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Three-Step Implicit Multistep Method for Solving Diabetes Mellitus Model

Woon Hui Ning[1], Syahirbanun Isa[1]*

[1] *Department of Mathematics and Statistics, Faculty of Applied Sciences and Technology, UTHM Kampus Cawangan Pagoh, Hab Pendidikan Tinggi Pagoh, KM 1, Jalan Panchor, 84600, Pagoh, Muar, Johor MALAYSIA*

*Corresponding Author: syahir@uthm.edu.my
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Abstract

Diabetes mellitus is a growing global health problem, especially in low- and middle-income countries. In this study, we compared the SEII$_T$ model with and without genetic factors to predict the trend of diabetes over a 5-year period using data from the Malaysian National Diabetes Registry 2020. The SEII$_T$ model categorizes the population into susceptible (S), exposed (E), infected (I), and infected with treatment (I_T). Three-step implicit multistep calculations were performed using MATLAB, where the Runge-Kutta fourth order (RK4) method was used for the initial solution, and the Adams-Bashforth and Adams-Moulton methods were used for prediction and correction, respectively. The results calculated using the three-step multistep method showed a similar trend in diabetes prevalence as the results of the reference study were solved using RK4. Comparison with the Malaysian National Diabetes Registry Report 2023 showed that the genetic model performed well in predicting the exposed and infected populations, but both models overestimated the susceptible and treated populations.

1. Introduction

Diabetes is a chronic disease that affects millions of people around the world, and its incidence is rising. It is characterized by increased blood glucose when the body cannot produce enough insulin or use it properly. Type 1 diabetes develops in childhood or young adulthood and is caused by the immune system attacking the pancreas's insulin-producing cells. Meanwhile, type 2 diabetes is the most common type of diabetes, and it can be caused by lifestyle factors such as obesity, inadequate food intake and physical inactivity. Gestational diabetes occurs during pregnancy. The diagnosis of diabetes is on the rise, especially in low and middle-income countries, and as a result, diabetes has become a new global health crisis. In addition to short-term health risks, diabetes can lead to serious complications, such as cardiovascular disease, renal failure and neuropathy, each of which places a significant economic burden on healthcare systems worldwide. The International Diabetes Federation estimates that more than 536 million people will be diagnosed with diabetes in 2021, expected to rise to 783 million by 2045 [1]. These rising numbers indicate the urgent need to understand better and control diabetes.

Researchers are using mathematical models to understand better, identify, solve, and predict diabetes. Asmaidi and Suryanto explored the SEII$_T$ model, which divides the population into susceptible (S), exposed (E), infected (I), and infected with treatment (I_T) groups while incorporating both treatment and genetic factors [2]. Their findings show that effective treatment can significantly reduce the prevalence of diabetes, emphasizing the importance of early intervention.

However, solving the equations of the SEII$_T$ model is challenging due to the complex interactions between these different groups. While exact solutions are often impractical, numerical methods offer approximate results. The Runge-Kutta method used to solve the diabetes mellitus model without genetic factors but considering

treatment, also faces challenges such as computational demands and complexity, particularly in the absence of genetic considerations [3].

Among the numerical methods, the multistep method is particularly useful for solving large and complicated equations. Unlike simpler methods that only use information from the previous step, multistep methods consider multiple previous points, making them more accurate and stable. The Adams-Moulton method is particularly effective in solving complex systems of equations, such as the diabetes complication model [4].

For this study, a three-step implicit multistep method has been chosen. This method uses data from the last three steps to compute the next value and is particularly effective for solving the SEII$_T$ model. The Runge-Kutta fourth order (RK4) method finds the three initial points. The predictor-corrector method first provides an initial estimate and then refines that estimate to improve accuracy [5]. Hence, Adams-Bashforth's four-step method and Adams-Moulton's three-step method are the predictor and corrector, respectively, to increase the accuracy of this study.

This study aims to apply the three-step implicit multistep method to solve the SEII$_T$ model and predict the trend of diabetes mellitus over the next five years using data from previous research and Malaysian datasets. The results will be compared to prior studies that utilized different methods and between two SEII$_T$ model variations using Malaysian data to evaluate their effectiveness.

2. Methodology

This section discusses the SEII$_T$ model, both with and without genetic factors, and presents the system of ordinary differential equations (ODEs) that define the model. Applying a three-step implicit multistep method to solve the system, including the necessary formulas, is also explained.

