

Mathematical modeling of biological systems using differential equations

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Abstract

Nonlinear interactions and temporal evolution in a biological system can be mathematically modeled by differential equations and can be analysed quantitatively. Combining biologically relevant growth, mortality, resource limitation, interaction, regulation, equilibrium, stability and numerical solution mechanisms, this study suggests an integrated framework. The novelty is to combine the three elements of nonlinear biological dynamics, Jacobian-based stability assessment, and comparative numerical evaluation, in a coherent modeling framework. The Euler, Heun, Midpoint, third-order Runge–Kutta (RK3) and fourth-order Runge–Kutta (RK4) methods were compared at a step size of 0.10. The results show that RK4 gives the highest accuracy of 98.8%, with the lowest RMSE of 0.012, and the lowest absolute error of 0.009 when compared to Euler with 91.6% accuracy and RMSE of 0.084. RK3 achieved 97.5% accuracy with 0.025 RMSE. These results confirm numerical reliability for studying nonlinear dynamics, equilibrium behavior, stability and responses of systems as a function of their parameters.

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I. Introduction

Mathematical modelling is now a very important tool for studying biological systems involving complex interactions, nonlinear behaviour and continuous time evolution. There are many variables involved in the description of the behavior of biological processes, such as growth of populations, appearance of diseases, dynamics of cells, interactions between organisms, biochemical reactions, or physiological regulation, which can be described using differential equations in a way that captures their relationships and interactions [1, 2]. These equations offer a quantitative means of describing rates of change and assessing the biological component's response to changes in the environmental conditions and/or system parameters. Models based on differential equations can help researchers to translate biological hypotheses into mathematical equations that can be systematically explored [3, 4, 5]. Ordinary differential equations are especially suitable for the representation of processes that depend on time, and nonlinear formulations useful to represent feedback, competition, cooperation, regulation and saturation effects that are often found in living systems [6, 7]. Mathematical models can be used to find steady-state solutions and analyze the stability of the solutions, so as to observe whether the biological systems tend to be stable or dynamic [8, 9]. Biological systems often, however, have uncertain parameters, strongly coupled interactions, and nonlinear response, which can make analytical solutions difficult. Thus, the numerical methods are needed to approximate the system trajectories and to investigate the behavior of the system for various conditions [10]. In this study, an integrated mathematical modeling framework is formulated, which consists of the governing differential equations and the biological parameters, as well as stability analysis and numerical simulation. The approach allows systematic study of biological dynamics, to interpret how the interactions work, and offers a flexible framework for predicting how the system will respond to different biological conditions [11, 12].

II. Biological System and Mathematical Formulation

Mathematically the biological system is represented by identifying interacting components, defining state variables, defining biological relationships, and formulating differential equations that describe the dynamic evolution of the state variables over time.

A. Model Assumptions and Biological Parameters

Model assumptions include the biological characteristics, constraints on interactions, characteristics of populations, and environmental influences. Parameters refer to the rate of growth, decay, population regulation, population competition, and interactions with the rest of the system [13], [14].

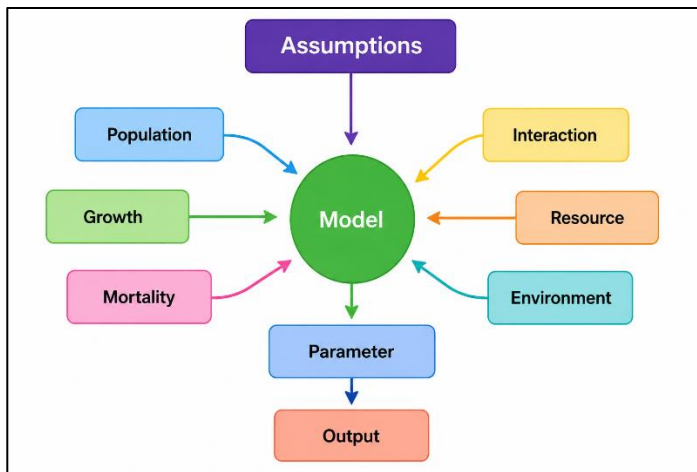


Figure 1

Biological Assumptions and Parameter Interaction Framework

The integration of biological assumptions, population factors, interactions, resources, and environmental influences is captured in the model through parameters to produce meaningful outputs from the biological systems shown in Figure 1.

