

Machine Learning Approach for SEIJR Model in Medical Diagnosis



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DEDICATION

I express my sincere gratitude and
profound admiration as I dedicate this
work to my beloved

Hazrat Muhammad (S.A.W),

My esteemed teachers

and

My dear Parents.

They have been a constant source of inspiration and
encouragement, guiding me towards greater ideals in life.

DECLARATION

I hereby affirm research work presented in this thesis is entirely my own, except where acknowledgments have been made. This thesis represents my own composition and has not been submitted, in whole or in part, for any other academic degree.

Date _____

(Zeeshan Shamshad)
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I am deeply thankful to **my Parents and siblings** for their constant support, encouragement, and genuine concern for my academic achievements. My **Parents** selfless prayers and heartfelt wishes have always been a guiding force in my life. I am also grateful to **my Father** for his continuous moral support.

(Zeeshan Shamshad)

PREFACE

Machine learning has emerged as a crucial tool for medical diagnostics and epidemiological modeling in recent years, providing new ways to comprehend and forecast the dynamics of infectious diseases [1]. A strong mathematical foundation for comprehending transmission and recovery dynamics is provided by the Susceptible-Exposed-Infected-Isolated-Recovered (SEIIR) model and other traditional compartmental frameworks [2]. However, their predictive accuracy is frequently diminished by scarce data, intricate nonlinear relationships between epidemiological variables, and uncertainty in parameter estimation [3,4]. This work uses cutting-edge machine learning techniques and Physics-Informed Neural Networks (PINNs) to improve the diagnostic and prediction capabilities of the SEIIR model in order to address these shortcomings [5-7]. The estimation of the epidemiological parameters and the identification of hidden relationships between disease compartments are made possible by artificial neural networks, which offer a potent data-driven method for approximating nonlinear system [8-10]. ANNs improve epidemic assessment and diagnostics forecasts by making it easier to investigate intricate relationships between infection stages, environmental variables, and intervention effects inside the SEIIR model. Disease modeling has also been transformed by the creation of Physics-Informed Neural Networks, which directly incorporate epidemiology differential equations during training [11-15]. PINNs ensure biological and physical consistency even with sparse or noisy data by including the mathematical equations driving disease dynamics, in contrast to solely data-driven techniques. Because it is consistent with both empirical data and theoretical epidemiology, this hybrid learning approach makes the trained model very useful for real-world disease predictions [16]. The SEIIR model's five fundamental compartments-Susceptible (S), Exposed (E), Infected (I),

Isolated (J), and Recovered (R)-collectively describe the temporal history of infection in a population and show how the disease develops. Metrics like the transmission rate, isolation rate, and recovery rate-all crucial for understanding epidemic behavior-can be adaptively learned by integrating machine learning into this framework. Additionally, a dependable technique for forecasting the course of a disease, spotting infection trends, and providing early diagnostic information is to minimize a combined loss function that accounts for both data fidelity framework [17-20].

This thesis is organized into three main parts. The first chapter introduces the details background of the study, including the research objectives and scope. The second chapter provides a review [21]. The third chapter mainly discuss the development of new epidemiological dissipativity and boundedness, the local stability of equilibria points, lyapunov stability of equilibria points, research methodology, results and discussion. This study emphasizes how machine learning and computation influenced by physics might revolutionize contemporary disease modeling. The study advances the creation of trustworthy, understandable, and data-efficient diagnostic models by fusing the analytical purity of epidemiological mathematics with the adaptive learning potential of neural networks. The ultimate goal of this effort is to improve the link between medical diagnosis and artificial intelligence by supporting disease prognosis, public health decision-making, and epidemic early detection.

Contents

Chapter 1	1
INTRODUCTION.....	1
1.1 Introduction	1
1.2 Background of Study	1
1.3 Research Problem and Statement	3
1.4 Mathematical Modeling.....	6
1.5 Basic Mathematical Models.....	6
1.5.1 SIR Model	9
1.5.2 SEIR Model	10
1.6 Important Terminologies	11
1.6.1 Lyapunov Function.....	11
1.6.2 Basic Reproduction Number	12
1.6.3 Optimal Control Solution Using Pontryagins Maximum Principle	14
1.6.4 Control Strategies for MPOX.....	15
1.7 Physics Informed Neural Network	17
Chapter 2	20
Performance Analysis of Mathematical Methods used to Forecast the 2022 New York City Mpox Outbreak.....	20
2.1 Introduction	20
2.2 Problem Formulation and Methodology	21
2.2.6 Retrospective Analysis of Forecasts.....	25
2.2.7 Forecast Performance.....	25
2.2.8 Improving Early Case Forecasts	26
2.3 Research Methodology	27
2.4 Results and Discussion	28
2.4.1 Exponential Model Performance	29
2.4.2 SEIR Model Performance	30
2.4.3 Replacing Exponential Model with SEIR Model	32
2.5.4 Sensitivity to Case Detection Rate	33
2.5 Conclusion	34
Chapter 3	35

Stability and Sensitivity Analysis of a Dynamical Model Mpox Disease with Physics Informed Machine Learning	35
3.1 Introduction	35
3.2 Problem Formulation	35
3.2.1 Epidemiological Dissipativity and Boundedness	36
3.2.2 The Local Stability of Equilibria Points	38
3.2.3 Lyapunov Stability of Equilibria Points	44
3.3 Research Methodology	53
3.4 Results and Discussion	53
3.4.1 SEIJR Model Simulation	53
3.4.2 Susceptible populations over Time	55
3.4.3 Exposed Population over Time	55
3.4.4 Infected Individuals Without Drug Resistance over Time	56
3.4.5 Infected Individuals with Drug Resistance over Time	57
3.4.6 Recovered Individuals over Time	58
3.4.7 Effect of θ (Infectious Reduction) on Total Infectious Individuals	59
3.4.8 Behavior of Vaccination Control over Time	60
3.4.9 Behavior of Awareness Control Variable over Time	60
3.4.10 SEIJR Dynamics under Different Initial Conditions	62
3.4.11 Lyapunov Function over Time	63
3.4.12 Phase Portrait: Infected vs Isolated	65
3.4.13 Total Infected Individuals over Time	67
3.4.14 Time Derivative of Lyapunov Function	67
3.4.15 Local Sensitivity Analysis	68
3.5 Conclusion	69
References	72

LIST OF FIGURES

Fig 1.1: SIR Epidemic Model Simulation	9
Fig 1.2: SEIR Epidemic Simulation.	11
Fig 1.3: Physics Informed Neural Networks Structure.	19
Fig 2.1: Comparison of Exponential and ARIMA Models for Weekly Mpox Case Forecasting.	30
Fig 2.2: Comparison of Model Fits and Forecasts for Weekly Reported Mpox Cases.	31
Fig 2.3: Comparison of Model Fits and Forecasts for Weekly Mpox Cases.	32
Figure 2.4: Comparison of two Models for Fitting and Forecasting Weekly Mpox Cases.	33
Fig 3.1: SEIJR Model Representation Graphically with PINNs for total Number of Population.	54
Fig 3.2: Susceptible Population over Time.	54
Fig.3.3: Exposed population over Time.	56
Fig 3.4: Infected Individuals without Drug Resistance over Time.	56
Fig 3.5: Infected Individuals with Drug Resistance over Time.	58
Fig 3.6: Recovered Population over Time.	58
Fig 3.7 Reduction Control Variable over Time.	59
Fig 3.8: Vaccination Control over Time.	59
Fig 3.9: Awareness Control Variable over Time.	61
Fig 3.10: SEIJR Dynamic Under Different Initial Conditions over Time	63
Fig 3.11: Lyapunov Function Variable over Time.	64
Fig 3.12: Phase Portrait Variable over Time.	65
Fig 3.13: Infected Individuals Variable over Time.	66

Fig 3.14: Derivative of Lyapunov Function Variable over Time	66
Fig 3.15: Sensitivity Analysis over Time.	69

LIST OF TABLES

Table 1.1: Parameters and variables description of the proposed model.....	5
Table 2.1: Calibrating parameters, bounds, and estimated values of Susceptible-Exposed-Infectious-Recovered model for August calibration.....	22

Chapter 1

INTRODUCTION

1.1 Introduction

The Monkeypox virus (MPXV), which belongs to the Orthopoxvirus genus, is caused by Mpox. Like cowpox, vaccinia, camelpox, and smallpox, Mpox has emerged as a major global public health concern [22]. Its quick cross-border spread has resulted in many hospitalizations and fatalities despite significant control efforts, necessitating better modeling and control techniques. To characterize the dynamics of infectious disease transmission and evaluate intervention strategies, mathematical models like SEIR and SEIJR are frequently employed. However, data restrictions and parameter estimation are common problems with traditional methods. However, data models the SEIJR dynamics of Mpox using Physics-Informed Neural Networks (PINNs) in order to overcome these difficulties. Even with sparse data, PINNs can accurately learn system parameters and hidden states by combining differential equations with observational data. In order measures, this paper proposes a PINN-based SEIJR model. The method provides an effective framework for comprehending and controlling Mpox epidemics by bridging theoretical epidemiology with machine learning.

1.2 Background of Study

Mpox (formerly known as Monkeypox) is a re-emerging zoonotic disease caused by the Monkeypox virus (MPXV), a double-stranded DNA virus of the Orthopoxvirus genus of the Poxviridae family. It is acquired in humans through direct contact with infected individuals, animals, or objects, and manifests clinically with fever, rash, lymphadenopathy, and pustular lesions [23]. Though the disease was formerly

geographically contained within Central and West Africa, the 2022–2023 global epidemics exhibited high human-to-human transmissibility, which prompted the World Health Organization (WHO) to declare it a public health emergency of international concern [24]. Insight into Mpox transmission mechanism is central to effective control and prevention of the disease, and mathematical modeling is a rudimentary instrument for simulating its nonlinear dynamics and predicting outbreak behavior [25]. Compartmental classical models such as SIR, SEIR, and SEIJR models have been used extensively to analyze epidemic dynamics, estimate the basic epidemiological parameters, and design control measures [26]. The basic reproduction number R_0 is a key parameter derived from the above models and it is the expected number of secondary infections caused by an infective individual in a fully susceptible population [27]. The sickness will progressively disappear and the disease-free equilibrium will become asymptotically stable locally if $R_0 < 1$, meaning that each infected individual typically infects fewer people than one another. On the other hand, if $R_0 > 1$, the infection continues or spreads, leading to an endemic equilibrium in which the illness spreads throughout the population [28]. R_0 , then, serves as a threshold indicator that establishes data, and parameter uncertainty make it difficult to estimate R_0 for Mpox, especially in the early stages of an outbreak. Predictive uncertainty and inaccurate parameter estimate results from traditional deterministic models’ frequent inability to manage sparse or noisy input [29]. Physics-Informed Neural Networks (PINNs) are a cutting-edge-driven modeling approach that incorporates epidemiological dynamics straight into neural network architectures in order to address these issues [30]. To ensure that the learned dynamics adhere to biological and epidemiological principles, PINNs incorporate the governing differential equations of disease transmission into their loss function, in contrast to purely statistical techniques

[31]. This hybrid approach enables that latent evolution of disease compartments, such as susceptible, exposed, infectious, isolated and recovered individuals, and the simultaneous learning of hidden parameters, such as contact rate, transmission rate, and recovery rate [32]. The following are some benefits of using PINNs for Mpox transmission: (i) using the limited epidemic data to directly R_0 and other important parameters, (ii) reconstructing unseen compartments such as isolated or asymptomatic individuals and (iii) better prediction of epidemic patterns under different control measures including immunization and isolation [33]. Additionally, the incorporation of real-world impacts like behavioral changes, vaccine inefficiencies, and environmental feedback mechanical rigor of SEIJR modeling improves interpretability and predictive accuracy, offering a strong basis for data-driven public health policy. In order to prevent Mpox from persisting, it is still crucial to keep $R_0 < 1$ through prompt interventions, whereas $R_0 > 1$ indicates the possibility of prolonged or recurring outbreaks that call for more stringent surveillance and efforts [34].

1.3 Research Problem and Statement

Mpox is a resurgent zoonotic viral disease that has serious social, economic, and health repercussions. Affected population have experienced psychological suffering, social stigma, and economic instability in addition to the disease's clinical symptoms, which include fever, rash, and lymphadenopathy [35]. The recent global outbreaks have been aggravated by factors such as delayed diagnosis, weak surveillance system, inadequate vaccination coverage, and waning immunity, which collectively increase the risk of reinfection and transmission [36,37]. These difficulties highlight how vital it is to develop, evaluate, and improve efficient intervention techniques in order to stop the spread of Mpox. Research on combining biological and social behavioral elements in

the control analysis is still lacking, despite the fact a number of mathematical models have been put out to examine the dynamics of Mpox transmission.