2.1 Diabetes Model With Genetic Factors

A mathematical model can be formulated as a system of ODEs to describe the dynamics of diabetes. Formulating and calculating the system of ODEs allows for predicting future diabetic populations. The system of ODEs of diabetes is built by forming a diabetes model SEII$_T$ with genetic factors and treatment [2]. The diagram of the diabetes model SEII$_T$ with genetic factors and treatment is shown in Fig. 1.

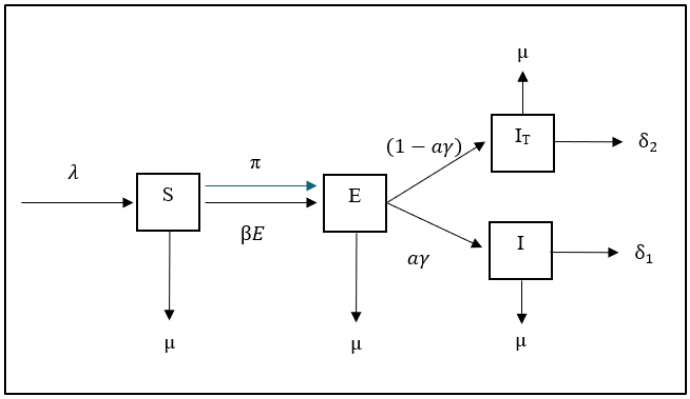

Fig. 1 Model SEII$_T$ with genetic factors and with treatment [2]

The model shows the relation of each parameter in this model. [2] analyses the stability results by examining the fixed points without disease and under endemic conditions, determined by the basic reproduction number. $\mathcal{R}_0$. Fixed points without disease stable for the condition $\mathcal{R}_0 < 1$ and fixed points endemic stable at $\mathcal{R}_0 > 1$.

The parameters of the SEII$_T$ model, along with genetic factors and treatment, are the basis for the calculations. Each parameter shows a part of the system and how it works in the model. These parameters decide how the model acts and match the real world. Table 1 lists the parameters and their meanings. Each parameter is used in the calculations to predict the diabetes trend over 5 years.

Table 1 Parameter of SEII$_T$ model with genetic factor.

Symbol	Meaning
N	Population
S	Susceptible
E	Exposed
I	Infected

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I_T	Infected with treatment
λ	Birth rate
μ	Mortality rate by nature
δ_1	Mortality rate by disease to population infected without treatment
δ_2	Mortality rate by disease to population infection with treatment
π	Population shift rate susceptible to exposed by genetic factor
β	Population shift rate susceptible to exposed without treatment by infective contact among population
α	Population shift rate exposed to infected without treatment
γ	Removal rate

The system of ODEs of the model $SEII_T$ for diabetes with genetic factors is formed as equation (1).

$$\begin{aligned}
\frac{dS}{dx} &= \lambda - (\pi + \mu + \beta E)S, \\
\frac{dE}{dx} &= (\pi + \beta E)S - (\mu + 1)E, \\
\frac{dI}{dx} &= \alpha\lambda E - (\mu + \delta_1)I, \\
\frac{dI_T}{dx} &= (1 - \alpha\gamma)E - (\mu + \delta_1)I_T, \\
N &= S + E + I + I_T.
\end{aligned} \tag{1}$$

To obtain the simplification for solving equation (1), the proportion of each population to the total population, N, is formed and is substituted and simplified into equation (2).

$$\begin{aligned}
\frac{ds}{dx} &= \frac{\lambda}{N}(1 - s) - (\pi + \beta eN - \delta_1 i - \delta_2 i_T)s, \\
\frac{de}{dx} &= (\pi + \beta eN)s - (1 + \frac{\lambda}{N} - \delta_1 i - \delta_2 i_T)e, \\
\frac{di}{dx} &= \alpha\gamma e - (\delta_1 + \frac{\lambda}{N} - \delta_1 i - \delta_2 i_T)i, \\
\frac{di_T}{dx} &= (1 - \alpha\gamma)e - (\delta_2 + \frac{\lambda}{N} - \delta_1 i - \delta_2 i_T)i_T,
\end{aligned} \tag{2}$$

Equation (2) will be used to solve and predict the trend of diabetes mellitus after five years.

2.2 Diabetes Model Without Genetic Factors

Genetic factors are one of the risk factors for diabetes, and genetic reasons can cause different types of diabetes. The most significant difference between the two models is that the one with genetic causes has an extra parameter 'π', leading to a slight difference in the final system ODEs. Fig.2 shows the diagram of the $SEII_T$ model without considering genetic factors referred to by Side [3].

