

Safety Verification of SEITR Epidemic Model on Recombination HIV and Hepatitis B Virus using Taylor Model

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Abstract—Human Immunodeficiency Virus (HIV) is an AIDS (Acquired Immuno Deficiency Syndrome) virus that attacks the immune system for which there is no cure. When the immune system has decreased, it is prone to diseases such as Hepatitis B disease. To reduce the error value of the number of subpopulations, we use an interval approximation. One of the simulation calculations that the number of variables initially intervals is Taylor model. Taylor's model can be used to verify that the number of people infected with HIV and Hepatitis B will not exceed the specified number of unsafe sets. To calculate the set of states that are reached by the system over a certain period of time, given the initial conditions and parameters. The initial condition is divided into three scenarios, an affordable set of states, safety verification can be done. As a result of the safety verification of the three scenarios provided there is no set of states that are not safe, so the results of all three scenarios are safe.

Index Terms—Recombination of HIV and Hepatitis B viruses, Taylor models, safety verification.

I. INTRODUCTION

MANY methods can solve a system model such as Runge Kutta. But most of these methods require a value from the initial condition of a single value. This contradicts the fact that most subpopulations whose single value is uncertain. One method that the initial condition could be intervals is Taylor model. The initial condition of the model calculated using Taylor model can be both interval and single. This reduces the error value and results in a value that is close to the actual value. System verification can be done in a model. System verification aims to determine the state of the variables, parameters and changes that occur in the specified system conditions. Verification completion can use a software, and one of the software used to verify the model or system is flow star. Flow star is one of the applications that simulates the model of the system using Taylor model. Often pandemic diseases include HIV and Hepatitis B. Researchers here want to verify the complexity of HIV and Hepatitis B recombination, whether within 5 years, the disease becomes an outbreak or not. Based on the above description the purpose of this study is to analyze the safety verification results of SEITR epidemic model on the recombination of HIV and Hepatitis B virus with Taylor model.

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Previous research related to safety verification is [1]. In the study, the authors presented a case study of a simple hybrid multi basalt control system that switches to different preset insulin delivery rates across different ranges of glucose levels. The study used the Dalla-Man model to model the patient's physiology and the hybrid automaton model of the controller. The purpose of that research is to verify that blood glucose levels remain in a safe range overnight using flow* software. They used 2 different control strategies defined by a set of insulin levels. And the result of the study is that strategy I and strategy II do not cause hypoglycemia and ketoacidosis, but their blood glucose is not in the euglycemic range. While blood glucose should be in the euglycemic range.

II. MODELS AND PRELIMINARIES

A. Mathematical Model

The model in this paper is a mathematical epidemic model constructed of type SEITR (Susceptible Exposed Infected Treatment Recovery). The model presented the progression of recombinant spread of HIV and Hepatitis B viruses. The population in the model was divided into 10 subpopulations. The subpopulations are the subpopulations of Susceptible (S_1), Exposed HIV (E_1), Exposed hepatitis B (E_2), Infected HIV (I_1), Infected Hepatitis B (I_2), Infected AIDS (I_3), Infected recombination HIV and hepatitis B (I_4), Treatment HIV (T_1), Treatment hepatitis B (T_2), Recovery (R) [2].

