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Mean Latin Hypercube Runge-Kutta Method to Solve the Influenza Model

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Abstract

In this study, we propose a suitable solution for a non-linear system of ordinary differential equations (ODE) of the first order with the initial value problems (IVP) that contains multi variables and multi-parameters with missing real data. To solve the mentioned system, a new modified numerical simulation method is created for the first time which is called Mean Latin Hypercube Runge-Kutta (MLHRK). This method can be obtained by combining the Runge-Kutta (RK) method with the statistical simulation procedure which is the Latin Hypercube Sampling (LHS) method. The present work is applied to the influenza epidemic model in Australia in 1919 for a previous study. The comparison between the numerical and numerical simulation results is done, discussed and tabulated. The behavior of subpopulations is shown graphically. MLHRK method can reduce the number of numerical iterations of RK, and the number of LHS simulations, thus it saves time, effort, and cost. As well as it is a faster simulation over the distribution of the LHS. The MLHRK method has been proven to be effective, reliable, and convergent to solve a wide range of linear and nonlinear problems. The proposed method can predict the future behavior of the population under study in analyzing the behavior of some epidemiological models.

Keywords: Nonlinear system of ordinary differential equations, Epidemic model, Runge-Kutta (RK) method, Latin Hypercube Sampling (LHS) method, Numerical simulation methods.

طريقة متوسط المكعب اللاتيني رونكا كوتا لحل نموذج الانفلونزا

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الخلاصة

في هذه الدراسة تم افتراض الحل المناسب لنظام غير خطي من المعادلات التفاضلية الاعتيادية (ODE) من الدرجة الأولى مع مسائل القيم الابتدائية (IVP) التي تحتوي على متغيرات متعددة ومعلمات متعددة مقدرة. لحل النظام المذكور، تم إنشاء طريقة محاكاة عددية جديدة معدلة تسمى (Mean Latin Hypercube Runge-Kutta) لأول مرة. يمكن الحصول على الطريقة المذكورة من خلال الجمع بين طريقة Runge-Kutta (RK) مع إجراء المحاكاة الإحصائية وهو طريقة أخذ عينات المكعب اللاتيني (LHS). تم تطبيق العمل الحالي على نموذج وباء الأنفلونزا في أستراليا عام 1919 لدراسة سابقة. تم إجراء المقارنة بين نتائج المحاكاة العددية والعديدية ومناقشتها وجدولتها. يظهر سلوك الوباء في المجتمع بيانياً.

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يمكن أن تقلل طريقة MLHRK من عدد التكرارات العددية لـ RK ، وعدد عمليات محاكاة LHS ، وبالتالي توفر الوقت والجهد والتكلفة. كذلك ، إنها محاكاة أسرع لتوزيع LHS. لقد ثبت أن طريقة MLHRK فعالة وموثوقة ومقاربة لحل مجموعة واسعة من المشكلات الخطية وغير الخطية. يمكن للطريقة المقترحة التنبؤ بالسلوك المستقبلي للسكان قيد الدراسة في تحليل سلوك بعض النماذج الوبائية.

1. Introduction:

The differential equation is very useful for modeling, simulating phenomena and understanding how the natural problem can be formulated not just a value or a set of values, but a function or a class of functions.

The problem of the present study, multi-parameters of the non-linear system of ordinary differential equations (ODE) with missing their real data is that matter needs to solve the system and to estimate their parameters in the same time. Epidemic refers to an increasing in the number of disease cases in the population of a particular region such as influenza, cholera, measles, malaria and others. The epidemic may be in one place, however if it spreads to other countries and it affects a large number of people, it may be called a pandemic. Two kinds of epidemic models social and biology epidemic models. The study of epidemiology has spread significantly; the problem was studied by several authors such as study the fitting curve of the influenza epidemic in Australia in 1919 [1]. 50-100 million deaths people were recorded who have been affected by the influenza epidemic that means the influenza epidemic is a global epidemic that is spreading very quickly across the world and infecting much of the population. Estimation of outstanding claims liability and sensitivity analysis. Herlambang and Tampubolon in 2008 studied estimation of outstanding claim liability and sensitivity analysis. probabilistic trend family (PTE) model [2]. Mutaqin, et al. in 2008 studied generating claim data of general insurance based on collective risk model and claim process [3]. Asmawati and Juliana in 2008 studied Combining individual learning ,and group discussion in calculus course [4]. Kinyanjui, et al. in 2015 studied Vaccine induced herd immunity for control of respiratory syncytial virus disease in a low-income country setting [5]. Beauparlant in 2016 studied a metapopulation model for the spread of *MRSA* in correctional facilities [6]. Leung, et al. in 2016 studied periodic solutions in a *SIRWS* model with immune boosting and cross-immunity [7]. Pei, et al. in 2019 studied predictability in process-based ensemble forecast of influenza [8]. The social epidemic problems attracted a lot of attention and was studied by several authors such as Sabaa, et al. studied approximate solutions for alcohol consumption model in Spain in 2019 [9]. Many authors proposed Runge-Kutta numerical method to solve the social epidemic models. Mohammed et al. discussed numerical solution for weight reduction model due to health campaigns in Spain in 2015 [10]. Sabaa and Mohammed in 2020 studied approximate solutions of nonlinear smoking habit model [11].

To produce data for the parameters of a real model random numbers are usually created in a sequence by a specific code for some programs in computer to generate them, this process is called simulation. In our study simulations process (LHS) is used. Elsevier and AB McBratney studied a conditioned Latin hypercube method for sampling in the presence of ancillary information in 2006 [12]. One of the statistical tasks is to determine the appropriate sample size for the study because this statistic largely depends on the sample size [10]. Inevitable epidemiological models are represented as a non-linear system of differential equations that have parameters missing their real data. These models are solved using a simulation approach to evaluate random parameters for deterministic epidemiological models that have specific distribution and approximate their solutions. The statistical simulations process (LHS) run multiple times to simulate the parameter values, then estimated parameters are combined with a reliable numerical method to be a numerical simulation method to simulate the parameter values to solve the influenza epidemic problem under study. Some authors solved the social epidemic models by numerical simulation methods such that

Mohammed, et al. in 2018 discussed the non-conventional hybrid numerical approach with multi-dimensional random sampling for cocaine abuse in Spain [13]. Mohammed, et al. in 2019 discussed Mean Monte Carlo finite difference method for random sampling of a nonlinear epidemic system [14]. Sabaa in 2019 proposed modified numerical simulation methods Mean Monte Carlo Runge-Kutta that was applied to two the social epidemic models, namely nonlinear smoking habit, and alcohol consumption model [15].

This research is arranged as follows: in Section 2, the mathematical model of an influenza epidemic is described. Statistical technique: Latin hypercube sampling (*LHS*) to simulate model's parameters is introduced in Section 3. In Section 4, numerical methods (Runge-Kutta) are presented. In Section 5, the modified process which is Mean Latin Hypercube Runge-Kutta (*MLHRK*) method is constructed as a suitable numerical simulation method to applied on the influenza epidemic model. In Section 6, the results of the current methods are discussed and shown tabulary and graphically the influenza epidemic model under study, the version (9.0) for *MATLAB* R2016a is used to obtain the results of the influenza epidemic model which is the present application. Finally, some conclusions for outcomes are mentioned in Section 7.

2. Mathematical Model:

Modeling is an important and powerful tool for understanding the effects and transmission of epidemic diseases [16]. Mathematical models are used to plan, implementation, comparison, evaluation, prevention, treatment, and other matters [17]. The mathematical models describe different processes in mathematics, physics, and biology [18]. The modeling requires an initial effort to reduce complexity. Examining the model is important to prevent the spread of the epidemic. The system consists four equations, and four variables which are $S(t)$, $E(t)$, $I(t)$, $R(t)$ represent healthy persons, infected persons that does not cause infection, the person is in the incubation period, infected persons and the cause infection after in the incubation period the persons who recover or die. So that our model is made (*SEIR*) with eight parameters $\beta, \mu, r, \delta, \sigma, \kappa, \alpha, \gamma$ that connect variables. The *SEIR* model is used to study disease progression and to obtain some estimates and comparisons [19]. The influenza model was introduced as a system of the first order nonlinear ordinary differential equations in equations (1-4):

$$S'(t) = -\beta \frac{IS}{N} - \mu S + rN + \delta R, \quad (1)$$

$$E'(t) = \beta \frac{IS}{N} - (\mu + \sigma + \kappa)E, \quad (2)$$

$$I'(t) = \sigma E - (\mu + \alpha + \gamma)I, \quad (3)$$

$$R'(t) = \kappa E + \gamma I - \mu R - \delta R. \quad (4)$$

Table 1. describes the variables of influenza model $S(t), E(t), I(t), R(t)$, and Table 2. describes the parameters of influenza model $\beta, \mu, r, \delta, \sigma, \kappa, \alpha, \gamma$, the initial conditions (random variables) of equations (1-4) are as follows : $S_0 = 4865.0000$, $E_0 = 9.0000000$, $I_0 = 68.000000$, $R_0 = 0.0000000$ for first wave, $S_0 = 0.3982$, $E_0 = 0.000010$, $I_0 = 0.000079$, $R_0 = 0.0000000$ for second wave, N is the total population such that $N = S + E + I + R$, and the time period is specified in days; (0,70) was used to obtain results by Samsuzzoha, Manmohan Singh and David Lucy [1].

Table 1- Description of variables for the influenza model, [1]

Variables	Description
$S(t)$	Proportion of susceptible population
$E(t)$	Proportion of exposed population
$I(t)$	Proportion of infective population
$R(t)$	Proportion of recovered population

Table 2- Description of parameters for the influenza model, [1]

Parameters	Description	Value of parameters
β	Contact rate	0.5020000
μ	Natural mortality rate	0.0003671
r	Birth rate	0.0006762
δ	Duration of immunity loss	0.0027400
σ	Mean duration of latency	0.6990000
κ	Recovery rate of latent	0.0001500
α	Flu induced mortality rate	0.0300000
γ	Mean recovery time for clinically ill	0.3600000

3. Methodology

In this section, statistical method (*LHS*) is used to simulate the model's parameters, numerical methods (*RK*) and modified numerical simulation method (*MLHRK*) is used to solve the system numerically and approximately.

