

BASIC EPIDEMIC MODEL OF DENGUE TRANSMISSION USING THE FRACTIONAL ORDER DIFFERENTIAL EQUATIONS

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Received: 27th Oct 2018

Revised: 27th Oct 2018

Accepted: 19th Dec 2018

DOI : <https://doi.org/10.22452/mjs.sp2019no1.1>

ABSTRACT Dengue is normally emerging in tropical and subtropical countries and now has become a serious health problem. In Malaysia, dengue is considered endemic for the past few years. A reliable mathematical model of dengue epidemic is crucial to provide some means of interventions in controlling the spread of the disease. Many mathematical models have been proposed and analyzed in the literature, but very little of them used fractional order derivative in analyzing the dengue transmission. In this paper, a study on a basic fractional order epidemic model of dengue transmission is conducted using the SIR-SI model, including the aquatic phase of the vector. The population size of the human is assumed to be constant. The threshold quantity R_0 is attained by the next generation matrix method. The preliminary result of the study is presented. It has shown that the disease-free equilibrium is locally asymptotically stable when $R_0 < 1$, and unstable when $R_0 > 1$. In other words, the dengue disease is eliminated if $R_0 < 1$, and it approaches a positive endemic equilibrium if $R_0 > 1$. Finally, some numerical results are presented based on the real data in Malaysia in 2016.

Keywords: Dengue, Epidemic, Fractional order, Stability, Reproduction number

ABSTRAK Denggi berlaku di negara-negara tropika dan sub-tropika dan kini telah menjadi masalah kesihatan utama. Di Malaysia, denggi telah pun disifatkan sebagai endemik untuk beberapa tahun yang lepas. Model matematik bagi wabak denggi yang boleh diandalkan adalah sangat penting sebagai intervensi dalam mengawal denggi dari terus merebak. Banyak model matematik telah dikemukakan dan dianalisa, namun tidak banyak daripada kajian yang ada menggunakan pembezaan melalui tertib pecahan dalam menganalisa penularan denggi. Di dalam artikel ini, kajian terhadap model penularan wabak denggi menggunakan kaedah tertib pecahan dijalankan. Ianya berdasarkan model SIR-SI serta mengambil kira fasa kehidupan vektor di dalam air. Saiz populasi manusia dianggap tetap. Nilai ambang R_0 , diperolehi menggunakan kaedah *the*

next-generation matrix. Penemuan awal kajian ini dibentangkan. Ianya telah diperlihatkan bahawa titik keseimbangan bebas penyakit adalah stabil apabila $R_0 < 1$, dan tidak stabil apabila $R_0 > 1$. Dalam kata lainnya, penyakit denggi dapat dihapuskan jika $R_0 < 1$, dan ianya akan mendekati titik keseimbangan endemic untuk $R_0 > 1$. Pada penghujung artikel ini, beberapa keputusan berangka dibentangkan berdasarkan data sebenar di Malaysia pada tahun 2016.

Kata kunci: Denggi, Kestabilan, Nombor pembiakan, Tertib pecahan, Wabak

INTRODUCTION

Dengue is listed second after malaria, as the most prevalent vector-borne disease in the world, caused by any of four closely related virus serotypes named DEN-1, DEN-11, DEN-III, and DEN-IV. The chance of contracting dengue virus has increased dramatically since the mid-90s. Now, dengue is becoming endemic in more than hundred countries (World Health Organization (WHO)).

Dengue virus is transferred to one individual by the bite of an infected *Aedes* female mosquito. Individuals who recuperate from one of the serotypes become constantly immune to it. However, they may become partially-immune or temporarily-immune or both to the other serotypes. Up to date, there is still no vaccine available for dengue patients. The efforts to prevent and control the spread of the dengue virus focus merely on the vector population, for instance, the implementation of the larvicides, residual treatment and space sprays.

Many mathematical models have been established in the literature to study the mechanism of the dengue transmission (Esteva & Vargas, 1998) (Esteva & Yang, 2015) (Syafuddin & Noorani, 2012). Most of these models were developed using the system of ordinary differential equation.

The integer order systems are ideal in modelling system like Markov system where the current state does not depend on the previous state. However, Sardar et al. (Sardar, Rana, & Chattopadhyay, 2014) explained that based on the entomological studies on the dengue transmission, memory and associative learning in the mosquito population and awareness in human population show a significant role in the transmission (McCall & Kelly, 2002). Since the behaviour of the trajectories of the fractional operator is non-local, it is one of the best ways to incorporate memory into the dynamical process (Agarwal, Ntouyas, Ahmad, & Alhothuali, 2013).