The absence of models that can account for isolated, poor vaccination and human behavioral changes under unclear data conditions is one of main limitations. Furthermore, when real-world data is noisy or incomplete, the majority of optimal frameworks now is use to produce incorrect results because they are extremely sensitive to parameter uncertainty, particularly in transmission rates, recovery rates, and vaccination efficacy [38,39]. The SEIJR model for Mpox transmission is the results of this study's extension of traditional SEIJR model by adding a compartment "J" TO reflect isolated infected persons in order to solve these issues. The following nonlinear autonomous system of differential equations governs the model:

$$\frac{dS}{dt} = b - \frac{\beta S(I+\theta J)}{N} - \eta S + \phi R, \quad (1.1)$$

$$\frac{dE}{dt} = \frac{\beta S(I+\theta J)E}{N} - (K + \eta)E, \quad (1.2)$$

$$\frac{dI}{dt} = KE - (\mu + \alpha_1 + \eta + P)I, \quad (1.3)$$

$$\frac{dJ}{dt} = \mu I - (\alpha_2 + \eta + \varepsilon)J, \quad (1.4)$$

$$\frac{dJ}{dt} = \mu I - (\alpha_2 + \eta + \varepsilon)J, \quad (1.5)$$

Table (1.1) describes all of the state variables and parameters. For biological realism, we assume that all variables and parameters are not negative. The model is examined using the following beginning conditions:

$$S(0) = S^0 > 0, E(0) = E^0 \geq 0, I(0) = I^0 \geq 0, J(0) = J^0 \geq 0, R(0) = R^0 > 0. \quad (1.6)$$

The current study offers Physics-Informed Neural Networks as a reliable and data-driven substitute for evaluating the SEIJR model in order to address these issues. PINNs allow the model to learn unknown parameters and recreate unseen compartments while

adhering to epidemiological principles by directly embedding the differential equations of the SEIJR framework into the neural network loss function [40]. In the contrast to conventional curve-fitting technique, PINNs make use of the governing equations as well as the available data, which allows them to manage data that is noisy, incomplete, or irregularly sampled. The suggested SEIJR-PINNs model can precisely of different control interventions like immunization, isolation, and treatment by fusing the mechanistic structure of SEIJR dynamics with the learning capabilities of deep neural networks.

Parameter	Description
$S(t)$	Initial number of Susceptible individuals
$E(t)$	Initial number of exposed individual
$I(0)$	Initial number of actively infected individual
$J(t)$	Initial number of drug-resistant
$R(0)$	Initial number of recovered individuals
b	Birth rate
β	Disease transmission rate
θ	Reduction in infectiousness of drug-resistant individual
η	Natural death rate
ϕ	Rate at which recovered lose immunity (R-S)
K	Incubation rate (E-I)
μ	Treatment rate for infected individuals
α_1	Disease-induced death rate in I class
α_2	Disease-induced death rate in J class
ε	Rate of dropout from J class

Table 1.1: Parameters and Variables Description of the Proposed Model.

1.4 Mathematical Modeling

By using compartmental frameworks that use differential equations to express transitions between disease state, mathematical modeling helps epidemiologists characterize and forecast the spread of infectious illnesses. In order to simulate disease processes and evaluate intervention techniques, these models integrate biological, environmental, and behavioral components [41]. Because Mpox, which is caused by the monkeypox virus, is mainly transmitted by direct contact, infected objects, or respiratory droplets, compartmental models are especially well-suited to documenting its modes of transmission and preventative strategies [42]. In order to improve parameter estimation, state prediction, and control strategy optimization, Physics-Informed Neural Networks have recently become a complex hybrid framework that blends machine learning and conventional epidemiology [43]. PINNs preserve flexibility to learn from sparse or noisy data while guaranteeing conformity with epidemiological laws by incorporating the governing differential equations of models such as a SEIR or SEIIR within a neural network's loss function. Estimating hidden variables, reconstructing unseen states, and dynamically calculating the time-varying reproduction number R_0 are all made possible by this method. For properly simulating mpox transmission and data-efficient tool overall [44].

1.5 Basic Mathematical Models

Epidemic models are mathematical frameworks for studying the dynamics of infectious disease spread in a population. The word mathematical model refers to a representation of a real-world system that employs mathematical expressions, tools, or processes. In epidemiology, these models enable researchers to capture disease propagation mechanisms, assess the effectiveness of various control efforts, and forecast future

outbreaks under various scenarios. They are also used to compare intervention options, analyze experimental or observational data, and determine long-term disease trends. Constructing a realistic epidemic model typically involves multiple steps.

First, the diseases biology and epidemiological aspects must be thoroughly characterized, including transmission pathways, incubation durations, recovery rate, and immunity loss. These characteristics are then converted into a series of mathematical equations—often systems of nonlinear differential equations—that describe the time evolution of various population groupings or compartments. For Mpox, the SEIJR model classifies the population into Susceptible (S), Exposed (E), Infected (I), Isolated (J), and Recovered (R). The individuals are transferred across compartments depending on parameters such as transmission rate (β), progression rate (κ), treatment resistance rate (μ), recovery rate (p), natural death rate (η), and immunity fading rate (ϕ).

Mathematical modeling has long been regarded as an important technique in epidemiology for studying the dynamics of infectious illnesses and forecasting their potential trajectories. Classical models, such as SIR and SEIR frameworks, lay the groundwork for including different transmission mechanisms, latency periods, and recovery process [45,46]. Extensions to these models, such as the SEIJR structure, allow researchers to account for drug resistance and decreasing immunity, providing a more complete picture of real-world settings. In recent years, several research have used mechanistic models to examine epidemics of emerging and re-emerging illnesses, such as Mpox. Mechanistic methods are especially useful for simulating the effects of epidemiological variables including contact rates, disease development, and intervention techniques. Compartmental models in the COVID-19 pandemic were effectively employed to forecast case number, examine the impact of non-

pharmaceutical interventions, and evaluate vaccination campaigns [47]. Comparable modeling of Mpox has been employed to estimate transmission parameters, identify vulnerable populations, and forecast peak outbreak under different intervention strategies. Strategies for control in infectious disease modeling are typically categorized into constant, optimal, or adaptive. Fixed control strategies are associated with fixed intervention levels, like constant immunization or social isolation. Optimal control theory is used to formulate intervention programs which minimize the disease burden as well as costs over a specified time frame. Adaptive control methods re-adjust interventions dynamically from real-time data and thus find particular favor in the context of rapidly expanding outbreaks. Targeted vaccinations, isolation of cases, and public education campaigns have been shown to significantly lower Mpox transmission, especially when aimed at high-sensitivity targets such as the transmission rate (β). Traditional differential equation models tend to have difficulty with sparse or noisy outbreak data, and estimation of parameters difficult. This is addressed by the current work incorporating a Physics-Informed Neural Network (PINN) architecture into the SEIJR model. The neural network is trained on existing Mpox data while being physically constrained by the governing SEIJR differential equations, which will make learned dynamics adhere to epidemiology principles. This PINN-SEIJR hybrid framework facilitates precise parameter estimation, unobserved state reconstruction, and enhanced outbreak prediction. This model updates predictions adaptively as new data arrives and helps optimize control interventions and sensitivity analysis for important parameters like β and κ [48,49]. The proposed PINN-SEIJR model generally improves upon conventional numerical solvers by integrating mechanistic insight with data-driven learning to offer a reliable framework for modeling mpox spread in Pakistan.

1.5.1 SIR Model

The SIR model depicts the transmission of an infectious illness by classifying the entire population into three categories. The first group is susceptible group (S), which includes those who are healthy but could get the disease. The infectious group (I) is the second group, which includes those who are currently infected and can spread the virus. The third group, the recovered group (R), includes people who have recovered and established immunity. The PINNs approach embeds SIR equations into the network, aligning data fitting with epidemiological dynamics. The mathematical model is as follows [50]:

$$\frac{dS}{dt} = -\phi SI, \quad (1.7)$$

$$\frac{dI}{dt} = \phi SI - \omega I, \quad (1.8)$$

$$\frac{dR}{dt} = \omega I. \quad (1.9)$$

With initial conditions $S_0 > 0, I_0 \geq 0, R_0 \geq 0$.

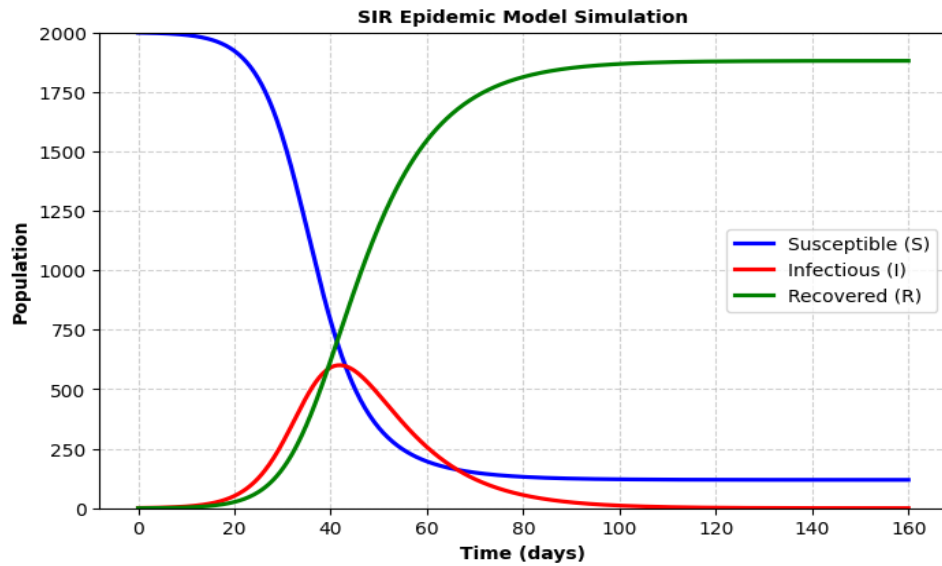


Fig 1.1: SIR Epidemic Model Simulation.

1.5.2 SEIR Model

The SEIR model expands on the standard SIR model by including an additional compartment to represent the latent period of infection. The entire population is separated into four compartments. The first type, susceptible (S), includes those who are healthy but can become ill. The second category exposed (E), includes people who have been infected but are not yet infectious. The third type, infectious (I), consists of people who can spread the disease to others. The fourth type, recovered (R), includes those who have recovered from the virus and are immune. The PINNs approach embeds SIR equations into the network, aligning data fitting with epidemiological dynamics.

The model is represented by the following system of differential equations:

$$\frac{dS}{dt} = \Lambda - \beta SI - \mu S, \quad (1.10)$$

$$\frac{dE}{dt} = \beta SI - (\sigma + \mu)E, \quad (1.11)$$

$$\frac{dI}{dt} = \sigma E - (\gamma + \mu)I, \quad (1.12)$$

$$\frac{dR}{dt} = \gamma I - \mu R. \quad (1.13)$$

Here, Λ is the recruitment rate of vulnerable individuals, and (β) is the transmission rate. The infected rate (σ) , recovery rate (γ) , and natural rate (μ) are all factors to consider. The model is considered under the following initial conditions:

$$S_0 > 0, E_0 \geq 0, I_0 \geq 0, R_0 \geq 0.$$

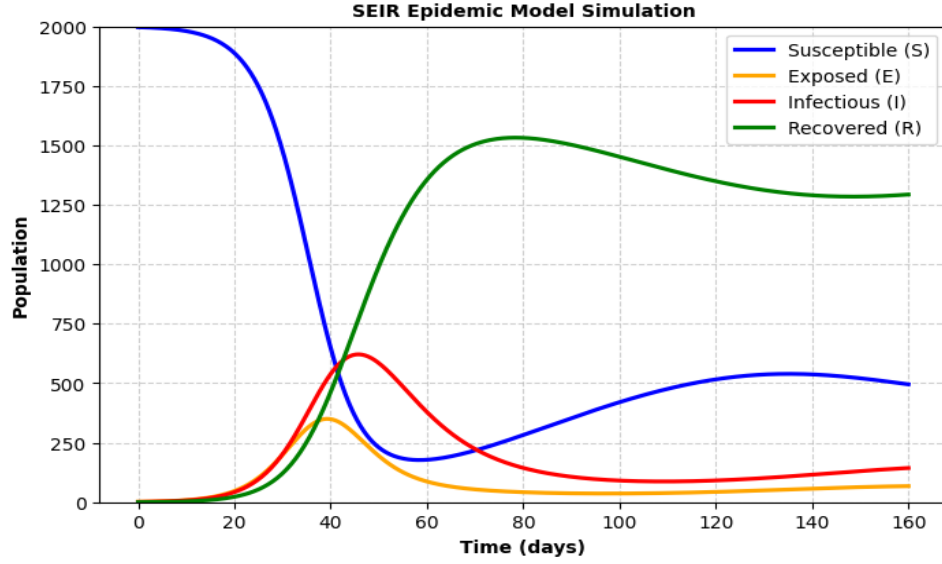


Fig 1.2: SEIR Epidemic Simulation.