$$\begin{aligned}
 \frac{dS}{dt} &= A - (\beta_1 I_1 + \beta_2 I_2 + \mu)S \\
 \frac{dE_1}{dt} &= \beta_1 S I_1 - (\gamma_1 + \mu)E_1 \\
 \frac{dE_2}{dt} &= \beta_2 S I_2 - (\gamma_2 + \mu)E_2 \\
 \frac{dI_1}{dt} &= \gamma_1 E_1 - (\theta + a_1 + \mu)I_1 + (1 - c_1)\psi_1 T_1 \\
 \frac{dI_2}{dt} &= \gamma_2 E_2 - (\omega_1 I_3 + a_2 + \mu)I_2 + (1 - c_2)\psi_2 T_2 \\
 \frac{dI_3}{dt} &= \theta I_1 - (\omega_1 I_2 + a_2 + \mu)I_3 + (1 - c_3)\psi_3 T_1 \\
 \frac{dI_4}{dt} &= \omega_1 I_3 I_2 + \omega_2 I_2 I_3 - (a_4 + \mu)I_4 + (1 - c_4)\psi_4 T_1 \\
 \frac{dT_1}{dt} &= a_1 I_1 + a_3 I_3 + a_4 I_4 - (1 - c_1)\psi_1 T_1 - (1 - c_3) \\
 &\quad - (1 - c_4)\psi_4 T_1 - c_4 \psi_2 T_2 - c_1 \psi_1 T_1 - c_3 \psi_3 T_1 \\
 &\quad - \mu T_1
 \end{aligned}$$

$$\frac{dT_2}{dt} = a_2 I_2 - (1 - c_2) \psi_2 T_2 + c_4 \psi_4 T_1 - \mu T_2 - c_2 \psi_2 T_2$$

$$\frac{dR}{dt} = c_1 \psi_1 T_1 + c_3 \psi_3 T_1 + c_2 \psi_2 T_2 - \mu R$$

where S represents the number of susceptible individuals, E_1 represents the number of exposed HIV, E_2 represents the number of hepatitis B, I_1 represents the number of individuals infected by HIV, I_2 represents the number of individuals infected by hepatitis B, I_3 represents the number of individuals infected by AIDS, I_4 represents the number of individuals infected by HIV and hepatitis B, T_1 represents the number of individuals being treated for HIV, T_2 represents the number of individuals being treated for hepatitis B, R represents the number of recovered individuals.

The parameters used are as follows: A denotes the number of births, μ denotes the death rate, β_i denotes the rate of contact between susceptible and infected individuals for $i = 1, 2$, γ_i denotes the rate of exposed individuals that entered the infected subpopulation for $i = 1, 2$, θ denotes HIV and AIDS transmission rate, a_j denotes the treatment rate for $j = 1, 2, 3, 4$, ω_i denotes the contact rate between HIV-infected individuals and individuals infected by hepatitis B virus for $i = 1, 2$, c_j denotes the opportunity for the individual to experience a better change in condition due to treatment for $j = 1, 2, 3, 4$ and ψ_j denotes the individual healing after treatment for $j = 1, 2, 3, 4$.

B. Safety Verification

The safety has the specification “no unsafe state can be reached”. Safety verification issues can be written, given the n -dimensional dynamic system, the initial set of $X_0 \in R^n$, unsafe set $U \subseteq R^n$, and time horizon $T > 0$. The safety verification issue is proving that $Reach_u(X_0, [0, T]) \cap U = \emptyset$. In safety verification, we can overapproximate the reachable states. If no unsafe state can be reached, then the system is safe. The nature of safety is very important for hybrid systems and verification can be done by calculating reachability in the hybrid space state.

C. Taylor's Model

Taylor's model was originally developed by Berz and Makino to provide over-approximation for continuous functionality. Taylor models (TM) can be applied to over-approximation for flowpipes.

Definition 1 ([3]): Taylor's model is denoted by a pair (p, I) where p is a polynomial on the \vec{x} variable set, starting in the domain interval D , and I is the remaining interval. TM may also be worth a real-value TM vector, or in a way both p and I are vector-valued and have the same dimensions.