The aims of this study are to formulate a fractional order dengue epidemic model and to study the stability of the disease-free equilibrium point. The generalized Adams-Bashforth-Moulton algorithm has been used to solve the system of differential equations (Garrappa, 2015). For our purposes, we have followed the dengue disease outbreak in Malaysia for the year 2016. In this paper, we presented the preliminary result of our study.

This paper is structured as follows. In section 2, the formulation of the model is given. The basic definition of the fractional calculus is included followed by the construction of the proposed model. Disease-free equilibrium point and its stability are discussed in section 3. Section 4 is reserved for numerical results for the model and discussions. The conclusion is presented in section 5.

FORMULATION OF THE MODEL

The history of fractional calculus started in 1695 when L'Hospitals asked in a letter to Leibniz for the n th derivative, $\frac{D^n x}{Dx^n}$, what is the result for when $n = 1/2$. For more than two centuries, fractional calculus is only popular around pure mathematics branch. However, a few years back, the study of fractional calculus has become researcher's interest in many application fields such as in engineering, genetics, biology, statistics, and even finance. Researchers believe that fractional calculus can give more genuine understandings of the real-world phenomena (Diethelm K., 2010).

There are many descriptions of fractional order differential equations introduced in the literature. Among the famous one are the Riemann-Liouville, Caputo and Grünwald-Letnikov. In this paper, the Caputo's definition is used as the initial conditions of the integer order differential equation can be taken without encountering any problems in obtaining the solutions (Diethelm & Freed, 2002).

Definition 1. *The Caputo derivative of fractional order α of a function $f: \mathbb{R}^+ \rightarrow \mathbb{R}$ is defined by the following equation*

$$D_C^\alpha f(x) = \frac{1}{\Gamma(n - \alpha)} \int_a^x \frac{d^n f}{d\varepsilon^n}(\varepsilon)(x - \varepsilon)^{n-\alpha-1} d\varepsilon$$

where α is the order of the derivative with $n-1 < \alpha < n$ and $n = [\alpha] + 1$. $\Gamma(n-\alpha)$ is the Euler gamma function.

In the formulation of the model, the total number of human and mosquito one serotype of dengue viruses. The dynamics of female *Aedes* mosquito includes aquatic phase, A_m , and adult mosquito stage. The adult stage is divided into two compartments which are susceptible M_s and infectious M_i . The total human population is partitioned into three compartments that are susceptible H_s , infectious H_i , and recovered H_r individuals. The derivation of the fractional order

population is assumed to be constant. We also assume that the infection is produced by only differential equation for the proposed host-vector model is based on the ordinary differential equation introduced by Bailey for a single serotype dengue transmission (Bailey, 1975) and SIR model established by Kermack and McKendrick (Kermack & McKendrick, 1996). The fractionalization is done following the work of Diethelm (Diethelm, 2013). The governing equation is as follows:

$$\begin{aligned}
 D^\alpha A_m &= q\phi \left(1 - \frac{A_m}{C}\right) M - (\sigma_A + \mu_A)A_m \\
 D^\alpha M_s &= \sigma_A A_m - \frac{b^\alpha \beta_m}{H} M_s H_i - \mu_m M_s \\
 D^\alpha M_i &= \frac{b^\alpha \beta_m}{H} M_s H_i - \mu_m M_i \\
 D^\alpha H_s &= \mu_h (H - H_s) - \frac{b^\alpha \beta_h}{H} H_s M_i \\
 D^\alpha H_i &= \frac{b^\alpha \beta_h}{H} H_s M_i - (\gamma_h + \mu_h) H_i \\
 D^\alpha H_r &= \gamma_h H_i - \mu_h H_r
 \end{aligned}
 \tag{1}$$

where the description of the parameters used in the model can be found in Table 1.

The effective contact rate to human $b\beta_h$, is defined as the average number of contacts per day that result in infection if the mosquito is infected. On the other hand, the effective contact rate $b\beta_m$, is the average number of

contacts per day that successfully transfer the infection (virus) to the vector. All parameters are assumed to be positive as the system monitors the dynamic of the human population.

Table 1: Parameter description of system (1) and their reasonable range of values.