1.6 Important Terminologies

1.6.1 Lyapunov Function

In this study, a Lyapunov function is built to examine the stability of the equilibrium point of the SEIJR Model established using the machine learning framework for medical diagnosis. The Lyapunov function is a mathematical measure of the system energy that is commonly employed to ensure the stability of nonlinear dynamical systems. Let $V(S, E, I, J, R)$ be a continuously differentiable function in the N neighborhood of the equilibrium point. The Lyapunov function for the SEIJR model is as follows:

$$V(S, E, I, J, R) = (S - S^*)^2 + (E - E^*)^2 + (I - I^*)^2 + (J - J^*)^2 + (R - R^*)^2, \quad (1.14)$$

$(S^*, E^*, I^*, J^*, R^*)$ are the equilibrium values of the corresponding compartments. To qualify as a

Lyapunov function, it must satisfy the following conditions:

$$1. V(S, E, I, J, R) > 0 \text{ for all } (S, E, I, J, R) \in N \setminus \{(S^*, E^*, I^*, J^*, R^*)\}, \quad (1.15)$$

$$2. \frac{dt}{dV} \leq 0 \text{ for all } (S, E, I, J, R) \in N(S, E, I, J, R), \quad (1.16)$$

$$3. V(S^*, E^*, I^*, J^*, R^*) = 0. \quad (1.17)$$

If these conditions apply, the SEIJR model's equilibrium point is stable according to Lyapunov. However, if any of these conditions fail, the system will become unstable. This Lyapunov approach, when combined with machine learning-based parameter optimization, ensures trustworthy stability assessment and enhanced predictive accuracy in medical diagnosis models.

1.6.2 Basic Reproduction Number

The basic reproduction number R_0 is the predicted number of secondary infections caused by a single infected individual in a perfectly susceptible population. In the context of the Machine Learning-based SEIJR model for medical diagnosis, this threshold parameter is critical in determining disease transmissibility and epidemic durability. The value of R_0 is not physiologically constant, but rather varies on a variety of epidemiological and environmental parameters, including transmission rate, detection efficiency, quarantine effectiveness, and population behavior, all of which can be dynamically changed using the machine learning framework. $R_0 > 1$ indicates that the infection will spread farther throughout the community, while $R_0 < 1$ indicates that the sickness will eventually die out. The greater the value of R_0 , the more difficult it is to contain the diseases spread. As a result, determining R_0 gives critical information on how much intervention—such as vaccination, isolation, or treatment—is required to prevent or eradicate an outbreak. Individuals in the SEIJR system are classified as susceptible (S), exposed (E), infectious (I), Isolated (J), and recovered (R). To compute R_0 , we use the Next Generation Matrix (NGM) approach with the Jacobian

matrix evaluated at Disease-Free Equilibrium. Let F signify the rate of new infections in the exposed and infected compartments, and V denote the rate of persons transferring between compartments via recovery, isolation, or mortality. The NGM is then provided:

$$J = FV^{-1}. \quad (1.18)$$

The fundamental reproduction number is defined as the spectral radius (dominant eigenvalue) of this matrix:

$$R_0 = \rho(FV^{-1}). \quad (1.19)$$

In the SEIJR model, infection concepts are essentially derived from the exposed and infectious compartment. Therefore, the matrices F and V can be expressed as follows:

$$F = \begin{bmatrix} 0 & \beta S^*/N^* \\ 0 & 0 \end{bmatrix}, \quad V = \begin{bmatrix} \alpha + \mu & 0 \\ -\alpha & \gamma + \delta + \mu + \kappa \end{bmatrix}. \quad (1.20)$$

In this equation, (β) represents the transmission rate and (α) represents the rate of progression from exposure to infection. The recovery rate (γ) , disease-induced death rate (δ) , natural mortality rate (μ) , and isolation rate (κ) are determined by the machine learning model. Using the Next Generation Method, we obtain:

$$R_0 = \frac{\beta \alpha S^*}{N^*(\alpha + \mu)(\gamma + \delta + \mu + \kappa)}. \quad (1.21)$$

This expression represents the estimated number of new infections caused by a single infected individual, taking into consideration both biological characteristics and ML-optimized isolation or detection dynamics. Machine learning improves the SEIJR frameworks flexibility by dynamically estimating parameters like β, κ and α based on real-time clinical or diagnostic data, resulting in data-driven and adaptable estimation of R_0 .

1.6.3 Optimal Control Solution Using Pontryagins Maximum

Principle

The optimal control problem for the Machine Learning-based SEIJR model in medical diagnostics seeks to limit the spread of illness while lowering the overall cost of implementing control options such as vaccine, isolation, and therapy. The model is represented by a set of ordinary differential equations that describe disease dynamics in the presence of time-dependent control factors.

Consider the state variables $X(t) = [S(t), E(t), I(t), J(t), R(t)]^T$ and the control functions $U(t) = [u_1(t), u_2(t), u_3(t)]^T$, where $u_1(t)$, $u_2(t)$, and $u_3(t)$ represent vaccination, isolation, and treatment efforts, respectively. The controlled SEIJR model can be expressed as follows:

Consider the state variables $X(t) = [S(t), E(t), I(t), J(t), R(t)]^T$ and the control functions $U(t) = [u_1(t), u_2(t), u_3(t)]^T$, where $u_1(t)$, $u_2(t)$, and $u_3(t)$ represent vaccination, isolation, and treatment efforts, respectively. The controlled SEIJR model can be expressed as follows:

$$\frac{dX}{dt} = F(X(t), U(t), t), X(0) = X_0. \quad (1.22)$$

where F define the systems dynamic behavior, including the effects of control variables and the machine learning-based estimation of time-varying parameters such as the transmission rate $\beta(t)$,

recovery rate $\gamma(t)$, and isolation rate $\kappa(t)$. The optimal control issue aims to find the control functions $U^*(t)$ that reduce the total number of infected and isolated individuals while reducing control expenditures. The relevant object function is presented as follows:

$$J[U] = \int_0^T A_1 I(t)^2 + A_2 J(t)^2 + \frac{1}{2} (B_1 u_1(t)^2 + B_2 u_2(t)^2 + B_3 u_3(t)^2) dt. \quad (1.23)$$

Where $A_i > 0$ are weights reflecting the importance of disease reduction, and $B_i > 0$ are cost coefficients expressing each controls implementation expense.

The purpose is to establish an optimal control, $U^*(t)$, such that

$$J[U^*] = \min_U J[U]. \quad (1.24)$$

object to SEIJR system limitations. Pontryagins Maximum Principle states that the essential conditions for optimality are established by defining the relevant adjoint

$$\frac{d\lambda}{dt} = -\frac{\partial F^T}{\partial \lambda} \lambda, \quad \lambda(T) = 0. \quad (1.25)$$

$\lambda(t)$ is the vector of adjoint variables associated with the system states. The optimal control functions, $u_i^*(t)$, are constructed from these necessary conditions and bounded inside the admissible control range, $0 \leq u_i(t) \leq 1$.

$$u_i^*(t) = \min \left(\max \left(0, -\frac{1}{B_i} \frac{\partial J}{\partial u_i} \right), 1 \right), i = 1, 2, 3 \quad (1.26)$$

The optimal control solution for the SEIJR model is defined as the pair $(X^*(t), U^*(t))$ that satisfies both the state and adjoint equations under the aforementioned optimality constraints. The use of machine learning algorithms improves this process by continuously updating parameter estimations and control effects in response to diagnostic data, resulting in more adaptive and precise disease transmission control.

1.6.4 Control Strategies for MPOX

A number of studies on Mpox transmission dynamics modeling, particularly those that use compartmental epidemic frameworks like the SEIR and SEIJR models, have integrated control strategies such as vaccination, isolation, and behavioral interventions

to evaluate disease management and mitigation efficiency [51]. These models investigate how various time-dependent control settings can minimize the number of infectious persons while slowing epidemic progression within given population. Generally, when the fundamental reproduction number $R_0 > 1$, the disease persists and expands throughout the population, while $R_0 < 1$ indicates that infections gradually fall and the outbreak can be eradicated. The SEIJR model, which divides the population into Susceptible (S), Exposed (E), Infected (I), Isolated (J), and Recovered (R) compartments, has been widely used to study emerging infectious disease such as Mpox. It captures critical biological and social processes such as incubation, detection, isolation, and immunity acquisition. However, many early models of Mpox dynamics ignored adaptive and time-dependent controls that represent actual public health policy and response efforts. Subsequent research has focused on the application of optimal control theory to epidemic management, adding dynamic vaccination and isolation restrictions to reduce Mpox transmission while balancing intervention costs [52,53]. In this context, immunization is thought to be the most effective preventive technique, particularly the use of smallpox-derived vaccines like the modified Vaccinia Ankara-Bavarian Nordic (MVA-BN), which the World Health Organization (WHO) has prequalified for Mpox prevention in 2024. The introduction of vaccination in the SEIJR framework successfully reduces the vulnerable populations (S), lowering R_0 and flattening epidemic peaks. According to the 2013 and 2024 National Institute of Health (NIH) guidelines for Mpox in Pakistan, optimal control models assess the best vaccination rate that reduces infections while accounting for restricted vaccine availability. Controlling Mpox transmission requires both isolation and contact tracing. The isolated class (J) in the SEIJR model reflects individuals who have been recognized and separated from the broader population upon diagnosis. Studies demonstrate that

increasing case detection efficiency and shortening the interval between infection and isolation can significantly reduce the infectious pool (I). In Pakistan, this has been highlighted through increased laboratory capacity, airport screening, and the development of isolation units in large hospitals. According to mathematical modeling, implementing isolation and vaccination measures at the same time reduces infection rates and overall disease burden in a synergistic manner. In addition to conventional control approaches, innovative techniques such as sliding mode control (SMC) and adaptive control algorithms have recently been proposed for epidemiological modeling due to their resilience and stability under uncertainty [54-57]. While SMC has been effectively employed in engineering systems, its extension to disease models, such as adaptive SMC for Mpox, opens up the possibility of robust real-time control in response to changing epidemic conditions. This study aims to develop and analyze a time-dependent optimal control framework within the SEIJR model for Mpox dynamics in Pakistan, incorporating vaccination, isolation, and awareness interventions to reduce the number of infectious individuals and the total cost of control implementation.

1.7 Physics Informed Neural Network

Physics-Informed Neural Networks (PINNs) are a class of machine learning models that combine data-driven methods with the governing laws of physics. Since their introduction by Raissi, Perdikaris and Karniadakis in 2019, PINNs have emerged as a crucial framework in scientific machine learning, an area of the study that aims to combine the interpretability and structure of physical systems with the predictive capability of deep learning. Large volumes of classified data are necessary for traditional neural networks to train models efficiently, but this can be difficult to come by in many fields of science and engineering. However, ordinary or partial differential equations (ODEs or PDEs) already reveal the underlying dynamics in the majority of

physical systems. In order to solutions that satisfy the data and the governing equations, PINNs take advantage of this information by directly integrating the physics into the learning process. To estimate the solution of a differential equations, such as $\mathcal{N}[u(x, t)] = 0$, here $\mathcal{N}$ represents a differential operator, a neural network $\mathcal{F}_\theta(x, t)$ with parameter θ is trained in conventional PINN architecture. During the training phase, a loss function is defined by combining two terms: (1) a physics loss term that penalizes violations of the governing equations at specific collocation sites, and (2) a data loss term that measures the error between the neural network outputs and observed data points. The model learns to fulfill both theoretical principles and actual facts by simultaneously minimizing both terms. A standard feedback neural network and typical PINN share a similar architecture. The output layer generates predictions for the physical variable of interest after the input layer receives spatial and temporal variables and hidden layers employ nonlinear activation functions such as the hyperbolic tangent (tanh) or ReLU. To make sure the solution satisfies the physical equations across the region, the collocation points are selected inside the domain to assess the physics loss. Stochastic gradient descent and Adam, two gradient-based optimization methods, are used to optimize the model parameters. Because of this structure, PINNs are mesh-free, continuous, and adaptable, enabling them to efficiently tackle high-dimensional and nonlinear problems. To make sure the solution satisfies the physical equations across the region, the collocation points are selected inside the domain to assess the physics loss. Stochastic gradient descent and Adam, two structure, PINNs are mesh-free, continuous, and adaptable, enabling them to efficiently tackle high-dimensional and nonlinear problems. Numerous fascinating extensions of PINNs have been made possible by recent study. To increase accuracy and efficiency, methods like adaptive sampling concentrate training on region with the highest physics residuals. The network

is progressively trained using curriculum learning strategies, which begin with easier activities and progress to more intricate dynamics [58-60]. Low-fidelity and high-fidelity data are combined in multi-fidelity PINNs to lower calculation costs without sacrificing accuracy. For real-world applications like climate prediction and epidemic forecasting, probabilistic and Bayesian PINNs have been created to quantify uncertainty in forecasts and parameter estimation. Furthermore, hybrid models have demonstrated significant promise in managing multi-scales and multi-physics systems by combining PINNs with transformers, graph neural networks, or conventional solvers. In the field of disease modeling, PINNs are especially valuable. Traditional epidemiological models like SIR, SEIR and SEIJR are expressed as systems of differential equations that describe the time evolution of susceptible, exposed, infected, isolated and recovered populations. PINNs can integrate these equations directly into the neural network's structure, allowing them to infer unknown parameters such as infection or recovery rates and predict future outbreak dynamics. This is particularly useful when data are incomplete or delayed, as the physical constraints ensure biologically meaningful results. By coupling data-driven inference with mechanistic models, PINNs provide a robust and interpretable framework for understanding disease spread and evaluating intervention strategies.