3.1 Latin Hypercube Sampling (*LHS*) Technique

Latin Hypercube Sampling is one of the known stratified statistical methods and type of stratified sampling that used to generate random samples for a multidimensional random distribution of a multidimensional model over the certain period in present study. It is fast method, and it is efficiency method that saves effort and time with a small number of sample elements. The results can be accurately reached. The sampling methods are different in the time and the results obtained. *LHS* is an appropriate method to solve any system because the system is made up of multiple variables and parameters to solve, therefore a stratif sampling becomes necessary. *LHS* provides more accurate, better simulation results and closer to the statistical values even if the number of iterations is few because it is often faster to reach a good representation of the probability distribution.

The name *LHS* is Latin squares sampling that $N \times N$ arrays contain various elements. Each element in a Latin square exactly occurs once in each row and column. The elements occur

once in each hyperplane when the *LHS* concept is applied to a multidimensional setting to make up a Latin hypercube. Each layer is represented by the elements in the hypercube, the layer is divided into equal intervals $[\frac{1}{N-1}, \frac{1}{N}]$ based on the number of samples required [20]. Before using this method we must create the random numbers then we create a sample that has a uniform distribution, after that we specify the number of simulations [21]. In addition *LHS* remember in which row and column the specific sample was taken, this is called a system mentioned in the approach compared with the rest of the methods such as *MC* it needs a large number of iterations in order to provide accurate simulation results because the sample comes from anywhere to distribute the inputs so this is without memory in the approach. Therefore it is sometimes inactive. *LHS* distributes the sample values even in small areas, while *MC* distributes the samples in large areas, and without cutting so that the *LHS* method is better than *MC* method [9, 19, 20].

3.2 Runge-Kutta (*RK*) Numerical Method

Runge-Kutta is one of the most famous multi-stage methods. Runge-Kutta techniques had been introduced around 1900 by C. Runge and M. W. Kutta. Runge-Kutta is an effective, iterative numerical method consisting of several stages, the arrangement of the method is determined by the number of stages, this method can be applied to the ordinary, partial, explicit, implicit, delaying differential equations etc [22]. It is easy to understand and implement. Runge-Kutta generates a series of approximate solutions converging to the exact solution. Runge-Kutta plays a major role in many branch of science, engineering and economics that frequently contain mathematical models of ordinary differential equations [23]. In our study, *RK* method is used to solve the nonlinear system of an influenza model of the first order *ODE* for initial value problems. Two types of Runge-Kutta numerical methods have been used.

3.2.1 Runge-Kutta of order four (*RK*₄):

Runge-Kutta of order four (*RK*₄) is suggested an approximation for solving the system of non-linear ordinary differential equations (*ODE*) of the first order with the initial value problem (*IVP*). The *RK*₄ is a numerical method that gives more accurate results than some other numerical methods such as Finite Difference (*FD*) method.

The general form of the first order for ordinary differential equation (*ODE*) can be written as follows:

$$y' = f(t, y), \quad a \leq t \leq b, \quad \text{with initial value } y(a) = a_0,$$

where f is nonlinear function, y is the dependent variable, t is the independent variable while a, b and a_0 are positive real constant values.

The most common form of the four-stage of the explicit *RK* method [23] is:

$$k_1 = hf_1(t_i, y_i) \tag{5}$$

$$k_2 = hf_2(t_i + \frac{h}{2}, y_i + \frac{k_1}{2}) \tag{6}$$

$$k_3 = hf_3(t_i + \frac{h}{2}, y_i + \frac{k_2}{2}) \tag{7}$$

$$k_4 = hf_4(t_i + h, y_i + k_3) \tag{8}$$

The general formula of y_{i+1} for the *RK*₄ method is

$$y_{i+1} = y_i + \frac{1}{6}(k_1 + 2k_2 + 2k_3 + k_4) \tag{9}$$

where f_1, f_2, f_3, f_4 are unknown function, t is a time and h is a step size

The most common form of the four-stage of the implicit *RK* method [23] is:

$$k_1 = f_1(t_i, y_i) \tag{10}$$

$$k_2 = f_2(t_i + \frac{h}{2}, y_i + \frac{hk_1}{2}) \tag{11}$$

$$k_3 = f_3(t_i + \frac{h}{2}, y_i + \frac{hk_2}{2}) \tag{12}$$

$$k_4 = f_4(t_i + h, y_i + hk_3) \tag{13}$$

The general formula of y_{i+1} for the RK_4 method is

$$y_{i+1} = y_i + \frac{h}{6} (k_1 + 2k_2 + 2k_3 + k_4) \tag{14}$$

where f_1, f_2, f_3, f_4 are unknown function, t is a time and h is a step size.

Now, to find k_{S1}, k_{E1}, k_{I1} and k_{R1} , we following the next steps in equations (10-14).

$$k_{S1} = hf_1(t_i, S_i, E_i, I_i, R_i) = h \left(\frac{-\beta}{N} I_i S_i - \mu S_i + rN + \delta R_i \right), \tag{15}$$

$$k_{E1} = hf_2(t_i, S_i, E_i, I_i, R_i) = h \left(\frac{\beta}{N} I_i S_i - (\mu + \sigma + \kappa) E_i \right), \tag{16}$$

$$k_{I1} = hf_3(t_i, S_i, E_i, I_i, R_i) = h (\sigma E_i - (\mu + \alpha + \gamma) I_i), \tag{17}$$

$$k_{R1} = hf_4(t_i, S_i, E_i, I_i, R_i) = h (\kappa E_i + \gamma I_i - \mu R_i - \delta R_i). \tag{18}$$

where $i = 0, 1, \dots, n - 1$.

In the same way, k_{S2}, k_{E2}, k_{I2} and k_{R2} can be found to obtain the second step in equations (15-18) where f_1, f_2, f_3, f_4 are unknown functions, t is a time and h is a step size:

$$k_{S2} = hf_1 \left(t_i + \frac{h}{2}, S_i + \frac{1}{2} k_{S1}, E_i + \frac{1}{2} k_{E1}, I_i + \frac{1}{2} k_{I1}, R_i + \frac{1}{2} k_{R1} \right) = h \left(\frac{-\beta}{N} \left(I_i + \frac{1}{2} k_{I1} \right) \left(S_i + \frac{1}{2} k_{S1} \right) - \mu \left(S_i + \frac{1}{2} k_{S1} \right) + rN + \delta \left(R_i + \frac{1}{2} k_{R1} \right) \right), \tag{19}$$

$$k_{E2} = hf_2 \left(t_i + \frac{h}{2}, S_i + \frac{1}{2} k_{S1}, E_i + \frac{1}{2} k_{E1}, I_i + \frac{1}{2} k_{I1}, R_i + \frac{1}{2} k_{R1} \right) = h \left(\frac{\beta}{N} \left(I_i + \frac{1}{2} k_{I1} \right) \left(S_i + \frac{1}{2} k_{S1} \right) - (\mu + \sigma + \kappa) \left(E_i + \frac{1}{2} k_{E1} \right) \right), \tag{20}$$

$$k_{I2} = hf_3 \left(t_i + \frac{h}{2}, S_i + \frac{1}{2} k_{S1}, E_i + \frac{1}{2} k_{E1}, I_i + \frac{1}{2} k_{I1}, R_i + \frac{1}{2} k_{R1} \right) = h \left(\sigma \left(E_i + \frac{1}{2} k_{E1} \right) - (\mu + \alpha + \gamma) \left(I_i + \frac{1}{2} k_{I1} \right) \right), \tag{21}$$

$$k_{R2} = hf_4 \left(t_i + \frac{h}{2}, S_i + \frac{1}{2} k_{S1}, E_i + \frac{1}{2} k_{E1}, I_i + \frac{1}{2} k_{I1}, R_i + \frac{1}{2} k_{R1} \right) = h \left(\kappa \left(E_i + \frac{1}{2} k_{E1} \right) + \gamma \left(I_i + \frac{1}{2} k_{I1} \right) - \mu \left(R_i + \frac{1}{2} k_{R1} \right) - \delta \left(R_i + \frac{1}{2} k_{R1} \right) \right). \tag{22}$$

where $i = 0, 1, \dots, n - 1$.

In the third stage, we try to find k_{S3}, k_{E3}, k_{I3} and k_{R3} by substituting in the system (1) as below in equations (19-22) where f_1, f_2, f_3, f_4 are unknown functions, t is a time and h is a step size:

$$k_{S3} = hf_1 \left(t_i + \frac{h}{2}, S_i + \frac{1}{2} k_{S2}, E_i + \frac{1}{2} k_{E2}, I_i + \frac{1}{2} k_{I2}, R_i + \frac{1}{2} k_{R2} \right) = h \left(\frac{-\beta}{N} \left(I_i + \frac{1}{2} k_{I2} \right) \left(S_i + \frac{1}{2} k_{S2} \right) - \mu \left(S_i + \frac{1}{2} k_{S2} \right) + rN + \delta \left(R_i + \frac{1}{2} k_{R2} \right) \right), \tag{23}$$

$$k_{E3} = hf_2 \left(t_i + \frac{h}{2}, S_i + \frac{1}{2} k_{S2}, E_i + \frac{1}{2} k_{E2}, I_i + \frac{1}{2} k_{I2}, R_i + \frac{1}{2} k_{R2} \right) = h \left(\frac{\beta}{N} \left(I_i + \frac{1}{2} k_{I2} \right) \left(S_i + \frac{1}{2} k_{S2} \right) - (\mu + \sigma + \kappa) \left(E_i + \frac{1}{2} k_{E2} \right) \right), \tag{24}$$

$$k_{I3} = hf_3 \left(t_i + \frac{h}{2}, S_i + \frac{1}{2} k_{S2}, E_i + \frac{1}{2} k_{E2}, I_i + \frac{1}{2} k_{I2}, R_i + \frac{1}{2} k_{R2} \right) = h \left(\sigma \left(E_i + \frac{1}{2} k_{E2} \right) - (\mu + \alpha + \gamma) \left(I_i + \frac{1}{2} k_{I2} \right) \right), \tag{25}$$

$$k_{R3} = hf_4 \left(t_i + \frac{h}{2}, S_i + \frac{1}{2} k_{S2}, E_i + \frac{1}{2} k_{E2}, I_i + \frac{1}{2} k_{I2}, R_i + \frac{1}{2} k_{R2} \right) = h \left(\kappa \left(E_i + \frac{1}{2} k_{E2} \right) + \gamma \left(I_i + \frac{1}{2} k_{I2} \right) - \mu \left(R_i + \frac{1}{2} k_{R2} \right) - \delta \left(R_i + \frac{1}{2} k_{R2} \right) \right). \tag{26}$$

where $i = 0, 1, \dots, n - 1$.

