AN INTRODUCTION TO MATHEMATICAL EPIDEMIOLOGY

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What is Epidemiology?

- Epidemiology is the subject that studies the patterns of health and illness which associated factors at the population level.
- The word "epidemiology" is derived from the Greek terms:
  - *epi* - meaning "upon"
  - *demos* - meaning "people"
  - *logos* - meaning "study"
- The origin of this word implies that epidemiology is concerned primarily with human populations.
- The role of the father of epidemiology is often assigned to the Greek physician Hippocrates (460-377 B.C.E.), who described the connection between disease and environment.

- The term "epidemiology" appears to have first been used to describe the study of epidemics in 1802 by the Spanish physician de Villalba in *Epidemiologia Espanola*.
- Until the twentieth century, epidemiological studies were mostly concerned with infectious diseases.
- Nowadays, the leading causes of deaths worldwide are diseases such as stroke and coronary heart disease, positioning diseases that do not transmit from one person to another as a central concern of epidemiology.
- Among infectious diseases, those that dominate worldwide as a cause of death include lower respiratory infections (such as pneumonia) and HIV.

A Brief History of Epidemic Diseases

- The plague of Athens struck the city between 430-426 B.C.E., described in detail by Thucydides.
- The causative agent of the Athens plague is still debated.
- Smallpox affected the Roman Empire and Egypt in 165-180 C.E.
- The Black Death, occurring during 1348-1350, devastated the Mediterranean and Europe, causing an estimated 50-100 million deaths.
- The pathogen responsible for the Black Death is believed to be the Yersinia pestis bacterium.

- A smallpox epidemic in the 16th century caused an estimated 35 million deaths among the Aztecs.
- In the early 20th century, an influenza pandemic killed an estimated 20 million people worldwide.
- Significant outbreaks continue to occur, such as the Bombay plague in 1905-1906, the 2003 SARS outbreak, and the 2009 H1N1 swine flu pandemic.
- The recent COVID-19 outbreak has strained health systems worldwide and profoundly affected social life. COVID-19 has caused approximately 6.98 million deaths worldwide. The total number of confirmed cases globally is around 769 million.

Modeling of Epidemic Diseases

- Although epidemiology has a long history, the mathematical study of diseases dates back approximately 350 years.
- The first statistical study is attributed to John Graunt, while the first epidemiological model is credited to Daniel Bernoulli.
- Louis Pasteur made groundbreaking discoveries in disease causes and prevention in the mid-19th century.
- Robert Koch identified the causes of tuberculosis, cholera, and anthrax, laying the foundation for modern bacteriology.

What is a Mathematical Model?

- A mathematical model is a description of a system using mathematical tools and language.
- The process of developing mathematical models is called mathematical modeling.
- In principle, mathematical modeling can be applied to any system, biological or otherwise.
- Mathematical models are formulated for the following aims:
  - To help explain a system.
  - To study the effects of its various components.
  - To make predictions about their behavior.

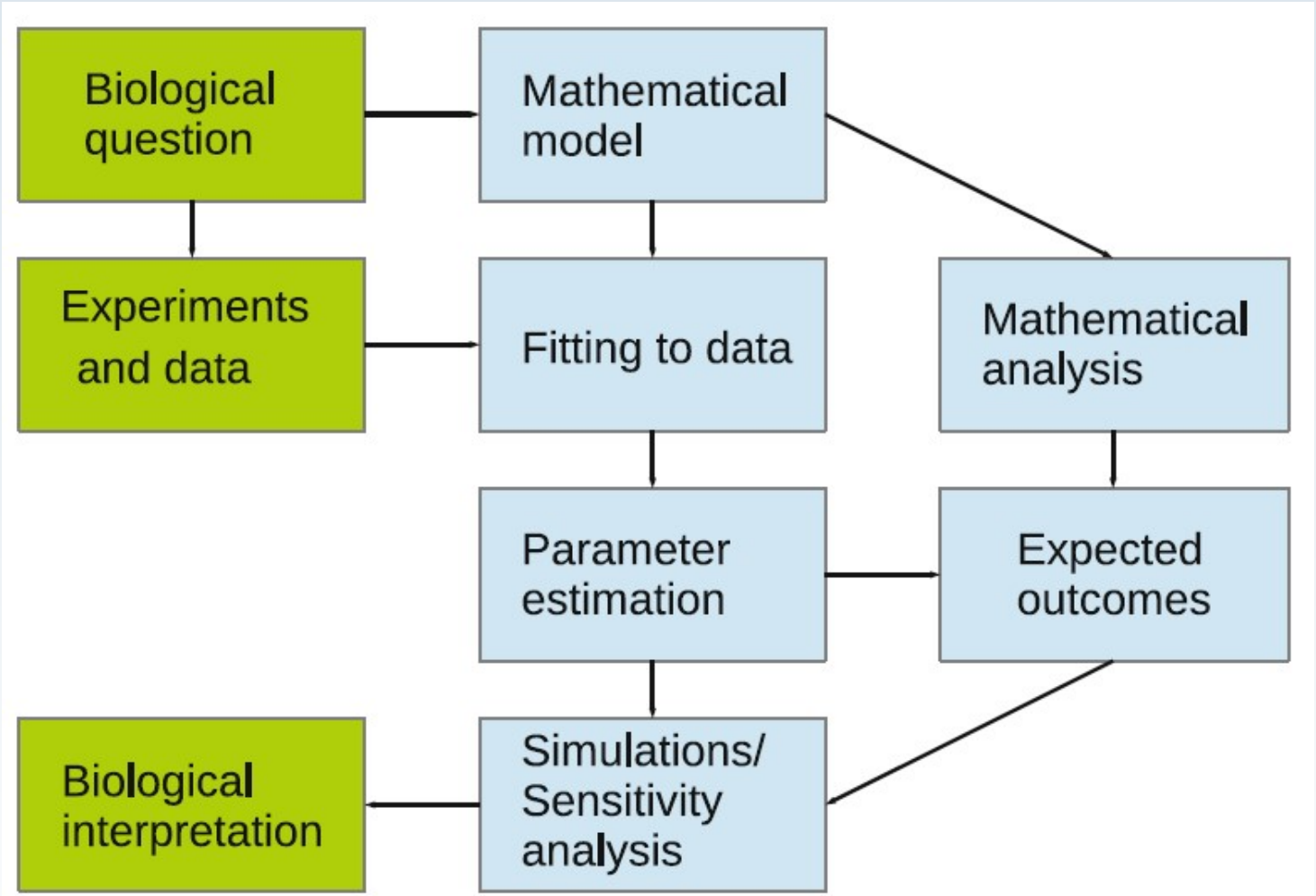

Figure 2.1: Modeling diagram.

Once a mathematical model is formulated, it can be investigated with a number of mathematical tools:

- It may be analyzed to produce critical quantities that govern the overall behavior of the solutions,
- It may be fitted to available data or used to stimulate experiments that can produce data,
- Parameters of the model may be estimated,
- It may be simulated to understand how important each parameter is to the solution.

After the model has been understood, we must address these questions:

- What did we learn about the real world from the model?
- Is our model's message supported by the information about the system?

Classification of Mathematical Models

- Mathematical models usually consist of parameters and variables that are connected by relationships.
- Models can be classified in multiple ways:
  - **Linear/nonlinear:** A model is classified as nonlinear if it contains a nonlinear dependence on the variables (e.g., a product of variables). Otherwise, it is classified as linear. The models we will construct and use in this study will be nonlinear.
  - **Static/dynamic:** A dynamic model accounts for time-dependent changes in the state of the system, while a static model calculates system quantities assuming that it does not change in time and thus is time-invariant. Dynamic models typically employ differential equations or difference equations. The models that we will consider in this study will be dynamic models.

- **Discrete/continuous:** Discrete models treat time or system states as discrete. Continuous models incorporate time and system states as continuous.
- **Deterministic/stochastic:** A deterministic model is one in which every set of variable states is uniquely determined by the parameters in the model and the initial state of the variables. Stochastic models are characterized by randomness, and variable states are described by probability distributions. The models that we will consider in this study will be deterministic models.

Mathematical Epidemiological Modeling

- Dividing a system into various compartments for modeling is called a compartmental model.
- Each compartment represents a specific state, and individuals move between these compartments according to certain rules.
- When a disease spreads in a population, it splits the population into non-intersecting classes.

- In one of the simplest scenarios, there are three such classes:
  - **Susceptible individuals:** The class of individuals who are healthy but can contract the disease. The size of this class is usually denoted by S.
  - **Infected individuals:** The class of individuals who have contracted the disease and are now sick with it. The size of this class is usually denoted by I.
  - **Recovered/Removed individuals:** The class of individuals who have recovered and cannot contract the disease again. The size of this class is usually denoted by R.

- The number of individuals in each of these classes changes with time, that is, $S(t), I(t)$ and $R(t)$ are functions of time t.
- The total population size N is the sum of the sizes of these three classes:

$$N(t) = S(t) + I(t) + R(t).$$

- Such a model is called an **SIR** model
- SIR models can be further categorised depending on the immunity against the infection:
  - **SI model:** No recovery,
  - **SIS model:** Recovery occurs but no immunity,
  - **SIR model:** Recovery and permanent immunity,
  - **SIRS model:** Recovery and temporary immunity.

Bernoulli's Model

- One of the pioneering studies in mathematical modeling is Bernoulli's investigation of the dynamics of smallpox ([2]).
- In this study, Bernoulli formulated the mathematical model as follows:

$$\begin{aligned} \frac{dS}{dt} &= -(\lambda+\mu)S, \\ \frac{dR}{dt} &= \lambda(1-d)S - \mu R, \end{aligned}$$

where S and R denotes the susceptible and recovered individuals respectively.

α = rate of the population that has gained immunity to the disease,

d = death rate induced by the disease,

μ = natural death rate,

λ = rate at which susceptibles become infected.

- It was known that the death rate d for several large cities was approximately $\frac{1}{13} \approx 7.7\%$.
- Bernoulli estimated $d = \frac{1}{8} \approx 12.5\%$ for Wroclaw, Poland.
- For Paris, assuming a life expectancy of 32 years, the calculated that 15% of susceptible individuals would die or equivalently, 85% would gain immunity.

Kermack-McKendrick SIR Model

- One of the first epidemic models proposed by Kermack and McKendrick in 1927 is an SIR model, described by the system ([3]):

$$\begin{aligned} S'(t) &= -\beta SI \\ I'(t) &= \beta SI - \alpha I, \\ R'(t) &= \alpha I. \end{aligned}$$

- The coefficient β is the constant of proportionality called the transmission rate.
- Individuals who recover or die leave the infected class at constant per capita probability per unit of time α, called recovery rate.

- There are several assumptions on the Kermack-McKendrick model:
  - There are no births and deaths in the population,
  - No one from the outside enters the population, and no one leaves the population,
  - All recovered individuals have complete immunity and cannot be infected again.

What is the Incidence Function?

- The number of individuals who become infected per unit of time in epidemiology is called incidence.
- In Kermack-McKendrick SIR model, incidence function have taken as

$$f(S, I) = \beta SI,$$

which called bilinear incidence or mass action incidence.

- An incidence function possesses the following properties [4]:

(i) $f : \mathbb{R}^2 \to \mathbb{R}_+$ is a differentiable function. $f(S, 0) = f(0, I) = 0$ for all $S, I \geq 0$ and $f(S, I) > 0$ for all $S, I > 0$,

(ii) There exists $\eta > 0$ such that $f(S, I) \leq \eta S$ for all $S, I \geq 0$,

(iii) $\frac{\partial f(S,I)}{\partial S} > 0$ and bounded for all $S \geq 0$ and $I > 0$,

(iv) $\frac{\partial f(S,I)}{\partial I} \geq 0$ for all $S, I \geq 0$,

(v) $I \frac{\partial f(S,I)}{\partial I} - f(S, I) \leq 0$ for all $S, I \geq 0$.

- Bilinear incidence rate implies that the number of individuals getting infected per unit of time increases as the number of susceptible individuals increases, which may not be a realistic assumption.
- To handle this concern, various alternative incidence rates have been proposed in the literature. For instance:

$$\textbf{Saturated incidence} \quad : \quad \frac{\beta SI}{1+\alpha_2 I},$$

$$\textbf{Beddington-DeAngelis incidence} \quad : \quad \frac{\beta SI}{1+\alpha_1 S+\alpha_2 I},$$

$$\textbf{Crowley-Martin incidence} \quad : \quad \frac{\beta SI}{(1+\alpha_1 S)(1+\alpha_2 I)}.$$

What is the Basic Reproduction Number?