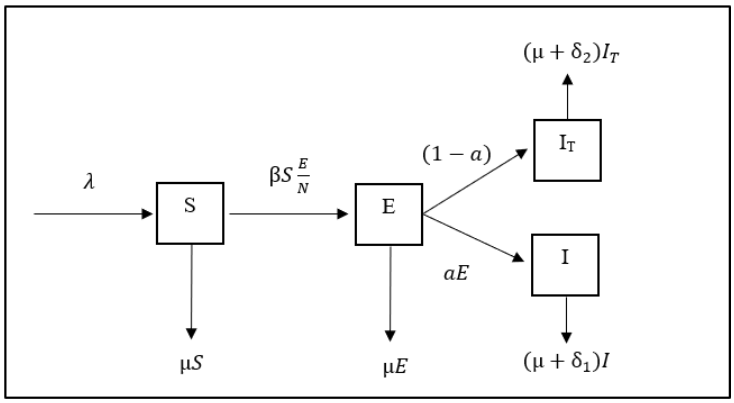

Fig. 2 Model SEIIT without genetic factors and with treatment.[3]

The parameters and the relationship of each parameter are drawn in the diagram. The stability is analysed by [6]. The results show that when the basic reproduction number $\mathcal{R}_0 < 1$, the disease-free equilibrium is stable. Conversely, when the basic reproduction number $\mathcal{R}_0 > 1$, the endemic equilibrium becomes stable.

Table 2 Parameter of SEIIT model without genetic factor.

Symbol	Meaning
N	Population
S	Susceptible
E	Exposed
I	Infected
I_T	Infected with treatment
λ	Birth rate
μ	Mortality rate by nature
δ_1	Mortality rate by disease to population infected untreated
δ_2	Mortality rate by disease to population infection treated
β	Population-shift rate susceptible to exposed untreated by invective contact among population
α	Population-shift rate exposed to infected untreated

Table 2 tabulates the meaning of the corresponding parameters appearing in the model. The parameter is important as it describes the model and will be used to form the system of ODEs of diabetes mellitus. The system of ODEs of the model $SEII_T$ with diabetes without genetic factors is formed as equation (3).

$$\begin{aligned}
\frac{dS}{dx} &= \lambda - \mu S - \beta S\frac{E}{N},\\
\frac{dE}{dx} &= \beta S\frac{E}{N} - \mu E - E,\\
\frac{dI}{dx} &= \alpha E - (\mu + \delta_1)I,\\
\frac{dI_T}{dx} &= (1-\alpha)E - (\mu + \delta_2)I_T,\\
N &= S + E + I + I_T.
\end{aligned} \tag{3}$$

Equation (3) is simplified to equation (4), and derivative S is simplified and replaced with derivative N. Equation (4) will be solved using a three-step implicit multistep method to predict the trend of diabetes over five years.

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$$\begin{aligned}
\frac{dN}{dx} &= \lambda - \mu N - \delta_1 I, -\delta_2 I_T, \\
\frac{dE}{dx} &= \beta(N - E - I - I_T)\frac{E}{N} - \mu E - E, \\
\frac{dI}{dx} &= \alpha E - (\mu + \delta_1) I, \\
\frac{dI_T}{dx} &= (1-\alpha) E - (\mu + \delta_2) I_T.
\end{aligned} \tag{4}$$

2.3 Three steps implicit multistep method

The linear multistep method approximates solutions to ODEs using previous points and their derivatives. This study employs a three-step implicit multistep method to solve the SEII$_T$ model. According to [7], its general form is shown as

$$\sum_{m=0}^{s} \alpha_m y_{i+m} = h \sum_{m=0}^{s} \beta_m f(t_{i+m}, y_{i+m}) \tag{5}$$

where α_m and β_m are constant coefficients, h is step size, s is the number of steps, y_{i+m} are the solution values and $f(t_{i+m}, y_{i+m})$ are the derivatives. The linear multistep method is divided into explicit ($\beta_s = 0$) and implicit ($\beta_s \neq 0$). The predictor-corrector technique is used for higher accuracy. the predictor estimates the solution while the corrector refines it. The four-step Adams-Bashforth method, an explicit method, will be the predictor to predict solutions and is expressed as

$$y_{i+1} = y_i + \frac{h}{24}[55 f(x_i, y_i) - 59 f(x_{i-1}, y_{i-1}) + 37 f(x_{i-2}, y_{i-2}) - 9 f(x_{i-3}, y_{i-3})] \tag{6}$$

The three-step Adams-Moulton method, an implicit method that considers the desired point on both sides will be the corrector to correct the predicted solution and is expressed as

$$y_{i+1} = y_i + \frac{h}{24}[9 f(x_{i+1}, y_{i+1}) + 19 f(x_i, y_i) - 5 f(x_{i-1}, y_{i-1}) + f(x_{i-2}, y_{i-2})] \tag{7}$$