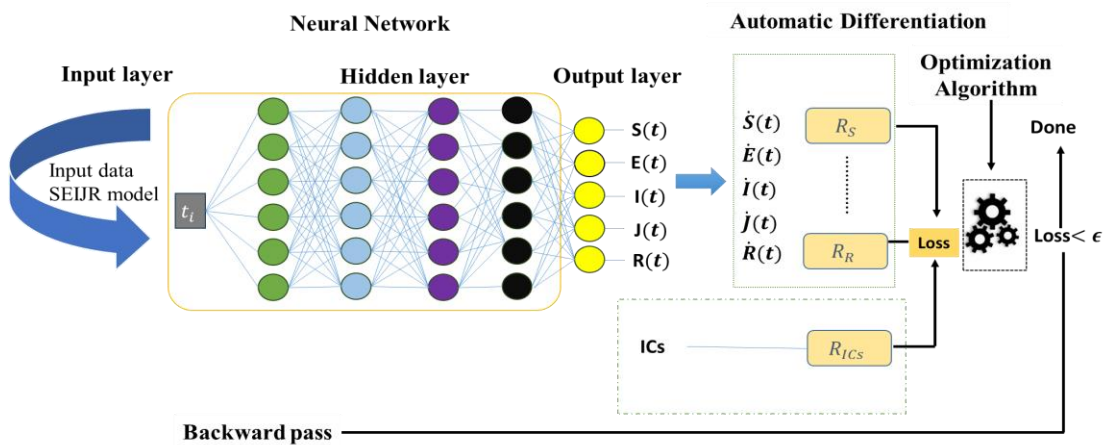


Fig 1.3: Physics Informed Neural Networks Structure.

Chapter 2

Performance Analysis of Mathematical Methods used to Forecast the 2022 New York City Mpox Outbreak

2.1 Introduction

The US Mpox outbreak centered in New York City (NYC) around the middle of 2022. To help with outbreak response, we sent the NYC Department of Health and Mental Hygiene real-time Mpox case projections. As the disease spread, forecasting techniques changed. Initially, we used exponential growth models to predict instances because we did not know the size of the at-risk population. We employed a susceptible-Exposed-Infectious-Recovered (SEIR) model when exponential development slowed. We investigated whether, with or without knowledge of the case detection rate, projections may have been enhanced by substituting our early exponential growth model with an SEIR model. The 2-week mean absolute error (MAE) increased from 53 cases/week (July 1-14) to 457 cases/week (July 15-28), indicating that predictions from exponential growth models did not perform well. Nevertheless, an SEIR model was able to correctly forecast the duration of the outbreak (7-week MAE: 13.4 cases/week) when exponential growth slowed, offering insight into the size of the vulnerable population. In retrospect, we discovered that the epidemiological features of the outbreak were not sufficiently understood to allow for the early parameterization of SEIR model. Early in the outbreak, however, an SEIR model might have been more accurate than exponential growth models if the at-risk population and case detection rate were known.

2.2 Problem Formulation and Methodology

We used a straightforward discrete-time Susceptible-Exposed-Infectious-Recovered (SEIR) model to predict the remainder of the outbreak (August 10-September 27, 2022) when case data indicated exiting exponential growth (i.e., week-to-week increments in case counts were no longer rising, approximating linear growth) and epidemiological observations from health authorities were sufficient to define a most-at-risk population. The following was the model's definition:

$$S_{t+1} = S_t - \beta_t \cdot S_t \cdot I_t - v_t \cdot \frac{S_t}{S_0}, \quad (2.1)$$

$$E_t = E_t + \beta_t \cdot S_t \cdot I_t - \alpha \cdot E_t, \quad (2.2)$$

$$I_{t+1} = I_t + \alpha \cdot E_t - \gamma \cdot I_t, \quad (2.3)$$

$$R_{t+1} = R_t + \gamma \cdot I_t + v_t \cdot \frac{S_t}{S_0}. \quad (2.4)$$

The numbers of susceptible, exposed, infectious, and recovered individuals at time t represented by the state variables S_t, E_t, I_t and R_t . The effective number of newly protected people each day is indicated by the vaccination term v_t , which is determined by multiplying the number of people who get at least one dose of JYNNEOS by the matching vaccine efficacy. Due to behavioral changes brought on by Mpox risk-reduction message, the transmission rate β_t is time-varying, starting at a higher level and falling over a 30-day period (see Supporting Information: Fig 2.1). The daily rate at which exposed individuals become infectious is represented by the parameter α , while the daily recovered rate of infectious individuals is represented by the parameter γ . Previous investigations have proved the mathematical features of the model, such as positivity, uniqueness, boundedness, and equilibria [61-63]. A Tree-Structured Parzen Estimator written in Optuna was used to calibrate the model parameters to observed

case data after they were chosen within reasonable limits from the literature [64]. Based on DOHMH estimates of sexual minority men at heightened risk, the at-risk population size (S_t, E_t, I_t and R_t) was set at 70180. The initial conditions $S_0 = 70,000, E_0 = 161, I_0 = 19$ and $R_0 = 0$ were obtained through calibration.

Table 2.1. Calibrating parameters, bounds, and estimated values of Susceptible-Exposed-Infectious-Recovered model for August calibration.

Parameter	Description	Calibration Bounds	Calibrated Value
R_0	Mpox basic reproduction number	0.5– 4.0	3.8
$1/\alpha$	Duration of incubation period	6.6– 10.9 days	7.5 days
$1/\gamma$	Duration of infectious period	14– 28 days	14 days
E_0	Number infected on May 2, 2022	1– 20 infections	19 infections
Behavior change effect	Reduction in susceptibility due to behavior change	0%–50% attack rate reduction	44% attack rate reduction
Behavior changes start date	Date when behavior change takes effect	June 30–July 30	<i>July 16</i>
Vaccine effectiveness	Proportion of vaccine recipients	55%– 95%	77%

	who become immune		
Case detection rate	Proportion of infections reported as cases	5%– 100%	6%

2.2.1 Methods

We first outline the steps taken to give the NYC DOHMH timely case predictions throughout the 2022 outbreak in our methodology section. Second, we outline how we evaluate prediction performance and suggest ways to make our projections better.

2.2.2 Responding to the Mpox Outbreak in Real Time

The NYC DOHMH asked for assistance in predicting mpox cases in June 2022. In the end, our quick response resulted in forecasts for July and August of 2022 that were utilized in the NYC DOHMH epidemic response. The datasets and techniques utilized for these projections are explained in this section.

2.2.3 Mpox Case Data

On May 19, 2022, the first Mpox case in NYC was tested, and on May 21, 2022, the results were verified. The NYC DOHMH submitted statistics on NYC Mpox cases from this period till July 28th, 2022. The cumulative case count is displayed on the nyc.gov Mpox information website [65]. We developed a Python-based web scraping tool to extract the listed cumulative cases at each timepoint after identifying timepoints when the website was modified using data from the Internet Archive’s Wayback Machine [66]. The inability to backdate these early data is one of their limitations. This meant

that increases in instances, including testing and reporting delays, happened at the time the case was reported. Since the testing and reporting delays had not been identified at the time of the study, we did not try to account for data analysis. The Mpox case count datasets were made publicly available on GitHub after July 28. Instead of counting cases on the data of reporting, 17 cases were counted on the day of specimen collection. Git was used to version-control the data, making it possible to compare older and more recent versions of the data to see backdated modifications and data cleaning.

2.2.4 Mpox Vaccine Data

The first doses of the Mpox vaccine were made available in NYC on July 6, 2022 [67]. Those who were 18 years of age or older, identified as guys who have sex with men, and had multiple or anonymous sex partners within the previous two weeks were the only ones eligible for the initial supply [68]. Midway through September, eligibility for the vaccine was expanded to include individuals who had multiple or anonymous sexual partners within the previous two weeks and who identified as either 1) a man (cisgender or transgender) who has sex with cisgender or transgender men or transgender women, 2) transgender non-conforming, or gender nonbinary regardless of the gender of one's sex partners, or 3) a sex worker and anyone engaging in survival sex or transactional sex (including in exchange for money, food, shelter, or other goods) of any sexual orientation or gender identity. Initially, news media coverage of DOHMH press releases provided information on the quantity of Mpox vaccination doses accessible in NYC; DOHMH confirmed this. Following August 18, 2022, weekly Mpox vaccination dosage data were made available in public repository maintained on GitHub and accessible via link from the DOHMH Mpox website [69]. Vaccinations were reported on the day of

the immunization event, as is customary, with retrospective updates for data cleaning and lagged reporting.

2.2.5 Forecasting Mpox Cases using Exponential Regression

We employed exponential regression to produce short-term projections early in outbreak (July 1st and 15th), assuming exponential growth would continue. The following exponential growth model was put into practice:

$$cases = B_0 e^{\beta_1 t}. \quad (2.5)$$

denotes the transmission rate per infectious individual less the disease recovery rate, n is the number of cases at $t = 0.21$. Using the R4.0 packages nlstools, we fit the model by minimizing squared error in relation to cumulative case data [70]. Forecasts with a two-week time horizon were made on June 30 and July 14.

2.2.6 Retrospective Analysis of Forecasts

After the outbreak ended in February 2023, we examined how well our forecasts performed, examined the characteristics of our forecasting models, and looked into ways to make them better.

2.2.7 Forecast Performance

The mean absolute error (MAE) of weekly case counts during the forecasting period was used to assess the model's performance.

$$MAE = \frac{1}{N} \sum_{i=0}^N |\hat{y}_i - y_i| \quad (2.6)$$

Where y_i is reported weekly case count for week i and $\hat{y}_i$ is the predicted case count for week i . In disease forecasting, MAE is a widely used statistics that enables a direct comparison between the model error and the outbreak's magnitude [71,72]. For forecasting produced throughout the outbreak, we assessed forecast performance.

Based on the kind of data each forecast was trained on, we assessed each one. The scraped data was used to train exponential models, which counted cases based on the date of reporting rather than the date of Mpox testing. Using the same scraped data, we assessed the performance of the exponential model. The datasets uploaded to GitHub, which allowed for back-dated modifications, were used to train the SEIR model, allowing cases to be counted on the testing date. Using the same GitHub data, we assessed the SEIR model's performance. In order to compare our predictions, we also assess an ARIMA model, which has also been used to predict Mpox cases. The Python library pmdarima was used to train ARIMA model with weekly seasonality [73]. The Diebold-Mariano test, which is frequently used to compare forecast performance, was employed to determine whether differences in forecast performance were significant [74].

2.2.8 Improving Early Case Forecasts

We retrospectively assess our early use of exponential models by directly comparing them “head-to-head” with SEIR models fitted to the same data after the DOHMH declared the NYC Mpox outbreak to be over in February 2023. This allowed us to determine whether early forecasts would have been better if the at-risk population size had been known at the outset.

We fitted an exponential growth model and recalibrated an SEIR model using DOHMH case data that had been right-censored as of July 15. The parameters of these models are shown in Supporting Information: Table 2.1. For the next two weeks, we forecasted weekly instances and compared them to reported counts.

We also evaluated whether improved parameter knowledge could lead to better early projections. As reported by public health researchers worldwide, the case detection rate

had the largest impact on SEIR model performance and the widest a priori uncertainty (Supporting Information: Table 2.1) [75].

With different assumptions for the case detection rate in mid-July predictions, we conducted two more studies. We first recalibrated an SEIR model utilizing right-censored data prior to July 15, assuming greater data availability. We fixed the detection rate at the ideal mid-August value (6%; Table 1). Second, we recalibrated another SEIR model with the detection rate at 52.5%, the median of the initial calibration range, under the assumption of decreased data availability. Supporting Information: Table 2.1 contains the parameters for both models. MAE was used to compare two-week forecasts from July 15 with reported numbers.