Parameter	Biological meaning	Range of values
q	Proportion of eggs that results in female mosquito	0-1
ϕ	Oviposition rate	0-11.2 per day
σ_A	Transition rate from aquatic stage to adult	0-0.19 per day
μ_A	Per capita mortality rate of aquatic stage	0.01-0.47 per day
$1/\mu_m$	Average lifespan of adult mosquito	0-42 days
$1/\mu_h$	Average lifespan of human	50-75 years
b	The biting rate	0-1 per day
β_m	Transmission probability from human to vector	0.375
β_h	Transmission probability from vector to human	0.375
γ_h	Recovery rate in the human population	0.083-0.33 per day
C	Mosquito carrying capacity	-

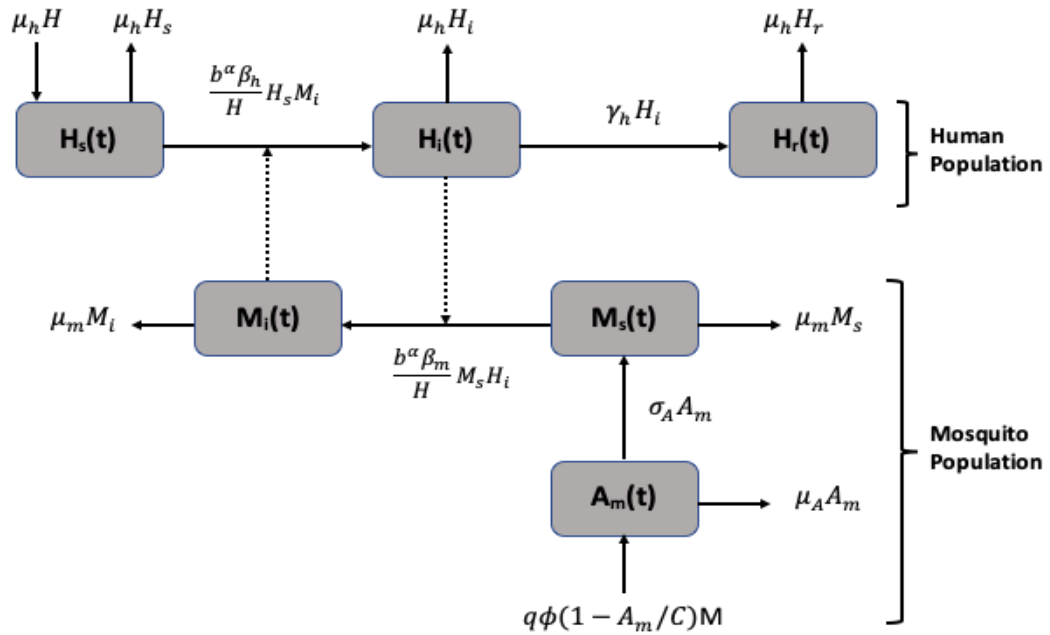


Figure 1: The schematic diagram of the dengue transmission model (1)

DISEASE-FREE EQUILIRIUM POINT AND LOCAL STABILITY

With the condition of $N_h = H = H_s + H_i + H_r$, we have $H_r = H - H_s + H_i$. Thus, we can now write down the corresponding system for human population exclusive of the H_r differential equation.

$$\begin{aligned}
 D^\alpha H_s &= \mu_h(H - H_s) - \frac{b^\alpha \beta_h}{H} H_s M_i \\
 D^\alpha H_i &= \frac{b^\alpha \beta_h}{H} H_s M_i - (\gamma_h + \mu_h) H_i \\
 D^\alpha A_m &= q\phi \left(1 - \frac{A_m}{C}\right) M - (\sigma_A + \mu_A) A_m \\
 D^\alpha M_s &= \sigma_A A_m - \frac{b^\alpha \beta_m}{H} M_s H_i - \mu_m M_s \\
 D^\alpha M_i &= \frac{b^\alpha \beta_m}{H} M_s H_i - \mu_m M_i
 \end{aligned} \tag{2}$$

Let the set Ω be the region of biological interest that is positively invariant with respect to model (2).