III. RESULTS AND DISCUSSIONS

In this paper, three scenarios were used. The scenario is used to find out if hiv virus recombination disease and hepatitis B within a certain period will be an outbreak or not. The initial condition of scenario 1 is adjusted to the data taken from the previous model [2] and the unsafe condition is obtained from twice the initial condition with the focus of

```

init
{
  S in [2900000, 3000000]
  E1 in [1000, 1050]
  E2 in [150, 200]
  I1 in [1040, 1050]
  I2 in [190, 200]
  I3 in [641, 641]
  I4 in [50, 70]
  T1 in [1267, 1267]
  T2 in [188, 188]
  R in [1112, 1112]
}

unsafe set
{
  E1 in [2000, 2100]
  E2 in [300, 400]
  I1 in [2080, 2100]
  I2 in [380, 400]
}

```

Fig. 1. The initial condition of the first scenario.

```

continuous reachability
{
  state var S, E1, E2, I1, I2, I3, I4, T1, T2, R, t

  par
  {
    A = 50000
    alpha1 = 0.784
    alpha2 = 0.984
    alpha3 = 0.694
    alpha4 = 0.774
    gamma1 = 1
    gamma2 = 1
    C1 = 0.434
    C2 = 0.869
    C3 = 0.4
    C4 = 0.452
    psi1 = 0.804
    psi2 = 0.883
    psi3 = 0.877
    psi4 = 0.883
    theta = 0.615
    mu = 0.013
    beta1 = 35e-26
    beta2 = 6e-26
    omega1 = 6e-26
    omega2 = 35e-26
  }
}

```

Fig. 2. System parameters.

research sub-population Exposed HIV (E_1), Exposed hepatitis B (E_2), Infected HIV (I_1), Infected Hepatitis B (I_2). The initial condition of the first scenario and its unsafe value can be seen in Fig. 1.

The initial condition of the second scenario is taken from the initial condition of the first scenario but the observed sub population is 20%. The initial condition of the third scenario is taken from the initial condition of scenario 1 but the observed sub population is lowered by 20% and unsafe conditions are still obtained from the initial two conditions. Numerical completion to optimize the system in this mass is completed using flow star with parameter value can be from [2], along with the parameter value of the system from this research.

After a safety trait verification calculation using Flow* is obtained, the E_1 for the first scenario from start to finish down. The number E_1 is down from the initial number of 1000-1050 to close to the value of 0. The image shows the number does not reach twice the initial amount. Therefore, the result is that the system satisfies the safety specification or the system is safe. The E_1 plot in the first scenario can be seen in Fig. 3.

The results of the next research are sub population E_2 . The resulting plot for E_2 can be seen in Fig. 4.

The result of the image can E_2 from start to finish down. The E_2 is down from the initial number of 150-200 to close to the value of 0. The image shows the number does not

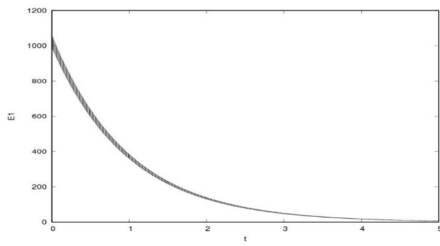


Fig. 3. The result of E_1 plot in the first scenario with a time of five years.

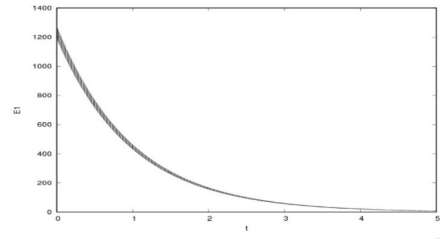


Fig. 7. The result of E_1 plot in the second scenario with a time of five years.

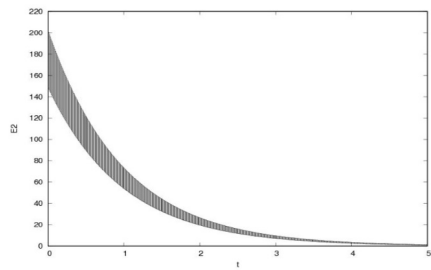


Fig. 4. The result of E_2 plot in the first scenario with a time of five years.