$$G(X) = rX \quad (1)$$

This equation (1) is intrinsic growth of a population, where the change in population is directly proportional to the size of the population and its intrinsic growth rate over time as there is no restriction on the population's size.

$$L(X) = 1 - \frac{X}{K} \quad (2)$$

Environmental limitation is described in equation (2) in terms of the carrying capacity which shows that the growth potential gradually decreases as the biological population approaches the maximum sustainable population.

$$G_{d(X)} = rX \left(1 - \frac{X}{K}\right) \quad (3)$$

Equation (3) is a combination of intrinsic growth and carrying capacity, resulting in density-dependent population dynamics with a high growth rate that slows down as the population approaches carrying capacity limits.

$$I(X, Y) = \alpha XY \quad (4)$$

In Equation (4) the interactions among the biological population are quantified as a function of the densities of these populations as well as the

interaction coefficient representing either competition, predation, cooperation or biological influence strength.

$$R(X, N) = \frac{\beta NX}{K_N + N} \quad (5)$$

This equation (5) represents the biological regulation that is dependent on resources, incorporating the factors of resource availability, population density, resource utilization, and saturation effects, and accounts for the fact that there are nonlinearities when essential resources become more abundant to populations.

B. Formulation of Governing Differential Equations

Biological state variables can change over time and are mathematically described by differential equations that contain growth, interaction, regulatory, mortality and environmental effects in one system of nonlinear dynamics.

$$\frac{dX}{dt} = rX \left(1 - \frac{X}{K}\right) - \alpha XY - \mu X \quad (6)$$

Equation (6) represents a nonlinear population evolution equation as it evolves over time, due to intrinsic growth, carrying-capacity limitation, biological interaction, and natural mortality, which describes primary population variation.

$$\frac{dY}{dt} = \eta \alpha XY - \delta Y \quad (7)$$

Equation (7) is the secondary population changes, which also involve interaction efficiency, encounter with primary population and natural decay, and are dynamic when the biological interaction process is in play.

$$\frac{dN}{dt} = \lambda(N_0 - N) - \frac{\beta NX}{K_N + N} \quad (8)$$

External replenishment, natural adjustment and population-dependent consumption are described by equation (8) and how nutrient concentrations vary as a dynamic response to the biological demand and environmental supply conditions.

$$\frac{dZ}{dt} = \gamma X - \omega Z \quad (9)$$

In equation (9), the activation of regulatory activity is balanced by the degradation of the natural environment, which means that the mechanisms of biological control change dynamically over time according to the changes in the population.

$$\frac{dB}{dt} = \rho XN - \sigma B \quad (10)$$

The changes in biomass over time, modeled by Equation (10), reflect population-resource utilization and biomass degradation, which reflect the influence of available nutrients, population abundance and natural biomass degradation processes.

$$\frac{dE}{dt} = \theta X - \varphi E + \psi N \quad (11)$$

The environmental response in equation (11) incorporates responses from population influences, natural environmental recovery and resource contributions and reflects dynamic interactions between biological activity, ecological conditions and available resources over time.

III. Proposed Mathematical Modeling Framework

The proposed framework combines the biological assumptions, governing equations, parameter definitions, stability evaluation, and numerical computation to systematically examine the complex interactions and to make accurate prediction of biological system behavior.

