = 25830958$

$I = 2267$

$R = 2265$

Therefore, $S = N - I + R = 25830958 - (2267 + 2265) = 25826426$

The duration of the disease ranges from 3 to 16 days [7], therefore we could roughly estimate the duration of the disease at the midpoint, i.e. 9 (approx.) days.

$D = 9$

$\gamma = \frac{1}{9} = 0.11$

The mortality rate of Yellow Fever is 0.13 [8] and the number of people susceptible is 25826426.

Therefore, β (the rate of infection) $= \frac{0.13}{25826426} = 5.03 \times 10^{-9}$

In order to use the SIR model to predict the evolution of the disease, it would be helpful if we could solve the system of differential equations. Unfortunately, we cannot completely solve these equations with an explicit formula solution. Therefore, we will use numerical approaches. We will use Runge Kutta method to extract the solution.

3.1 Runge-Kutta (RK4) Method

For each day, we will calculate the values of S, I and R using

$$k_1^S = -\beta S_n I_n$$

$$k_1^I = \beta S_n I_n - \gamma I_n$$

$$k_1^R = \gamma I_n$$

$$k_2^S = -\beta\left(S_n + \frac{k_1^S \Delta t}{2}\right)(I_n + \frac{k_1^I \Delta t}{2})$$

$$k_2^I = \beta\left(S_n + \frac{k_1^S \Delta t}{2}\right)\left(I_n + \frac{k_1^I \Delta t}{2}\right) - \left(I_n + \frac{k_1^I \Delta t}{2}\right)$$

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$$k_2^R = \gamma\left(I_n + \frac{k_1^I \Delta t}{2}\right)$$

$$k_3^S = -\beta\left(S_n + \frac{k_2^S \Delta t}{2}\right)\left(I_n + \frac{k_2^I \Delta t}{2}\right)$$

$$k_3^I = \beta\left(S_n + \frac{k_2^S \Delta t}{2}\right)\left(I_n + \frac{k_2^I \Delta t}{2}\right) - \left(I_n + \frac{k_2^I \Delta t}{2}\right)$$

$$k_3^R = \gamma\left(I_n + \frac{k_2^I \Delta t}{2}\right)$$

$$k_4^S = -\beta(S_n + k_3^S \Delta t)(I_n + k_3^I \Delta t)$$

$$k_4^I = \beta(S_n + k_3^S \Delta t)(I_n + k_3^I \Delta t) - (I_n + k_3^I \Delta t)$$

$$k_4^R = \gamma(I_n + k_3^I \Delta t)$$

$$S_{n+1} = S_n + \frac{\Delta t}{6}(k_1^S + 2k_2^S + 2k_3^S + k_4^S)$$

$$I_{n+1} = I_n + \frac{\Delta t}{6}(k_1^I + 2k_2^I + 2k_3^I + k_4^I)$$

$$R_{n+1} = R_n + \frac{\Delta t}{6}(k_1^R + 2k_2^R + 2k_3^R + k_4^R)$$

We take the initial values as

$$S_0 = 25826426$$

$$I_0 = 2267$$

$$R_0 = 2265$$

$$\gamma = 0.11$$

$$\beta = 5.03 \times 10^{-9}$$

We will do this explicitly for the transition from t = 0 to t = 1. Using those equations the following values for S, I and R can be calculated.