- The persistence of infection in mathematical epidemic models depends upon the threshold.
- This threshold is known as the basic reproduction number and denoted by $\mathcal{R}_0$.
- Epidemiologically, $\mathcal{R}_0$, gives the number of secondary cases produced by a single infectious individual in a population consisting only of susceptible individuals.
- Several techniques have been developed to derive the next-generation matrix from compartmental models.
- Here, two different approaches that can be used for continuous and discrete models will be presented.

Calculation $\mathcal{R}_0$ for Continuous Models

This method can be used for determining the next-generation matrix from ordinary differential equation compartment models.

- Let x and y be the vector of variables in the infected compartments and noninfected compartments, respectively.
- Arrange the equations so that the first n components of the system correspond to the infected compartments. Let
- $F_i(x, y)$ be the rate of appearance of new infections in compartment i,
- $V_i^+(x, y)$ and $V_i^-(x, y)$ be the the remaining transitional terms into and out from the compartment i, respectively, such as births, deaths, recovery, etc.
- Let $V_i(x, y) = V_i^-(x, y) - V_i^+(x, y)$.
- The next-generation matrix is defined as FV^{-1} and the basic reproduction number is

$$\mathcal{R}_0 = \rho(FV^{-1}),$$

where ρ denotes the spectral radius and

$$F = \left[\frac{\partial F_i(E_0)}{\partial x_j}\right], \quad V = \left[\frac{\partial V_i(E_0)}{\partial x_j}\right].$$

An Example for Computing $\mathcal{R}_0$

Let's consider the smoking model given in [14]

$$\begin{aligned}
\frac{dP}{dt} &= \lambda - \beta\frac{2PL}{P+L} - (d+\mu)P \\
\frac{dL}{dt} &= \beta\frac{2PL}{P+L} - (\zeta + d + \mu)L \\
\frac{dS}{dt} &= \zeta L - (\delta + d + \mu)S \\
\frac{dQ}{dt} &= \delta S - (\mu + d)Q
\end{aligned}$$

Here, P, L, S, and Q denote the number of potential, occasional, chain, and quit smoker individuals, respectively. The smoke-free equilibrium given as $E_0 = \left(\frac{\lambda}{d+\mu}, 0, 0, 0\right)$.

λ = The recruitment rate of the non-smoking class from the larger embedding population,

β = The transmission rate of non-smokers into smoking class,

d = The natural death rate,

μ = Death rate induced by smoking,

ζ = The rate at which occasional smokers being chain smokers,

δ = The rate at which chain smokers that quit smoking.

It is enough that consider only infected compartments. Let $x = (x_1, x_2) = (L, S)$ be the vector of infected variables. Then

$$\begin{aligned} F_1(x) &= \frac{2\beta PL}{P+L}, \\ F_2(x) &= 0, \\ V_1 = V_1^-(x) - V_1^+(x) &= (\zeta + d + \mu)L, \\ V_2 = V_2^-(x) - V_2^+(x) &= (\delta + d + \mu)S - \zeta L, \end{aligned}$$

and

$$\begin{aligned} F &= \begin{pmatrix} 2\beta & 0 \\ 0 & 0 \end{pmatrix}, \\ V &= \begin{pmatrix} \zeta + d + \mu & 0 \\ -\zeta & \delta + d + \mu \end{pmatrix}. \end{aligned}$$

Then we have

$$FV^{-1} = \begin{pmatrix} 2\beta & 0 \\ 0 & 0 \end{pmatrix} \begin{pmatrix} \frac{1}{\zeta+d+\mu} & 0 \\ \frac{\zeta}{(\zeta+d+\mu)(\delta+d+\mu)} & \frac{1}{\delta+d+\mu} \end{pmatrix} = \begin{pmatrix} \frac{2\beta}{\zeta+d+\mu} & 0 \\ 0 & 0 \end{pmatrix}.$$

Therefore

$$R_0 = \rho(FV^{-1}) = \frac{2\beta}{\zeta + d + \mu}.$$

Calculation $\mathcal{R}_0$ for Discrete Models

Here we present a method can be used to calculation of the $\mathcal{R}_0$ for discrete epidemic models ([16]).

- Let $x = (x_1, x_2, \ldots, x_n)$ denote the n states of a population.
- Reorder the states so that the first m states are infected states, and the remaining $n - m$ states are uninfected states.
- Assume there exists a unique disease-free equilibrium E_0.
- Then the Jacobian matrix evaluated at E_0 has the following form:

$$J = \begin{pmatrix} F + T & 0 \\ A & C \end{pmatrix},$$

where the $m \times m$ submatrices F and T are non-negative, 0 is the zero matrix, and $F + T$ is irreducible. Assume $\rho(C), \rho(T) < 1$.

- Then

$$\mathcal{R}_0 = \rho(F[I - T]^{-1}).$$

An Example for Computing $\mathcal{R}_0$

- Let's consider the model

$$\begin{aligned} S_{n+1} &= \frac{A + S_n}{1 + \beta I_n + d} \\ I_{n+1} &= \frac{I_n + \beta S_{n+1} I_n}{1 + d + \gamma + \varepsilon}. \end{aligned}$$

- The disease-free equilibrium given as $E_0 = \left(\frac{A}{d}, 0\right)$.
- Rearrange variables in the model as (I_n, S_n). Then $E_0 = \left(0, \frac{A}{d}\right)$.

Then we have

$$J(E_0) = \begin{pmatrix} F+T & 0 \\ A & C \end{pmatrix} = \begin{pmatrix} \frac{\frac{\beta A}{d}}{1+d+\gamma+\varepsilon} + \frac{1}{1+d+\gamma+\varepsilon} & 0 \\ -\frac{\frac{\beta A}{d}}{1+d} & \frac{1}{1+d} \end{pmatrix}.$$

Here, the submatrices F and T are non-negative, $F+T$ is irreducible, and $\rho(T), \rho(C) < 1$. Then

$$\mathcal{R}_0 = \rho(F(1-T)^{-1}) = \frac{\beta A}{d(d+\gamma+\varepsilon)}.$$

Some Mathematical Definitions

Definition

Consider the differential equation system

$$\frac{dx}{dt} = f(x), \tag{6.1}$$

where $x = (x_1, x_2, \ldots, x_n)$ and $f = (f_1, f_2, \ldots, f_n)$. If $f(x^*) = 0$, then x^* is called an equilibrium point of the system (6.1).

Definition

Consider the difference equation system

$$x_{n+1} = f(x_n), \tag{6.2}$$

where $x_n = (x_n^1, x_n^2, \ldots, x_n^k)$ and $f = (f_1, f_2, \ldots, f_n)$. If $f(x^*) = x^*$, then x^* is called an equilibrium point of the system (6.2).

Definition

Let x^* be an equilibrium point of the continuous system (6.1). Then x^* is said to be stable if, for any given $\varepsilon > 0$, there exists $\delta > 0$ such that for every solution $x = x(t)$ satisfying

$$\|x_0 - x^*\| < \delta,$$

we have

$$\|x(t) - x^*\| < \varepsilon.$$

An equilibrium point that is no stable is unstable.

Definition

Let x^* be an equilibrium point of the discrete system (6.2). Then x^* said to be stable if, for any given $\varepsilon > 0$, there exists $\delta > 0$ such that for every solution $f^n(x_0)$ satisfying

$$\|x_0 - x^*\| < \delta,$$

we have

$$\|f^n(x_0) - x^*\| < \varepsilon, \quad \forall n \in \mathbb{N}.$$

An equilibrium point that is no stable is unstable.

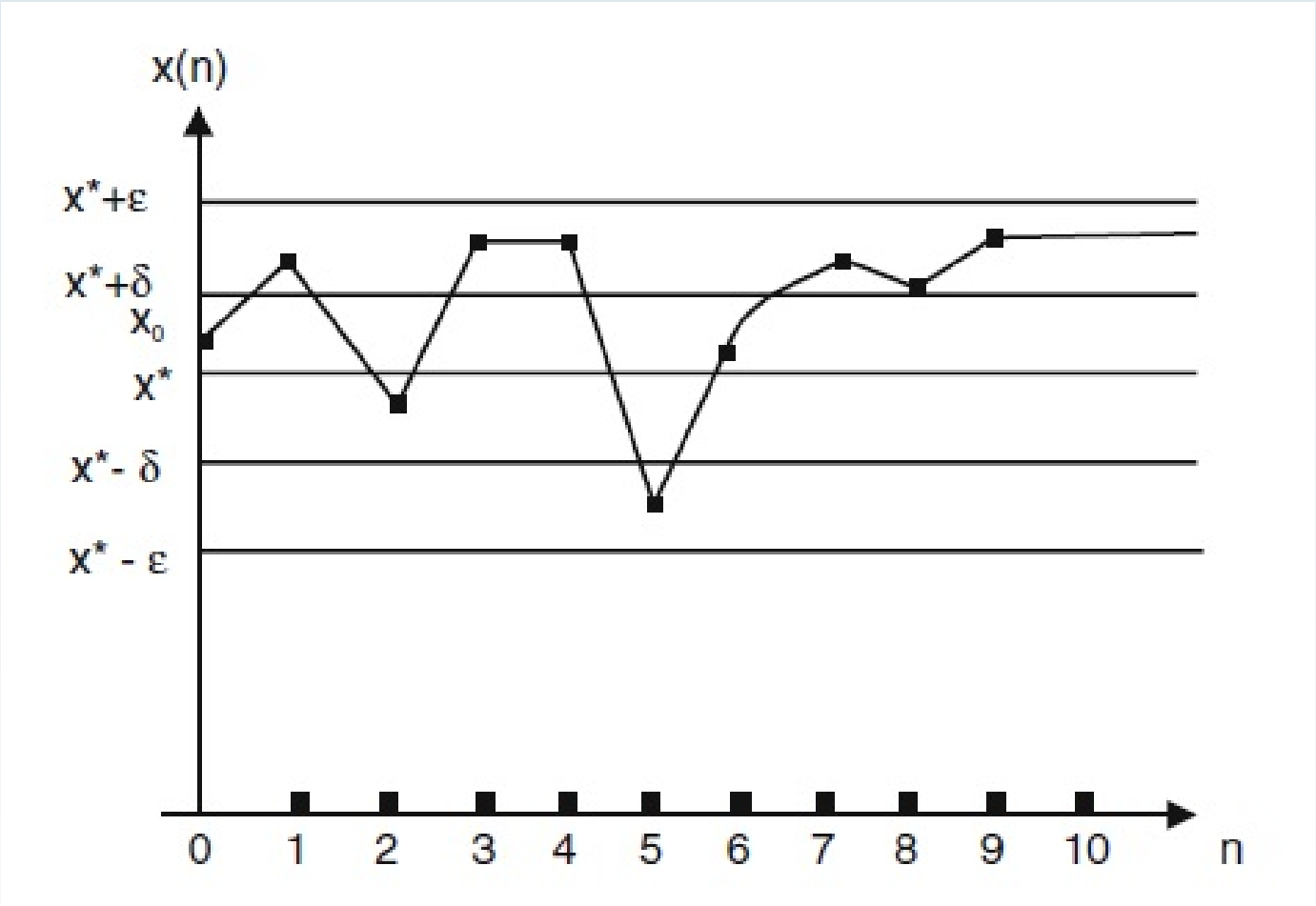

Figure 6.1: Stable equilibrium x^*.