The RK4 method was used to find the three initial points before applying Adams-Bashforth and Adams-Moulton methods. The RK4 method applies the following equation to calculate y_1, y_2 and y_3.

$$\begin{aligned}
k_1 &= hf(x_i, y_i), \\
k_2 &= hf(x_i + \frac{h}{2}, y_i + \frac{k_1}{2}), \\
k_3 &= hf(x_i + \frac{h}{2}, y_i + \frac{k_2}{2}), \\
k_4 &= hf(x_i + h, y_i + k_3), \\
y_{i+1} &= y_i + \frac{1}{6}(k_1 + 2k_2 + 2k_3 + k_4).
\end{aligned} \tag{8}$$

Then the y_4 and the subsequent y_i are calculated by the predictor and corrector methods, which are given by the equation of (6) and (7).

3. Result and Discussion

The three-step implicit multistep method will solve the diabetes mellitus model $SEII_T$ with and without genetic factors. The Adams-Bashforth method will be used as a predictor, and the Adams-Moulton method will be used as a predictor. MATLAB will be used to calculate and predict the trend of diabetes mellitus.

3.1 $SEII_T$ Model Without Genetic Factors Using Data From Makassar

[3] obtained the initial value and data from Makassar City Health Office and Central of Statistics and solved it using the RK4 method. The parameter of the $SEII_T$ model without genetic factor is shown in Table 3. Therefore, the same parameter and initial value are used in this study to predict the same model with three-step multistep methods with step size 0.01.

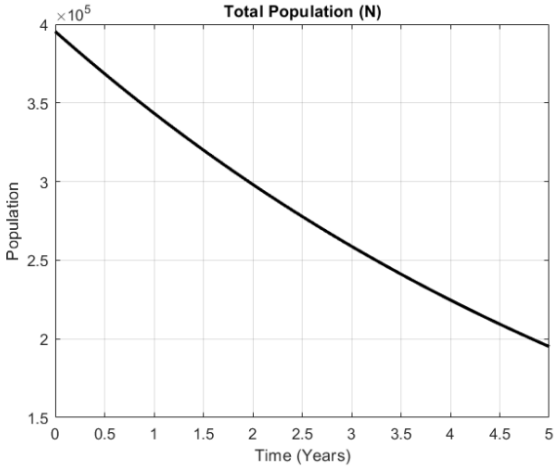
Table 3 Parameters from reference [3]

Symbol	Value
λ	2
μ	0.13869
δ_1	0.06654
δ_2	0.09281
β	0.88187
α	0.0009

The initial condition for the total population, N, is 395,406; the exposed population, E, is 9,304; the infected population, I, is 4,779, and the infected with treatment population, I_T, is 3,426 [3]. The prediction using MATLAB will be conducted with parameters set at a step size of 0.01. The prediction results over five years are shown in Table 4, and the graphs are shown in Fig.3(a) to Fig. 3(d).

Table 4 Result of model SEIIT without genetic factor for $\boldsymbol{h = 0.01}$

	N	E	I	I_T
Year 1	343,460.46	3,355.98	8,463.42	3,321.27
Year 2	298,177.42	1,210.51	8,541.93	2,852.51
Year 3	258,838.67	436.64	7,551.80	2,341.51
Year 4	224,706.7	157.50	6,365.16	1,885.93
Year 5	195,102.82	56.81	5,261.55	1,506.40



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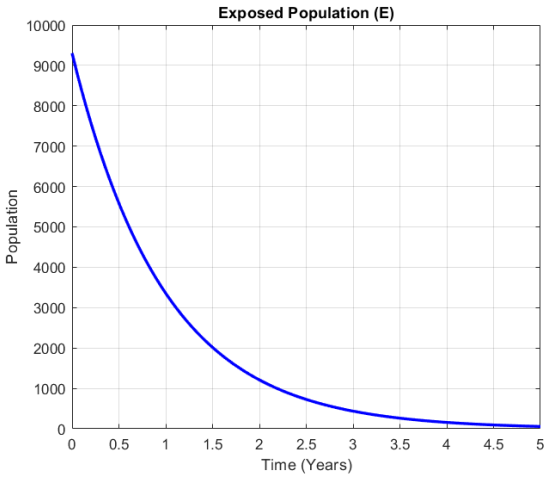