$$\Omega = \{(A_m, M_s, M_i, H_s, H_i) \in \mathbb{R}_+^5: H_s + H_i \leq H, A_m \leq kH, M_s + M_i \leq mH\},$$

where k is the number of larvae per human and m is the number of female mosquito per human. System (2) can be written as follows:

$$\frac{dX}{dt} = M(X)X + F, \tag{3}$$

where here, $\frac{dX}{dt} = D^\alpha(A_m, M_s, M_i, H_s, H_i)$ and $F = (0,0,0, \mu_h H, 0)$. Meanwhile, $M(X)$ is the matrix with all off-diagonal entries are nonnegative value, and known as Metzler matrix. The Metzler matrix is in the following form

$$M(X) = \begin{pmatrix} \frac{-q\phi(M_s + M_i)}{C} - (\sigma_A + \mu_A) & q\phi & q\phi & 0 & 0 \\ \sigma_A & -\frac{b^\alpha \beta_m}{H} H_i - \mu_m & 0 & 0 & 0 \\ 0 & \frac{b^\alpha \beta_m}{H} H_i & -\mu_m & 0 & 0 \\ 0 & 0 & 0 & -\mu_h - \frac{b^\alpha \beta_h}{H} M_i & 0 \\ 0 & 0 & 0 & \frac{b^\alpha \beta_h}{H} M_i & -(\gamma_h + \mu_h) \end{pmatrix}$$

Since $F \geq 0$, we can say that system (3) is positively invariant in \mathbb{R}_+^5 . Meaning that, any solution of the equation departing from an initial state in the positive orthant \mathbb{R}_+^5 will remain forever in \mathbb{R}_+^5 . This implies that the

closed set Ω is positively invariant with respect to the system (2) (Rodrigues et al., 2012).

Now we let $v = (A_m, M_s, M_i, H_s, H_i) \in \mathbb{R}_+^5: H_s + H_i \leq H, A_m \leq kH, M_s + M_i \leq mH$. Since $m \geq \frac{\sigma_A}{\mu_A} k$, it can be shown that v is

positively invariant with respect to (3). Hence, we suppose that m and k are chosen such that,

$$m \geq \frac{\sigma_A}{\mu_A} k \tag{4}$$

To evaluate the equilibrium point, we let $D^\alpha A_m = 0, D^\alpha M_s = 0, D^\alpha M_i = 0, D^\alpha H_s = 0, D^\alpha H_i = 0$. The fractional order system (2) has two disease-free equilibrium (DFE). The first one is the straightforward trivial equilibrium E_0 . Here, $A_m = 0$,

indicates of the none existence of mosquito population, hence, no dengue outbreaks. This DFE is not of our interest since this state does not represent the real situation for the region that we considered in the real data set.

$$E_0 = (0,0,0, H, 0)$$

The second DFE obtained is given by

$$E_1 = (\bar{A}_m, \bar{M}_s, 0, H, 0)$$

where \bar{A}_m and \bar{M}_s are given by the following equation:

$$\bar{A}_m = C(1 - \frac{1}{R_m}) \quad \text{and} \quad \bar{M}_s = \frac{\sigma_A \bar{A}_m}{\mu_m}$$

Hence,

$$E_1 = (C(1 - \frac{1}{R_m}), \frac{C\sigma_A}{\mu_m}(1 - \frac{1}{R_m}), 0, H, 0)$$

where $R_m = \frac{q\phi\sigma_A}{\mu_m(\sigma_A + \mu_A)}$. R_m represent the basic offspring of the mosquito population. This is biologically interesting when $R_m > 1$, in which mosquito population exist. This is the case when disease is eradicated without taking any action on the eliminating of the mosquito population.

The basic reproduction number R_0 , is a very important threshold quantity in investigating the stability of the equilibrium point of the system. In general, R_0 is biologically defined as the expected number of secondary infections in a completely susceptible population. The interpretations of R_0 in terms of the stability are as follows

- If $R_0 < 1$, the transmission sequences are not self-contained, hence, incapable to create a major epidemic.
- If $R_0 = 1$, the infectious is maintained, no major outbreaks.
- If $R_0 > 1$, the number of infected individuals will increase as infectious take over, hence, the disease will persist

In this paper, the next generation matrix is used to obtain the R_0 for system (2).

$$R_0^2 = \frac{b^{2\alpha} \beta_m \beta_h \bar{M}_s}{(\gamma_h + \mu_h) \mu_m H}$$

$$R_0 = \sqrt{\frac{b^{2\alpha} \beta_m \beta_h \bar{M}_s}{(\gamma_h + \mu_h) \mu_m H}} \tag{5}$$

The calculated R_0 is not only depend on the biting rate parameter as in the integer order case but also a memory dependent threshold quantity since $R_0 \propto b^\alpha$ (Hamdan & Kilicman,

2018). It can be observed that if the order α is decreasing, the value of b^α will also be decreasing. This result in a less efficient the average bite rate by each mosquito per day (Sardar, Rana, & Chattopadhyay, 2014).