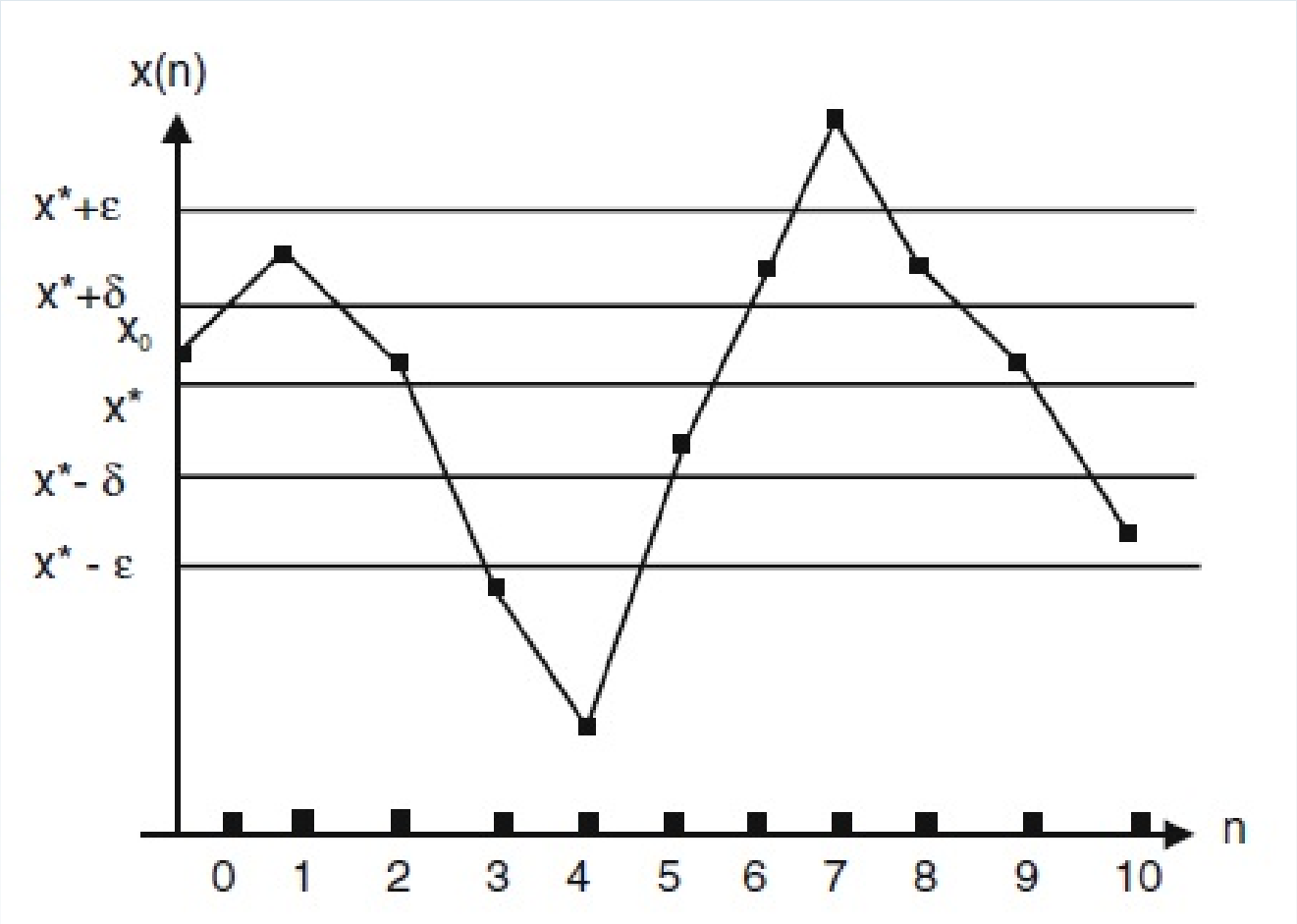

Figure 6.2: Unstable equilibrium x^*.

Definition

Let x^* be a stable equilibrium point of the continuous system (6.1). x^* is called locally asymptotically stable if there exists a $\delta > 0$ such that for $\|x_0 - x^*\| < \delta$, we have

$$\lim_{t \to \infty} x(t) = x^*.$$

Definition

Let x^* be a stable equilibrium point of the discrete system (6.2). x^* is called locally asymptotically stable if there exists a $\delta > 0$ such that for $\|x_0 - x^*\| < \delta$, we have

$$\lim_{n \to \infty} x_n = x^*.$$

- If $\delta \to \infty$, then x^* is globally asymptotically stable.

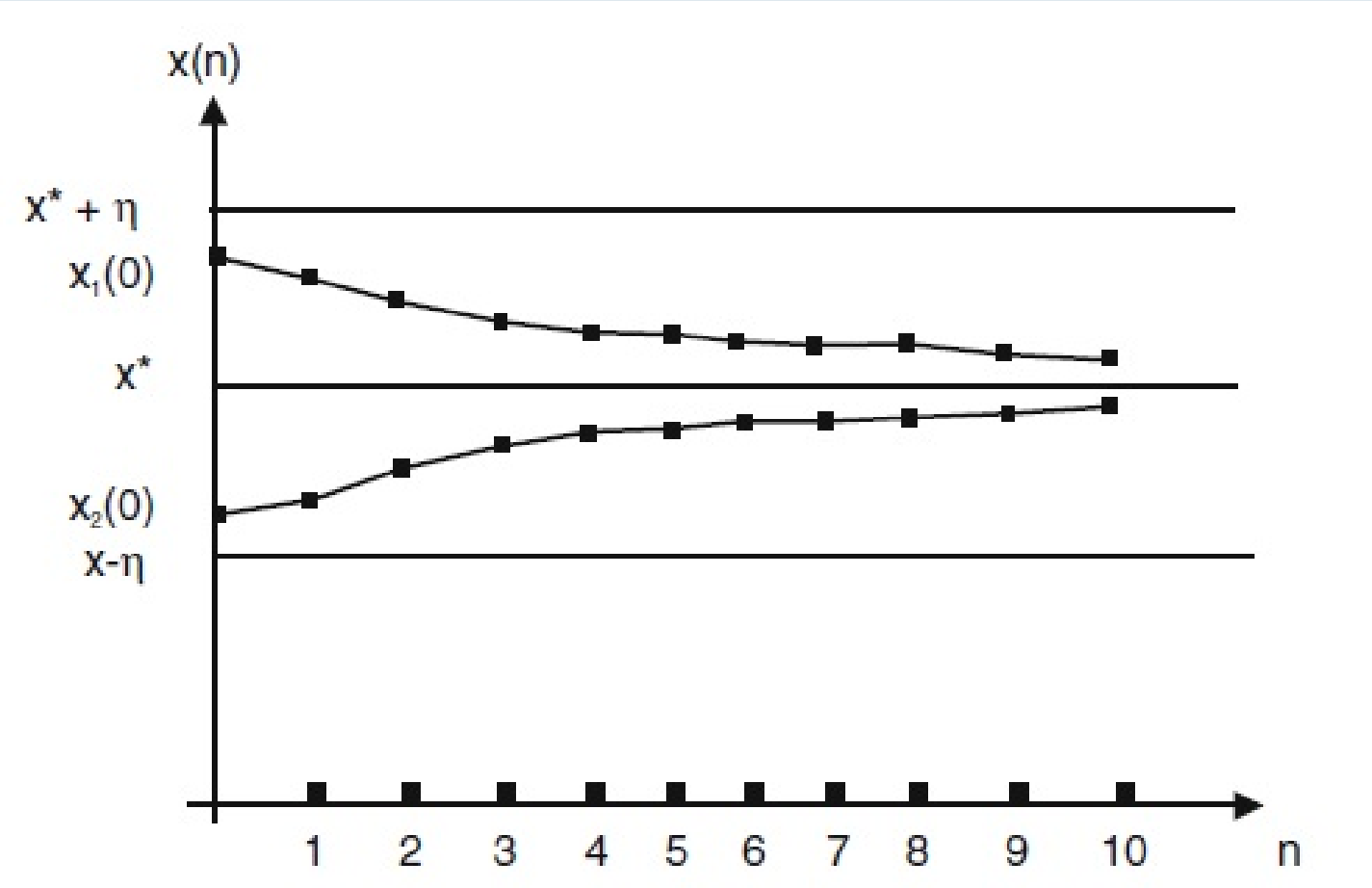

Figure 6.3: Asymptotically stable equilibrium x^*.

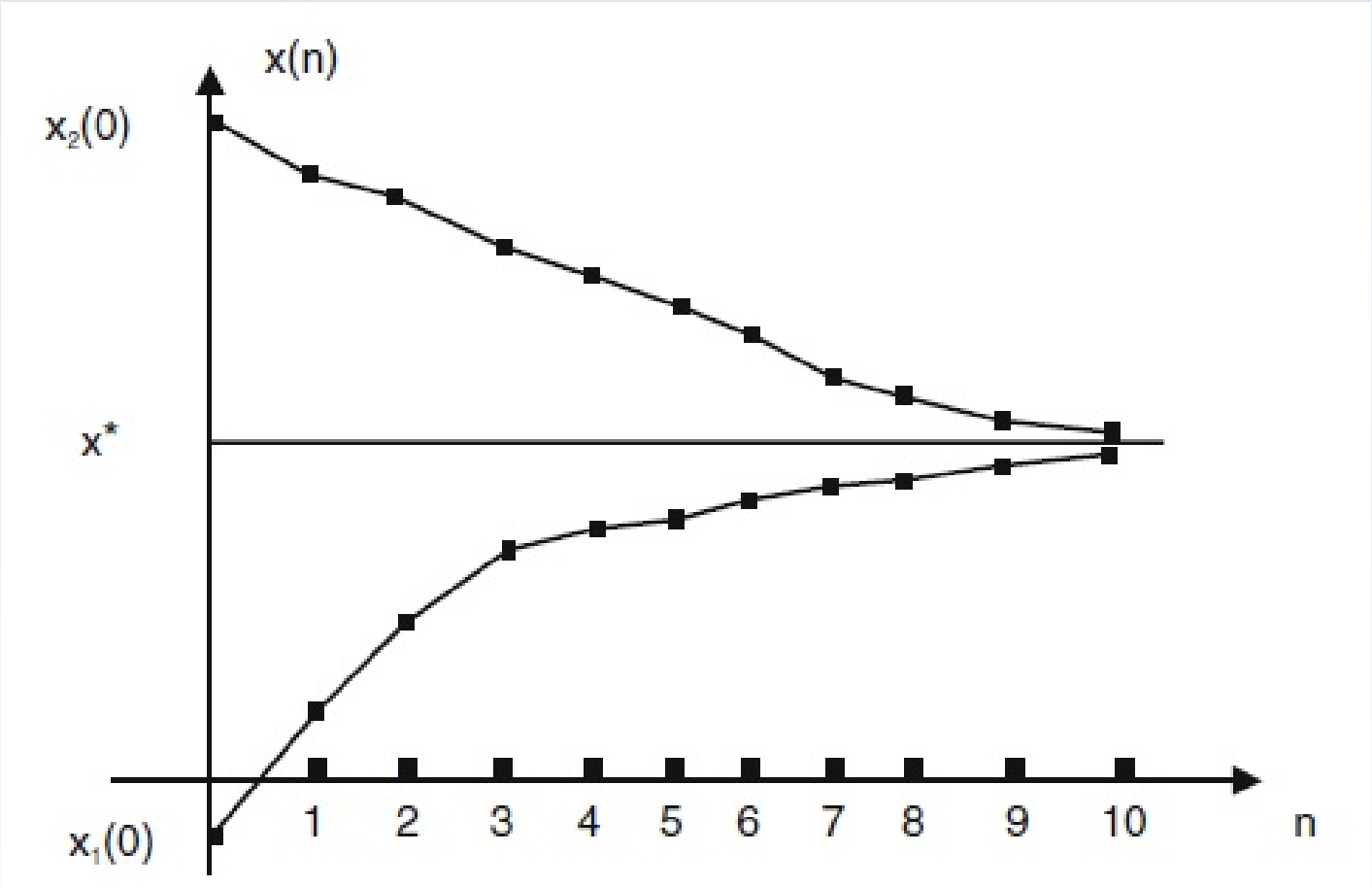

Figure 6.4: Globally asymptotically stable equilibrium x^*.

Definition (Schur-Cohn Criterion)

Let x^* be an equilibrium point of the continuous system (6.1), and $J(x^*)$ be the Jacobian matrix of f at x^*. Also, let λ_i, $i = 1, 2, \ldots, n$ are be the characteristic roots of $J(x^*)$. Then

(i) If λ_i's have negative real parts, then x^* is locally asymptotically stable.

(ii) If the real parts of λ_i's are zero, then x^* is stable but not asymptotically stable.

(iii) If λ_i's have positive real parts, then x^* is unstable.