The fourth stage needs to find k_{S4}, k_{E4}, k_{I4} and k_{R4} as below, in equations (23-26) where f_1, f_2, f_3, f_4 are unknown functions, t is a time and h is a step size:

$$k_{S4} = hf_1(t_i + h, S_i + k_{S3}, E_i + k_{E3}, I_i + k_{I3}, R_i + k_{R3})$$

$$= h \left(\frac{-\beta}{N} (I_i + k_{I3})(S_i + k_{S3}) - \mu(S_i + k_{S3}) + rN + \delta(R_i + k_{R3}) \right), \tag{27}$$

$$k_{E4} = hf_2(t_i + h, S_i + k_{S3}, E_i + k_{E3}, I_i + k_{I3}, R_i + k_{R3})$$

$$= h \left(\frac{\beta}{N} (I_i + k_{I3})(S_i + k_{S3}) - (\mu + \sigma + \kappa)(E_i + k_{E3}) \right), \tag{28}$$

$$k_{I4} = hf_3(t_i + h, S_i + k_{S3}, E_i + k_{E3}, I_i + k_{I3}, R_i + k_{R3})$$

$$= h \left(\sigma(E_i + k_{E3}) - (\mu + \alpha + \gamma)(I_i + k_{I3}) \right), \tag{29}$$

$$k_{R4} = hf_4(t_i + h, S_i + k_{S3}, E_i + k_{E3}, I_i + k_{I3}, R_i + k_{R3})$$

$$= h \left(\kappa(E_i + k_{E3}) + \gamma(I_i + k_{I3}) - \mu(R_i + k_{R3}) - \delta(R_i + k_{R3}) \right). \tag{30}$$

where $i = 0, 1, \dots, n - 1$.

3.2.2 Runge-Kutta of order four (RK₄₅):

Runge-Kutta of order four (RK₄₅) is presented an approximation for solving the system of non-linear ordinary differential equations (ODE) of the first order with the initial value problem (IVP). It is a suitable method to obtain stable results.

The most common form of the six-stage of the explicit RK method is:

$$k_1 = hf_1(t_i, y_i) \tag{31}$$

$$k_2 = hf_2\left(t_i + \frac{h}{4}, y_i + \frac{k_1}{4}\right) \tag{32}$$

$$k_3 = hf_3\left(t_i + \frac{3h}{8}, y_i + \frac{3k_1}{32} + \frac{9k_2}{32}\right) \tag{33}$$

$$k_4 = hf_4\left(t_i + \frac{12h}{13}, y_i + \frac{1932k_1}{2197} - \frac{7200k_2}{2197} + \frac{7296k_3}{2197}\right) \tag{34}$$

$$k_5 = hf_5\left(t_i + h, y_i + \frac{439k_1}{219} - 8k_2 + \frac{3680k_3}{513} - \frac{845k_4}{4104}\right) \tag{35}$$

$$k_6 = hf_6\left(t_i + \frac{h}{2}, y_i - \frac{8k_1}{27} + 2k_2 - \frac{3544k_3}{2565} + \frac{1859k_4}{4104} - \frac{11k_5}{40}\right) \tag{36}$$

The general formula of y_{i+1} for the RK₄ method is

$$y_{i+1} = y_i + \frac{25k_1}{216} + \frac{1408k_3}{2565} + \frac{2197k_4}{4104} - \frac{1k_5}{5} \tag{37}$$

where $f_1, f_2, f_3, f_4, f_5, f_6$ are unknown function, t is a time and h is a step size.

Now, To find k_{S1}, k_{E1}, k_{I1} and k_{R1} , we following the next steps in equations (38-41) where f_1, f_2, f_3, f_4 are unknown functions, t is a time and h is a step size:

$$k_{S1} = hf_1(t_i, S_i, E_i, I_i, R_i)$$

$$= h \left(\frac{-\beta}{N} I_i S_i - \mu S_i + rN + \delta R_i \right), \tag{38}$$

$$k_{E1} = hf_2(t_i, S_i, E_i, I_i, R_i)$$

$$= h \left(\frac{\beta}{N} I_i S_i - (\mu + \sigma + \kappa) E_i \right), \tag{39}$$

$$k_{I1} = hf_3(t_i, S_i, E_i, I_i, R_i)$$

$$= h \left(\sigma E_i - (\mu + \alpha + \gamma) I_i \right), \tag{40}$$

$$k_{R1} = hf_4(t_i, S_i, E_i, I_i, R_i)$$

$$= h \left(\kappa E_i + \gamma I_i - \mu R_i - \delta R_i \right). \tag{41}$$

where $i = 0, 1, \dots, n - 1$.

In the same way, k_{S2}, k_{E2}, k_{I2} and k_{R2} can be found to obtain the second step in equations (42-45) where f_1, f_2, f_3, f_4 are unknown functions, t is a time and h is a step size:

$$k_{S2} = hf_1\left(t_i + \frac{h}{4}, S_i + \frac{1}{4}k_{S1}, E_i + \frac{1}{4}k_{E1}, I_i + \frac{1}{4}k_{I1}, R_i + \frac{1}{4}k_{R1}\right)$$

$$= h \left(\frac{-\beta}{N} \left(I_i + \frac{1}{4}k_{I1} \right) \left(S_i + \frac{1}{4}k_{S1} \right) - \mu \left(S_i + \frac{1}{4}k_{S1} \right) + rN + \delta \left(R_i + \frac{1}{4}k_{R1} \right) \right), \tag{42}$$

$$k_{E2} = hf_2\left(t_i + \frac{h}{4}, S_i + \frac{1}{4}k_{S1}, E_i + \frac{1}{4}k_{E1}, I_i + \frac{1}{4}k_{I1}, R_i + \frac{1}{4}k_{R1}\right)$$

$$= h \left(\frac{\beta}{N} \left(I_i + \frac{1}{4} k_{I1} \right) \left(S_i + \frac{1}{4} k_{S1} \right) - (\mu + \sigma + \kappa) \left(E_i + \frac{1}{4} k_{E1} \right) \right), \tag{43}$$

$$k_{I2} = hf_3 \left(t_i + \frac{h}{4}, S_i + \frac{1}{4} k_{S1}, E_i + \frac{1}{4} k_{E1}, I_i + \frac{1}{4} k_{I1}, R_i + \frac{1}{4} k_{R1} \right) \\ = h \left(\sigma \left(E_i + \frac{1}{4} k_{E1} \right) - (\mu + \alpha + \gamma) \left(I_i + \frac{1}{4} k_{I1} \right) \right), \tag{44}$$

$$k_{R2} = hf_4 \left(t_i + \frac{h}{4}, S_i + \frac{1}{4} k_{S1}, E_i + \frac{1}{4} k_{E1}, I_i + \frac{1}{4} k_{I1}, R_i + \frac{1}{4} k_{R1} \right) \\ = h \left(\kappa \left(E_i + \frac{1}{4} k_{E1} \right) + \gamma \left(I_i + \frac{1}{4} k_{I1} \right) - \mu \left(R_i + \frac{1}{4} k_{R1} \right) - \delta \left(R_i + \frac{1}{4} k_{R1} \right) \right). \tag{45}$$

where $i = 0, 1, \dots, n - 1$.

In the third stage, try to find k_{S3}, k_{E3}, k_{I3} and k_{R3} by substituting in the system (1) as below in equations (46-49) where f_1, f_2, f_3, f_4 are unknown functions, t is a time and h is a step size:

$$k_{S3} = hf_1 \left(t_i + \frac{3h}{8}, S_i + \frac{3}{32} k_{S1} + \frac{9}{32} k_{S2}, E_i + \frac{3}{32} k_{E1} + \frac{9}{32} k_{E2}, I_i + \frac{3}{32} k_{I1} + \frac{9}{32} k_{I2}, R_i + \frac{3}{32} k_{R1} + \frac{9}{32} k_{R2} \right) \\ = h \left(\frac{-\beta}{N} \left(I_i + \frac{3}{32} k_{I1} + \frac{9}{32} k_{I2} \right) \left(S_i + \frac{3}{32} k_{S1} + \frac{9}{32} k_{S2} \right) - \mu \left(S_i + \frac{3}{32} k_{S1} + \frac{9}{32} k_{S2} \right) + rN + \delta \left(R_i + \frac{3}{32} k_{R1} + \frac{9}{32} k_{R2} \right) \right), \tag{46}$$

$$k_{E3} = hf_2 \left(t_i + \frac{3h}{8}, S_i + \frac{3}{32} k_{S1} + \frac{9}{32} k_{S2}, E_i + \frac{3}{32} k_{E1} + \frac{9}{32} k_{E2}, I_i + \frac{3}{32} k_{I1} + \frac{9}{32} k_{I2}, R_i + \frac{3}{32} k_{R1} + \frac{9}{32} k_{R2} \right) \\ = h \left(\frac{\beta}{N} \left(I_i + \frac{3}{32} k_{I1} + \frac{9}{32} k_{I2} \right) \left(S_i + \frac{3}{32} k_{S1} + \frac{9}{32} k_{S2} \right) - (\mu + \sigma + \kappa) \left(E_i + \frac{3}{32} k_{E1} + \frac{9}{32} k_{E2} \right) \right), \tag{47}$$

$$k_{I3} = hf_3 \left(t_i + \frac{3h}{8}, S_i + \frac{3}{32} k_{S1} + \frac{9}{32} k_{S2}, E_i + \frac{3}{32} k_{E1} + \frac{9}{32} k_{E2}, I_i + \frac{3}{32} k_{I1} + \frac{9}{32} k_{I2}, R_i + \frac{3}{32} k_{R1} + \frac{9}{32} k_{R2} \right) \\ = h \left(\sigma \left(E_i + \frac{3}{32} k_{E1} + \frac{9}{32} k_{E2} \right) - (\mu + \alpha + \gamma) \left(I_i + \frac{3}{32} k_{I1} + \frac{9}{32} k_{I2} \right) \right), \tag{48}$$

$$k_{R3} = hf_4 \left(t_i + \frac{3h}{8}, S_i + \frac{3}{32} k_{S1} + \frac{9}{32} k_{S2}, E_i + \frac{3}{32} k_{E1} + \frac{9}{32} k_{E2}, I_i + \frac{3}{32} k_{I1} + \frac{9}{32} k_{I2}, R_i + \frac{3}{32} k_{R1} + \frac{9}{32} k_{R2} \right) \\ = h \left(\kappa \left(E_i + \frac{3}{32} k_{E1} + \frac{9}{32} k_{E2} \right) + \gamma \left(I_i + \frac{3}{32} k_{I1} + \frac{9}{32} k_{I2} \right) - \mu \left(R_i + \frac{3}{32} k_{R1} + \frac{9}{32} k_{R2} \right) - \delta \left(R_i + \frac{3}{32} k_{R1} + \frac{9}{32} k_{R2} \right) \right). \tag{49}$$

where $i = 0, 1, \dots, n - 1$.