2.3 Research Methodology

In this study, a Physics-Informed Neural Networks (PINN) architecture is used to solve a system of nonlinear ordinary differential equations (ODEs) that reflect the disease transmission mechanism. By embedding the ODEs and their beginning conditions into the loss function, the disease model-defined by epidemiological compartments like susceptible, exposed, infected, recovered, or any extended structure-is immediately integrated into the learning process of the neural network. The PINN learns the solution by minimizing the residuals of the epidemiology ODEs at a collection of collocation locations dispersed throughout the time domain, as opposed to producing numerical solution data beforehand. The network can enforce the biological dynamics precisely as specified by the model equations by using automatic differentiation to calculate the necessary derivatives. Gradient-based techniques are used to adjust the network parameters until the total loss (ODE residual loss + initial-condition loss + optional data-fitting loss) is minimized. In order for the PINN to concurrently satisfy the epidemiological equations and observable epidemic patterns, an extra data-misfit

component is added to the loss function when actual case-data are available. In order to estimate disease trajectories, handle noisy or inadequate surveillance data, and capture the nonlinear behavior inherent in infectious-disease dynamics, our physics-guided learning methodology offers a mesh-free, flexible, and reliable solution.

2.4 Results and Discussion

We provided real-time Mpox forecasts to NYC health authorities during the 2022 outbreak. Early forecasts, based on simple exponential regression and a 2-week horizon, performed poorly-first underestimating and then overestimating cases with large error. Latter forecasts using an SEIR model accurately captured the remainder of the outbreak, with errors small relative to observed cases. However, an SEIR model would not have produced accurate early-outbreak predictions without prior knowledge of the case detection rate, which only became available after calibration to later case data. Our findings show that when important epidemiological inputs, including the size of the susceptible population and the case detection rate, are known beforehand, a deterministic SEIR model can predict Mpox outbreaks with high accuracy. Infection-induced or vaccine-induced immunity depletes susceptible, causing an epidemic slowdown in SEIR models. Compared to Viruses like influenza or SARS-Cov-2, Mpox is especially well adapted to SEIR modeling since immunity is long-lasting, reinfection is uncommon, and immune escape variations are rare. To our knowledge, our study is the first to empirically assess SEIR forecasting performance-in comparison to exponential and ARIMA models-under different assumptions about epidemiological knowledge and data availability in a single setting, despite previous work suggesting that Mpox transmission dynamics resemble n sub-epidemic models struggled to anticipate with our findings. Population-based surveillance at the beginning of an outbreak may provide crucial information for precise early prediction because case

detection rates have a significant impact on early forecasts. Such surveillance can assist convert case-based surveillance into population-level estimates of the infection burden, show how many illnesses are being overlooked, and pinpoint the groups where transmission is taking place. Early Mpox testing in NYC was limited to identified high-risk populations, such as males who have sex with men and those who participate in transactional sex, which may have created blind spots where infected people were unable to get tested. While research and surveillance testing are less constrained and could be used to produce the population level data required for efficient public health planning, diagnostic tests are subject to stringent regulatory limits that may limit their early availability. There are various limitations to our study. Early data lacked back-dating to test dates, making it unable to account for reporting delays, and forecasts were based only on detected case counts rather than direct estimates of case detection rates. Although our estimations are consistent with previous Mpox studies, expectations of high vaccine efficacy, and realistic public health response effects, these limitations hindered our ability to accurately estimate epidemiological parameters. The expected, constant case detection rate, which probably changed over time as testing became more accessible and well-known, had a significant impact on forecast accuracy.

2.4.1 Exponential Model Performance

Early in the pandemic, exponential models performed poorly. Our team only gave DOHMH one-week and two-week estimates since we anticipated that performance would be subpar in the long run. With a mean absolute error (MAE) of 53 cases per week, the epidemic grew faster than the model indicated over the two weeks that followed the July 1st forecast. In comparison to the reported weekly cases, this inaccuracy was significant (Fig. 2.1). A new exponential forecast was prepared after July 15th, this time overestimating cases by an MAE of 457 instances per week. In

comparison to weekly cases, this was once more significant (Fig. 2.1). Interestingly, by the end of the second forecast period, reported cases were no longer increasing exponentially; instead, the epidemic was developing linearly over the second half of July, with consistent week-to-week increments. The Diebold-Mariano test revealed that the difference was not significant ($p = 0.374$), but the MAE of all exponential forecasts was 255 cases/week, which was lower than our ARIMA benchmark (59 cases/week).

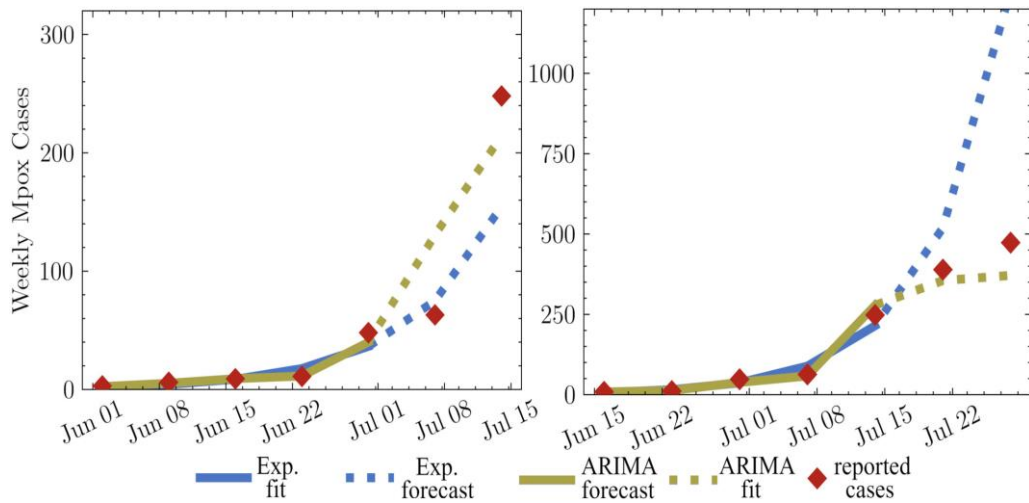


Fig 2.1: Comparison of Exponential and ARIMA Models for Weekly Mpox Case Forecasting.

Forecasts of Mpox cases on (A) July 1st and (B) July 15th were performed using exponential (blue) models, with an Auto-Regressive-Integrated-Moving-Average (ARIMA) model (yellow) serving as a comparator. Forecasts are shown as dashed lines, and the model's fits to the data are shown as solid lines. As the outbreak stopped growing exponentially, the July 15th forecast performance of exponential model declined.

2.4.2 SEIR Model Performance

As soon as data for the second half of July were available, we started SEIR modeling, which revealed linear growth. For the duration of the outbreak, the SEIR model performed better than the exponential model and produced precise forecasts. The most

recent data available at the time of our team's August 19th 7-week estimate was from August 9th. The SEIR model's mean absolute error for the seven-week projection period was 13.4 instances per week. This was a tiny percentage of weekly instances during this time (Fig. 2.2), and the Diebold–Mariano test showed that it significantly surpassed the ARIMA benchmark (140 cases/week) ($p = 0.01$). As soon as data for the second half of July were available, we started SEIR modeling, which revealed linear growth. For the duration of the outbreak, the SEIR model performed better than the exponential model and produced precise forecasts. The most recent data available at the time of our team's August 19th 7-week estimate was from August 9th. The SEIR model's mean absolute error for the seven-week projection period was 13.4 instances per week. This was a tiny percentage of weekly instances during this time (Fig. 2.2), and the Diebold-Mariano test showed that it significantly surpassed the ARIMA benchmark (140 cases/week) ($p = 0.01$).

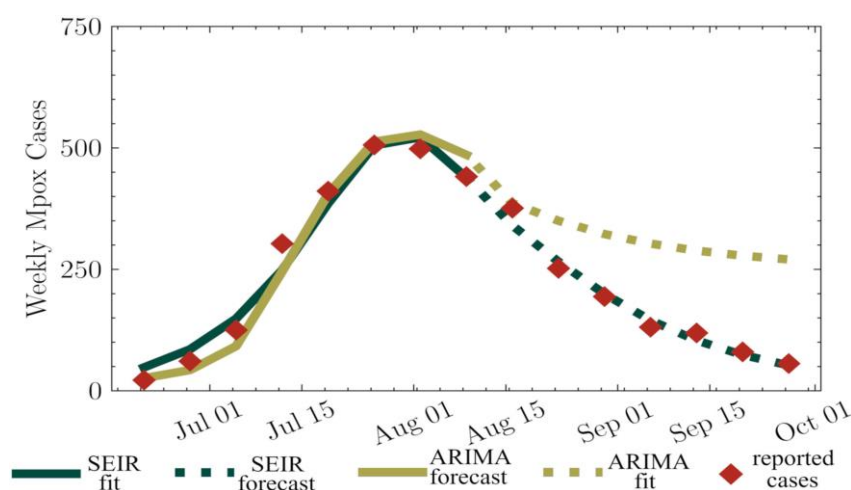


Fig 2.2: Comparison of Model Fits and Forecasts for Weekly Reported Mpox Cases. On August 19, Mpox cases were predicated using a Susceptible-Exposed-Infectious-Recovered (SEIR) (green) model. As a comparative, an Auto-Regressive-Integrated-Moving-Average (ARIMA) model (yellow) was employed. Data from the start of the outbreak until August 10th was used to calibrate the models. The solid-line shows how

well the models fit the calibration data. Seven weeks from the last day of data, models were employed to forecast (dash-line).

2.4.3 Replacing Exponential Model with SEIR Model

In retrospect, we looked at whether employing an SEIR model rather than an exponential model would have improved the July 15th forecast. We created a two-week forecast by calibrating an exponential model (Fig. 23A) and an SEIR model (Figure 3B) using right-censored daily case data (prior to July 15th). Compared to the exponential model trained and assessed on the right-censored daily case data (MAE: 861 cases/week), the SEIR model forecast had an MAE of 365 cases/week, which was less than half. The inaccuracy, however, was still a significant portion of daily instances and failed to forecast a slowdown in the epidemic's expansion that happened soon after the July 15th datapoint.

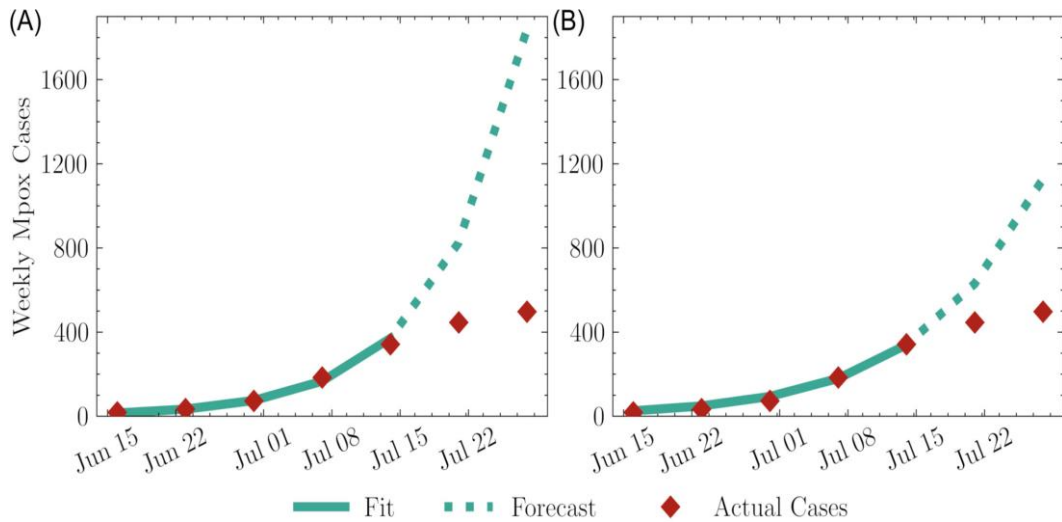


Fig 2.3: Comparison of Model Fits and Forecasts for Weekly Mpox Cases.

We fitted an exponential model (Panel A) and a Susceptible-Exposed-Infectious-Recovered (SEIR) model (Panel B) to see if the latter could have improved our July 15th forecast. Both models were fitted using publicly available DOHMH data that has been right-censored after July 14. Solid lines are used to show model fits. For the period

of July 15-28, case forecasts were created (shown by dashed lines). Similar errors to the exponential model were produced by the SEIR model, which predicted exponential growth across the prediction horizon.

2.5.4 Sensitivity to Case Detection Rate

The case detection rate had a significant impact on forecast performance. The re-calibrated SEIR model would have significantly overestimated cases using a naïve estimate of the case detection rate without fitting to any case data (Fig. 2.4A). When compared to the naïve case detection rate, using an SEIR model calibrated to additional case detection information not available at the time of forecasting (the optimal case detection rate from our August model) reduced error by more than a factor of two (Figure 4B); MAE decreased from 394 cases/week to 151 cases/week. Additionally, the infection point of the case counts within the 2-week prediction horizon was accurately predicted by the SEIR model with the best-informed case detection rate.