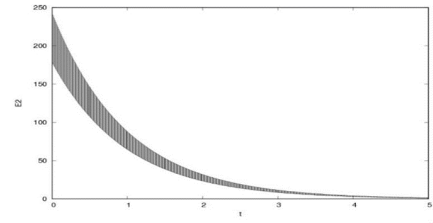


Fig. 8. The result of E_2 plot in the second scenario with a time of five years.

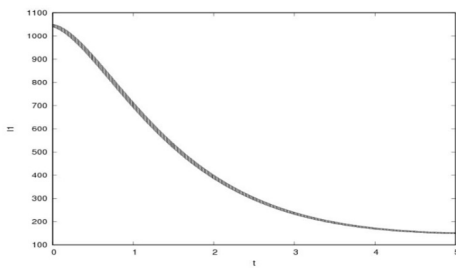


Fig. 5. The result of I_1 plot in the first scenario with a time of five years.

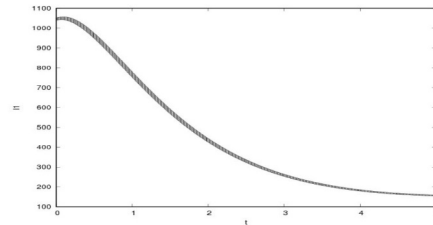


Fig. 9. The result of I_1 plot in the second scenario with a time of five years.

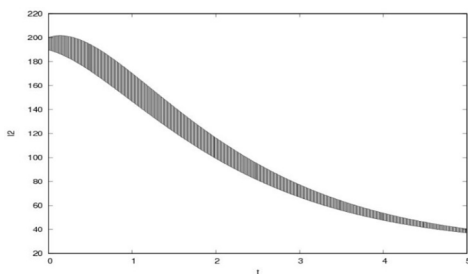


Fig. 6. The result of plot I_2 in the first scenario with a time of five years.

reach twice the initial amount, therefore the system is safe. The resulting plot of I_1 can be seen in Fig. 5.

The result of the image can I_1 from start to finish down. The number I_1 the population is down from the initial number of 1140 -1150 to 150-155. The image shows the number does not reach twice the initial amount, therefore the system is safe. The resulting plot I_2 can be seen in Fig. 6.

The results of the image can be seen that I_2 is initially constant a few months ago until the end went down. The number I_2 initially 190 -200 a few months ago dropped to the end of the year to 40-45. The image shows the number does not reach twice the initial amount, therefore the system

is safe. The second check is in the second scenario. The result of E_1 plot in the second scenario can be seen in Fig. 7.

The result of the image is that E_1 from start to finish down. The E_1 is down from the initial number of 1200-1260 to close to the value of 0. The image shows the number does not reach twice the initial amount, therefore the system is safe. The result of E_2 plot in the second scenario can be seen in Fig. 8.

The result of the image can E_2 from start to finish down. The number E_2 is down from the initial number of 180-240 to close to the value of 0. The image shows the number does not reach twice the initial amount, therefore the system is safe. The result of I_1 plot in the second scenario can be seen in Fig. 9.

The result of the image can I_1 from start to finish down. The I_1 the number of people down from the beginning was 1140-1150 to 160-165. The image shows the number does not reach twice the initial amount, therefore the system is safe. The result I_2 the second scenario can be seen in Fig. 10.

The result of the image can be I_2 initially only rose slightly a few months ago until the end of the fall. The I_2 initially 190-200 rose slightly in the months to 195-210 then dropped by the end of the year to 40-45. The image shows the number does not reach twice the initial amount, therefore the system is safe. The third check is in scenario 3, the result of the plot E_1 the third scenario can be seen in Fig. 11.

The result of the image can E_1 from start to finish down. The E_1 is down from a starting number of 800-840 to close

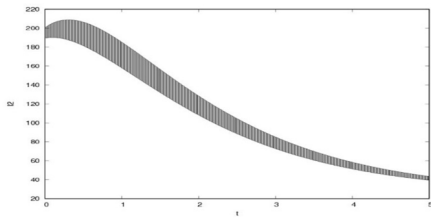


Fig. 10. The result of I_2 plot in the second scenario with a time of five years.