$$k_1^S = -\beta S_0 I_0$$

$$= -5.03 \times 10^{-9} \times 25826426 \times 2267$$

$$= -294.49899394226$$

$$k_1^I = \beta S_0 I_0 - \gamma I_0$$

$$= 5.03 \times 10^{-9} \times 25826426 \times 2267 - 0.11 \times 2267$$

$$= 45.128993942260024$$

$$k_1^R = \gamma I_0$$

$$= 0.11 \times 2267$$

$$= 249.37$$

$$k_2^S = -\beta\left(S_0 + \frac{k_1^S \Delta t}{2}\right)\left(I_0 + \frac{k_1^I \Delta t}{2}\right)$$

$$= -5.03 \times 10^{-9} \times \left(25826426 - \frac{294.49899394226}{2}\right) \times \left(2267 + \frac{45.128993942260024}{2}\right)$$

$$= -297.428582507639$$

$$k_2^I = \beta\left(S_0 + \frac{k_1^S \Delta t}{2}\right)\left(I_0 + \frac{k_1^I \Delta t}{2}\right) - \left(I_0 + \frac{k_1^I \Delta t}{2}\right)$$

$$= 5.03 \times 10^{-9} \times \left(25826426 + \frac{-294.49899394226}{2}\right) \times \left(2267 + \frac{45.128993942260024}{2}\right) - \left(2267 + \frac{45.128993942260024}{2}\right)$$

$$= 45.5764878408149$$

$$k_2^R = \gamma\left(I_0 + \frac{k_1^I \Delta t}{2}\right)$$

$$= 0.11 \times \left(2267 + \frac{45.128993942260024}{2}\right)$$

$$= 251.852094666824$$

$$k_3^S = -\beta\left(S_0 + \frac{k_2^S \Delta t}{2}\right)\left(I_0 + \frac{k_2^I \Delta t}{2}\right)$$

$$= -5.03 \times 10^{-9} \times \left(25826426 + \frac{-297.428582507639}{2}\right)\left(2267 + \frac{45.5764878408149}{2}\right)$$

$$= -297.457631748614$$

$$k_3^I = \beta\left(S_0 + \frac{k_2^S \Delta t}{2}\right)\left(I_0 + \frac{k_2^I \Delta t}{2}\right) - \left(I_0 + \frac{k_2^I \Delta t}{2}\right)$$

$$= 5.03 \times 10^{-9} \times \left(25826426 + \frac{-297.428582507639}{2}\right) \times \left(2267 + \frac{45.5764878408149}{2}\right) - \left(2267 + \frac{45.5764878408149}{2}\right)$$

$$= 45.580924917369200$$

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$$k_3^R = \gamma\left(I_0 + \frac{k_2^I \Delta t}{2}\right)$$

$$= 0.11 \times \left(2267 + \frac{45.5764878408149}{2}\right)$$

$$= 251.876706831244$$

$$k_4^S = -\beta(S_0 + k_3^S \Delta t)(I_0 + k_3^I \Delta t)$$

$$= -5.03 \times 10^{-9} \times (25826426 - 297.457631748614) \times (2267 + 45.580924917369200)$$

$$= -300.41681152467$$

$$k_4^I = \beta(S_0 + k_3^S \Delta t)(I_0 + k_3^I \Delta t) - (I_0 + k_3^I \Delta t)$$

$$= 5.03 \times 10^{-9} \times (25826426 - 297.457631748614) \times (2267 + 45.580924917369200) - (2267 + 45.580924917369200)$$

$$= 46.032909783759950$$

$$k_4^R = \gamma(I_0 + k_3^I \Delta t)$$

$$= 0.11 \times (2267 + 45.580924917369200)$$

$$= 254.38390174091$$

$$\therefore S_1 = S_0 + \frac{\Delta t}{6}(k_1^S + 2k_2^S + 2k_3^S + k_4^S)$$

$$= 25826426 + \frac{1}{6}(-294.49899394226 - 2 \times 297.428582507639 - 2 \times 297.457631748614 - 300.41681152467)$$

$$= 25826128.551961 \approx 25826129$$

$$\therefore I_1 = I_0 + \frac{\Delta t}{6}(k_1^I + 2k_2^I + 2k_3^I + k_4^I)$$

$$= 2267 + \frac{1}{6}(45.128993942260024 + 45.5764878408149 + 45.580924917369200 + 46.032909783759950)$$

$$= 2312.57945487373 \approx 2312$$

$$\therefore R_1 = R_0 + \frac{\Delta t}{6}(k_1^R + 2k_2^R + 2k_3^R + k_4^R)$$

$$= 2265 + \frac{1}{6}(249.37 + 251.852094666824 + 251.876706831244 + 254.38390174091)$$

$$= 2516.86858412284 \approx 2517$$

Here we use MATLAB to evaluate S, I, R over a two month period. **Table: 3.1** shows the result.