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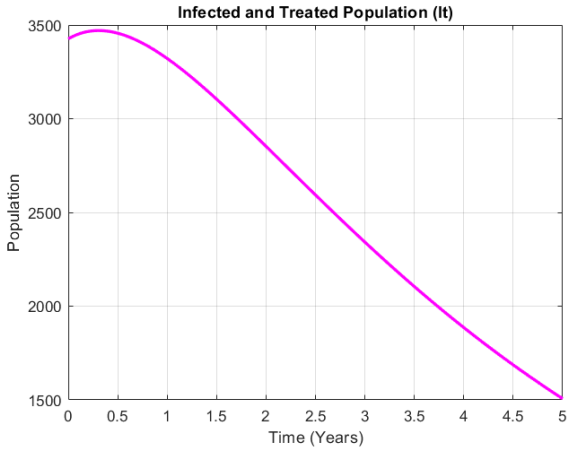


(d)

Fig. 3 Graph of result SEIIT without genetic factors in $\boldsymbol{h = 0.01}$. (a) Total population (b) Exposed population (c) infected population (d) Infected with treatment population

Over five years, the total population, *N*, shows the most drastic decrease, indicating that the management or preventive measures successfully reduce the cases of diabetes. The numbers decrease from about 343,460 in the first year to almost 195,103 by the fifth year, showing a very strong downward trend and predicting a decline in the incidence of diabetes. This trend follows the general finding of the study conducted by [3], where there was a consistent drop in the total population. However, the reduction from our model was larger likely due to small variations in the algorithm's iterative steps.

The estimated number of people exposed, *E* decreased sharply from 3,355.98 in year 1 to 1,210.51 in year 2, probably due to increased diagnostic efforts and interventions identifying previously undiagnosed cases. Then, this population drastically declines to 56.81 by year 5, suggesting that long-term management and prevention strategies are in place and effectively reduce the incidence of new exposures. Our model shows a higher initially exposed population than the reference study. However, both show a similar downtrend over the five years.

The infected population, *I*, increased from 4,779 to 8,463.42 in the first year due to delayed diagnosis, lack of awareness and poor early intervention efforts. However, by the fifth year, the number dropped to 5,261.55, indicating the impact of effective intervention and treatment programs to reduce active diabetes cases. These programs may include increased public health awareness, improved healthcare services, and improved at-risk or already diagnosed management strategies. The treated population, I_T, declines from 3,321.27 to 1,506.40 during the same period, indicating an improvement in the effectiveness of treatment and, likely, a decrease in the necessity for aggressive treatments. Our model outputs for infected and infected with treated populations align with the reference study, although our numbers are slightly higher. This may imply that our model will tend to overestimate the infected populations initially, after which corrective measures would bring the values closer to real-life trends. Despite minor differences, both models successfully capture the dynamics of diabetes management over time.

The comparison was carried out at two different time steps, $h_1 = 0.01$ and $h_2 = \frac{1}{365}$. Time step $h_2 = \frac{1}{365}$ enabled prediction to be made daily, and $h_1 = 0.01$ was selected in line with the already available reference method. The difference recorded between the two-time steps in results decreased gradually with time in all variables (N, E, I, I_T). The difference estimated as $h_2 - h_1$, were between $3.7899\times10^{-7}$and -4.149×10^{-6} in the first year but became negligible with errors in the range -3.6×10^{-8} and 4.81×10^{-8} by year 5.

3.2 Comparison of SEII$_T$ Model Predictions With and Without Genetic Factors Using Malaysian Data

The parameter was obtained from the Malaysia National Diabetes Registry Report 2020 [8], as shown in Table 5. The parameter and initial value will be used to predict diabetes trends of SEII$_T$ Model Predictions With and Without Genetic Factors by using $h = \frac{1}{365}$.