The fourth stage needs to find k_{S4}, k_{E4}, k_{I4} and k_{R4} as below, in equations (50-53) where f_1, f_2, f_3, f_4 are unknown functions, t is a time and h is a step size:

$$k_{S4} = hf_1 \left(t_i + \frac{12h}{13}, S_i + \frac{1932}{2197} k_{S1} - \frac{7200}{2197} k_{S2} + \frac{7296}{2197} k_{S3}, E_i + \frac{1932}{2197} k_{E1} - \frac{7200}{2197} k_{E2} + \frac{7296}{2197} k_{E3}, I_i + \frac{1932}{2197} k_{I1} - \frac{7200}{2197} k_{I2} + \frac{7296}{2197} k_{I3}, R_i + \frac{1932}{2197} k_{R1} - \frac{7200}{2197} k_{R2} + \frac{7296}{2197} k_{R3} \right)$$

$$= h \left(\frac{-\beta}{N} \left(I_i + \frac{1932}{2197} k_{I1} - \frac{7200}{2197} k_{I2} + \frac{7296}{2197} k_{I3} \right) \left(S_i + \frac{1932}{2197} k_{S1} - \frac{7200}{2197} k_{S2} + \frac{7296}{2197} k_{S3} \right) - \mu \left(S_i + \frac{1932}{2197} k_{S1} - \frac{7200}{2197} k_{S2} + \frac{7296}{2197} k_{S3} \right) + rN + \delta \left(R_i + \frac{1932}{2197} k_{R1} - \frac{7200}{2197} k_{R2} + \frac{7296}{2197} k_{R3} \right) \right), \quad (50)$$

$$k_{E4} = hf_2 \left(t_i + \frac{12h}{13}, S_i + \frac{1932}{2197} k_{S1} - \frac{7200}{2197} k_{S2} + \frac{7296}{2197} k_{S3}, \right. \\ \left. E_i + \frac{1932}{2197} k_{E1} - \frac{7200}{2197} k_{E2} + \frac{7296}{2197} k_{E3}, I_i + \frac{1932}{2197} k_{I1} - \frac{7200}{2197} k_{I2} \right. \\ \left. + \frac{7296}{2197} k_{I3}, R_i + \frac{1932}{2197} k_{R1} - \frac{7200}{2197} k_{R2} + \frac{7296}{2197} k_{R3} \right) \\ = h \left(\frac{\beta}{N} \left(I_i + \frac{1932}{2197} k_{I1} - \frac{7200}{2197} k_{I2} + \frac{7296}{2197} k_{I3} \right) \left(S_i + \frac{1932}{2197} k_{S1} - \frac{7200}{2197} k_{S2} + \frac{7296}{2197} k_{S3} \right) - \right. \\ \left. (\mu + \sigma + \kappa) \left(E_i + \frac{1932}{2197} k_{E1} - \frac{7200}{2197} k_{E2} + \frac{7296}{2197} k_{E3} \right) \right), \quad (51)$$

$$k_{I4} = hf_3 \left(t_i + \frac{12h}{13}, S_i + \frac{1932}{2197} k_{S1} - \frac{7200}{2197} k_{S2} + \frac{7296}{2197} k_{S3}, \right. \\ \left. E_i + \frac{1932}{2197} k_{E1} - \frac{7200}{2197} k_{E2} + \frac{7296}{2197} k_{E3}, I_i + \frac{1932}{2197} k_{I1} - \frac{7200}{2197} k_{I2} \right. \\ \left. + \frac{7296}{2197} k_{I3}, R_i + \frac{1932}{2197} k_{R1} - \frac{7200}{2197} k_{R2} + \frac{7296}{2197} k_{R3} \right) \\ = h \left(\sigma \left(E_i + \frac{1932}{2197} k_{E1} - \frac{7200}{2197} k_{E2} + \frac{7296}{2197} k_{E3} \right) - (\mu + \alpha + \gamma) \left(I_i + \frac{1932}{2197} k_{I1} - \frac{7200}{2197} k_{I2} + \right. \right. \\ \left. \left. \frac{7296}{2197} k_{I3} \right) \right), \quad (52)$$

$$k_{R4} = hf_4 \left(t_i + \frac{12h}{13}, S_i + \frac{1932}{2197} k_{S1} - \frac{7200}{2197} k_{S2} + \frac{7296}{2197} k_{S3}, \right. \\ \left. E_i + \frac{1932}{2197} k_{E1} - \frac{7200}{2197} k_{E2} + \frac{7296}{2197} k_{E3}, I_i + \frac{1932}{2197} k_{I1} - \frac{7200}{2197} k_{I2} \right. \\ \left. + \frac{7296}{2197} k_{I3}, R_i + \frac{1932}{2197} k_{R1} - \frac{7200}{2197} k_{R2} + \frac{7296}{2197} k_{R3} \right) \\ = h \left(\kappa \left(E_i + \frac{1932}{2197} k_{E1} - \frac{7200}{2197} k_{E2} + \frac{7296}{2197} k_{E3} \right) + \gamma \left(I_i + \frac{1932}{2197} k_{I1} - \frac{7200}{2197} k_{I2} + \right. \right. \\ \left. \left. \frac{7296}{2197} k_{I3} \right) - \mu \left(R_i + \frac{1932}{2197} k_{R1} - \frac{7200}{2197} k_{R2} + \frac{7296}{2197} k_{R3} \right) - \delta \left(R_i + \frac{1932}{2197} k_{R1} - \frac{7200}{2197} k_{R2} + \right. \right. \\ \left. \left. \frac{7296}{2197} k_{R3} \right) \right). \quad (53)$$

where $i = 0, 1, \dots, n - 1$.

The fifth stage needs to find k_{S5}, k_{E5}, k_{I5} and k_{R5} As below, in equations (54-57) where f_1, f_2, f_3, f_4 are unknown functions, t is a time and h is a step size:

$$k_{S5} = hf_1 \left(t_i + h, S_i + \frac{439}{216} k_{S1} - 8k_{S2} + \frac{3680}{513} k_{S3} - \frac{845}{4104} k_{S4}, \right. \\ \left. E_i + \frac{439}{216} k_{E1} - 8k_{E2} + \frac{3680}{513} k_{E3} - \frac{845}{4104} k_{E4}, I_i + \frac{439}{216} k_{I1} - 8k_{I2} \right. \\ \left. + \frac{3680}{513} k_{I3} - \frac{845}{4104} k_{I4}, R_i + \frac{439}{216} k_{R1} - 8k_{R2} + \frac{3680}{513} k_{R3} - \frac{845}{4104} k_{R4} \right) \\ = h \left(\frac{-\beta}{N} \left(I_i + \frac{439}{216} k_{I1} - 8k_{I2} + \frac{3680}{513} k_{I3} - \frac{845}{4104} k_{I4} \right) \left(S_i + \frac{439}{216} k_{S1} - 8k_{S2} + \frac{3680}{513} k_{S3} - \right. \right. \\ \left. \left. \frac{845}{4104} k_{S4} \right) - \mu \left(S_i + \frac{439}{216} k_{S1} - 8k_{S2} + \frac{3680}{513} k_{S3} - \frac{845}{4104} k_{S4} \right) + rN + \delta \left(R_i + \frac{439}{216} k_{R1} - \right. \right. \\ \left. \left. 8k_{R2} + \frac{3680}{513} k_{R3} - \frac{845}{4104} k_{R4} \right) \right), \quad (54)$$

$$\begin{aligned}
 k_{E5} &= hf_2 \left(t_i + h, S_i + \frac{439}{216} k_{S1} - 8k_{S2} + \frac{3680}{513} k_{S3} - \frac{845}{4104} k_{S4}, \right. \\
 &\quad \left. E_i + \frac{439}{216} k_{E1} - 8k_{E2} + \frac{3680}{513} k_{E3} - \frac{845}{4104} k_{E4}, I_i + \frac{439}{216} k_{I1} - 8k_{I2} \right. \\
 &\quad \left. + \frac{3680}{513} k_{I3} - \frac{845}{4104} k_{I4}, R_i + \frac{439}{216} k_{R1} - 8k_{R2} + \frac{3680}{513} k_{R3} - \frac{845}{4104} k_{R4} \right) \\
 &= h \left(\frac{\beta}{N} \left(I_i + \frac{439}{216} k_{I1} - 8k_{I2} + \frac{3680}{513} k_{I3} - \frac{845}{4104} k_{I4} \right) \left(S_i + \frac{439}{216} k_{S1} - 8k_{S2} + \frac{3680}{513} k_{S3} - \right. \right. \\
 &\quad \left. \left. \frac{845}{4104} k_{S4} \right) - (\mu + \sigma + \kappa) \left(E_i + \frac{439}{216} k_{E1} - 8k_{E2} + \frac{3680}{513} k_{E3} - \frac{845}{4104} k_{E4} \right) \right), \tag{55}
 \end{aligned}$$