Definition (Schur-Cohn Criterion)

Let x^* be an equilibrium point of the discrete system (6.2), and

$$p(\lambda) = \lambda^n + a_1\lambda^{n-1} + \cdots + a_n$$

be the characteristic polynomial of the system. Then x^* is locally asymptotically stable if and only if

(i) $p(1) > 0$,

(ii) $(-1)^n p(-1) > 0$,

(iii) The $(n-1) \times (n-1)$ matrices

$$B_{n-1}^{\pm} = \begin{pmatrix} 1 & 0 & \cdots & 0 & 0 \\ p_1 & 1 & \cdots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ p_{n-3} & p_{n-4} & \cdots & 1 & 0 \\ p_{n-2} & p_{n-3} & \cdots & p_1 & 1 \end{pmatrix} \pm \begin{pmatrix} 0 & 0 & \cdots & 0 & p_n \\ 0 & 0 & \cdots & p_n & p_{n-1} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & p_n & \cdots & p_4 & p_3 \\ p_n & p_{n-1} & \cdots & p_3 & p_2 \end{pmatrix}$$

are positive innerwise.

Definition (Positively Invariant Set)

A subset $\Omega \subseteq \mathbb{R}^n$ is said to be positively invariant with respect to the continuous system (6.1) if, for every $x_0 \in \Omega$ and $t \geq 0$, $x(t) \in \Omega$.

Definition (Positive Definite Function)

Let x^* be an equilibrium point of the continuous system (6.1). A function $V : \mathbb{R}^n \to \mathbb{R}$ is said to be positive definite at x^* if it satisfies the following conditions:

(i) $V(x^*) = 0$,

(ii) $V(x) > 0$ for all $x \in B(x^*, \delta)$ and $\delta > 0$.

Definition (Lyapunov Function)

Let x^* be an equilibrium point of the continuous system (6.1), the set Ω be positively invariant and $V : \Omega \to \mathbb{R}$ be positive definite at x^*. If

$$\lim_{\|x\| \to \infty} V(x) = \infty,$$

then the function V is said to be a Lyapunov function.

Definition (Lyapunov Function)

Let x^* be an equilibrium point of the discrete system (6.2), the set Ω be positively invariant and $V_n : \Omega \to \mathbb{R}$ be positive definite at x^*. If

- V_n is continuous on Ω,
- $\Delta V_n(x) \leq 0$, for all $x \in \Omega$, $x \neq x^*$.

then the function V_n is said to be a Lyapunov function.

Definition (Lyapunov Stability Theorem)

Let x^* be an equilibrium point of the continuous system (6.1) and V be a Lyapunov function. If

$$V(x) < 0$$

for all $x \neq x^*$, then x^* is globally asymptotically stable.

Definition (Lyapunov Stability Theorem)

Let x^* be an equilibrium point of the discrete system (6.2) and V be a Lyapunov function. If

- $\Delta V_n(x) < 0$ for all $x \neq x^*$,
- $\lim_{\|x\| \to \infty} V_n(x) = \infty$,

then x^* is globally asymptotically stable.

Definition (LaSalle's Invariance Principle)

Let x^* be an equilibrium point of the continuous system (6.1). Suppose $\Omega \subset \mathbb{R}^n$ is a bounded and positively invariant set. Let $V : \Omega \to \mathbb{R}$ be a Lyapunov function such that for every $x \in \Omega$,

$$V'(x) \leq 0.$$

Define the invariant set

$$M = \{x \in \Omega \mid V'(x) = 0\}.$$

If M contains only the equilibrium point x^*, then x^* is globally asymptotically stable.

Definition (LaSalle's Invariance Principle)

Let x^* be an equilibrium point of the discrete system (6.2). Suppose $\Omega \subset \mathbb{R}^n$ is a bounded and positively invariant set. Let $V_n : \Omega \to \mathbb{R}$ be a Lyapunov function such that for every $x \in \Omega$,

$$\Delta V_n(x) \leq 0.$$

Define the invariant set

$$M = \{x \in \Omega \mid \Delta V_n(x) = 0\}.$$

If M contains only the equilibrium point x^*, then x^* is globally asymptotically stable.

Definition

Let $\Gamma(u_0, t)$ be a solution orbit of (6.1) with initial point $u_0 = (x_0, y_0)$. In this case,

(i) The part of the solution orbit for $t \leq t_0$ is called the **negative orbit** and denoted by $\Gamma^-(u_0, t)$.

(ii) The part of the solution orbit for $t \geq t_0$ is called the **positive orbit** and denoted by $\Gamma^+(u_0, t)$.

Definition

Let $\Gamma(u_0, t)$ be a solution orbit of (6.1) with initial point $u_0 = (x_0, y_0)$ and let solutions be bounded. In this case,

(i) The set that the negative orbit converges to is called the α-**limit set**:

$$\alpha(u_0) = \left\{ a \in \mathbb{R}^2 \mid \exists \{t_i\}_{i=1}^{-\infty} \text{ such that } \lim_{t_i \to \infty} (x(t_i), y(t_i)) = a \right\}$$

(ii) The set that the positive orbit converges to is called the ω-**limit set**:

$$\omega(u_0) = \left\{ a \in \mathbb{R}^2 \mid \exists \{t_i\}_{i=1}^{-\infty} \text{ such that } \lim_{t_i \to \infty} (x(t_i), y(t_i)) = a \right\}$$

Theorem (Poincaré-Bendixson Theorem)

Let $\Gamma^+(u_0, t)$ be the positive orbit contained in a closed and bounded region in the plane. Assume that its ω-limit set contains no equilibrium points. Then one of the following holds:

(i) $\Gamma^+(u_0, t)$ is a periodic orbit (i.e., $\Gamma^+(u_0, t) = \omega(u_0)$).

(ii) $\omega(u_0)$ is a periodic orbit.

Theorem (Poincaré-Bendixson Trichotomy)

Let $\Gamma^+(u_0, t)$ be the positive orbit contained in a closed and bounded region D in the plane. Assume D contains a finite number of equilibrium points. Then one of the following holds:

(i) $\omega(u^0)$ is an equilibrium point.

(ii) $\omega(u^0)$ is a periodic orbit.

(iii) $\omega(u^0)$ consists of a finite number of equilibrium points and contains orbits Γ_i such that each Γ_i's α- and ω-limit sets contain one of these equilibrium points.

Theorem (Bendixson's Criterion)

Let $D \subseteq \mathbb{R}^2$ be a simply connected open set. If

$$\operatorname{div}(f, g) \equiv \frac{\partial f}{\partial x} + \frac{\partial g}{\partial y}$$

is nonzero and does not change sign in D, then the system has no periodic orbits in D.

Theorem (Dulac's Criterion)

Let $D \subseteq \mathbb{R}^2$ be a simply connected open set and $B : D \to \mathbb{R}$ be a function with first partial derivatives. If

$$\operatorname{div}(Bf, Bg) = \frac{\partial (Bf)}{\partial x} + \frac{\partial (Bg)}{\partial y}$$

is nonzero and does not change sign in D, then the system has no periodic solutions in D. B is called a **Dulac function**.

Relation Between Difference and Differential Equations

- A mathematical model is established with the help of differential equations and difference equations.
- Discrete-time epidemic models have an important place in mathematical epidemiology.
- However, research on discrete-time epidemic models is currently very scarce in the literature.
- Defining the model discretely or examining the continuous model by discretizing it has many advantages in mathematical epidemiology.

- Collecting epidemic data generally in separate time units (such as daily, monthly, annual) is just one of these advantages.
- For this reason, it may be more useful to use discrete-time models in the mathematical modeling of epidemic diseases.
- These models are more advantageous than continuous ones.
- On the other hand, difference equations are discrete analogues of ordinary differential equations and are used to study their numerical solutions.

- In cases where analytical solutions of the differential equation system cannot be obtained, a discrete equation related to the relevant equation can be used.
- Therefore, there is a need to discretize the system to calculate good analytical approximations of the solutions.
- Recently, the nonstandard finite difference scheme was proposed by Mickens ([5, 6, 7]) and has attracted great attention.
- An important advantage of the Mickens method is that it provides more effective preservation of global asymptotic stability (compared to the Euler and Runga Kutta methods).

Euler Method

Consider the first-order differential equation

$$\frac{dy}{dt} = f(t, y(t)), \quad y(t_0) = y_0, \quad t_0 \leq t \leq b.$$

Let us divide the interval $[t_0, b]$ into N equal subintervals. The size of each subinterval is called step size of the method and is denoted by $h = \frac{b-t_0}{N}$. This step size defines the nodes $t_0, t_1, \ldots, t_N$, where $t_j = t_0 + jh$. To derive the discrete equation, the derivative $\frac{dy}{dt}$ is approximated by a difference quotient,

$$\frac{dy}{dt} \approx \frac{y(t+h) - y(t)}{h}.$$

Substituting this value into the differential equation gives

$$y(t+h) = y(t) + hf(t, y(t)).$$

For $t = t_0 + nh$, we obtain

$$y(t_0 + (n+1)h) = y(t_0 + nh) + hf(t_0 + nh, y(t_0 + nh))$$

for $n = 0, 1, \ldots, N-1$.
Adapting the difference equation notation and replacing $y(t_0 + nh)$ by $y(n)$ gives

$$y(n+1) = y(n) + hf(n, y(n)).$$

This equation defines Euler's algorithm, which approximates the solutions of the differential equation at the node points.

An NSFD Method

- In [5, 6, 7], a nonstandard finite difference (NSFD) method was introduced.
- The NSFD method is based on two fundamental principles:
  - The substitution of discrete first-order derivatives with an expression of the form:

$$\frac{dy}{dt} = \frac{y_{n+1} - y_n}{\varphi(h)},$$

    where h denotes the time step size, and φ represents the denominator function satisfying $\varphi(h) = h + O(h^2)$.
  - Utilization of nonlocal approximations for replacing linear or nonlinear functions of y, such as $y^2 \approx y_{n+1}y_n$.

- It's crucial to recognize that here isn't a unique NSFD scheme for a given differential equation.
- Therefore, the dynamical properties of an NSFD scheme must undergo analysis to verify whether it maintains dynamical consistency with its original continuous equation or not.

A Novel Hepatitis B Epidemic Model

- Recently, together with my PhD student Kemal Türk, we developed and analyzed a new Hepatitis B epidemic model.
- The model employed a Beddington-DeAngelis type incidence rate and included a constant vaccination rate.
- We ensured the model's properties such as non-negativity, boundedness, the basic reproduction number $\mathcal{R}_0$, stability nature, and bifurcation analysis.
- Using the Bendixson theorem, we demonstrated that the disease-free equilibrium is globally asymptotically stable when $\mathcal{R}_0 < 1$.
- We identified a transcritical bifurcation phenomenon occurring when $\mathcal{R}_0 = 1$.

- It was concluded, utilizing Dulac's criteria, that the endemic equilibrium is globally asymptotically stable when $\mathcal{R}_0 > 1$.
- Additionally, we derived a discrete system of difference equations by constructing a non-standard finite difference (NSFD) scheme from the continuous model.
- We showed that solutions of this discrete system maintain dynamic consistency for all finite step sizes.
- The theoretical results were further validated and visualized through numerical simulations.
- These simulations also illustrated that the NSFD scheme outperforms Euler or RK4 schemes, as indicated by our theoretical findings.
- Our study has been published in the Q1 quadrant journal "Journal of Applied Mathematics and Computing".

- Hepatitis B is one of the most dangerous epidemic diseases, causing the deaths of a large number of people.
- Hepatitis B infection is a viral disease that affects the liver and is caused by the Hepatitis B virus.
- If not detected early and treated, this disease can lead to cirrhosis, liver cancer, or liver failure, making it a global health issue.
- It is known that Hepatitis B causes an average of 800,000 deaths per year, and it is estimated that there are more than 350 million chronic carriers.

- The Hepatitis B virus can be transmitted through body fluids such as blood and semen.
- Vaccination programs are implemented to prevent the spread of Hepatitis B and are quite effective in controlling the disease ([8, 9, 10]).
- Various studies have been conducted to analyze the spread dynamics of Hepatitis B ([9, 10, 11, 12, 13]).
- Motivated by these studies, we developed a new approach to model the spread dynamics of Hepatitis B [19].

Constructing of the Model

Let us divide the population into the classes S, I and R, representing the susceptible, infected, and recovered individuals, respectively. Let's make the following assumptions on the model:

- Initially, the sizes of subpopulations $S(0), I(0), R(0)$ are non-negative.
- Newborn individuals enter the susceptible class.
- The incidence rate is of Beddington-DeAngelis type.
- Infected individuals can transmit the disease.
- Vaccinated individuals move to the recovered class.
- Recovered individuals have permanent immunity to the disease.