Table 5 Parameters from Malaysia

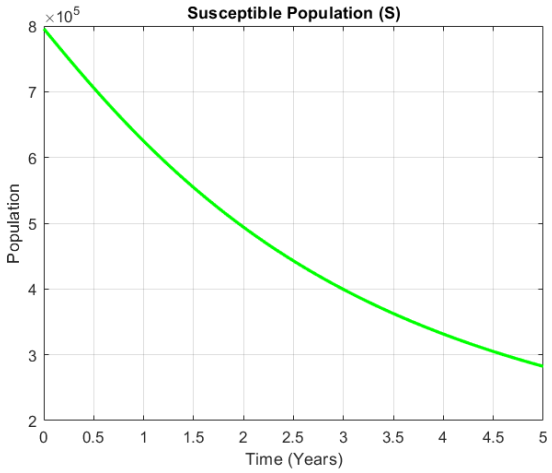
Symbol	Value
λ	0.0159
μ	0.0131

δ_1	0.1
δ_2	0.02
π	0.25
β	0.501
α	0.25
γ	0.1

The initial condition for the susceptible population, S, is 795,692, the exposed population, E, is 92,426, the infected population, I, is 902,991 and the infected with treatment population, I_T, is 270,898. The SEII$_T$ model, both with and without genetic factors, will be employed to forecast the populations S, E, I, and I_T over five years, using a step size of $\frac{1}{365}$. In the model without genetic factors, which focuses on predicting the total population, the susceptible population S will be computed using the formula $S = N - E - I - I_T$. The result of model SEII$_T$ with and without genetic factors is shown in Table 6. While the Fig.4 (a) to Fig.4 (d) and Fig.5 (a) to Fig.5 (d) show the graph of results for model SEII$_T$ with and without genetic factors, respectively, in susceptible, exposed, infected, and infected with treatment population.

Table 6 Result of model SEIIT with and without genetic factors in $\boldsymbol{h = \frac{1}{365}}$

Model	Year	S	E	I	I_T
SEII$_T$ with genetic factors	1	624,905.10	167,683.75	871,900.86	397,517.29
	2	493,975.67	164,781.27	851,498.46	551,751.60
	3	399,368.05	140,445.13	828,441.82	693,751.99
	4	331,495.25	115,393.86	800,033.07	815,084.81
	5	282,377.28	95,103.50	767,074.21	917,452.01
SEII$_T$ without genetic factor	1	702,380.28	85,670.95	827,472.05	327,793.00
	2	617,805.28	78,444.97	758,371.23	377,664.19
	3	541,993.41	70,971.43	694,917.61	420,475.18
	4	467,247.53	63,471.58	636,475.65	456,356.00
	5	408,353.75	56,146.23	582,527.93	485,589.09



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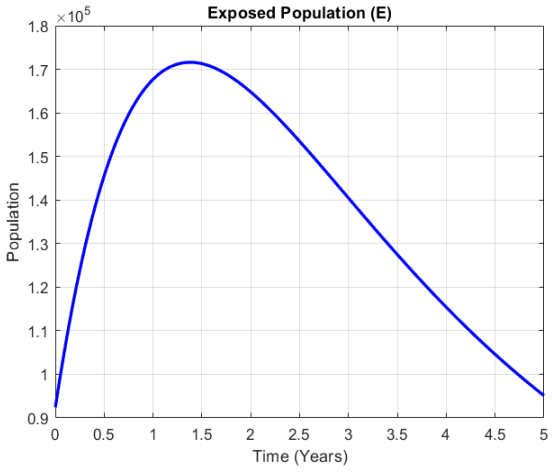

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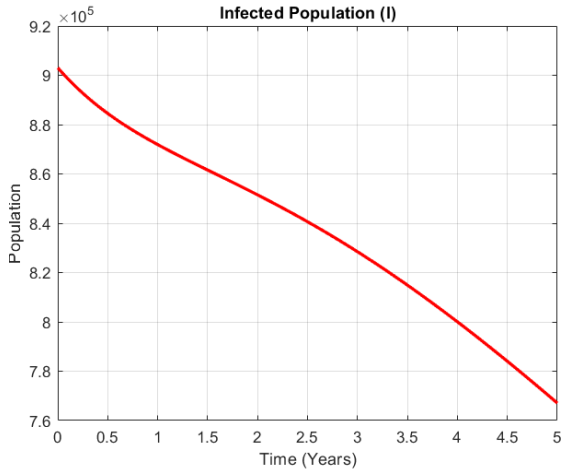

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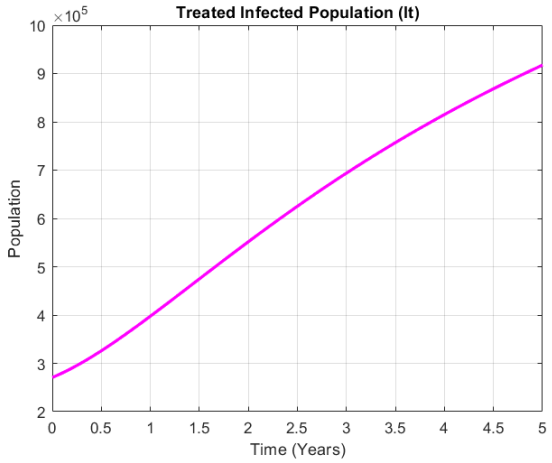
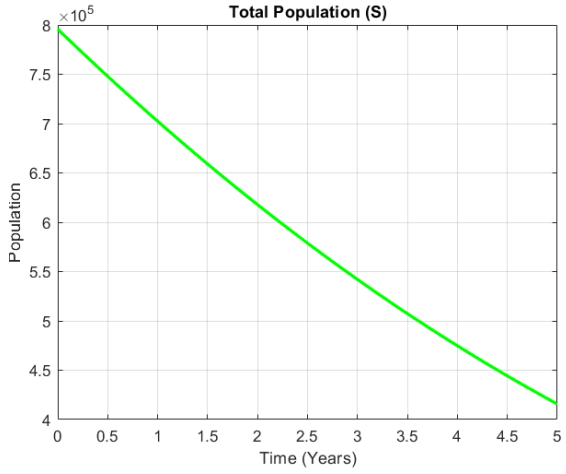