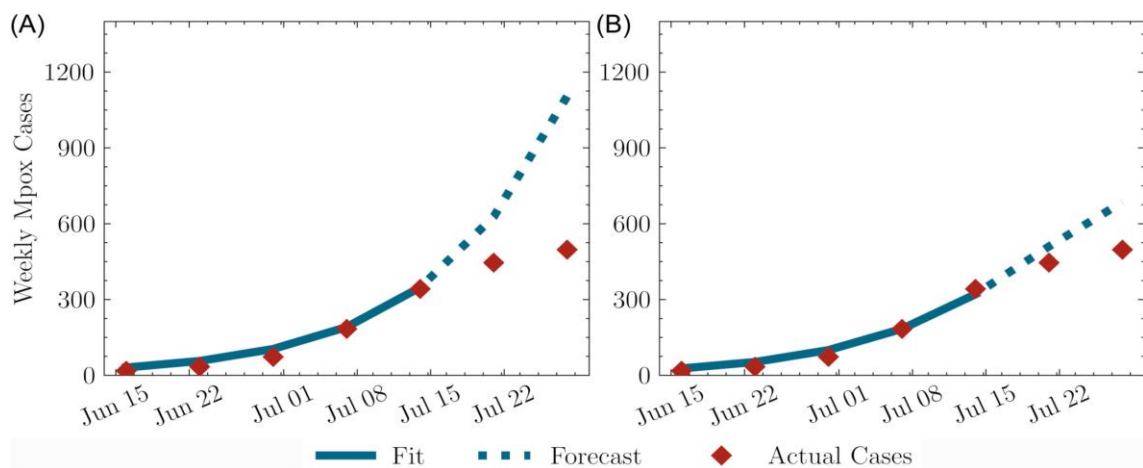


Fig 2.4: Comparison of two Models for Fitting and Forecasting weekly Mpox Cases.

Early in the outbreak, case detection rate had a significant impact on the performance of the Susceptible-Exposed-infectious-Recovered (SEIR) model. From July 15 to July 28, SEIR models predict cases using (Panel A) a naïve case detection rate and (Panel B) an optimized case detection rate. The SEIR model accurately forecasted when the

outbreak will stop experiencing exponential growth using an optimal case detection rate.

2.5 Conclusion

We have count projections to the NYC DOHMH when became the global epicenter of the 2022 Mpox outbreak. The performance of our early exponential models was subpar. The rest of the outbreak is precisely predicted by an SEIR model that trained on a larger data series. Accurate forecasting would not have been possible with an earlier SEIR model implementation unless case detection rates and susceptible populations were known beforehand. Early and more precise epidemic projections could be made possible by population-based surveillance to determine variables like case detection rate.

Chapter 3

Stability and Sensitivity Analysis of a Dynamical Model Mpox Disease with Physics Informed Machine Learning

3.1 Introduction

According to World Health Organization, a worldwide Mpox outbreak began in Pakistan in April 2023. A Susceptible-Exposed-Infected-Isolated-Recovered (SEIJR) model was created to simulate Mpox dynamics in order to overcome forecasting difficulties brought on by a lack of viral data and complicated transmission. The model combines data-driven learning with the SEIJR equations and integrates with a Physics-Informed Neural Networks (PINNs) to improve forecast accuracy and stability using early outbreak data for parameter estimation. Sensitivity analysis revealed that the most important component was the transmission rate (β), whereas the rates of isolation (μ), recovery (ρ), and progression (κ) successfully decreased infections. By focusing on (β), control techniques including mask wearing, immunization, and social separation can greatly reduce the transmission of disease

3.2 Problem Formulation

The progression of an infectious disease is described by the SEIJR compartmental model (Susceptible-Exposed-Infected-Isolated-Recovered), in which some infected persons are isolated (J) and many have varying infectiousness. The objective is to estimate unobserved compartments and unknown model parameters from noisy and incomplete clinical surveillance data using machine learning.

Mathematical Model [61-65];

$$\frac{dS}{dt} = \mathfrak{b} - \frac{\beta S(I+\theta J)}{N} - \eta S + \phi R, \quad (3.1)$$

$$\frac{dE}{dt} = \frac{\beta S(I+\theta J)E}{N} - (K + \eta)E, \quad (3.2)$$

$$\frac{dI}{dt} = KE - (\mu + \alpha_1 + \eta + \mathfrak{P})I, \quad (3.3)$$

$$\frac{dJ}{dt} = \mu I - (\alpha_2 + \eta + \varepsilon)J, \quad (3.4)$$

$$\frac{dR}{dt} = \mathfrak{P}I + \varepsilon J - (\phi + \eta)R. \quad (3.5)$$

Classification and distribution of observations are given below;

Total Population

$$N = S(0) + E(0) + I(0) + J(0) + R(0), \quad (3.6)$$

$$N = 99990 + 5 + 3 + 2 + 0 = 100,000. \quad (3.7)$$

3.2.1 Epidemiological Dissipativity and Boundedness

In epidemiological dissipativity and boundedness, we demonstrate that the developed model is bounded which is biologically feasible region with negative divergence, possesses a positively invariant region in R_+^5 . Restricting our attention to biologically feasible solutions, we prove that positive octant is invariant and that parameters provide explicit upper bounds for system trajectories. We considered SEIJR in the form variables i.e., $z_1, \dots, z_5$ as follow;

$$z_1(t) = S(t), \quad z_2(t) = E(t), \quad z_3(t) = I(t), \quad z_4(t) = J(t) \quad \text{and} \quad z_5(t) = R(t). \quad (3.8)$$

We reduce SEIJR model into the following simplified form;

$$\dot{z}_1(t) = f_1(z), \dots, \dot{z}_5(t) = f_5(z), \quad (3.9)$$

$$z_1(t_0) = z_{10}, \dots, z_5(t_0) = z_{50} \quad t_0 \in [0, T), \quad (3.10)$$

Here;

$$z = z(t) = \sum_{k=1}^5 z_k, \quad z_k > 0, \quad k = 1, 2, \dots, 5 \quad (3.11)$$

SEIJR model is modified as follow;

$$f_1(z) = b - \frac{\beta z_1(z_3(t) + \theta z_4(t))}{N} - \eta z_1(t) + \phi z_5(t), \quad (3.12)$$

$$f_2(z) = \frac{\beta z_1(z_3(t) + \theta z_4(t))z_2}{N} - (K + \eta)z_2(t), \quad (3.13)$$

$$f_3(z) = Kz_2(t) - (\mu + \alpha_1 + \eta + P)z_3(t). \quad (3.14)$$

$$f_4(z) = \mu z_3(t) - (\alpha_2 + \eta + \varepsilon)z_4(t), \quad (3.15)$$

$$f_5(z) = Pz_3(t) + \varepsilon z_4(t) - (\Phi + \eta)z_5(t). \quad (3.16)$$

Let

$$R_+^5 = \{ z = (z_1, \dots, z_5) \in R^+, z_k > 0 \}. \quad (3.17)$$

Condition 1. “Let $\beta \leq k\alpha_2, \eta > A$ and $P < \alpha_1$. Consider the problem (3.9) – (3.10) with $t_0 = 0$ ”.

“**Theorem 1.** Assume that the condition 1 is holds. Then the system (3.10) is with the negative divergence and dissipative”.

Proof. It is evident from Equation (3.10), we can simplify the following form;

$$\frac{\partial f_1}{\partial z_1} + \frac{\partial f_2}{\partial z_2} + \frac{\partial f_3}{\partial z_3} + \frac{\partial f_4}{\partial z_4} + \frac{\partial f_5}{\partial z_5}, \quad (3.18)$$

$$\frac{\partial}{\partial z_1} \left(b - \frac{\beta z_1(z_3(t) + \theta z_4(t))}{N} + \phi z_5(t) \right) - \eta z_1(t) = -\eta - \frac{\beta(z_3(t) + \theta z_4(t))}{N}, \quad (3.19)$$

$$\frac{\partial}{\partial z_2} \left(\frac{\beta z_1(\theta z_4(t) + z_3(t))z_2}{N} - (K + \eta)z_2(t) \right) = \frac{\beta z_1(z_3(t) + \theta z_4(t))}{N} - (K + \eta), \quad (3.20)$$

$$\frac{\partial}{\partial z_3} (Kz_2(t) - (\mu + \alpha_1 + \eta + P)z_3(t)) = -(\mu + \alpha_1 + \eta + P), \quad (3.21)$$

$$\frac{\partial}{\partial z_4} (\mu z_3(t) - (\alpha_2 + \eta + \varepsilon)z_4(t)) = -(\alpha_2 + \eta + \varepsilon), \quad (3.22)$$

$$\frac{\partial}{\partial z_5} (Pz_3(t) + \varepsilon z_4(t) - (\Phi + \eta)z_5(t)) = -(\Phi + \eta), \quad (3.23)$$

$$\frac{\partial f_1}{\partial z_1} + \frac{\partial f_2}{\partial z_2} + \frac{\partial f_3}{\partial z_3} + \frac{\partial f_4}{\partial z_4} + \frac{\partial f_5}{\partial z_5} = -\frac{\beta(z_3(t) + \theta z_4(t))}{N} - \eta + \frac{\beta z_1(z_3(t) + \theta z_4(t))}{N} - \quad (3.24)$$

$$(K + \eta) - (\mu + \alpha_1 + \eta + P) - (\alpha_2 + \eta + \varepsilon) - (\Phi + \eta).$$

Using condition 1 we get:

$$\Omega = \{z \in R_+^5: (b_1 + b_2)z_3 + (\beta_1 + \beta_2)z_4 \leq \mathbb{K}_2 - b\}. \quad (3.25)$$

3.2.2 The Local Stability of Equilibria Points

The stability characteristics of the system's equilibria points will be determined

(3.3.1). Let's

$$\beta_r(z) = \{z \in R^5, \|z - \bar{z}\| R^4 < r\}. \quad (3.26)$$

Condition 2. Let's assume the following.

$$(k\alpha_2 + \eta - \alpha_1)^2 \geq 4\alpha_1 k\eta, \quad (3.27)$$

“Theorem 2. Assume that the condition 2 is satisfied. The points $\mathcal{P}_0 = \mathcal{P}_0(0,0,0,0,0)$, $\mathcal{P}_i = \mathcal{P}_i\left(z_{1i}, 0, \frac{b}{p}, \frac{b\alpha}{p\epsilon}, 0\right)$, $i = 1,2,3$ and $\mathcal{P}_3 = \mathcal{P}_3(0, kb, 0,0,0)$ are the equilibria points of the system (3.9) in R_+^5 ”.

Proof. Substituting Eqs. (3.9) and (3.10), and resulting systems are obtained as follow;

$$b - \left[\frac{\beta(z_3(t) + \theta z_4(t))}{N} - \eta \right] z_1(t) + \phi z_5(t) = 0, \quad (3.28)$$

$$\left[\frac{\beta z_1(z_3(t) + \theta z_4(t)) z_2}{N} - (K + \eta) \right] z_2(t) = 0, \quad (3.29)$$

$$K z_2(t) - (\mu + \alpha_1 + \eta + \mathcal{P}) z_3(t) = 0, \quad (3.30)$$

$$\mu z_3(t) - (\alpha_2 + \eta + \epsilon) z_4(t) = 0, \quad (3.31)$$

$$\mathcal{P} z_3(t) + \epsilon z_4(t) - (\Phi + \eta) z_5(t) = 0, \quad (3.32)$$

Point of equilibrium is $\mathcal{P}_0 = (0,0,0,0,0)$ as obtained from Eqs. (3.11) and rest of solution is deduced as follow;

$$b - \left[\frac{\beta(z_3(t) + \theta z_4(t))}{N} - \eta \right] z_1(t) + \phi z_5(t) = 0, \quad (3.33)$$

$$\left[\frac{\beta z_1(z_3(t) + \theta z_4(t)) z_2}{N} - (K + \eta) \right] z_2(t) = 0, \quad (3.34)$$

$$K z_2(t) - (\mu + \alpha_1 + \eta + \mathcal{P}) z_3(t) = 0, \quad (3.35)$$

$$\mu z_3(t) - (\alpha_2 + \eta + \varepsilon)z_4(t) = 0, \quad (3.36)$$

$$Pz_3(t) + \varepsilon z_4(t) - (\Phi + \eta)z_5(t) = 0, \quad (3.37)$$

Suppose $z_1 = 0, z_2 = 0$. From equations (3.33) we get

$$K \cdot 0 = (\mu + \alpha_1 + \eta + p)z_3, \quad (3.38)$$

$$z_3 z_5 = 0 = \frac{b}{p}, \quad (3.39)$$

$$\mu \frac{b}{p} = (\alpha_2 + \eta + \varepsilon)z_4, \quad (3.40)$$

$$z_4 = \frac{b\alpha}{p\varepsilon}, \quad (3.41)$$

$$P \frac{b}{p} + \varepsilon \frac{b\alpha}{p\varepsilon} - (\phi + \eta)z_5 = 0, \quad (3.42)$$