Theorem 1. *The trivial disease-free equilibrium E_0 , is locally asymptotically stable if $R_0 < 1$ and the condition of $R_m < 1$ is satisfied, otherwise it is unstable.*

Proof. The disease-free equilibrium is locally asymptotically stable if all the eigenvalues, $\lambda_i, i = 1, 2, \dots, 5$ of the Jacobian matrix $J(E_0)$ satisfy the following condition (Matignon, 1996).

$$|\arg(\lambda_i)| > \frac{\alpha\pi}{2}$$

The Jacobian matrix of the system evaluated at the equilibrium point E_0 :

$$J(E_0) = \begin{pmatrix} -(\sigma_A + \mu_A) & 0 & 0 & 0 & 0 \\ \sigma_A & -\mu_m & 0 & 0 & 0 \\ 0 & 0 & -\mu_m & 0 & 0 \\ 0 & 0 & -b^\alpha \beta_h & -\mu_h & 0 \\ 0 & 0 & b^\alpha \beta_h & 0 & -(\gamma_h + \mu_h) \end{pmatrix}$$

It is clearly shown that all eigenvalues are negative real parts;

$-(\sigma_A + \mu_A), -\mu_m, -\mu_h, -(\gamma_h + \mu_h)$. Hence, E_0 is locally asymptotically stable.

Theorem 2. *The DFE E_1 , is locally asymptotically stable if $R_0 < 1$ and is unstable if $R_0 > 1$.*

Proof. Following the stability condition by Matignon, the Jacobian matrix of the system (2) evaluated at the equilibrium point E_1 , we have

$$J(E_1) = \begin{pmatrix} -R_m(\sigma_A + \mu_A) & 0 & 0 & 0 & 0 \\ \sigma_A & -\mu_m & 0 & 0 & \frac{b^\alpha \beta_m}{H} \bar{M}_s \\ 0 & 0 & -\mu_m & 0 & \frac{b^\alpha \beta_m}{H} \bar{M}_s \\ 0 & 0 & -b^\alpha \beta_h & -\mu_h & 0 \\ 0 & 0 & b^\alpha \beta_h & 0 & -(\gamma_h + \mu_h) \end{pmatrix}$$

The calculated eigenvalues are $\lambda_1 = -R_m(\sigma_A + \mu_A), \lambda_2 = -\mu_m, \lambda_3 = -\mu_h$. The other roots are determined by solving the quadratic equation:

$$\lambda^2 + (\mu_m + \gamma_h + \mu_h)\lambda + \mu_m(\gamma_h + \mu_h)(1 - R_0) = 0$$

Obviously, the roots are negative real parts for when $R_0 < 1$. Hence, proved that E_1 is locally asymptotically stable if $R_0 < 1$ and is unstable if $R_0 > 1$, and the condition of $R_m > 1$ is satisfied.

NUMERICAL RESULTS AND DISCUSSION

In the case of fractional order differential equation, there is no general analytical method in solving the nonlinear systems. In fact, the fractional differential equations are difficult to solve numerically, compared to the integer order ODE. However, several analytical method and numerical schemes have been developed to solve the system. For instance, Diethelm and Freed introduced a new algorithm known as FracPECE, the generalization of the classical PECE type method (Diethelm & Freed, 1999).

In this study, the values related to the human describe the reality of an infected period in Malaysia. The data used is based on the dengue fever cases recorded in Malaysia for 2016, taken from The Ministry of Health Malaysia (From the Desk of the Director-General of Health Malaysia), (Dengue Situation Updates 2016, n.d.). However, for the mosquito population we have selected information from various sources due to the limited sources available in Malaysia.

In this work, we have not established any new numerical scheme. We used the available Matlab code (fde12) developed by Garrappa (Garrappa, 2015), based on the work of Diethelm and Freed. As of in the classical integer order derivative, we used Matlab ODE solver, ode45. The numerical simulations are done using the parameter values in Table 2 for the system (2) (see (Hamdan & Kilicman, 2019) for references). The initial conditions for the problem: $H_{s0} = H - H_{i0}$, $H_{i0} = 2511$, $A_{m0} = kH$, $M_{s0} = mH$, with the final time, $t_f = 52$ weeks. The initial values are chosen based on the real data in Malaysia for year 2016.

However, the choice of the parameter values is carefully selected to suit the demographic factor of Malaysia.