(d)

Fig. 4 Graph of result SEIIT with genetic factors and with treatment in $\boldsymbol{h} = \frac{\mathbf{1}}{\mathbf{365}}$ (a) Susceptible population (b) Exposed population (c) infected population (d) Infected with treatment population



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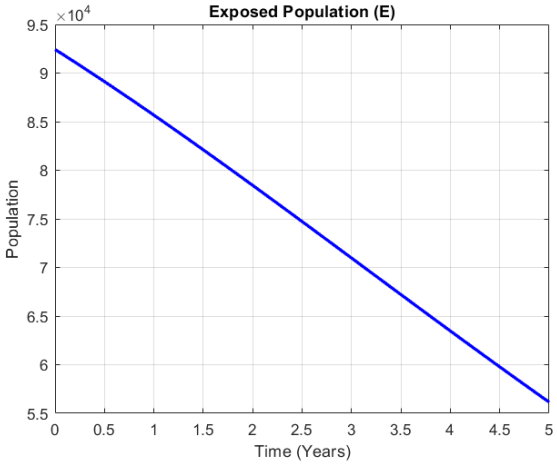

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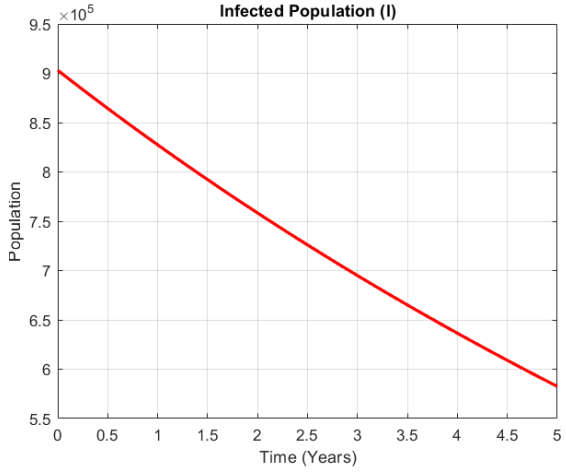

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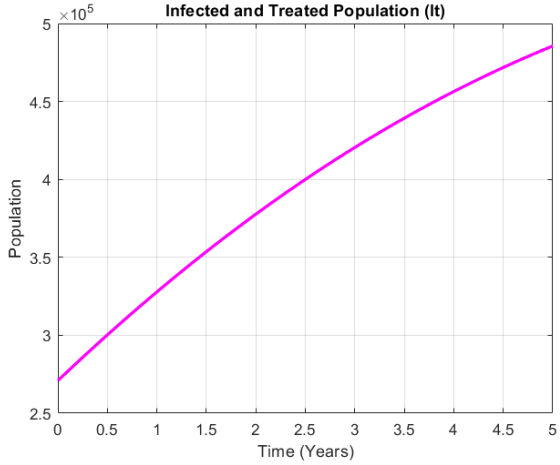

(d)

Fig. 5 Graph of result SEIIT without genetic factors and with treatment in $\boldsymbol{h} = \frac{\mathbf{1}}{\mathbf{365}}$(a) Susceptible population (b) Exposed population (c) infected population (d) Infected with treatment population

The susceptible population, S, declines significantly in both models, as shown in Table 6, Fig.4 (a) and Fig5(a). With genetic factors, it decreases from 624,905.10 in year 1 to 282,377.28 in year 5, while without genetic factors, it declines from 702,380.28 to 408,353.75. Including genetic factors enables earlier identification of at-risk populations, improving targeted interventions and management.

Fig.4 (b) and Fig.5 (b) show that the exposed population, E, behaves differently in both models. In the model with genetic factors, the value increases from 92,426 to 167,683.75 in the first year, followed by a decrease to 95,103.50 by the fifth year. However, without genetic factors, the exposed population starts lower at 85,670.95 in year 1 and decreases to 56,146.23 by year 5. This suggests that genetic predisposition leads to a higher initial exposure due to identifying at-risk individuals.