Now consider $z_3 = 0, z_4 = 0, z_5 = 0$. Then the second simplifies to $(k + \eta)z_2 = 0$.

$$z_2 = 0, \quad (3.43)$$

$$z_2 = 0, k \times 0 = (\mu + \alpha_1 + \eta + p)z_3, \quad (3.44)$$

$$z_3 = 0, \quad (3.45)$$

$$\text{Set } z_1 = 0, z_2 = 0, z_3 = 0, z_4 = 0, \quad (3.46)$$

$$P \times 0 + \varepsilon \times 0 = (\phi + \eta)z_5, \quad (3.47)$$

$$z_5 = 0, \quad (3.48)$$

Now solving y_1

$$u_1 z_1^2 + u_2 z_1 + u_3 = 0, \quad (3.49)$$

Where;

$$u_1 = \alpha_2, u_2 = k\alpha_2 + \eta - \alpha_1, u_3 = k\eta, \quad (3.50)$$

By condition 2, we get

$$u_2^2 - 4u_1 u_3 \geq 0, \quad (3.51)$$

Thus; by solving (3.49) we have

$$z_{11} = \frac{-u_2 + \sqrt{u_2^2 - 4u_1u_3}}{2u_1}, \quad z_{12} = \frac{-u_2 - \sqrt{u_2^2 - 4u_1u_3}}{2u_1}, \quad (3.52)$$

Suppose $z_1 = z_3 = z_4 = z_5 = 0$. and $z_2 \neq 0$. The second equation of (3.40) yields $z_2 = k_6$, indicating that the point $E_5 (0, k_6, 0, 0, 0)$ is likewise a stable point for the system (3.9). From (3.38), we may conclude that the stable points for (3.9) are $P_i (z_1, 0, \frac{6}{p}, \frac{6\alpha}{p_\varepsilon}, 0, 0)$.

$$\frac{-u_2 \pm \sqrt{u_2^2 - 4u_1u_3}}{2u_1} \geq 0, \quad (3.53)$$

Linearized matrix of Eqn. (3.3.1) is;

$$\frac{Df}{Dz} = \begin{bmatrix} \frac{\partial f_1}{\partial z_1} & \frac{\partial f_1}{\partial z_2} & \frac{\partial f_1}{\partial z_3} & \frac{\partial f_1}{\partial z_4} & \frac{\partial f_1}{\partial z_5} \\ \frac{\partial f_2}{\partial z_1} & \frac{\partial f_2}{\partial z_2} & \frac{\partial f_2}{\partial z_3} & \frac{\partial f_2}{\partial z_4} & \frac{\partial f_2}{\partial z_5} \\ \frac{\partial f_3}{\partial z_1} & \frac{\partial f_3}{\partial z_2} & \frac{\partial f_3}{\partial z_3} & \frac{\partial f_3}{\partial z_4} & \frac{\partial f_3}{\partial z_5} \\ \frac{\partial f_4}{\partial z_1} & \frac{\partial f_4}{\partial z_2} & \frac{\partial f_4}{\partial z_3} & \frac{\partial f_4}{\partial z_4} & \frac{\partial f_4}{\partial z_5} \\ \frac{\partial f_5}{\partial z_1} & \frac{\partial f_5}{\partial z_2} & \frac{\partial f_5}{\partial z_3} & \frac{\partial f_5}{\partial z_4} & \frac{\partial f_5}{\partial z_5} \end{bmatrix} = \begin{bmatrix} K_{11}(z) & 0 & K_{13}(z) & K_{14}(z) & K_{15}(z) \\ K_{21}(z) & K_{22}(z) & K_{23}(z) & K_{24}(z) & 0 \\ 0 & K_{32}(z) & K_{33}(z) & 0 & 0 \\ 0 & 0 & K_{43}(z) & K_{44}(z) & 0 \\ 0 & 0 & z_{1n} & 0 & -c \end{bmatrix} \quad (3.54)$$

Here

$$\begin{aligned} \frac{\partial f_1}{\partial z_1} &= -\frac{\beta(z_3(t) + \theta z_4(t))}{N} - \eta, \frac{\partial f_1}{\partial z_2} = 0, \frac{\partial f_1}{\partial z_3} = -\frac{\beta z_1(t)}{N}, \frac{\partial f_1}{\partial z_4} \\ &= -\frac{\beta \theta z_1(t)}{N}, \end{aligned} \quad (3.55)$$

$$\frac{\partial f_1}{\partial z_5} = \phi,$$

$$\begin{aligned} \frac{\partial f_2}{\partial z_1} &= \frac{\beta z_2(t)(z_3(t) + \theta z_4(t))}{N}, \frac{\partial f_2}{\partial z_2} \\ &= \frac{\beta z_1(t)(z_3(t) + \theta z_4(t))}{N} - (K + \eta), \end{aligned} \quad (3.56)$$

$$\frac{\partial f_2}{\partial z_3} = \frac{\beta z_1(t)z_2(t)}{N}, \frac{\partial f_2}{\partial z_4} = \frac{\theta \beta z_1(t)z_2(t)}{N}, \frac{\partial f_2}{\partial z_5} = 0,$$

$$\frac{\partial f_3}{\partial z_1} = 0, \frac{\partial f_3}{\partial z_2} = k, \frac{\partial f_3}{\partial z_3} = -(\mu + \alpha_1 + \eta + \mathcal{P}), \frac{\partial f_3}{\partial z_4} = 0, \frac{\partial f_3}{\partial z_5} = 0, \quad (3.57)$$

$$\frac{\partial f_4}{\partial z_1} = 0, \frac{\partial f_4}{\partial z_2} = 0, \frac{\partial f_4}{\partial z_3} = \mu, \frac{\partial f_4}{\partial z_4} = -(\alpha_2 + \eta + \varepsilon), \frac{\partial f_4}{\partial z_5} = 0, \quad (3.58)$$

$$\frac{\partial f_5}{\partial z_1} = 0, \frac{\partial f_5}{\partial z_2} = 0, \frac{\partial f_5}{\partial z_3} = \mathcal{P}, \frac{\partial f_5}{\partial z_4} = \varepsilon, \frac{\partial f_5}{\partial z_5} = -(\Phi + \eta), \quad (3.59)$$

where:

$$\mathbb{K}_{11}(z) = -\eta - \beta \frac{(\theta z_4(t) + z_3(t))}{N}, \mathbb{K}_{14}(z) = -\beta \frac{\theta z_1(t)}{N}, \mathbb{K}_{13}(z) = \quad (3.60)$$

$$-\beta \frac{z_1(t)}{N}, \mathbb{K}_{15}(z) = \phi, \mathbb{K}_{21}(z) = \beta \frac{(z_3(t) + \theta z_4(t))z_2(t)}{N},$$

$$\mathbb{K}_{22}(z) = -(k + \eta) + \beta z_1(t) \frac{(\theta z_4(t) + z_3(t))}{N}, \mathbb{K}_{23}(z) = \beta \frac{z_1(t)z_2(t)}{N}$$

$$\mathbb{K}_{24}(z) = \frac{\theta \beta z_1(t)z_2(t)}{N}, \mathbb{K}_{32}(z) = k, \mathbb{K}_{33}(z) = -(\mu + \alpha_1 + \eta +$$

$$\mathcal{P}), \mathbb{K}_{43}(z) = \mu, \mathbb{K}_{44}(z) = -(\alpha_2 + \eta + \varepsilon).$$

Jacobian matrix of Eqn. (3.9) at equilibrium points is defined:

$$A_0 = \frac{DF}{Dz}(0) = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 6 & 0 & 0 & 0 \\ 0 & 0 & -\eta_3 & 0 & 0 \\ 0 & 0 & 0 & -\eta_4 & 0 \\ 0 & 0 & d_n & 0 & -c \end{bmatrix}, \quad (3.61)$$

The linearized matrices of (3.9) based on the other stability points $\mathcal{P}_i$ are as follows.

$$A_i = \begin{bmatrix} \mathbb{K}_{11}(\mathcal{P}_i) & 0 & \mathbb{K}_{13}(\mathcal{P}_i) & \mathbb{K}_{14}(\mathcal{P}_i) & \mathbb{K}_{15}(\mathcal{P}_i) \\ \mathbb{K}_{21}(\mathcal{P}_i) & \mathbb{K}_{22}(\mathcal{P}_i) & \mathbb{K}_{23}(\mathcal{P}_i) & \mathbb{K}_{24}(\mathcal{P}_i) & 0 \\ 0 & \mathbb{K}_{32}(\mathcal{P}_i) & \mathbb{K}_{33}(\mathcal{P}_i) & 0 & 0 \\ 0 & 0 & \mathbb{K}_{43}(\mathcal{P}_i) & \mathbb{K}_{44}(\mathcal{P}_i) & 0 \\ 0 & 0 & \mathbb{K}_{1n} & 0 & -c \end{bmatrix}, \quad (3.62)$$

The linearized matrices of Eqn. (3.9) corresponding to additional stability points

$\mathcal{P}_3 (0, kA, 0, 0, 0)$ are as follows.

$$A_3 = \begin{bmatrix} \mathbb{K}_{11}(\mathbb{P}_3) & 0 & \mathbb{K}_{13}(\mathbb{P}_3) & \mathbb{K}_{14}(\mathbb{P}_3) & \mathbb{K}_{15}(\mathbb{P}_3) \\ \mathbb{K}_{21}(\mathbb{P}_3) & \mathbb{K}_{22}(\mathbb{P}_3) & \mathbb{K}_{23}(\mathbb{P}_3) & \mathbb{K}_{24}(\mathbb{P}_3) & 0 \\ 0 & \mathbb{K}_{32}(\mathbb{P}_3) & \mathbb{K}_{33}(\mathbb{P}_3) & 0 & 0 \\ 0 & 0 & \mathbb{K}_{43}(\mathbb{P}_3) & \mathbb{K}_{44}(\mathbb{P}_3) & 0 \\ 0 & 0 & \mathbb{K}_{1n} & 0 & -c \end{bmatrix}, \quad (3.63)$$

Condition 3. “Assume the following assumptions are satisfied”.

$$\begin{aligned} \mathbb{K}_{22} < 0, \mathbb{K}_{33} < 0, (\mathbb{K}_{11} + \mathbb{K}_{44}) \leq 0, (\mathbb{K}_{11} - \mathbb{K}_{44})^2 \geq 4(\mathbb{K}_{11}\mathbb{K}_{44} + \mathbb{K}_{13}\mathbb{K}_{12}\mathbb{K}_{43}, \mathbb{K}_3 \\ \geq K\alpha \end{aligned}$$

$$(\mathbb{K}_{11} + \mathbb{K}_{44}) \pm \sqrt{(\mathbb{K}_{11} - \mathbb{K}_{44})^2 - 4\mathbb{K}_{31}\mathbb{K}_{12}\mathbb{K}_{43}} \leq 0. \quad (3.64)$$

Let $\mathbb{K}_{jk} = \mathbb{K}_{jk}(\mathbb{P}_i)$ i.e., $i = 1, 2, 3$.

“Theorem 3. The point E_0 is a saddle point for the system of (3.9).”

Proof. The matrix A_0 eigenvalues are $\lambda_1 = 0, \lambda_2 = \mathbf{b}_2, \lambda_3 = -\eta_3, \lambda_4 = -\eta_4$, and $\lambda_5 = -c$. Since $\mathbf{b}_2, \eta_3$, and η_4, c all +ve values, however A_0 are non-positive. This shows that A_0 is a saddle point of Eqs. (3.9).

“Theorem 4. Let Conditions (2) and (3) hold. Then $\mathbb{P}_i$ are locally stable points for the system (3.9). Moreover, $\mathbb{P}_i$ are saddle points, when $\mathbb{K}_{22} \geq 0, \mathbb{K}_{33} \geq 0, (\mathbb{K}_{11} + \mathbb{K}_{44}) \geq 0$ and $\mathbb{K}_{11}\mathbb{K}_{44} + \mathbb{K}_{31}\mathbb{K}_{12}\mathbb{K}_{43} \geq 0$ ”.