Table: 3.1

Time (Days)	S	I	R	S+I+R
1	25826426	2267	2265	25830958
2	25826129	2312	2517	25830958
3	25825825	2359	2774	25830958
4	25825516	2406	3036	25830958
5	25825200	2455	3303	25830958
6	25824878	2504	3576	25830958
7	25824549	2555	3854	25830958
8	25824214	2606	4138	25830958
9	25823872	2658	4428	25830958
10	25823523	2712	4723	25830958
11	25823168	2766	5024	25830958
12	25822805	2822	5331	25830958
13	25822435	2878	5645	25830958
14	25822057	2936	5965	25830958
15	25821672	2995	6291	25830958
16	25821279	3055	6624	25830958
17	25820878	3117	6963	25830958
18	25820470	3179	7309	25830958
19	25820052	3243	7663	25830958
20	25819627	3308	8023	25830958
21	25819193	3375	8390	25830958
22	25818750	3442	8766	25830958
23	25818299	3511	9148	25830958
24	25817838	3582	9538	25830958
25	25817368	3654	9936	25830958
26	25816889	3727	10342	25830958
27	25816400	3802	10756	25830958
28	25815902	3878	11178	25830958

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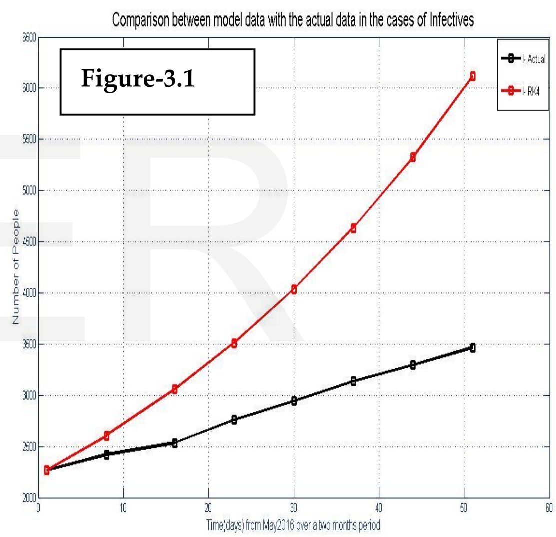
29	25815393	3956	11609	25830958
30	25814875	4035	12048	25830958
31	25814345	4116	12497	25830958
32	25813806	4198	12954	25830958
33	25813255	4283	13420	25830958
34	25812694	4368	13896	25830958
35	25812120	4456	14382	25830958
36	25811536	4545	14877	25830958
37	25810940	4636	15382	25830958
38	25810332	4729	15897	25830958
39	25809712	4824	16422	25830958
40	25809080	4920	16958	25830958
41	25808435	5019	17504	25830958
42	25807777	5119	18062	25830958
43	25807106	5222	18630	25830958
44	25806421	5326	19211	25830958
45	25805723	5433	19802	25830958
46	25805011	5541	20406	25830958
47	25804284	5652	21022	25830958
48	25803543	5765	21650	25830958
49	25802788	5880	22290	25830958
50	25802017	5998	22943	25830958
51	25801231	6117	23610	25830958
52	25800429	6240	24289	25830958
53	25799612	6364	24982	25830958
54	25798777	6492	25689	25830958
55	25797926	6621	26411	25830958
56	25797059	6753	27146	25830958
57	25796174	6888	27896	25830958
58	25795271	7025	28662	25830958
59	25794351	7165	29442	25830958
60	25793412	7308	30238	25830958

However, in order for the model to be valid and allow informing government policy, it obviously needs to correspond fairly close to reality.