- Based on these assumptions, a new Hepatitis B epidemic model has been developed with the following system of differential equations:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \frac{\beta SI}{1+\alpha_1 S+\alpha_2 I} - (p+\mu)S, \\
\frac{dI}{dt} &= \frac{\beta SI}{1+\alpha_1 S+\alpha_2 I} - (\mu+\nu+\sigma)I, \\
\frac{dR}{dt} &= pS+\nu I-\mu R.
\end{aligned}$$

- Here,

$$S(0)>0,\ I(0)>0,\ R(0)>0,$$

and all parameters are non-negative.

Here are the definitions of the parameters:

- Λ: The recruitment rate into the population,
- β: The transmission rate of the disease,
- α_1: The effect of susceptible individuals on the transmission rate,
- α_2: The effect of infected individuals on the transmission rate,
- p: The vaccination rate,
- μ: The natural death rate,
- σ: The disease-induced death rate,
- ν: The recovery rate.

- Here, the parameters α_1 and α_2 can cause a saturation effect in the transmission rate as the number of susceptible and infected individuals increases.
- This is the fundamental difference between the Beddington-DeAngelis incidence rate and the bilinear incidence rate.

Dynamical Analysis of the Model

- Since the first two equations in the system are independent of the variable R, it is sufficient to examine the following reduced model:

$$\begin{aligned} \frac{dS}{dt} &= \Lambda - \frac{\beta SI}{1+\alpha_1 S+\alpha_2 I} - (p+\mu)S, \\ \frac{dI}{dt} &= \frac{\beta SI}{1+\alpha_1 S+\alpha_2 I} - (\mu+\nu+\sigma)I. \end{aligned} \tag{8.1}$$

- It can be easily seen that the set

$$\Omega = \left\{ (S,I) \in \mathbb{R}^2_+ \mid S+I \leq \frac{\Lambda}{\mu} \right\} \tag{8.2}$$

is a positively invariant set for the solutions of the model (8.1).

- Additionally, the system has two equilibrium points $E_0 = (S_0, I_0)$ and $E^* = (S^*, I^*)$, where

$$\begin{aligned} S_0 &= \frac{\Lambda}{p+\mu}, \\ I_0 &= 0, \\ S^* &= \frac{\mu+\nu+\sigma+\alpha_2\Lambda}{\beta-\alpha_1(\mu+\nu+\sigma)+\alpha_2(p+\mu)}, \\ I^* &= \frac{\beta\Lambda-(p+\mu+\alpha_1\Lambda)(\mu+\nu+\sigma)}{(\mu+\nu+\sigma)(\beta-\alpha_1(\mu+\nu+\sigma)+\alpha_2(p+\mu))}. \end{aligned}$$

- The basic reproduction number is calculated as:

$$\mathcal{R}_0 = \frac{\beta\Lambda}{(p+\mu+\alpha_1\Lambda)(\mu+\nu+\sigma)}$$

- E_0 is always exists while E^* is exists if and only if $\mathcal{R}_0 > 1$.

Theorem

The equilibrium E_0 is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.

Proof.

The Jacobian matrix at E_0 is given by

$$J_0 = \begin{pmatrix} -(p+\mu) & -\mathcal{R}_0(\mu+\nu+\sigma) \\ 0 & (\mathcal{R}_0-1)(\mu+\nu+\sigma) \end{pmatrix}.$$

From this, the eigenvalues of J_0 are

$$\lambda_1 = -(p+\mu), \quad \lambda_2 = (\mu+\nu+\sigma)(\mathcal{R}_0-1).$$

For $\mathcal{R}_0 < 1$, both λ_1 and λ_2 are negative, implying that E_0 is locally asymptotically stable. For $\mathcal{R}_0 > 1$, λ_2 is positive, implying that E_0 is unstable. □

Theorem

If $\mathcal{R}_0 < 1$, then E_0 is globally asymptotically stable.

Proof.

Since E^* does not exist for $\mathcal{R}_0 < 1$, the only equilibrium point of system (8.1) is E_0. Thus, solutions push towards the I-axis. According to (8.2), solutions are bounded and the S-axis is positively invariant. Moreover, since E_0 is locally asymptotically stable, by the Bendixson's Trichotomy, all positive solutions of model (8.1) converge to E_0. Therefore, E_0 is globally asymptotically stable. □

Theorem

If $\mathcal{R}_0 > 1$, then the equilibrium E^* is locally asymptotically stable.

Proof.

The Jacobian matrix at E^* can be calculated as

$$J^* = \begin{pmatrix} -\frac{[\beta\Lambda - a(b+\alpha_1\Lambda)](\beta-\alpha_1 a)}{\beta(a+\alpha_2\Lambda)} - b & -\frac{a^2[\beta+\alpha_2(b+\alpha_1\Lambda)]}{\beta(a+\alpha_2\Lambda)} \\ \frac{[\beta\Lambda - a(b+\alpha_1\Lambda)](\beta-\alpha_1 a)}{\beta(a+\alpha_2\Lambda)} & \frac{a^2[\beta+\alpha_2(b+\alpha_1\Lambda)]}{\beta(a+\alpha_2\Lambda)} - a \end{pmatrix},$$

where

$$a = \mu + \nu + \sigma, \quad b = p + \mu.$$

For the eigenvalues of the matrix to be negative, it should satisfy $\mathrm{Tr}(J^*) < 0$ and $\det(J^*) > 0$. □

Proof (Continued).

After long mathematical calculations, the trace and determinant can be computed as

$$\mathrm{Tr}(J^*) = -\frac{(\mathcal{R}_0-1)a^2(b+\alpha_1\Lambda)[\mathcal{R}_0 b+(\mathcal{R}_0-1)\alpha_1\Lambda+\alpha_2\Lambda]}{\beta\Lambda(a+\alpha_2\Lambda)} - b,$$

$$\det(J^*) = \frac{(\mathcal{R}_0-1)a^2(b+\alpha_1\Lambda)\left[\mathcal{R}_0 ab+(\mathcal{R}_0-1)a\alpha_1\Lambda+\alpha_2 b\right]}{\beta\Lambda(a+\alpha_2\Lambda)}.$$

Therefore, for $\mathcal{R}_0 > 1$, the trace is negative and the determinant is positive, which implies that E^* is locally asymptotically stable. □

Theorem

If $R_0 > 1$, then E^* is globally asymptotically stable.

Proof.

Let

$$f(S,I) = \Lambda - \frac{\beta SI}{1+\alpha_1 S+\alpha_2 I} - (p+\mu)S,$$
$$g(S,I) = \frac{\beta SI}{1+\alpha_1 S+\alpha_2 I} - (\mu+\nu+\sigma)I$$

be defined. Let $B : \Omega \to \mathbb{R}$, $B(S,I) = I^{-1}$ be a Dulac function. Then, for every $(S,I) \in \Omega$,

$$\frac{\partial(Bf)}{\partial S} + \frac{\partial(Bg)}{\partial I} = -\frac{\beta(1+\alpha_2 I)}{(1+\alpha_1 S+\alpha_2 I)^2} - \frac{p+\mu}{I} - \frac{\alpha_2\beta S}{(1+\alpha_1 S+\alpha_2 I)^2} < 0.$$

Thus, the (8.1) model has no periodic orbits in Ω. Since solutions are bounded and E_0 is unstable for $\mathcal{R}_0 > 1$, by Dulac's Criterion, E^* is globally asymptotically stable. □

Theorem

At $R_0 = 1$, the model undergoes a transcritical bifurcation.

Proof.

Let the (8.1) model be written as $S = \gamma_1$ and $I = \gamma_2$ as follows:

$$f_1(\gamma_1, \gamma_2) = \Lambda - \frac{\beta\gamma_1\gamma_2}{1 + \alpha_1\gamma_1 + \alpha_2\gamma_2} - (p + \mu)\gamma_1,$$

$$f_2(\gamma_1, \gamma_2) = \frac{\beta\gamma_1\gamma_2}{1 + \alpha_1\gamma_1 + \alpha_2\gamma_2} - (\mu + \nu + \sigma)\gamma_2.$$

The Jacobian matrix at E_0 point of (8.1) model for $\mathcal{R}_0 = 1$ and $\beta = \beta^* = \frac{(p+\mu+\alpha_1\Lambda)(\mu+\nu+\sigma)}{\Lambda}$ is

$$J = \begin{pmatrix} -(p + \mu) & -\frac{\beta^*\Lambda}{p+\mu+\alpha_1\Lambda} \\ 0 & \frac{\beta^*\Lambda}{p+\mu+\alpha_1\Lambda} - (\mu + \nu + \sigma) \end{pmatrix}.$$

Proof (Continued).

One of the eigenvalues of J is zero, indicating the presence of a bifurcation. Let the left and right eigenvectors corresponding to the zero eigenvalue be denoted by $u = [u_1, u_2]^T$ and $w = [w_1, w_2]$, respectively. Then the components of u and w can be calculated as follows:

$$u_1 = 0, \quad u_2 = 1, \quad \text{and} \quad w_1 = -\frac{\beta^* \Lambda}{(p+\mu)(p+\mu+\alpha_1 \Lambda)}, \quad w_2 = 1.$$

The bifurcation constants can be computed as

$$\xi_1 = \sum_{i,j,k=1}^{2} u_k w_i w_j \frac{\partial^2 f_k(E_0)}{\partial \gamma_i \partial \gamma_j} = -\frac{2\beta S_0}{(1+\alpha_1 S_0)^2}\left(\alpha_2 + \frac{\beta^* \Lambda}{(p+\mu)(p+\mu+\alpha_1 \Lambda)}\right) < 0,$$

$$\xi_2 = \sum_{i,k=1}^{2} v_k w_i \frac{\partial^2 f_k(E_0)}{\partial \gamma_i \partial \beta^*} = \frac{S_0}{1+\alpha_1 S_0} > 0.$$

Therefore, by Theorem 4.1 in [18], the (8.1) model undergoes a transcritical bifurcation at $\mathcal{R}_0 = 1$. □

Constructing of the NSFD Scheme

- Let the numerical approximations of $S(t), I(t)$, and $R(t)$ at discrete time points $t = nh$, $n \in \mathbb{N}_0$ be denoted by S_n, I_n, and R_n, respectively, where h is the time step size.
- The model is discretized using Mickens' approach as follows:

$$\begin{aligned}
\frac{S_{n+1} - S_n}{\varphi(h)} &= \Lambda - \frac{\beta S_{n+1} I_n}{1 + \alpha_1 S_n + \alpha_2 I_n} - (p + \mu) S_{n+1}, \\
\frac{I_{n+1} - I_n}{\varphi(h)} &= \frac{\beta S_{n+1} I_n}{1 + \alpha_1 S_n + \alpha_2 I_n} - (\mu + \nu + \sigma) I_{n+1}, \qquad (8.3) \\
\frac{R_{n+1} - R_n}{\varphi(h)} &= p S_{n+1} + \nu I_{n+1} - \mu R_{n+1}.
\end{aligned}$$

- Here,

$$S_0 > 0, \quad I_0 > 0, \quad R_0 > 0,$$

.

- The denominator function is

$$\varphi(h) = \frac{e^{\mu h} - 1}{\mu}.$$

- The denominator function is chosen to ensure the boundedness of the solutions.
- Since the first two equations are independent of R_n, it is sufficient to investigate the following system written in explicit form:

$$\begin{aligned} S_{n+1} &= \frac{\Lambda\varphi + S_n}{1 + \varphi(\phi + p + \mu)}, \\ I_{n+1} &= \frac{I_n + \varphi\phi S_{n+1}}{1 + \varphi(\mu + \nu + \sigma)}. \end{aligned} \tag{8.4}$$

- Here, $\phi = \phi(S, I) = \frac{\beta I}{1+\alpha_1 S+\alpha_2 I}$.

- For this model, the set

$$\Omega_d = \left\{ (S_n, I_n) \in \mathbb{R}^2_+ \mid S_n + I_n \leq \frac{\Lambda}{\mu} \right\}$$

  is a positively invariant region.
- The system (8.4) has exactly the same equilibrium points as the continuous model: E_0 and E^*.
- Now, the stability behavior of these equilibria will be examined.