A. Model Architecture and Interaction Mechanisms

The model architecture structures the biological components as interdependent state variables, and mechanisms of interactions are modeled as competition, cooperation, regulation, feedback, utilization of resources and responses that depend on the populations of the components across the system.

$$\frac{dX}{dt} = rX \left(1 - \frac{X}{K}\right) - \alpha XY \quad (12)$$

Combining the factors of intrinsic growth, carrying capacity limits, and interpopulation interactions, Equation (12) provides a comprehensive description of coupled population dynamics, thus revealing how the evolution of populations is influenced by biological dependencies in a constrained environment over time.

$$I(X, Y) = \frac{\alpha XY}{(1 + \beta X)} \quad (13)$$

A nonlinear interaction strength between populations is quantified by Equation (13) and accounts for saturation effects, which means that biological influence becomes stronger when the density is increased, but gets lesser at high density.

$$X(t) = X(0) + \int [0 \text{ to } t] \left[rX(\tau) \left(1 - \frac{X(\tau)}{K}\right) - \alpha X(\tau)Y(\tau) \right] d\tau \quad (14)$$

$$C(t) = \int [0 \text{ to } t] \alpha X(\tau)Y(\tau) d\tau \quad (15)$$

By integrating growth and interaction over time, equation (14) represents responses to the population, which are cumulative in nature and therefore provide a representation of biological changes from the initial population to the end of the observation period. By integrating the intensity of the interactions between the populations, as a function of their population size, Equation (15) measures accumulated biological interactions over time, thus providing a quantitative estimate of the overall ecological influence between the interdependent biological populations during evolution.

$$M(t) = \sqrt{[X(t)^2 + Y(t)^2 + Z(t)^2]} \quad (16)$$

The nonlinear, root-based model in equation (16) is used to calculate the overall magnitude of multiple biological state variables, which gives one single, quantitative measure of combined system activity and response.

$$R(t) = \sqrt{[(\alpha XY)^2 + (\beta YZ)^2 + (\gamma XZ)^2]} \quad (17)$$

Combining the different parts of the interaction into one response magnitude as in equation 17 represents the combined effect of all the interaction pairs and their corresponding values of the coefficients in the modelled system.

B. Stability Analysis of the Biological System

Stability analysis is based on the Jacobian matrices and eigenvalues, to measure the state of equilibrium and ascertain whether the small perturbation decays or grows or remains constant, consequently, the long-term behavior of the biological system.

$$F(X^*, Y^*) = 0 \quad (18)$$

When biological variables do not change in time, the solution to equation (18) represents equilibrium states for the modeled system that are useful for studying the long-time behavior and stability of the system.

$$J = \left[\frac{\partial F_1}{\partial X} \quad \frac{\partial F_1}{\partial Y} \right] \quad (19)$$

The governing functions are used to generate the Jacobian matrix by differentiation at each equilibrium point in order to provide the local system behavior and sensitivity to be used in the subsequent mathematical stability assessment procedures in equation (19).

$$\lambda^2 - \text{Tr}(J)\lambda + \text{Det}(J) = 0 \quad (20)$$

The characteristic polynomial in Equation (20) allows the computation of the eigenvalues of the Jacobian matrix, which can be used to mathematically describe the local dynamic behavior and stability of the system close to a biological equilibrium state.

$$\lambda = \frac{\text{Tr}(J) \pm \sqrt{\text{Tr}(J)^2 - 4\text{Det}(J)}}{2} \quad (21)$$

The roots of the eigenvalues of equation (21) are obtained from trace and determinant of the matrix, which indicate the nature of the biological system perturbations around equilibrium, and thus the local stability of the biological system.

$$S = \sqrt{\lambda_1^2 + \lambda_2^2} \quad (22)$$

Individual eigenvalue contributions are aggregated into the overall dynamic response with the help of a root-based magnitude measure, given by Equation (22), which gives a quantitative measure of the overall

intensity of the dynamic response around the equilibrium state of the biological system.

$$SI(T) = \int [0 \text{ to } T] |X(t) - X^*| dt \quad (23)$$

Equation (23) calculates the cumulated deviation from the steady state value over time by integrating, thereby describing transient instability and the speed with which biological state variables move towards the steady state.