Both models show a decreasing trend for the infected population, I, which is clearly illustrated in Fig.4 (c) and Fig. 5(c). The model with genetic factors decreases from 871,900.86 in year 1 to 767,074.21 in year 5, while the model without genetic factors drops from 827,472.05 in year 1 to 582,527.93 in year 5. Models without genetic factors showed greater declines, which may reflect the greater impact of lifestyle or environmental changes.

The infected with treatment population, I_T, shows a significant increase in the model with genetic factors, rising from 397,517.29 in year 1 to 917,452.01 in year 5, indicating higher treatment demand. In the model without genetic factors, this population grows from 327,793.00 in year 1 to 485,589.09 in year 5, suggesting a lesser intensity of management needs.

A comparison is made between the predicted data calculated using the $SEII_T$ model based on the Malaysian National Diabetes Registry Report 2020 [8] and actual data recorded in the Malaysian National Diabetes Registry Report 2023 [9] to provide a comprehensive analysis of diabetes trends in Malaysia. The predicted third-year data from the $SEII_T$ model based on the 2020 dataset is compared with the 2023 data by calculating the relative error.

Table 7 Comparison of model SEIIT with and without genetic factors in year 2023

Model	Stage	Predicted	Actual	Relative error (%)
$SEII_T$ with genetic factors	S	399,368.05	1,085,380	63.20
	E	140,445.13	126,088	11.39
	I	828,441.82	870,771	4.86
	I_T	693,751.99	236,177	193.74
$SEII_T$ without genetic factor	S	541,993.41	1,085,380	50.06
	E	70,971.43	126,088	43.71
	I	694,917.61	870,771	20.20
	I_T	420,475.18	236,177	78.03

Table 7 shows the comparison between the $SEII_T$ model predictions and the actual data from the Malaysian National Diabetes Registry Report 2023 which provides crucial insights into the model's effectiveness. Both models underestimated the real values for the susceptible population. The genetic model performed slightly worse, with a larger error rate of 63.20%, compared to the without-genetic model at 50.06%. Conversely, the projections on the exposed population, E were closer to reality, where the genetic model performed better with an error of only 11.39%, compared to 43.71% for the without a genetic model. This indicates that genetic determinants play a vital role in explaining exposure patterns.

In the infected population, the accuracy of the genetic model was quite high, with an error of only 4.86%, which was better than the 20.20% without the genetic model. This suggests that predictions that include genetic predisposition are more reliable. However, the greatest difference was found in the treated population, where the genetic model overestimated the number of people treated by 193.74%. Meanwhile, the non-genetic model was overestimated by 78.03%. This could mean that both models overestimate the number of people who received or responded to treatment.

Overall, the genetic model better predicted the exposed and infected populations. However, both models need further improvement to predict susceptible and treated populations more accurately. The results suggest that further model improvements are needed to reflect real trends better and provide better predictions

4. Conclusion

The three-step multistep approach was compared with the RK4 method over five years. Both methods predicted well for the susceptible, S, exposed, E, infected, I, and infected with treated populations, I_T, showing similar trends. The multistep method requires fewer function evaluations per step but is more sensitive to initial conditions, while the RK4 method was better at handling rapid changes.

The strengths and weaknesses of the model were identified when comparing the prediction results of the SEIIT model with the actual data from the Malaysian National Diabetes Registry Report 2023. The genetic model better predicted the exposed and infected populations, with predictions of 140,445.13 and 828,441.82, respectively, close to the actual values of 126,088 and 870,771. This indicates the importance of genetic factors. However, both models underestimated the susceptible population and overestimated the treated population. The genetic model predicted 399,368.05 for the susceptible population, higher than the actual 1,085,380, and 693,751.99 for the treated population, compared to the actual 236,177. The model without genetic factors showed smaller discrepancies, predicting 541,993.41 for susceptible populations and 420,475.18 for treated populations. These results suggest the models need refinement, and incorporating additional factors or exploring hybrid models could improve accuracy and stability in predicting diabetes trends for better healthcare planning and treatment strategies.

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Conflict of Interest

Authors declare that there is no conflict of interests regarding the publication of the paper.

Author Contribution

The authors confirm contribution to the paper as follows: ***study conception and design:*** *Woon Hui Ning; Syahirbanun Isa,* ***data collection:*** *Woon Hui Ning;* ***analysis and interpretation of results:*** *Woon Hui Ning; Syahirbanun Isa;* ***draft manuscript preparation:*** *Woon Hui Ning, Syahirbanun Isa. All authors reviewed the results and approved the final version of the manuscript.*

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