Table 2: Parameter values

Parameter	Values
H	31200000
q	0.8
ϕ	7.5
σ_A	0.08
μ_A	0.25
μ_m	0.11
μ_h	0.0000365
b	0.8
β_m	0.375
β_h	0.375
γ_h	0.334
C	kH
k	3
m	6

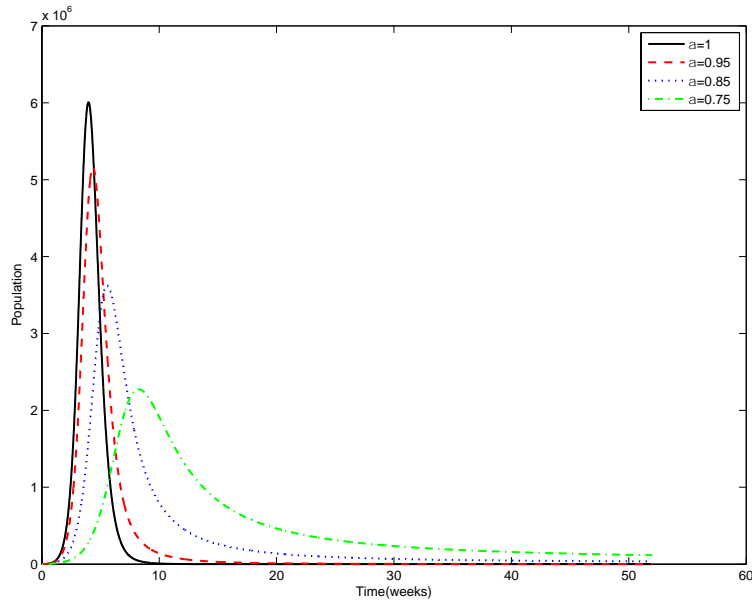


Figure 2: Solution to the classical model versus the solution of the fractional model (2) with various value of α for the infected human population.

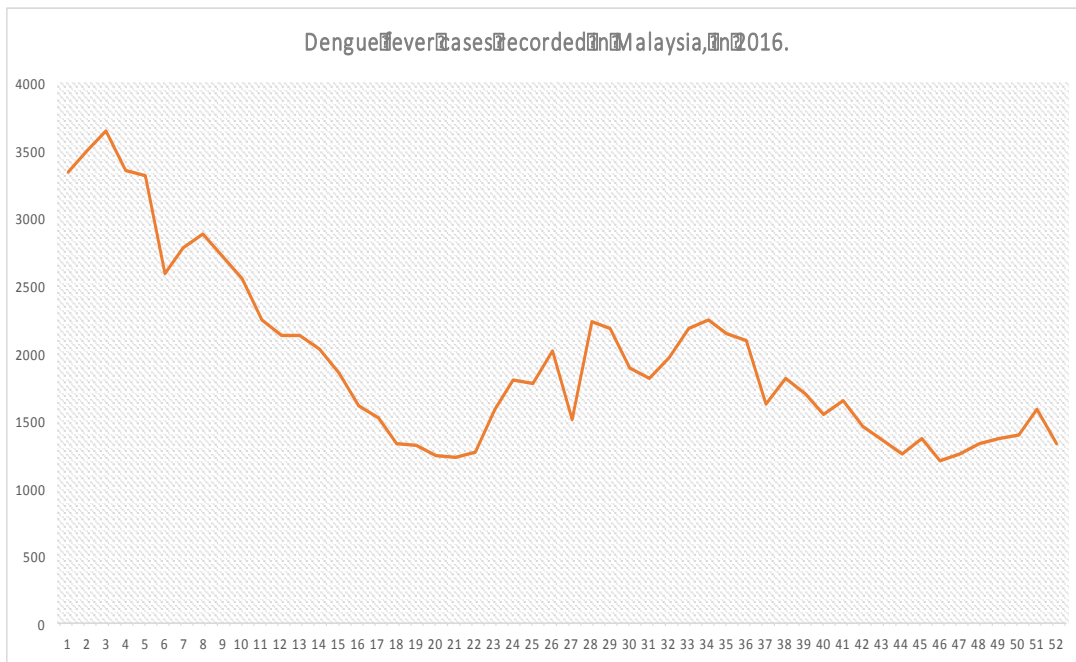


Figure 3: Number of dengue cases recorded in Malaysia, in 2016.