$$\begin{aligned}
 k_{I5} &= hf_3 \left(t_i + h, S_i + \frac{439}{216} k_{S1} - 8k_{S2} + \frac{3680}{513} k_{S3} - \frac{845}{4104} k_{S4}, \right. \\
 &\quad \left. E_i + \frac{439}{216} k_{E1} - 8k_{E2} + \frac{3680}{513} k_{E3} - \frac{845}{4104} k_{E4}, I_i + \frac{439}{216} k_{I1} - 8k_{I2} \right. \\
 &\quad \left. + \frac{3680}{513} k_{I3} - \frac{845}{4104} k_{I4}, R_i + \frac{439}{216} k_{R1} - 8k_{R2} + \frac{3680}{513} k_{R3} - \frac{845}{4104} k_{R4} \right) \\
 &= h \left(\sigma \left(E_i + \frac{439}{216} k_{E1} - 8k_{E2} + \frac{3680}{513} k_{E3} - \frac{845}{4104} k_{E4} \right) - (\mu + \alpha + \gamma) \left(I_i + \frac{439}{216} k_{I1} - \right. \right. \\
 &\quad \left. \left. 8k_{I2} + \frac{3680}{513} k_{I3} - \frac{845}{4104} k_{I4} \right) \right), \tag{56}
 \end{aligned}$$

$$\begin{aligned}
 k_{R5} &= hf_4 \left(t_i + h, S_i + \frac{439}{216} k_{S1} - 8k_{S2} + \frac{3680}{513} k_{S3} - \frac{845}{4104} k_{S4}, \right. \\
 &\quad \left. E_i + \frac{439}{216} k_{E1} - 8k_{E2} + \frac{3680}{513} k_{E3} - \frac{845}{4104} k_{E4}, I_i + \frac{439}{216} k_{I1} - 8k_{I2} \right. \\
 &\quad \left. + \frac{3680}{513} k_{I3} - \frac{845}{4104} k_{I4}, R_i + \frac{439}{216} k_{R1} - 8k_{R2} + \frac{3680}{513} k_{R3} - \frac{845}{4104} k_{R4} \right) \\
 &= h \left(\kappa \left(E_i + \frac{439}{216} k_{E1} - 8k_{E2} + \frac{3680}{513} k_{E3} - \frac{845}{4104} k_{E4} \right) + \gamma \left(I_i + \frac{439}{216} k_{I1} - 8k_{I2} + \right. \right. \\
 &\quad \left. \left. \frac{3680}{513} k_{I3} - \frac{845}{4104} k_{I4} \right) - \mu \left(R_i + \frac{439}{216} k_{R1} - 8k_{R2} + \frac{3680}{513} k_{R3} - \frac{845}{4104} k_{R4} \right) - \delta \left(R_i + \frac{439}{216} k_{R1} - \right. \right. \\
 &\quad \left. \left. 8k_{R2} + \frac{3680}{513} k_{R3} - \frac{845}{4104} k_{R4} \right) \right). \tag{57}
 \end{aligned}$$

where $i = 0, 1, \dots, n - 1$.

The sixth stage needs to find k_{S6}, k_{E6}, k_{I6} and k_{R6} as below, in equations (58-61) where f_1, f_2, f_3, f_4 are unknown functions, t is a time and h is a step size:

$$\begin{aligned}
 k_{S6} &= hf_1 \left(t_i + \frac{h}{2}, S_i - \frac{8}{27} k_{S1} + 2k_{S2} - \frac{3544}{2565} k_{S3} + \frac{1859}{4104} k_{S4} - \frac{11}{40} k_{S5}, \right. \\
 &\quad \left. E_i - \frac{8}{27} k_{E1} + 2k_{E2} - \frac{3544}{2565} k_{E3} + \frac{1859}{4104} k_{E4} - \frac{11}{40} k_{E5}, I_i - \frac{8}{27} k_{I1} + 2k_{I2} \right. \\
 &\quad \left. - \frac{3544}{2565} k_{I3} + \frac{1859}{4104} k_{I4} - \frac{11}{40} k_{I5}, R_i - \frac{8}{27} k_{R1} + 2k_{R2} - \frac{3544}{2565} k_{R3} \right. \\
 &\quad \left. + \frac{1859}{4104} k_{R4} - \frac{11}{40} k_{R5} \right) \\
 &= h \left(\frac{-\beta}{N} \left(I_i - \frac{8}{27} k_{I1} + 2k_{I2} - \frac{3544}{2565} k_{I3} + \frac{1859}{4104} k_{I4} - \frac{11}{40} k_{I5} \right) \left(S_i - \frac{8}{27} k_{S1} + 2k_{S2} - \right. \right. \\
 &\quad \left. \left. \frac{3544}{2565} k_{S3} + \frac{1859}{4104} k_{S4} - \frac{11}{40} k_{S5} \right) - \mu \left(S_i - \frac{8}{27} k_{S1} + 2k_{S2} - \frac{3544}{2565} k_{S3} + \frac{1859}{4104} k_{S4} - \frac{11}{40} k_{S5} \right) + \right. \\
 &\quad \left. rN + \delta \left(R_i - \frac{8}{27} k_{R1} + 2k_{R2} - \frac{3544}{2565} k_{R3} + \frac{1859}{4104} k_{R4} - \frac{11}{40} k_{R5} \right) \right), \tag{58}
 \end{aligned}$$

$$\begin{aligned}
 k_{E6} &= hf_2 \left(t_i + \frac{h}{2}, S_i - \frac{8}{27}k_{S1} + 2k_{S2} - \frac{3544}{2565}k_{S3} + \frac{1859}{4104}k_{S4} - \frac{11}{40}k_{S5}, \right. \\
 &\quad E_i - \frac{8}{27}k_{E1} + 2k_{E2} - \frac{3544}{2565}k_{E3} + \frac{1859}{4104}k_{E4} - \frac{11}{40}k_{E5}, I_i - \frac{8}{27}k_{I1} + 2k_{I2} \\
 &\quad - \frac{3544}{2565}k_{I3} + \frac{1859}{4104}k_{I4} - \frac{11}{40}k_{I5}, R_i - \frac{8}{27}k_{R1} + 2k_{R2} - \frac{3544}{2565}k_{R3} \\
 &\quad \left. + \frac{1859}{4104}k_{R4} - \frac{11}{40}k_{R5} \right) \\
 &= h \left(\frac{\beta}{N} \left(I_i - \frac{8}{27}k_{I1} + 2k_{I2} - \frac{3544}{2565}k_{I3} + \frac{1859}{4104}k_{I4} - \frac{11}{40}k_{I5} \right) \left(S_i - \frac{8}{27}k_{S1} + 2k_{S2} - \right. \right. \\
 &\quad \left. \left. \frac{3544}{2565}k_{S3} + \frac{1859}{4104}k_{S4} - \frac{11}{40}k_{S5} \right) - (\mu + \sigma + \kappa) \left(E_i - \frac{8}{27}k_{E1} + 2k_{E2} - \frac{3544}{2565}k_{E3} + \frac{1859}{4104}k_{E4} - \right. \right. \\
 &\quad \left. \left. \frac{11}{40}k_{E5} \right) \right), \tag{59}
 \end{aligned}$$

$$\begin{aligned}
 k_{I6} &= hf_3 \left(t_i + \frac{h}{2}, S_i - \frac{8}{27}k_{S1} + 2k_{S2} - \frac{3544}{2565}k_{S3} + \frac{1859}{4104}k_{S4} - \frac{11}{40}k_{S5}, \right. \\
 &\quad E_i - \frac{8}{27}k_{E1} + 2k_{E2} - \frac{3544}{2565}k_{E3} + \frac{1859}{4104}k_{E4} - \frac{11}{40}k_{E5}, I_i - \frac{8}{27}k_{I1} + 2k_{I2} \\
 &\quad - \frac{3544}{2565}k_{I3} + \frac{1859}{4104}k_{I4} - \frac{11}{40}k_{I5}, R_i - \frac{8}{27}k_{R1} + 2k_{R2} - \frac{3544}{2565}k_{R3} \\
 &\quad \left. + \frac{1859}{4104}k_{R4} - \frac{11}{40}k_{R5} \right) \\
 &= h \left(\sigma \left(E_i - \frac{8}{27}k_{E1} + 2k_{E2} - \frac{3544}{2565}k_{E3} + \frac{1859}{4104}k_{E4} - \frac{11}{40}k_{E5} \right) - (\mu + \alpha + \gamma) \left(I_i - \right. \right. \\
 &\quad \left. \left. \frac{8}{27}k_{I1} + 2k_{I2} - \frac{3544}{2565}k_{I3} + \frac{1859}{4104}k_{I4} - \frac{11}{40}k_{I5} \right) \right), \tag{60}
 \end{aligned}$$

$$\begin{aligned}
 k_{R6} &= hf_4 \left(t_i + \frac{h}{2}, S_i - \frac{8}{27}k_{S1} + 2k_{S2} - \frac{3544}{2565}k_{S3} + \frac{1859}{4104}k_{S4} - \frac{11}{40}k_{S5}, \right. \\
 &\quad E_i - \frac{8}{27}k_{E1} + 2k_{E2} - \frac{3544}{2565}k_{E3} + \frac{1859}{4104}k_{E4} - \frac{11}{40}k_{E5}, I_i - \frac{8}{27}k_{I1} + 2k_{I2} \\
 &\quad - \frac{3544}{2565}k_{I3} + \frac{1859}{4104}k_{I4} - \frac{11}{40}k_{I5}, R_i - \frac{8}{27}k_{R1} + 2k_{R2} - \frac{3544}{2565}k_{R3} \\
 &\quad \left. + \frac{1859}{4104}k_{R4} - \frac{11}{40}k_{R5} \right) \\
 &= h \left(\kappa \left(E_i - \frac{8}{27}k_{E1} + 2k_{E2} - \frac{3544}{2565}k_{E3} + \frac{1859}{4104}k_{E4} - \frac{11}{40}k_{E5} \right) + \gamma \left(I_i - \frac{8}{27}k_{I1} + 2k_{I2} - \right. \right. \\
 &\quad \left. \left. \frac{3544}{2565}k_{I3} + \frac{1859}{4104}k_{I4} - \frac{11}{40}k_{I5} \right) - \mu \left(R_i - \frac{8}{27}k_{R1} + 2k_{R2} - \frac{3544}{2565}k_{R3} + \frac{1859}{4104}k_{R4} - \frac{11}{40}k_{R5} \right) - \right. \\
 &\quad \left. \delta \left(R_i - \frac{8}{27}k_{R1} + 2k_{R2} - \frac{3544}{2565}k_{R3} + \frac{1859}{4104}k_{R4} - \frac{11}{40}k_{R5} \right) \right). \tag{61}
 \end{aligned}$$

where $i = 0, 1, \dots, n - 1$.