C. Numerical Solution of Differential Equations

Numerical methods numerically solve the differential equations by integrating them in discrete time, allowing for simulation of the biological trajectories when they are nonlinear, as well as parameter-dependent responses, transient dynamics, and convergence to the equilibrium or not under given conditions.

$$X_{n+1} = X_n + hF(t_n, X_n) \quad (24)$$

A numerical simulation of a continuous system dynamics is obtained by the numerical approximation of its dynamics with the help of equation (24): current value, rate of change, and step size.

$$X_{n+1} = X_n + \left(\frac{h}{2}\right) (k_1 + k_2) \quad (25)$$

$$k_1 = F(t_n, X_n) \quad (26)$$

$$k_2 = F(t_n + h, X_n + hk_1) \quad (27)$$

Including two estimated slopes for each computational interval in the average (as in Equation (25)) leads to a greater numerical accuracy than Euler integration, while minimizing approximation errors, and allows more accurate biological state predictions than Euler integration. The initial Runge-Kutta slope is calculated from the current time and biological state in equation (26), and is the rate of system change for the system at that instant in time and state. The second slope is calculated with a new biological state and time according to equation (27) and fed into the system with the predicted change. Further the second slope is calculated based on a new biological state and time given by equation (27) and fed into the system with a prediction of change, thus increasing the accuracy of the subsequent numerical estimate of the biological state.

$$X_{n+1} = X_n + \left(\frac{h}{6}\right) (k_1 + 2k_2 + 2k_3 + k_4) \quad (28)$$

The four weighted slope estimates in each time interval are summed in equation (28) giving extremely close numerical solutions to the nonlinear biological dynamics with computational stability throughout the simulation time.

$$X(t) = X_0 + \int F(\tau, X(\tau)) d\tau \quad (29)$$

Equation (29) is a biological state evolution, with an integral interpretation of the differential equations that describe the state evolution of a living system over time.

$$RMSE = \sqrt{\left[\left(\frac{1}{N}\right) \sum_{i=1}^N (X_i - \hat{X}_i)^2\right]} \quad (30)$$

The numerical prediction error is calculated from equation (30) and it is a quantitative measure of how accurate the computational solution is at each time step across observations and serves as an overall measure of the accuracy of the computational solution.

$$E(T) = \int [0 \text{ to } T] |X_{exact(t)} - X_{numerical(t)}| dt \quad (31)$$

Accumulated absolute differences between the exact and numerical solutions over the entire simulation interval is measured in Equation (31), which includes a wide range of biological system evolution approximation error.

IV. Result and Discussion

Variations in biological populations, in the equilibria, and in the stability properties of the system are shown as a function of the parameter conditions in the simulation and significant relationships between the strength of the interactions, the regulating mechanisms and the overall behavior are brought out.

Table 1
Comparative Performance of Differential Equation Numerical Methods

Numerical Method	Step Size	RMSE	Absolute Error	Computation Time (s)	Accuracy (%)
Euler Method	0.10	0.084	0.071	0.42	91.6
Heun Method	0.10	0.052	0.044	0.58	94.8
Midpoint Method	0.10	0.041	0.035	0.63	95.9
RK3	0.10	0.025	0.021	0.79	97.5
RK4	0.10	0.012	0.009	0.94	98.8

Table 1 shows a comparison between the performance of the five methods of the numerical solution of differential equations in terms of error, computation time and accuracy. Euler has the highest RMSE of 0.084 but achieves the highest level of accuracy of 91.6% with the lowest amount of computation time. The differences among numerical methods in terms of error and computational efficiency are shown in Figure 2.

Heun Method and Mid-point Method are the two improved methods that improve accuracy to 94.8% and 95.9% respectively. To obtain the accuracy of 97.5% and RMSE of 0.025, RK3 is further reduced.