Figure 2 represents the trajectories of the infected human population for the classical integer order derivative and fractional order derivative with various values of α and Figure 3 is the plot of the dengue fever cases in Malaysia (2016). We can see through Figure 2, the maximum peak of the infected human solution for both integer order ODE and fractional order differential equation is in between 0 to 10 weeks, which agreed well with the real data value. We observed that in the

fractional order case, the maximum peak of the infectious human population significantly drops as the value of order decreasing. However, the solutions required more time to achieve their steady state. In other words, one can say that the spread of the dengue disease can be reduced but needs more time to be eradicated. The order α can be represented as an index of memory, thus, $\alpha \rightarrow 0$, indicates an increase of memory in both human and mosquito population.

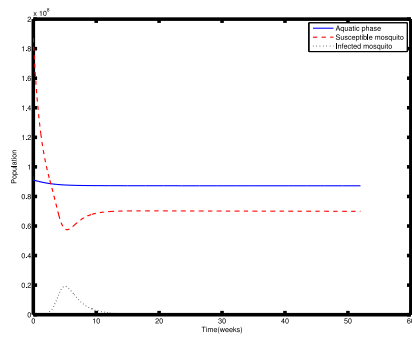


Figure 4a: Solution of the fractional order vector model, for $\alpha = 0.95$.

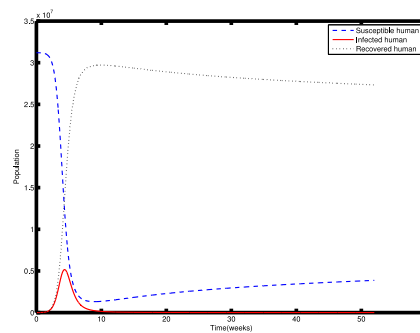


Figure 4b: Solution of the fractional order for the the human model, for $\alpha = 0.95$.

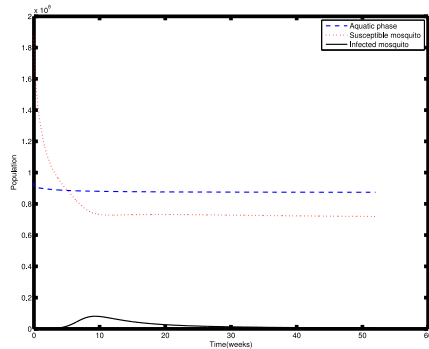


Figure 5a: Solution of the fractional order for the vector model, for $\alpha = 0.75$.

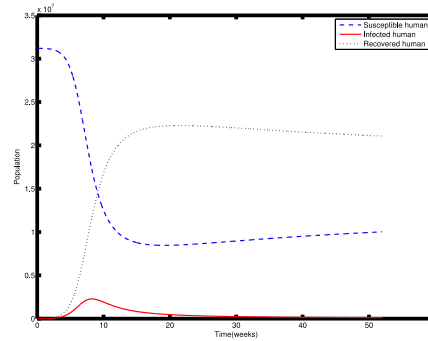


Figure 5b: Solution of the fractional order for the human model, for $\alpha = 0.75$.

Figure 4a, 4b and 5a, 5b revealed that the solution of the susceptible human population in the fractional order does not fall

drastically in a relatively short period for the small value of α . We observed that the speed

of convergence for the fractional order system is slower than the integer order system, and this explained the significance of time needed for the population to reach the disease-free state. Meanwhile, in Figure 6a, 6b and Figure 7a, 7b, it is shown that the solutions converge to the disease-free equilibrium for $\alpha = 0.5, 0.55$ in a very short period of time. These results verified

the local stability theorem in section 3 for the disease-free equilibrium. However, we noticed that the order α , gives a significant effect on the results of the stability of the system. The required time to eliminate the disease clearly depends on the memory effect on the host and vector population, at least, to this study.

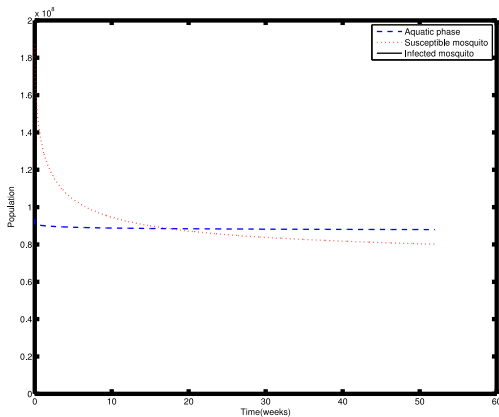


Figure 6a: Solution of the fractional order for the vector model, for $\alpha = 0.55$.