3.3 Mean Latin Hypercube Runge-Kutta (MLHRK) Method:

The modified method is the first time mentioned that integrates the results between the statistical simulations of random sampling with the classic numerical iterative approach of Runge-Kutta (RK) formula. Whereas, the samples are estimated by LHS random process before solving the system by the RK method. These samples contain the number of LHS simulation values for each parameter that was generated by code in MATLAB [9]. This method has been suggested to calculate the numerical simulation solution obtained for each subgroup. The MLHRK method is performed using the Matlab program. The MLHRK method is more effective than classical numerical methods that depend on a limited time. This method is applied to solve the influenza epidemic model in the current study. The Latin Hypercube sampling is repeated (200,500) times to simulate values of parameters as random sample. The modified method is called Mean Latin Hypercube Runge-Kutta method The modified process is called Mean Latin Hypercube Runge-Kutta method which is abbreviated by

(*MLHRK*). The scenario of the suggested method in our study is as follows : reliable numerical methods have firstly been used for solving nonlinear ordinary differential equations of the first order to prove the solutions of the system under study. The numerical simulation solutions for the influenza epidemic in Australia [1] are obtained using a modified process that combines the numerical method *RK* and the statistical random sampling technique *LHS*. The aim of this study to solve nonlinear ordinary differential equations of the first order for the influenza epidemic model by using *MLHRK* method under initial conditions. This modified approach simulates the rate of model parameters by *LHS* technology before integration with iterations of *RK*. The steps of the *MLHRK* method are summarized:

Step 1: All parameters have been simulated as *LHS* sample for n -times at once.

Step 2: For each random parameter, one value is specified and replaced in the system.

Step 3: Solve the system m -times iterations numerically by *RK*. The last iterative solution is the final solution.

Step 4: Repeat steps 1, and 2 for n -simulations times.

Step 5: Calculate the mean final solutions (*MLHRK*) of the model from step 4. The number of simulations is the total number of variables in the model present studied. The algorithm is displayed as a flow chart to the model under study.

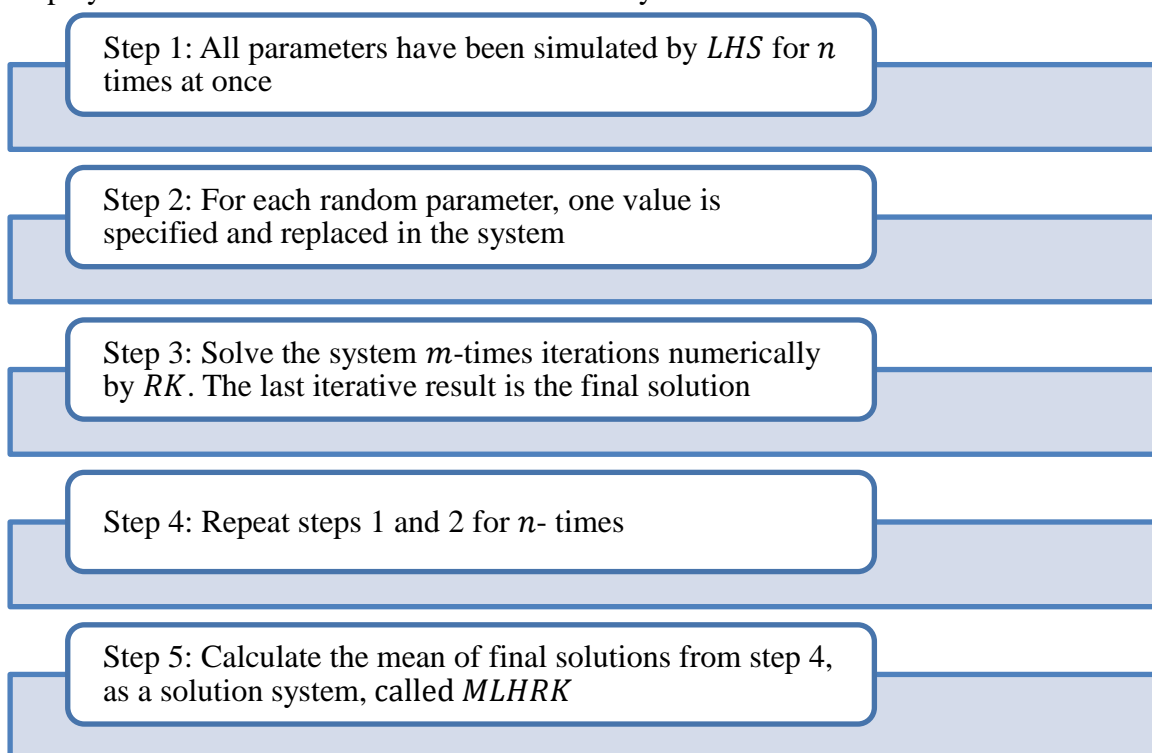


Figure 1- MLHRK procedur

6. Results and Discussion

Several numerical statistical results of the influenza epidemic have been discussed through 70 days. Suppose m is the number of iterations, p is the number of simulations of *MC*, and *LHS* operations and h is the step size. The parameters are treated as random variables having uniform distribution over predicted values from previous study. The results have been calculated by the Matlab program, and Figures have been drawn by the Magic plot program. It is found that the proposed method is effective, reliable, and suitable in solving such problems and there is a convergence between their results as it is shown in Tables 3 and 5. Error is a measure of the convergence of a solution to the methods. For this, the absolute error of

MLHRK method is less than the absolute error of *MMCRK* method as it is shown in the Tables 4 and 6, where the absolute error is the difference between RK numerical, and *MLHRK* numerical simulation results for both orders 4, and 4 and 5. The errors of *MLHRK*₄, and *MLHRK*₄₅ are less than the errors of *MMCRK*₄, and *MMCRK*₄₅, respectively. Therefore, *MLHRK* method is better than the *MMCRK* method. The *MMCRK*, and *MLHRK* solutions for influenza model in 70 days are inside the predicted interval of numerical.

From the Tables (3-6), we conclude, with the greater number of simulations, the best results for the old method *MMCRK* are got. While the increasing number of simulations does not affect the accuracy of the results in our new method *MLHRK*. Therefore, the proposed method *MLHRK* is not need more repetitions to get good results as in the other numerical simulation methods like *MMCRK* that needs more repetitions to get accurate results. It is clear in this study, 500 repetitions at $h=0.04$ need more time than 200 repetitions with the same step size, the *MLHRK* gets accurate results with 200 repetitions while *MMCRK* gets the accuracy with 500 repetitions under the same step size.

The proposed *MLHRK* method gives values closer to the RK numerical solutions than the *MMCRK* method for both orders 4 and, 4 and 5 as it is shown in Figures (1- 4).

7. Conclusion

The influenza model has been studied to understand, to analyze and to interpret the behavior of epidemic dynamics. Mean Latin Hypercube Runge-Kutta (*MLHRK*) method is an iterative algorithm which has been presented to calculate the numerical statistical solution for the influenza epidemic problem.

The new modified approach, namely Mean Latin Hypercube Runge-Kutta (*MLHRK*) method is discussed to solve influenza model wherein the sample is frequently and randomly divided into groups. The *RK* method is used to find numerical deterministic solutions to the influenza model when the model parameters are constants, while the *MLHRK* method is used when the randomization in the model becomes necessary with parameters model are treated as random variables. There are many techniques to solve epidemiological models and evaluate performance by applying a form of segmentation like Mean Monte Carlo Finite Difference (*MMCFD*) and Mean Latin Hypercube Finite Difference (*MLHFD*). The accuracy and efficiency of *MLHRK* method have been demonstrated by studying the convergence. The error of *MLHRK* method is less than *MMCRK* method. Therefore, *MLHRK* method is better than *MMCRK* method. The advantage of *MLHRK* method over *RK* method is that it can reduce the number of numerical iterations of *RK* as well as it is a faster simulation over the distribution of the LHS randomized group samples. *MLHRK* method is an upgrade to the previous numerical simulation process which is Mean Monte Carlo Runge-Kutta (*MMCRK*). *MLHRK* method is collected the last iteration of *RK* in each simulation, finally taking the average for the simulation iterations results as a final solution to the method. In the present work, the *MLHRK* results are tabulated with the *RK* results as well as the *MMCRK* results for the influenza pandemic model.

The numerical results of Runge-kutta of order 4 (*RK*₄) and Runge-kutta of order 4 and 5 (*RK*₄₅) methods are compared with other statistical numerical results of Mean Latin Hypercube Runge-Kutta (*MLHRK*), and Mean Monte Carlo Runge-Kutta (*MMCRK*) methods in the time interval (0,70). It is found that these proposed methods are effective, reliable, and suitable in solving such problems. *MLHRK* considers a middle between the statistical simulation process and numerical methods. The convergence of numerical and numerical statistical methods has been discussed. *MLHRK* method is better than the *MMCRK* method. The *MLHRK* method gives values closer to the *RK* numerical solutions than the *MMCRK* method. The results have been calculated by the Matlab program and the figures have been drawn by the Magic plot program.

Table 3- Numerical and numerical simulation results with 200 simulations for influenza model in 70 days.