- For simplicity, let's express the system as

$$F(S,I) = \frac{\Lambda\varphi + S_n}{1+\varphi(\phi+p+\mu)},$$
$$G(S,I) = \frac{I_n + \varphi\phi S_{n+1}}{1+\varphi(\mu+\nu+\sigma)}. \tag{8.5}$$

- In this case, the Jacobian matrix at an equilibrium $E = (S, I)$ of the discrete system (8.4) is

$$J(E) = \begin{pmatrix} \frac{\partial F}{\partial S}(S,I) & \frac{\partial F}{\partial I}(S,I) \\ \frac{\partial G}{\partial S}(S,I) & \frac{\partial G}{\partial I}(S,I) \end{pmatrix}.$$

Theorem

The equilibrium E_0 is locally asymptotically stable if $\mathcal{R}_0 < 1$ independent of h, and unstable if $\mathcal{R}_0 > 1$.

Proof.

The Jacobian matrix at E_0 is

$$J(E_0) = \begin{pmatrix} \frac{1}{1+\varphi(p+\mu)} & -\frac{\mathcal{R}_0\varphi(h)(\mu+\nu+\sigma)}{1+\varphi(h)(p+\mu)} \\ 0 & \frac{1+\mathcal{R}_0\varphi(h)(\mu+\nu+\sigma)}{1+\varphi(h)(\mu+\nu+\sigma)} \end{pmatrix}.$$

Therefore, the eigenvalues are

$$\lambda_1 = \frac{1}{1+\varphi(p+\mu)}, \quad \lambda_2 = \frac{1+\mathcal{R}_0\varphi(h)(\mu+\nu+\sigma)}{1+\varphi(h)(\mu+\nu+\sigma)}.$$

Clearly, if $\mathcal{R}_0 < 1$, then $|\lambda_{1,2}| < 1$ for each h. Thus, E_0 is locally asymptotically stable. Conversely, if $\mathcal{R}_0 > 1$, then $\lambda_2 > 1$, implying that E_0 is unstable. □

Theorem

The equilibrium E^* is locally asymptotically stable if $\mathcal{R}_0 > 1$ independent of h.

Proof.

The Jacobian at E^* is given by

$$J(E^*) = \begin{pmatrix} \frac{1}{x} + \frac{\alpha_1 t I^*}{x^2} & -\frac{(1+\alpha_1 S^*)t}{x^2} \\ \frac{1}{xy}\left[z + \frac{\alpha_1 t I^*}{x}(z-x)\right] & \frac{1}{y}\left[1 + \frac{t(1+\alpha_1 S^*)(x-z)}{x^2}\right] \end{pmatrix},$$

where

$$\begin{aligned} x &= 1 + \varphi(\phi^* + p + \mu) > 1, \\ y &= 1 + \varphi(\mu + \nu + \sigma) > 1, \\ z &= \varphi\phi^* > 0, \\ t &= \frac{\beta\varphi(\varphi\Lambda + S^*)}{(1 + \alpha_1 S^* + \alpha_2 I^*)} > 0. \end{aligned}$$

Proof (Continued).

Then,

$$\mathrm{Tr}(J(E^*)) = \frac{1}{x} + \frac{\alpha_1 t I^*}{x^2} + \frac{1}{y}\left[1 + \frac{1(1+\alpha_1 S^*)(x-z)}{x^2}\right],$$

$$\det(J(E^*)) = \frac{1}{x^2 y}(x + t(1 + \alpha_1 S^* + \alpha_1 I^*)).$$

For $|\mathrm{Tr}(J)| < 1 + \det(J) < 2$, E^* is locally asymptotically stable ([17]). This is ensured when $R_0 > 1$. □

Numerical Simulations

- Simulations are important tools to evaluate the suitability of the proposed mathematical model for real-world scenarios.
- Here, some numerical simulations will be provided to validate the theoretical results.
- Additionally, a comparison between the Euler and RK4 schemes will be made with the proposed NSFD scheme.
- Simulations are performed using MATLAB software.

Parameter	Value	Parameter	Value
Λ	0.5	p	0.00002
β	0.3 or 2	μ	0.06
α_1	0.8	ν	0.9
α_2	0.6	σ	0.08

Table 8.1: Parameter values used in simulations.

Example ($\mathcal{R}_0 < 1$ Case)

- According to the parameters given in Table 8.1, we have

$$\mathcal{R}_0 = 0.31353151869 < 1 \text{ and } E_0 = (8.33055648117, 0).$$

- In Figures below, a comparison of numerical solutions obtained from the Euler, RK4, and the proposed NSFD schemes for the Hepatitis B model is provided.
- The initial conditions are chosen as $S(0) = 100$, $I(0) = 40$, and the time step size $h = 4$.
- The Euler and RK4 schemes lead to negative populations and solutions do not converge to the equilibrium point.
- However, the proposed NSFD scheme does not suffer from these issues and provides consistent results.
- In Figures below, the NSFD scheme is simulated for different time step sizes, showing consistent results.

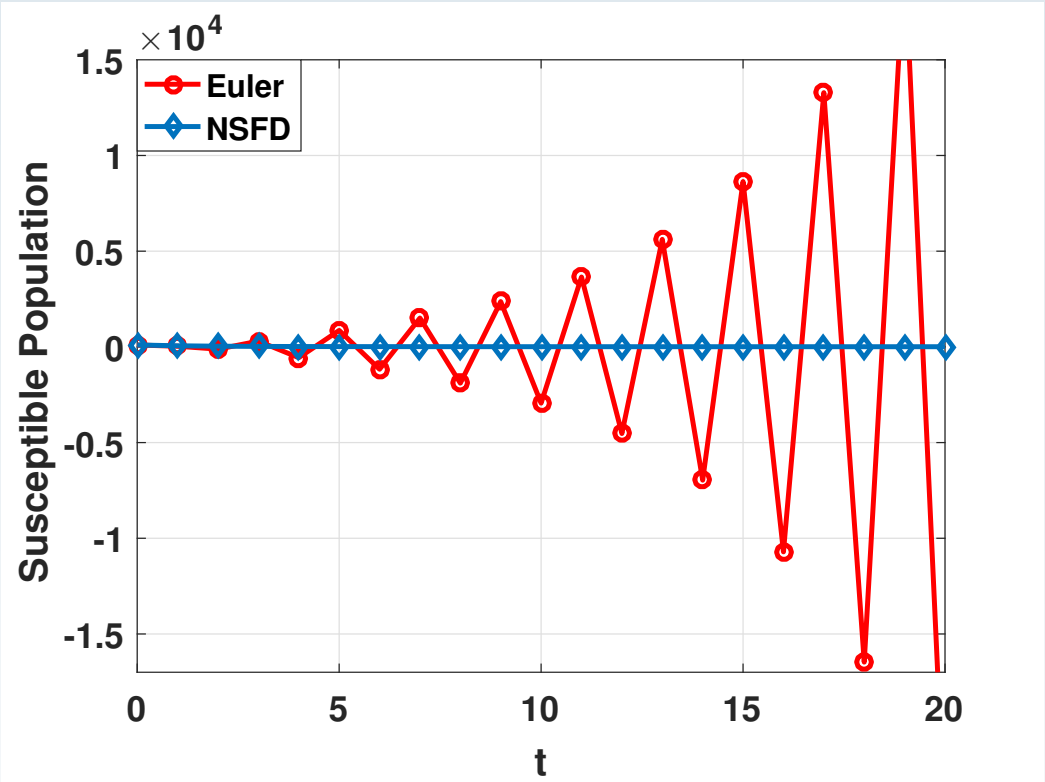

Figure 8.1: Comparison of numerical solutions obtained from Euler and NSFD schemes.

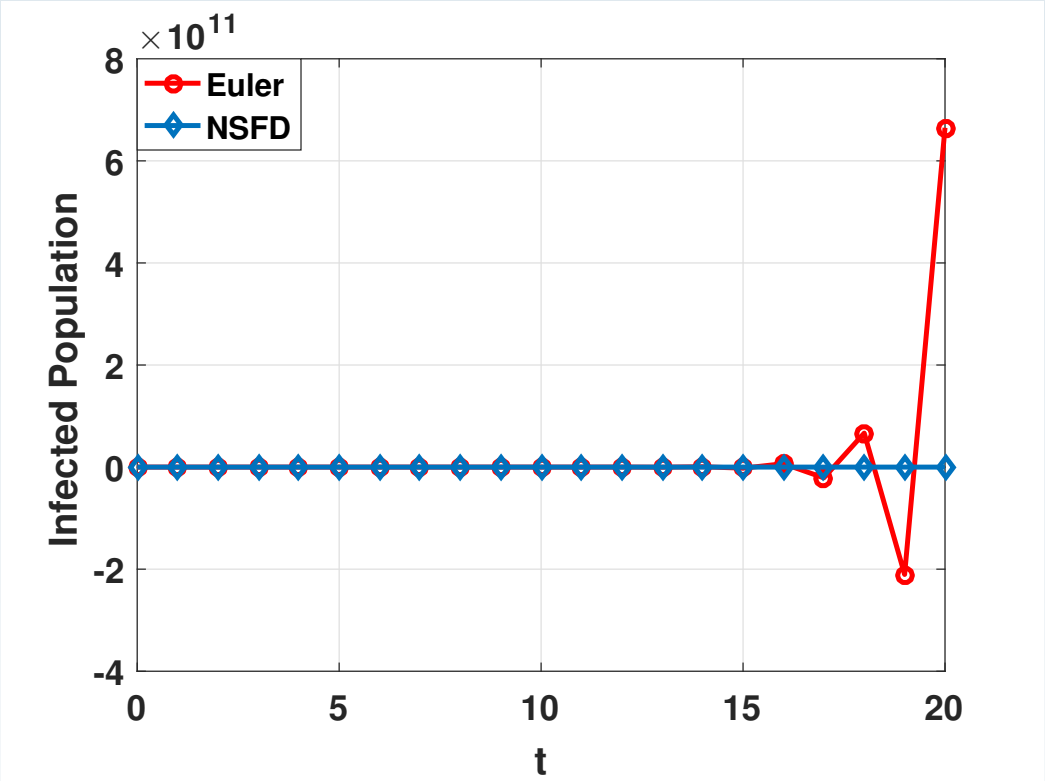

Figure 8.2: Comparison of numerical solutions obtained from Euler and NSFD schemes.

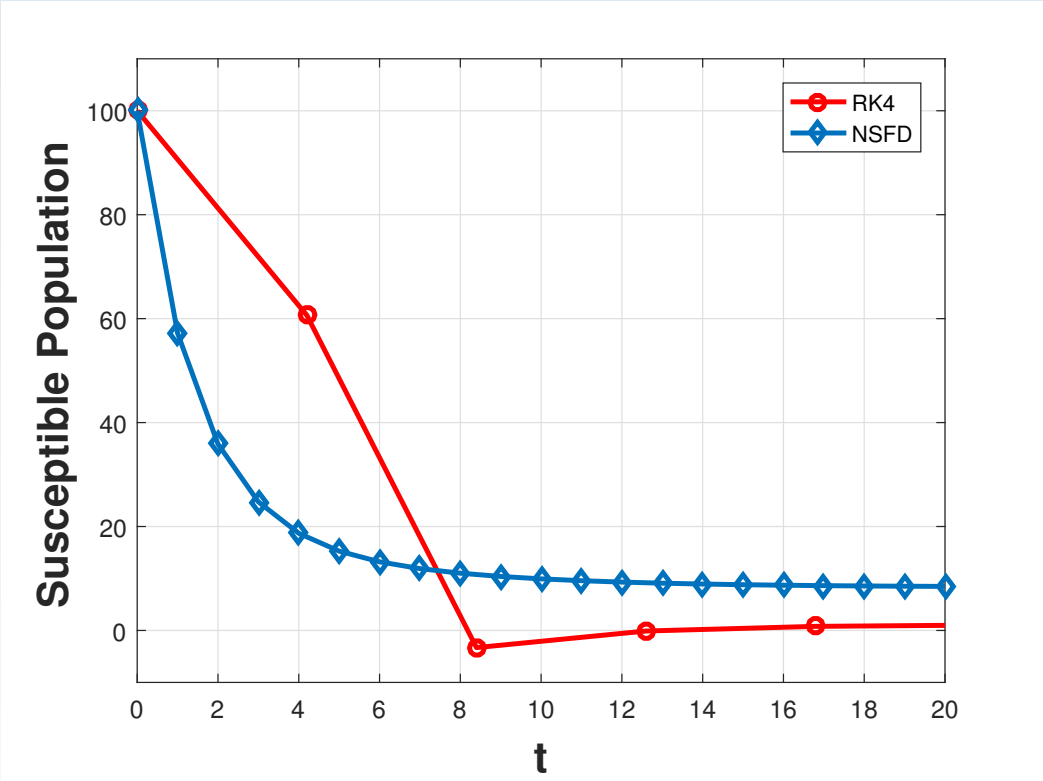

Figure 8.3: Comparison of numerical solutions obtained from Euler and NSFD schemes.