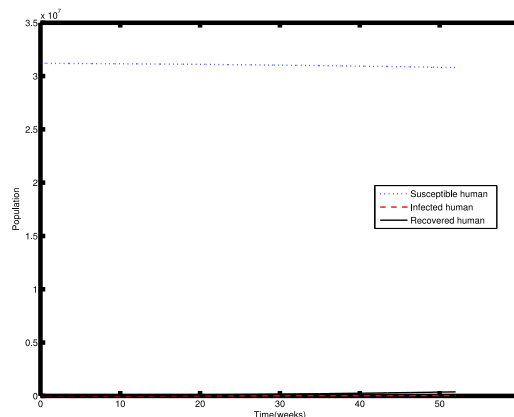


Figure 6b: Solution of the fractional order for the human model, for $\alpha = 0.5$.

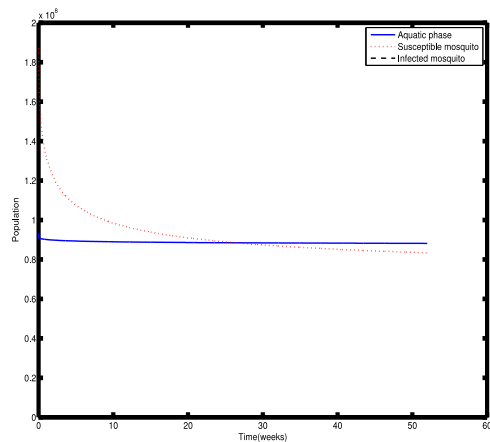


Figure 7a: Solution of the fractional order for the vector model, for $\alpha = 0.5$.

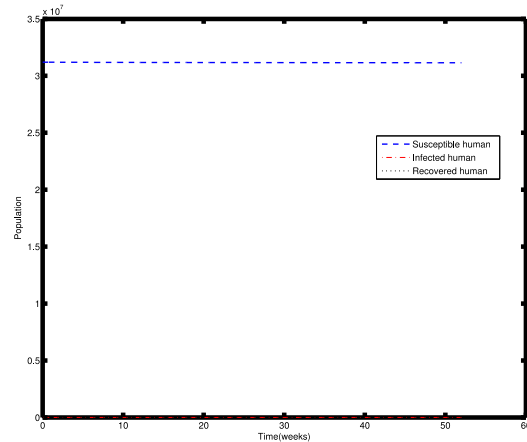


Figure 7b: Solution of the fractional order for human model, for $\alpha = 0.5$.

CONCLUSION

In this paper, we have proposed and analyzed a fractional order dengue epidemic model. The hypothetical and epidemiological findings of this study are summarized as follows:

- The disease-free equilibrium of system (2) is locally asymptotically stable if the corresponding $R_0 < 1$.
- Although the equilibrium points of fractional order system and integer order system are equal, the solution of the fractional order model approaches the fixed point over a longer period (Demirci, Unal, & Ozalp, 2011).
- The memory of the mosquito and human population represented by the order of the differential equation has a significant effect on the period of the disease elimination.
- An increase in order (memory) of human and mosquito population ($\alpha \rightarrow 0$), will decrease the abundance of infectious mosquito, hence, reduce the dengue transmission in a population.

The obtained results are significant with a real-life situation of dengue transmission. For

ACKNOWLEDGEMENTS

This work is supported by the Ministry of Higher Education Malaysia and Universiti Teknologi MARA (UiTM). This work is also partially funded by the Universiti Putra Malaysia providing Putra Grant GP-IPS/2018/9625000.

instance, mosquito does not casually feed on host blood, but they somehow use their experience about human spot and defensiveness in selecting the host (Sardar et al., 2014). Thus, plenty of time and effort are needed to completely eradicate the disease, in terms of the elimination of the *Aedes* mosquito, in which reflects the results obtained in Figure 6 and 7.

We can say that from the preliminary results obtained, fractional order derivative gives us a more realistic way to model vector-borne disease dynamics as it possesses memory. In this study, we can conclude that smaller value of α , gives a better approximation in reducing the intensity of the dengue transmission. However, a thorough analysis needs to be done on the parameter values and α value chosen, so that this model can be used to successfully predict the long-term behaviour of the disease, especially in Malaysia. A model of fractional order dengue with control parameters will be our future study. This model will be developed to see how effective the current control strategies used by the government specifically in Malaysia and how does the order α , and control parameter affect the stability of the model.

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