Variables	Step size h (day^{-1})	RK_4	MLHRK4	MMCRK4	RK_{45}	MLHRK45	MMCRK45
$S(t)$	0.5	0.59720331	0.60910438	0.61407354	0.59720329	0.60910436	0.61407353
	0.25	0.59715737	0.60914557	0.61412602	0.59715736	0.60914555	0.61412600
	0.04	0.59711877	0.60918342	0.61417319	0.59711877	0.60918341	0.61417319
$E(t)$	0.5	0.00224669	0.00179916	0.00171281	0.00224670	0.00179916	0.00171282
	0.25	0.00224599	0.00177358	0.00168868	0.00224599	0.00177358	0.00168868
	0.04	0.00224539	0.00175238	0.00166868	0.00224539	0.00175238	0.00166868
$I(t)$	0.5	0.00473296	0.00378715	0.00358140	0.00473297	0.00378716	0.00358140
	0.25	0.00473178	0.00373198	0.00352907	0.00473178	0.00373198	0.00352907
	0.04	0.00473076	0.00368628	0.00348572	0.00473076	0.00368628	0.00348572
$R(t)$	0.5	0.38142439	0.37020568	0.36639393	0.38142440	0.37020569	0.36639394
	0.25	0.38146692	0.37028761	0.36646455	0.38146694	0.37028763	0.36646457
	0.04	0.38150269	0.37035259	0.36652021	0.38150269	0.37035259	0.36652022

Table 4- Absolute Error (AE) between numerical and numerical simulation results with 200 simulations for influenza model in 70 days

Variables	Step size h (day^{-1})	AE for RK4 and MLHRK4	AE for RK4 and MMCRK4	AE for RK45 and MLHRK45	AE for RK45 and MMCRK45
$S(t)$	0.5	0.01190107	0.01687023	0.01190107	0.01687024
	0.25	0.01198819	0.01696865	0.01198819	0.01696865
	0.04	0.01206465	0.01705442	0.01206465	0.01705442
$E(t)$	0.5	0.00044754	0.00053388	0.00044754	0.00053388
	0.25	0.00047241	0.00055731	0.00047241	0.00055731
	0.04	0.00049301	0.00057672	0.00049301	0.00057672
$I(t)$	0.5	0.00094581	0.00115157	0.00094581	0.00115157

	0.25	0.00099979	0.00120271	0.00099979	0.00120271
	0.04	0.00104448	0.00124504	0.00104448	0.00124504
R(t)	0.5	0.01121871	0.01503046	0.01121871	0.01503047
	0.25	0.01117931	0.01500237	0.01117931	0.01500237
	0.04	0.01115010	0.01498248	0.01115010	0.01498248

Table 5-Numerical and numerical simulation results with 500 simulations for influenza model in 70 days

Variables	Step size h (day^{-1})	RK_4	MLHRK4	MMCRK4	RK_{45}	MLHRK45	MMCRK45
S(t)	0.5	0.59720331	0.61016727	0.61288480	0.59720329	0.61016726	0.61288479
	0.25	0.59715737	0.61021177	0.61293555	0.59715736	0.61021175	0.61293553
	0.04	0.59711877	0.61025230	0.61298126	0.59711877	0.61025230	0.61298126
E(t)	0.5	0.00224669	0.00177515	0.00172169	0.00224670	0.00177515	0.00172169
	0.25	0.00224599	0.00175031	0.00169747	0.00224599	0.00175031	0.00169747
	0.04	0.00224539	0.00172973	0.00167739	0.00224539	0.00172973	0.00167739
I(t)	0.5	0.00473296	0.00369642	0.00358722	0.00473297	0.00369642	0.00358722
	0.25	0.00473178	0.00364310	0.00353507	0.00473178	0.00364310	0.00353507
	0.04	0.00473076	0.00359893	0.00349188	0.00473076	0.00359893	0.00349188
R(t)	0.5	0.38142439	0.36939055	0.36704081	0.38142440	0.36939056	0.36704083
	0.25	0.38146692	0.36946747	0.36711051	0.38146694	0.36946749	0.36711052
	0.04	0.38150269	0.36952835	0.36716539	0.38150269	0.36952836	0.36716540

Table 6-Absolute Error (AE) between numerical and numerical simulation results with 500 simulations for influenza model in 70 days

Variables	Step size h (day^{-1})	AE for RK4 and MLHRK4	AE for RK4 and MMCRK4	AE for RK45 and MLHRK45	AE for RK45 and MMCRK45
S(t)	0.5	0.01296396	0.01568150	0.01296397	0.01568150

	0.25	0.01305439	0.01577818	0.01305439	0.01577818
	0.04	0.01313353	0.01586249	0.01313353	0.01586249
$E(t)$	0.5	0.00047155	0.00052500	0.00047155	0.00052500
	0.25	0.00049568	0.00054853	0.00049568	0.00054853
	0.04	0.00051567	0.00056800	0.00051567	0.00056800
$I(t)$	0.5	0.00103655	0.00114575	0.00103655	0.00114575
	0.25	0.00108868	0.00119670	0.00108868	0.00119670
	0.04	0.00113183	0.00123888	0.00113183	0.00123888
$R(t)$	0.5	0.01203384	0.01438358	0.01203384	0.01438358
	0.25	0.01199945	0.01435642	0.01199945	0.01435642
	0.04	0.01197434	0.01433730	0.01197434	0.01433730

Table 7- Predicted interval of numerical simulation results with 500 simulations for influenza model in 70 days.

Variables	Step size h (day^{-1})	MLHRK4	MMCRK4	MLHRK45	MMCRK45
$S(t)$	0.5	[0.351101467962179, 0.895619597016719]	[0.359742130259010, 0.886651778145059]	[0.351101428240616, 0.895619613803351]	[0.359742071783190, 0.886651797827509]
	0.25	[0.351420402152609, 0.895652764062866]	[0.360089071512295, 0.886705727496761]	[0.351420373345214, 0.895652762695949]	[0.360089028752050, 0.886705725302930]
$E(t)$	0.5	[0.000384019645701, 0.003625380625017]	[0.000420050272981, 0.003540872886166]	[0.000384019780925, 0.003625381610702]	[0.000420050448261, 0.003540874304606]
	0.25	[0.000376700227764, 0.003574775934314]	[0.000412249213634, 0.003496157020491]	[0.000376700271277, 0.003574776386625]	[0.000412249256735, 0.003496157507734]
$I(t)$	0.5	[0.000902936431770, 0.007432508394284]	[0.000420050272981, 0.003540872886166]	[0.000902936653220, 0.007432510571505]	[0.001006120837582, 0.006953824570379]
	0.25	[0.000893897570153, 0.007350003304441]	[0.000996076132565, 0.006865136055881]	[0.000893897638856, 0.007350003927862]	[0.000996076198154, 0.006865136652129]
$R(t)$	0.5	[0.112027579234225, 0.600690300179813]	[0.001006120594320, 0.006953822030645]	[0.112027561777776, 0.600690337676898]	[0.121517392921282, 0.593779332386679]
	0.25	[0.112041999544785, 0.600437901904896]	[0.121542496550874, 0.593537050877795]	[0.112042001570227, 0.600437928733691]	[0.121542499236846, 0.593537083223483]

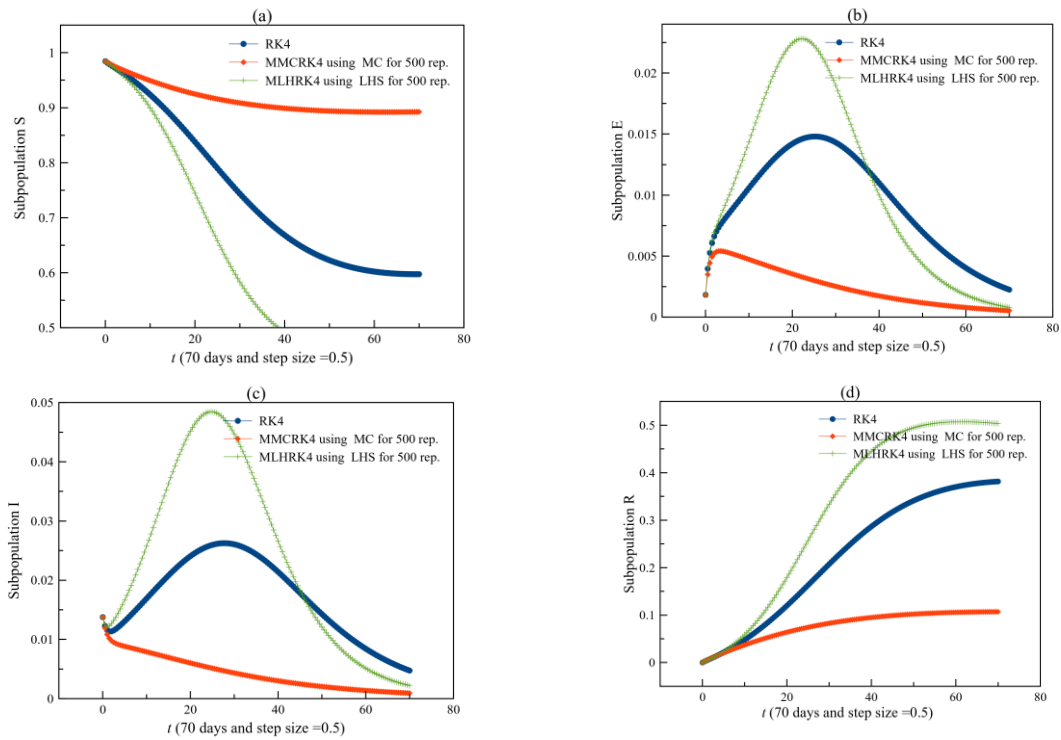


Figure 1- Comparison RK_4 numerical and $MMCRK_4$ and $MLHRK_4$ numerical simulation solutions for influenza model of $S(t), E(t), I(t), R(t)$ in 1919 when step size $h = 0.5$ and simulation $p = 500$.