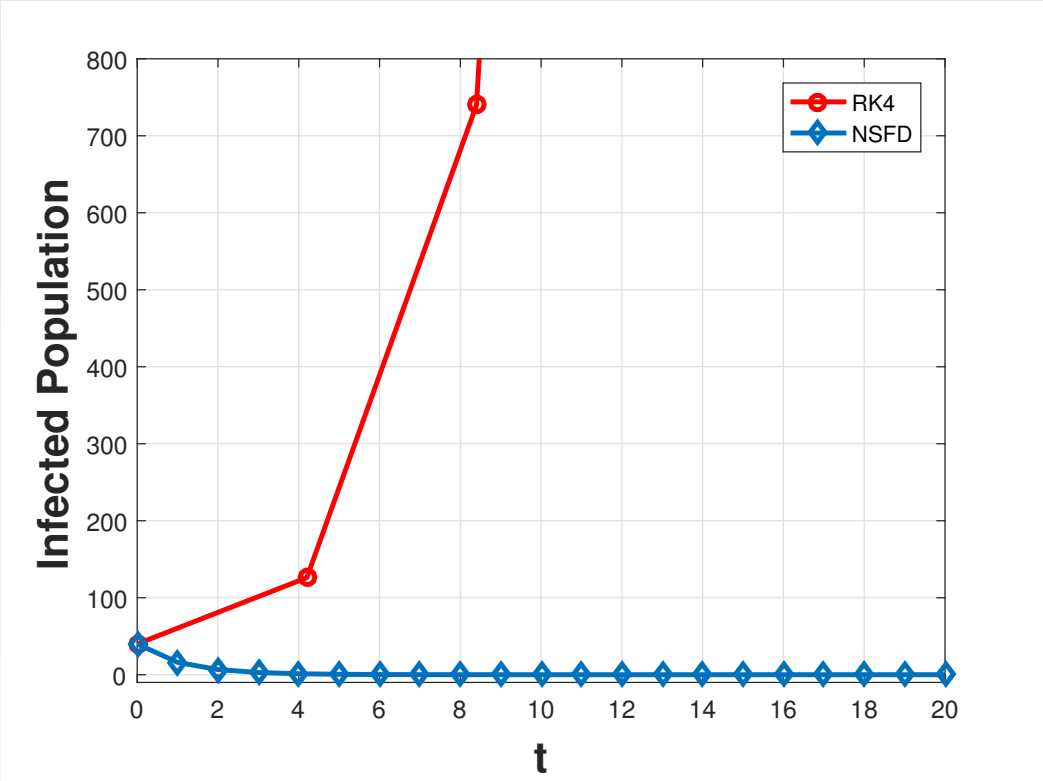

Figure 8.4: Comparison of numerical solutions obtained from Euler and NSFD schemes.

Example (Case of $\mathcal{R}_0 > 1$)

- Here, unlike the previous example, $\beta = 2$ is chosen. All other parameter values remain the same.
- In this case,

$$\mathcal{R}_0 = 2.09021012464 > 1 \text{ and } E^* = (1.11294571815, 0.41653942114).$$

- Figures given below shows the simulation of the global asymptotic stability of E^* in the $S - I$ phase plane.
- Here, the NSFD scheme is used for $h = 0.08$.
- Given figures presents a simulation showing the effect of the vaccination rate p on susceptible and infected populations.
- Figures, also simulate the effect of parameters α_1 and α_2 on susceptible and infected populations, respectively.

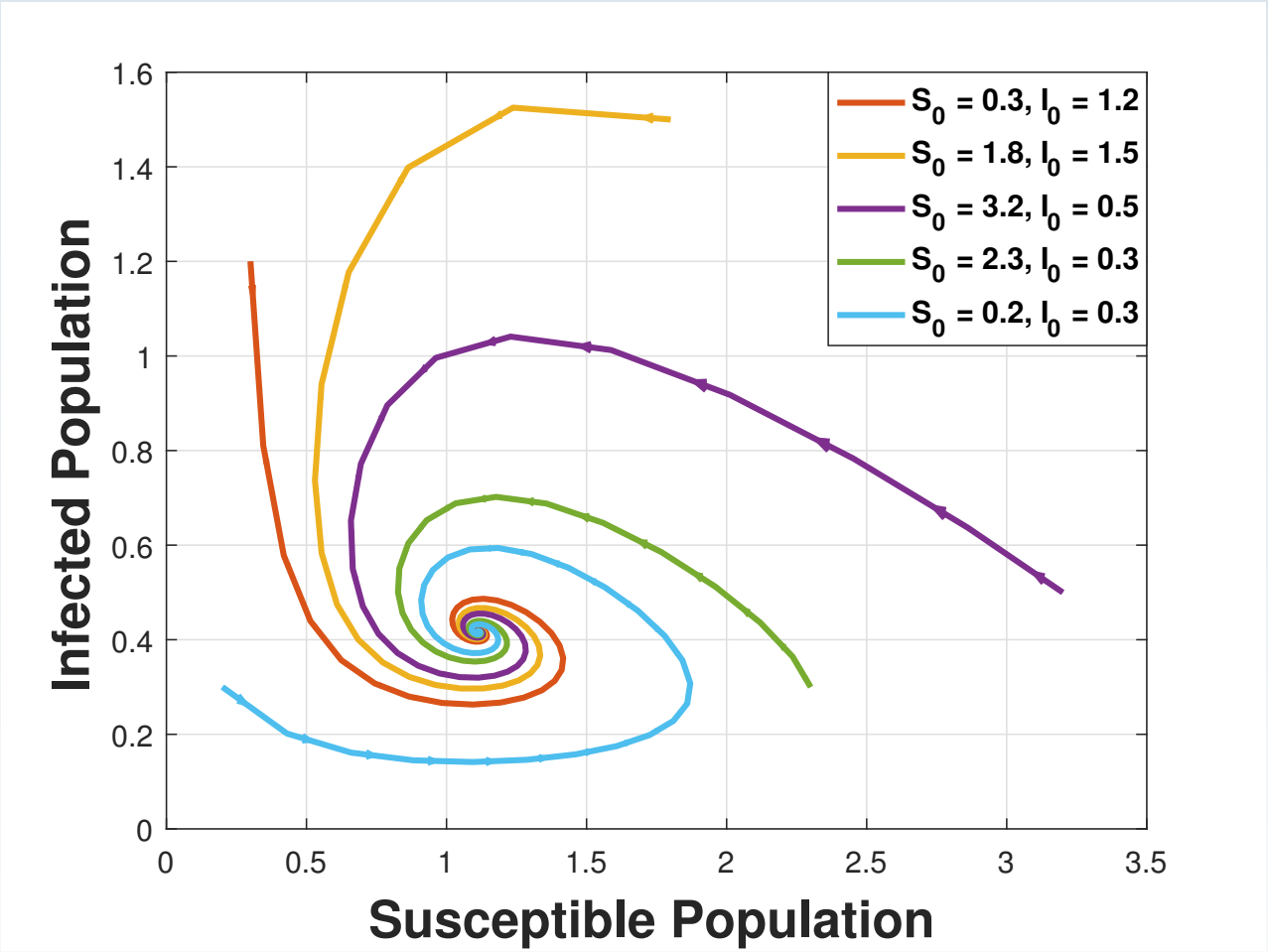

Figure 8.5: Global asymptotic stability of E^* with the NSFD scheme for $h = 0.08$.

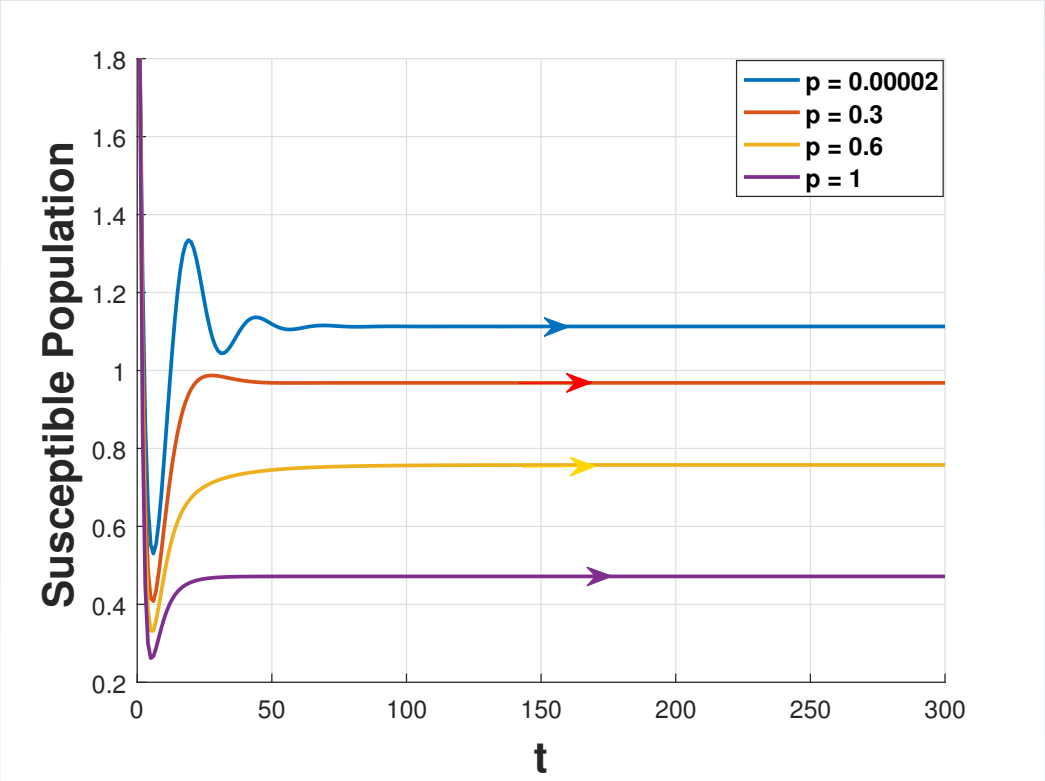

Figure 8.6: The effect of vaccination rate p on susceptibleindividuals.

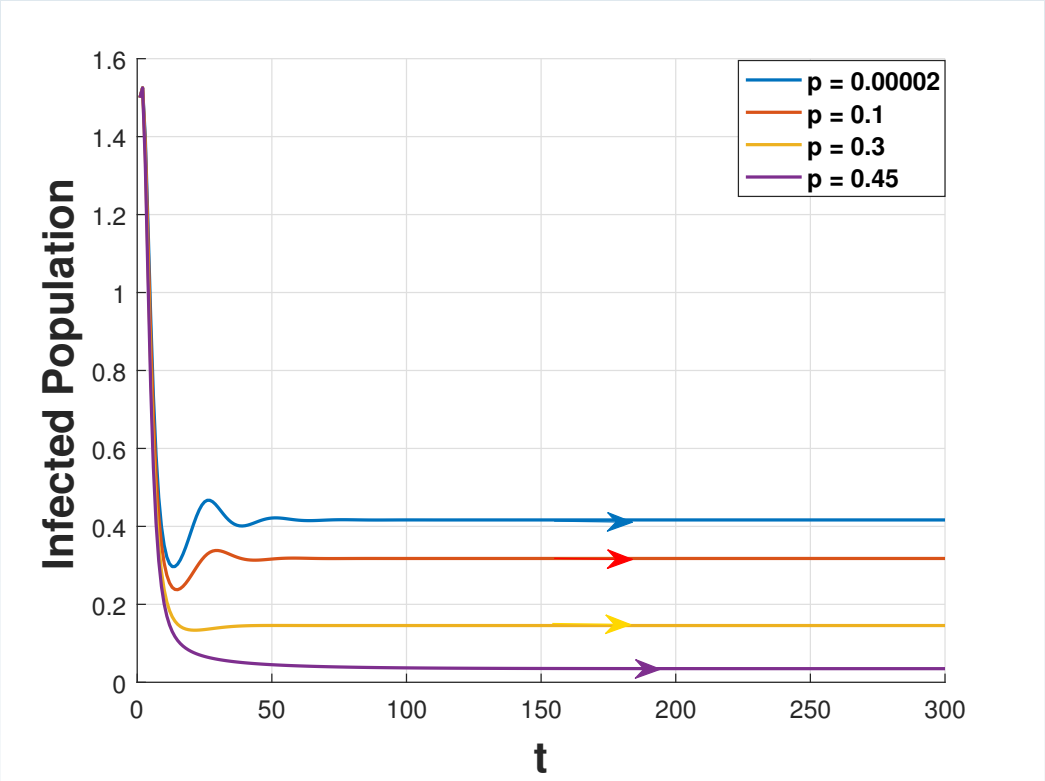

Figure 8.7: The effect of vaccination rate p on infected individuals.