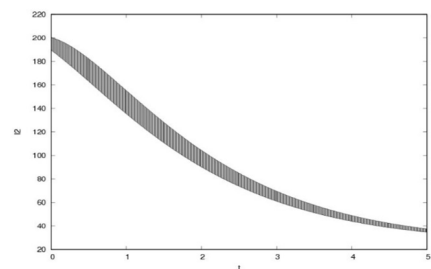


Fig. 14. The result of I_2 plot in the third scenario with a time of five years.

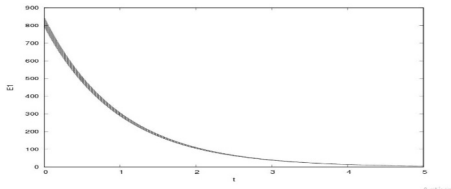


Fig. 11. The result of E_1 plot in the third scenario with a time of five years.

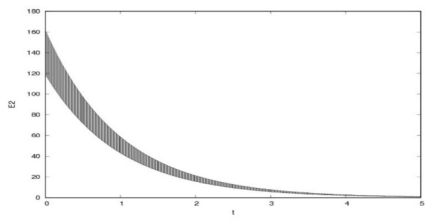


Fig. 12. The result of E_2 plot in the third scenario with a time of five years.

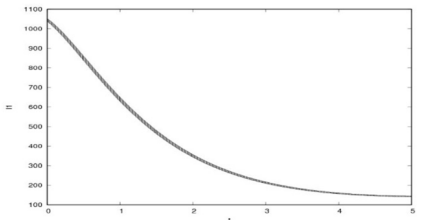


Fig. 13. The result of I_1 plot in the third scenario with a time of five years.

to 0. The image shows the number does not reach twice the initial amount, therefore the system is safe. The result of E_2 plot in the third scenario can be seen in Fig. 12.

The result of the image can E_2 from start to finish down. The number E_2 is down from the initial number of 120-160 to close to the value of 0. The image shows the number does not reach twice the initial amount, therefore the system is safe. The result of I_1 plot in the third scenario can be seen in Fig. 13.

The result of the image can I_1 from start to finish down. The I_1 the number of people down from the beginning was 1140-1150 to 140-145. The image shows the number does not reach twice the initial amount, therefore the system is safe. The result I_2 in third scenario can be seen in Fig. 14.

The result of the image can be I_2 the beginning to the end of the drop. The I_2 is initially 190-200 then dropped until the end of the year to 33-38. The image shows the number does not reach twice the initial amount, therefore the system is safe.

TABLE I
RUNNING TIME AND VERIFICATION RESULTS OF EACH SCENARIO

No	Initial condition	Running time	Verification time	Verification results
1	First scenario	72 s	1.9 s	safe
2	Second scenario	71 s	1.9 s	safe
3	Third scenario	66 s	1.9 s	safe

IV. CONCLUSIONS

The results of safety verification of four subpopulations E_1 , E_2 , I_1 , I_2 are described in Table I. The verification result of these three scenarios is that it is safe or not to be an outbreak of the disease for either the E_1 , E_2 , I_1 sub-population or the I_2 .

REFERENCES

- [1] X. Chen, S. Dutta, and S. Sankaranarayanan, "Formal verification of a multi-basal insulin infusion control model." in *ARCH@ CPSWeek, 2017*, pp. 75-91.
- [2] A. Zuhriah, "Analisa dinamik dari model matematika rekombinasi antara hiv dan virus hepatitis b," Master's thesis, Institut Teknologi Sepuluh Nopember, 2016.
- [3] X. Chen, "Reachability analysis of non-linear hybrid systems using taylor models," Ph.D. dissertation, Fachgruppe Informatik, RWTH Aachen University, 2015.