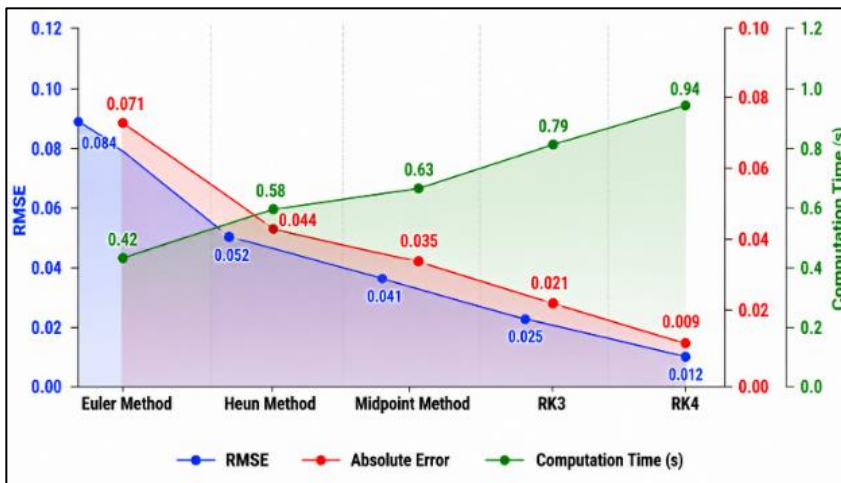


Figure 2
Comparative Performance of Numerical Methods Based on RMSE, Absolute Error, and Computation Time

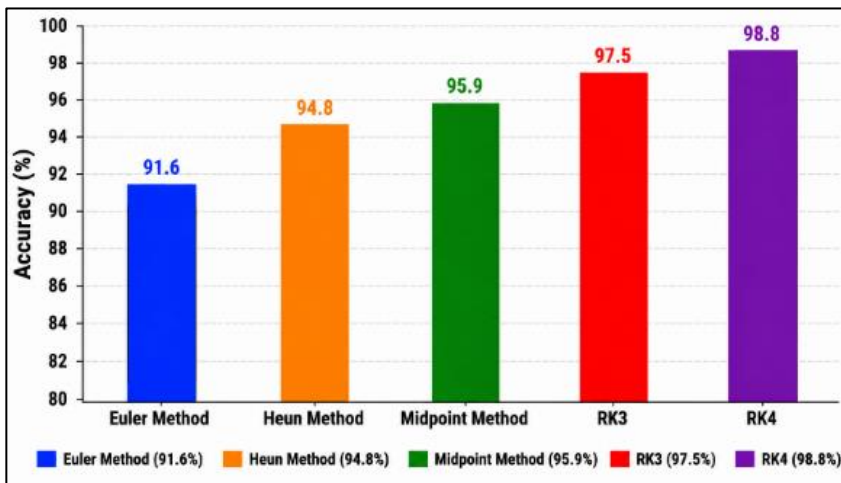


Figure 3
Comparative Accuracy Analysis of Numerical Methods for Differential Equation Solutions

Comparative Accuracy Analysis of Numerical Methods for Differential Equation Solutions compared in Figure 3, with RK4 being more accurate. RK4 gives the highest accuracy of 98.8%, minimum RMSE of 0.012 and absolute error of 0.009 and has a higher computational time.

V. Conclusion

The study proposed a mathematical model of biological system analysis based on the differential equations that describe the dynamic interaction of system, its temporality and regulation. Assumptions, state variables and parameters were used in the formulation of the model and were biologically relevant, representing growth, decay, competition, cooperation and feedback processes. Both stability analysis and numerical solution techniques gave insight into equilibrium behavior and system responses to the small perturbations applied, as well as considering the nonlinear dynamics of the system under varying conditions. Results of the simulations showed that the biological parameters can have a substantial effect on the population dynamics, the equilibrium states and stability of the population.

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