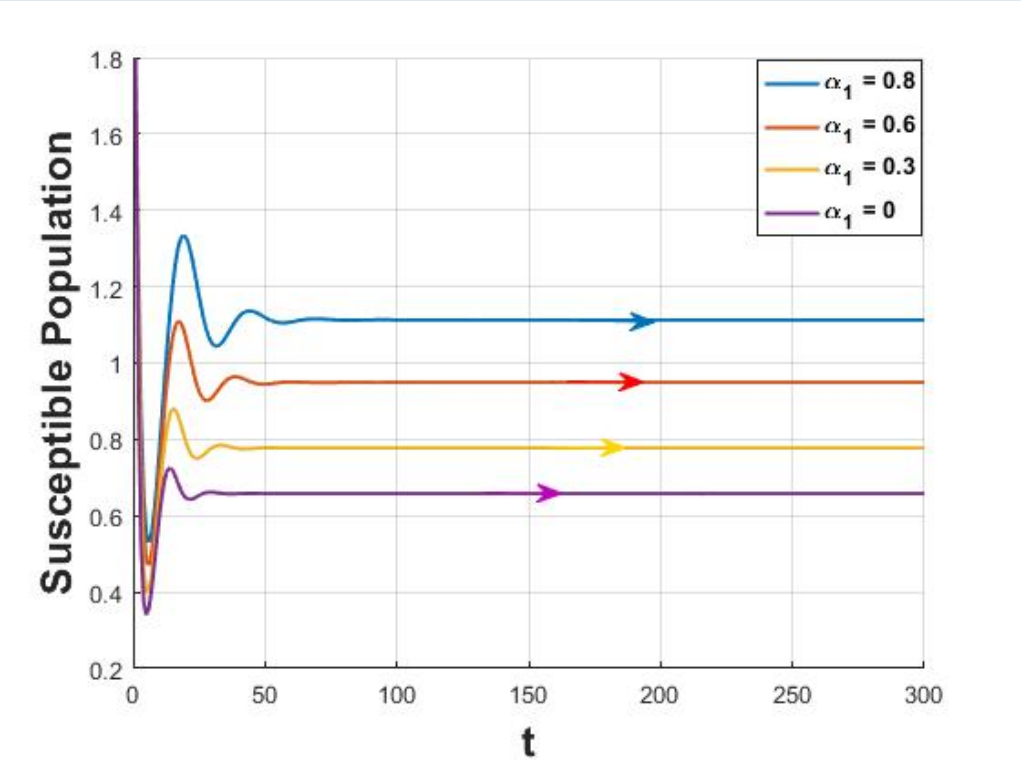

Figure 8.8: The effect of α_1 on susceptible individuals.

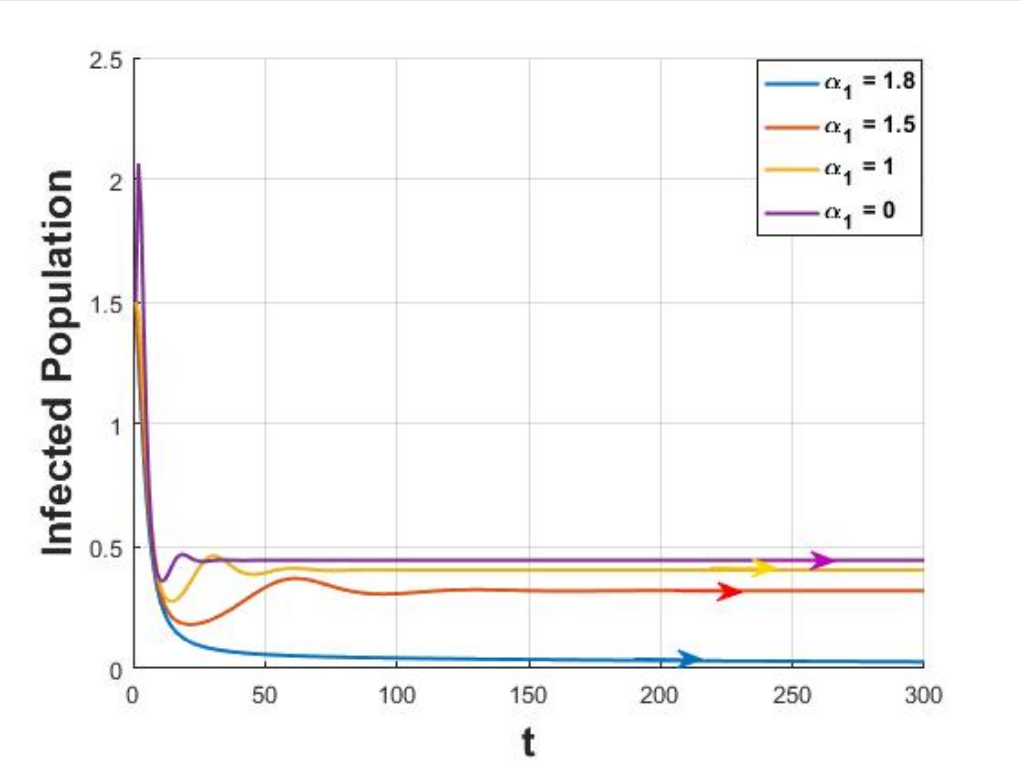

Figure 8.9: The effect of α_1 on infected individuals.

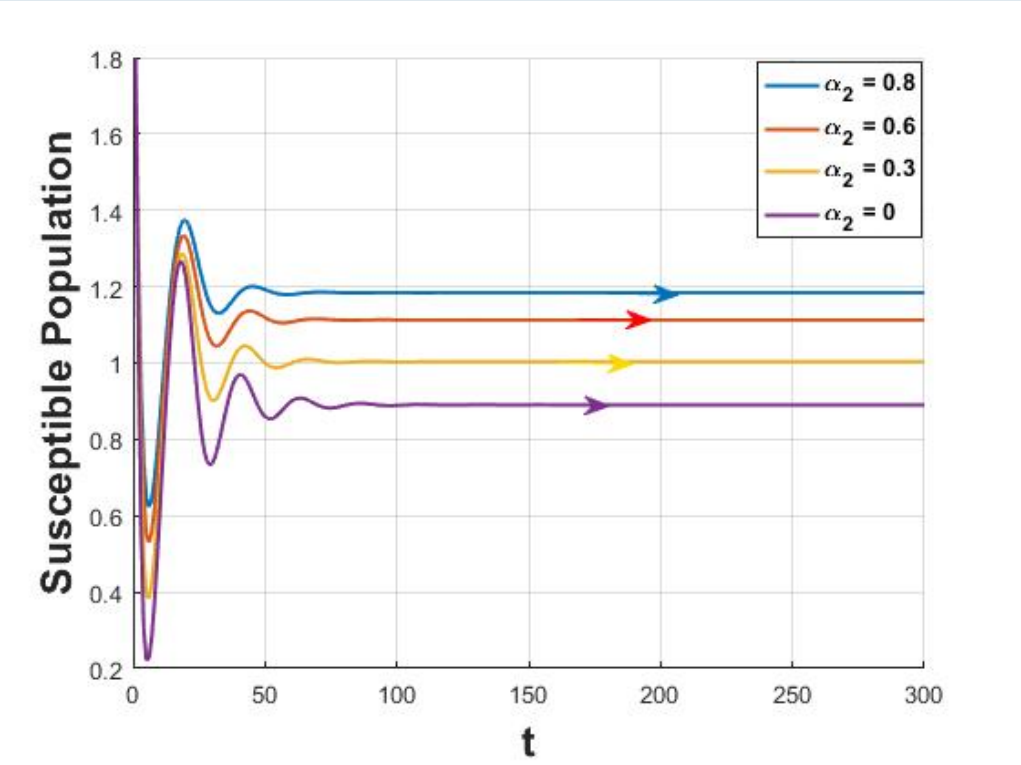

Figure 8.10: The effect of α_2 on susceptible individuals.

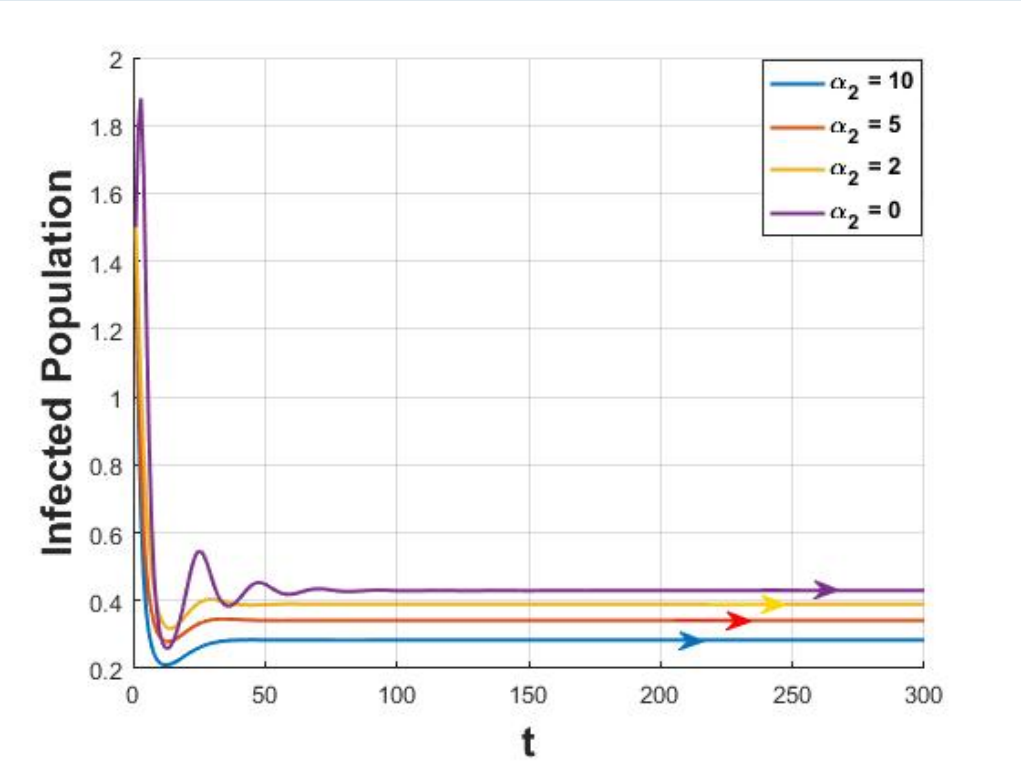

Figure 8.11: The effect of α_2 on infected individuals.

Obtained Results and Novelty in the Literature

- The obtained results provide important insights into reducing the spread of Hepatitis B.
- It can be said that the disease will be eradicated as long as the $\mathcal{R}_0$ threshold is below 1.
- Measures should be taken to reduce the transmission rate for this purpose.
- The most important way to achieve this is to increase vaccination programs and raise awareness among individuals to take preventive measures against the spread of the disease.

- Additionally, maintaining the birth rate within a certain range in the population will also be effective in reducing this threshold below 1.
- The accuracy of these predictions has been supported by numerical simulations.
- While there are models for Hepatitis B considering vaccination and different incidence rates in the literature, there is no model including both vaccination and Beddington-DeAngelis incidence rate.
- In this study, a more general model than those given in the literature has been considered, and both continuous and discrete structures have been investigated.

- Unlike classical methods in the literature, an NSFD approach has been used for discretization.
- It has been shown that the proposed discrete scheme provides dynamically consistent results with the continuous model.
- Therefore, the application of a discretization method that provides more successful results than classical methods has been presented.
- The advantages of this approach have been validated through numerical simulations.

Conjecture. The DFE point E^0 of the discrete HBV model (8.4) is GAS if $\mathcal{R}_0 < 1$, and the EE point E^* is GAS if $\mathcal{R}_0 > 1$, for all time-step sizes h.

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