The **Table-3.2** below compares the data collected from the SIR model (using RK4) for the number of people infected and the real life data of the number of people infected.

Table: 3.2		
Time (Days)	I-Actual	I-Model
1	2267	2267
8	2420	2606
16	2536	3055
23	2758	3511
30	2945	4035
37	3137	4636
44	3294	5326
51	3464	6117

Using the value of **Table-3.2** we can plot a graph using MATLAB which compares the model data to the actual data for the number of people infected (**Figure-3.1**).



As the graph demonstrates, the real data does not correspond very well to the data received from the model. The model has overestimated the number of individuals who can become infected with Yellow fever. This is often because of the many limitations. One of the main limitations includes the incorrect beta and gamma values that were calculated. Once fixing the beta and gamma values, we were able to find another gamma value that resulted in similar values to the real data. The suitable gamma value is 0.121407977.

The **Table: 3.3** below compares the data collected from the fitted model for the number of people infected and the real life data of the number of people infected.

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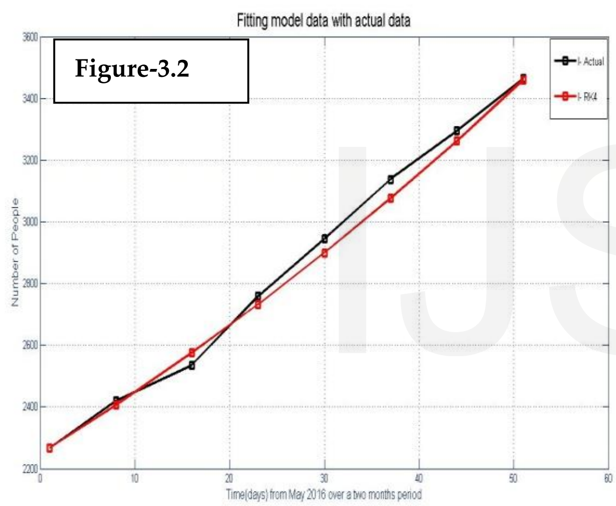
Table: 3.3

Time (Days)	I-Fitted	I-Actual
1	2267	2267
8	2406	2420
16	2575	2536
23	2732	2758
30	2899	2945
37	3075	3137
44	3262	3294
51	3460	3464

Using the value of **Table-3.3** we can plot a graph using MATLAB which compares curve fitted data with real data for the number of people infected (**Figure-3.2)**



Result Discussion

Although, this doesn't match the graph exactly, it shows a much better correlation of the number of individuals infected. Therefore, in order to improve the model, many changes should be done, together with altering the gamma value. The value that we eventually used to alter the model, led to being in several decimal places. This goes to illustrate the necessary precision required as very little deviance will cause massive changes. This can be because the gamma is calculated through extreme simplification, leaving great possibilities for more room for errors.

Furthermore, it is tough to differentiate between the number of people who have died and also the number of people who have survived with permanent immunity as they both fall under the same class of being 'recovered'. It is also a fact that rate of recovery is faster that the time scale of birth and death. The model is used to estimate future predictions of the disease and consequently, it will facilitate to determine practical components like the quantity of beds required in the hospitable, number of vaccination and reallocation costs etc.

Conclusion

The results obtained from modeling data will lead to completely different views and interpretations. This is due to the unequal distribution of knowledge across the globe whereby in countries like Angola, there is little access to the statistics which makes it troublesome to form constructive predictions regarding the outbreak. Through our research, we have gained further insight into the uses of mathematical modeling so as to work out the outbreak of diseases similarly as evaluating its flaws. Having chosen Yellow Fever as the diseases of concentration, as it is incredibly relevant to this situation in continent, it has enabled a practical understanding of its rate of transmission.

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