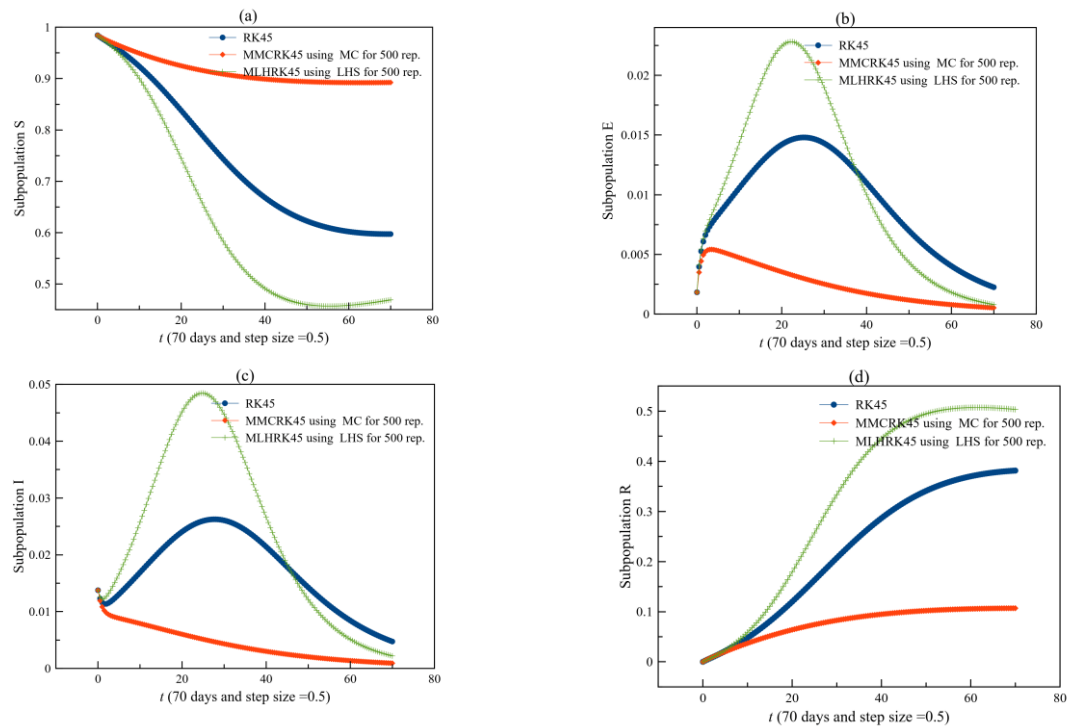


Figure 2- Comparison RK_{45} numerical and $MMCRK_{45}$ and $MLHRK_{45}$ numerical simulation solutions for influenza model of $S(t), E(t), I(t), R(t)$ in 1919 when step size $h = 0.5$ and simulation $p = 500$.

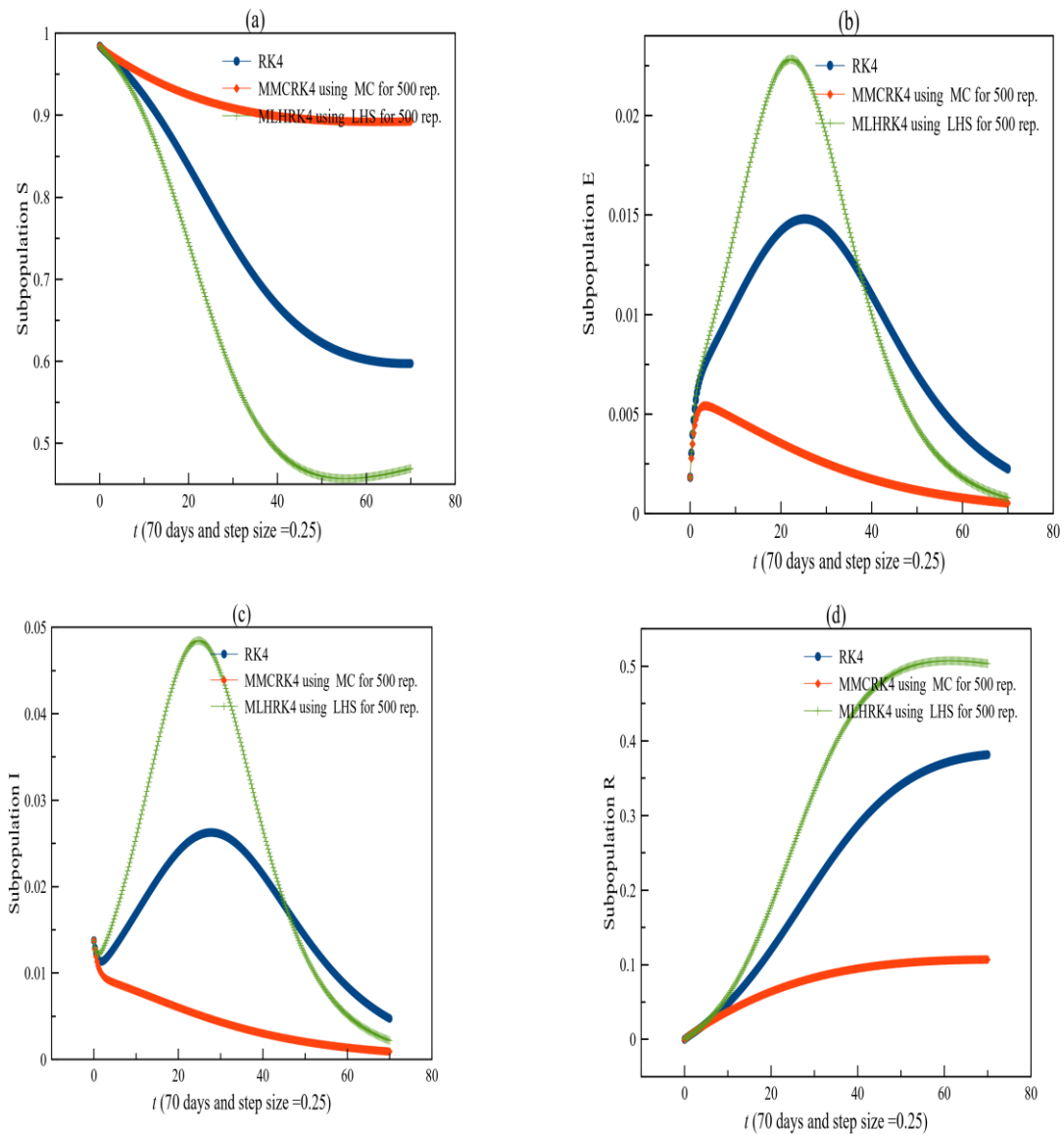


Figure 3-Comparison RK_4 numerical and $MMCRK_4$ and $MLHRK_4$ numerical simulation solutions for influenza model of $S(t), E(t), I(t), R(t)$ in 1919 when step size $h = 0.25$ and simulation $p = 500$.

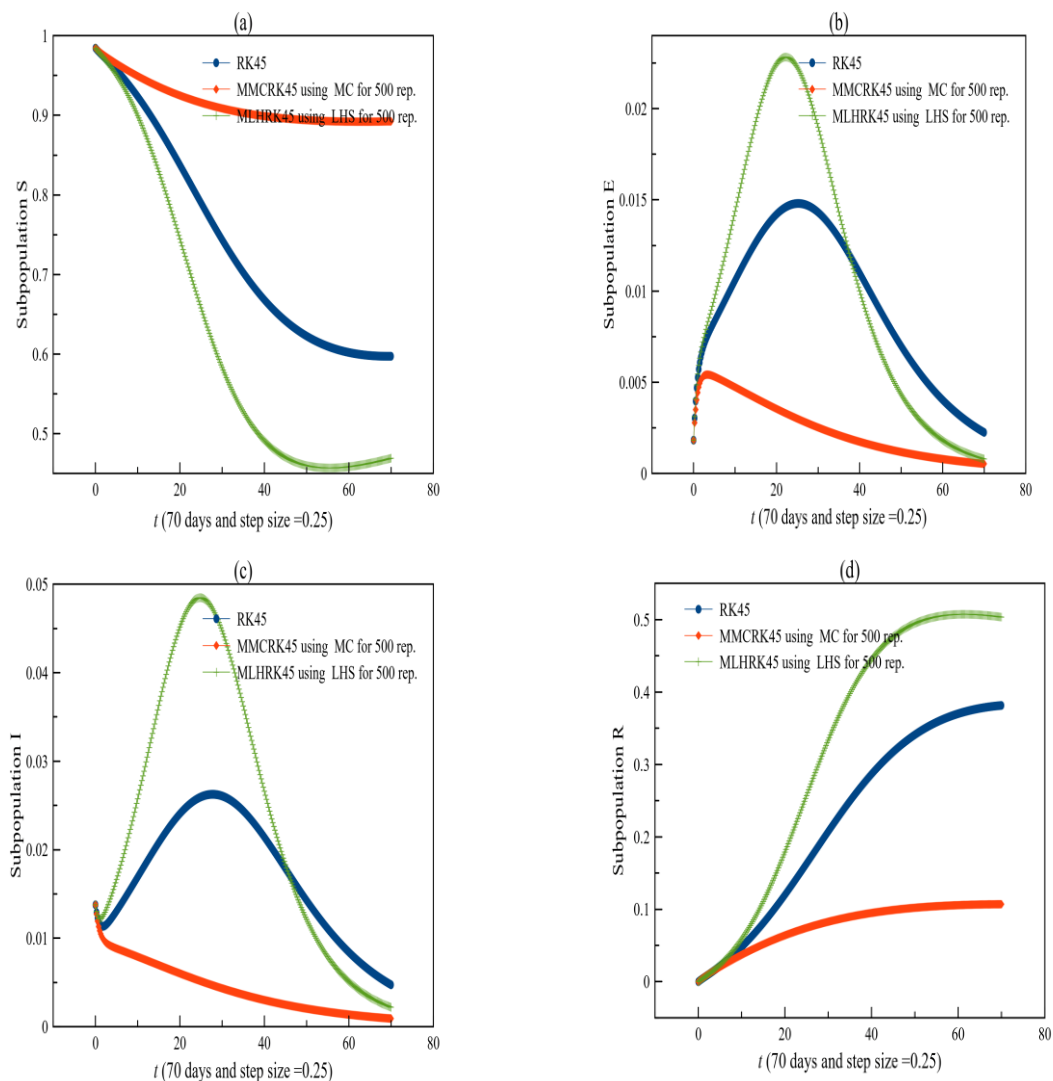


Figure 4-Comparison RK_{45} numerical and $MMCRK_{45}$ and $MLHRK_{45}$ numerical simulation solutions for influenza model of $S(t), E(t), I(t), R(t)$ in 1919 when step size $h = 0.25$ and simulation $p = 500$.

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