Proof. We compute an eigenvalue of A_i as follow;

$$A_i - \lambda I = \begin{bmatrix} \mathbb{K}_{11} - \lambda & 0 & \mathbb{K}_{13} & \mathbb{K}_{14} & \mathbb{K}_{15} \\ \mathbb{K}_{21} & \mathbb{K}_{22} - \lambda & \mathbb{K}_{23} & \mathbb{K}_{24} & 0 \\ 0 & \mathbb{K}_{32} & \mathbb{K}_{33} - \lambda & 0 & 0 \\ 0 & 0 & \mathbb{K}_{43} & \mathbb{K}_{44} - \lambda & 0 \\ 0 & 0 & \mathbb{K}_{1n} & 0 & -c - \lambda \end{bmatrix}, \quad (3.65)$$

$$= (c + \lambda) \begin{bmatrix} \mathbb{K}_{11} - \lambda & 0 & \mathbb{K}_{13} & \mathbb{K}_{14} \\ \mathbb{K}_{21} & \mathbb{K}_{22} - \lambda & \mathbb{K}_{23} & \mathbb{K}_{24} \\ 0 & \mathbb{K}_{32} & \mathbb{K}_{33} - \lambda & 0 \\ 0 & 0 & \mathbb{K}_{43} & -c - \lambda \end{bmatrix}, \quad (3.66)$$

$$(c + \lambda)[\prod_{k=1}^4[(\mathbb{K}_{kk} - \lambda)] + \mathbb{K}_{21}\mathbb{K}_{32}\mathbb{K}_{43}(\mathbb{K}_{44} - \lambda) + \mathbb{K}_{13}\mathbb{K}_{32}(\mathbb{K}_{22} - \lambda)(\mathbb{K}_{44} - \lambda)] = 0, \quad (3.67)$$

From Eqn. (3.67), we compute eigenvalue i.e., $\lambda_1 = -c$.

$$\prod_{k=1}^4[(\mathbb{K}_{kk} - \lambda)] + \mathbb{K}_{21}\mathbb{K}_{32}\mathbb{K}_{43}(\mathbb{K}_{44} - \lambda) + \mathbb{K}_{13}\mathbb{K}_{32}(\mathbb{K}_{22} - \lambda)(\mathbb{K}_{44} - \lambda) = 0, \quad (3.68)$$

Let $\lambda_2 = \mathbb{K}_{22}, \lambda_3 = \mathbb{K}_{33}$. The roots of λ_4 and λ_5 will be the solution to the following equations.

$$(\mathbb{K}_{11} - \lambda)(\mathbb{K}_{44} - \lambda) + \mathbb{K}_{31}\mathbb{K}_{12}\mathbb{K}_{43} = 0, \quad (3.69)$$

Expanding,

$$\mathbb{K}_{11}\mathbb{K}_{44} - \mathbb{K}_{11}\lambda - \mathbb{K}_{44}\lambda + \lambda^2 + \mathbb{K}_{31}\mathbb{K}_{12}\mathbb{K}_{43} = 0, \quad (3.70)$$

Arranging as the quadratic equations

$$\lambda^2 - (\mathbb{K}_{11} + \mathbb{K}_{44})\lambda + \mathbb{K}_{11}\mathbb{K}_{44} + \mathbb{K}_{31}\mathbb{K}_{12}\mathbb{K}_{43} = 0, \quad (3.71)$$

$$\lambda_{4,5} = \frac{(\mathbb{K}_{11} + \mathbb{K}_{44}) \pm \sqrt{(\mathbb{K}_{11} + \mathbb{K}_{44})^2 - 4(\mathbb{K}_{11}\mathbb{K}_{44} + \mathbb{K}_{31}\mathbb{K}_{12}\mathbb{K}_{43})}}{2}, \quad (3.72)$$

$$= \frac{(\mathbb{K}_{11} + \mathbb{K}_{44}) \pm \sqrt{(\mathbb{K}_{11} - \mathbb{K}_{44})^2 - 4(\mathbb{K}_{11}\mathbb{K}_{44} + \mathbb{K}_{31}\mathbb{K}_{12}\mathbb{K}_{43})}}{2}, \quad (3.73)$$

When

$$(\mathbb{K}_{11} - \mathbb{K}_{44})^2 \geq 4(\mathbb{K}_{11}\mathbb{K}_{44} + \mathbb{K}_{31}\mathbb{K}_{12}\mathbb{K}_{43}), \quad (3.74)$$

Furthermore, for $\mathbb{K}_{22} \geq 0, \mathbb{K}_{33} \geq 0, (\mathbb{K}_{11} + \mathbb{K}_{44}) \geq 0$, and $\mathbb{K}_{11}\mathbb{K}_{44} + \mathbb{K}_{31}\mathbb{K}_{21}\mathbb{K}_{43} \geq 0$,

“Theorem 5. Let the Conditions 2 holds. The point $\mathcal{P}_3$ is a saddle point”.

Proof. The following equations provide the solutions for an eigenvalue of A_3 .

$$A_3 - \lambda I = \begin{bmatrix} \mathbb{K}_{11} & 0 & \mathbb{K}_{13} & \mathbb{K}_{14} & \mathbb{K}_{15} \\ \mathbb{K}_{21} & \mathbb{K}_{22} & \mathbb{K}_{23} & \mathbb{K}_{24} & 0 \\ 0 & \mathbb{K}_{32} & \mathbb{K}_{33} & 0 & 0 \\ 0 & 0 & \mathbb{K}_{43} & \mathbb{K}_{44} & 0 \\ 0 & 0 & \mathbb{K}_{1n} & 0 & -c \end{bmatrix} - \lambda \begin{bmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix}, \quad (3.75)$$

$$A_3 - \lambda I = \begin{bmatrix} \mathbb{K}_{11} - \lambda & 0 & \mathbb{K}_{13} & \mathbb{K}_{14} & \mathbb{K}_{15} \\ \mathbb{K}_{21} & \mathbb{K}_{22} - \lambda & \mathbb{K}_{23} & \mathbb{K}_{24} & 0 \\ 0 & \mathbb{K}_{32} & \mathbb{K}_{33} - \lambda & 0 & 0 \\ 0 & 0 & \mathbb{K}_{43} & \mathbb{K}_{44} - \lambda & 0 \\ 0 & 0 & \mathbb{K}_{1n} & 0 & -c - \lambda \end{bmatrix}, \quad (3.76)$$

Consider the sub-block matrix 3×3

$$\begin{bmatrix} \mathbb{K}_{33} - \lambda & 0 & 0 \\ \mathbb{K}_{43} & \mathbb{K}_{44} - \lambda & 0 \\ \mathbb{K}_{1n} & 0 & -c - \lambda \end{bmatrix}, \quad (3.77)$$

This is a lower-triangular matrix, so its determinant is product of the diagonal entries

$$(\mathbb{K}_{33} - \lambda)(\mathbb{K}_{44} - \lambda)(-c - \lambda) = 0, \quad (3.78)$$

Hence the eigenvalues of this block are

$$\lambda_3 = \mathbb{K}_{33}, \lambda_4 = \mathbb{K}_{44}, \lambda_0 = -c, \quad (3.79)$$

The remaining eigenvalue now consider the top left top 2×2 block

$$\begin{bmatrix} \mathbb{K}_{11} - \lambda & 0 \\ \mathbb{K}_{21} & \mathbb{K}_{22} - \lambda \end{bmatrix}, \quad (3.80)$$

This is top triangular, so its eigenvalues are

$$(\mathbb{K}_{11} - \lambda)(\mathbb{K}_{22} - \lambda) = 0, \quad (3.81)$$

$$\lambda_1 = \mathbb{K}_{11}, \lambda_2 = \mathbb{K}_{22}, \quad (3.82)$$

Hence, $\lambda_0 = -c, \lambda_1 = \mathbb{K}_{11}, \lambda_2 = \mathbb{K}_{22}, \lambda_3 = \mathbb{K}_{33}, \lambda_4 = \mathbb{K}_{44}$ are eigenvalues of A_3 .

3.2.3 Lyapunov Stability of Equilibria Points

To examine the stability, we used Lyapunov Stability of Equilibria Points criteria, we used following theorem.

“Theorem 6. The system (3.9) is not stable at the equilibria $\mathcal{P}_0(0)$ in the Lyapunov sense”.

Proof. With a positive eigenvalue at $\mathcal{P}_0$, Eqn. (3.3.1) is unstable at point $\mathcal{P}_0$. We now examine the equilibrium points $\mathcal{P}_i$ and prove the result.

“Theorem 7. Assume that the Conditions 2 and 3 are satisfied. Then the system (3.9) is asymptotically stable at the equilibria points $\mathcal{P}_i$ in the sense of Lyapunov”.

Proof. To compute equilibrium criteria, we suppose the following matrix;

$$A_i = \begin{bmatrix} \mathbb{K}_{11}(\mathcal{P}_i) & 0 & \mathbb{K}_{13}(\mathcal{P}_i) & \mathbb{K}_{14}(\mathcal{P}_i) & \mathbb{K}_{15}(\mathcal{P}_i) \\ \mathbb{K}_{21}(\mathcal{P}_i) & \mathbb{K}_{22}(\mathcal{P}_i) & \mathbb{K}_{23}(\mathcal{P}_i) & \mathbb{K}_{24}(\mathcal{P}_i) & 0 \\ 0 & \mathbb{K}_{32}(\mathcal{P}_i) & \mathbb{K}_{33}(\mathcal{P}_i) & 0 & 0 \\ 0 & 0 & \mathbb{K}_{43}(\mathcal{P}_i) & \mathbb{K}_{44}(\mathcal{P}_i) & 0 \\ 0 & 0 & \mathbb{K}_{1n} & 0 & -c \end{bmatrix}, \quad (3.83)$$

Where $\mathbb{K}_{kj} = \mathbb{K}_{kj}(\mathcal{P}_i)$. Consider the Lyapunov equation

$$B_i A_i + A_i^T B_i = -I, \quad (3.84)$$

Where;

$$B_i = \begin{bmatrix} \mathfrak{b}_{11} & \mathfrak{b}_{12} & \mathfrak{b}_{13} & \mathfrak{b}_{14} & \mathfrak{b}_{15} \\ \mathfrak{b}_{21} & \mathfrak{b}_{22} & \mathfrak{b}_{23} & \mathfrak{b}_{24} & \mathfrak{b}_{25} \\ \mathfrak{b}_{31} & \mathfrak{b}_{32} & \mathfrak{b}_{33} & \mathfrak{b}_{34} & \mathfrak{b}_{35} \\ \mathfrak{b}_{41} & \mathfrak{b}_{42} & \mathfrak{b}_{43} & \mathfrak{b}_{44} & \mathfrak{b}_{45} \\ \mathfrak{b}_{51} & \mathfrak{b}_{52} & \mathfrak{b}_{53} & \mathfrak{b}_{54} & \mathfrak{b}_{55} \end{bmatrix}, \mathfrak{b}_{kj} = \mathfrak{b}_{kj}(i), \mathfrak{b}_{kj} = \mathfrak{b}_{jk}, \quad (3.85)$$

It is clear that

$$B_i A_i = \begin{bmatrix} \mathfrak{b}_{11} & \mathfrak{b}_{12} & \mathfrak{b}_{13} & \mathfrak{b}_{14} & \mathfrak{b}_{15} \\ \mathfrak{b}_{21} & \mathfrak{b}_{22} & \mathfrak{b}_{23} & \mathfrak{b}_{24} & \mathfrak{b}_{25} \\ \mathfrak{b}_{31} & \mathfrak{b}_{32} & \mathfrak{b}_{33} & \mathfrak{b}_{34} & \mathfrak{b}_{35} \\ \mathfrak{b}_{41} & \mathfrak{b}_{42} & \mathfrak{b}_{43} & \mathfrak{b}_{44} & \mathfrak{b}_{45} \\ \mathfrak{b}_{51} & \mathfrak{b}_{52} & \mathfrak{b}_{53} & \mathfrak{b}_{54} & \mathfrak{b}_{55} \end{bmatrix} \begin{bmatrix} \mathbb{K}_{11} & 0 & \mathbb{K}_{13} & \mathbb{K}_{14} & \mathbb{K}_{15} \\ \mathbb{K}_{21} & \mathbb{K}_{22} & \mathbb{K}_{23} & \mathbb{K}_{24} & 0 \\ 0 & \mathbb{K}_{32} & \mathbb{K}_{33} & 0 & 0 \\ 0 & 0 & \mathbb{K}_{43} & \mathbb{K}_{44} & 0 \\ 0 & 0 & \mathbb{K}_{1n} & 0 & -c \end{bmatrix} = \quad (3.86)$$

$$[ck_j],$$

$$A_i^T = \begin{bmatrix} \mathbb{K}_{11} & \mathbb{K}_{21} & 0 & 0 & 0 \\ 0 & \mathbb{K}_{22} & \mathbb{K}_{32} & 0 & 0 \\ \mathbb{K}_{13} & \mathbb{K}_{23} & \mathbb{K}_{33} & \mathbb{K}_{43} & \mathbb{K}_{1n} \\ \mathbb{K}_{14} & \mathbb{K}_{24} & 0 & \mathbb{K}_{44} & 0 \\ \mathbb{K}_{15} & 0 & 0 & 0 & -c \end{bmatrix} = \begin{bmatrix} \mathfrak{b}_{11} & \mathfrak{b}_{12} & \mathfrak{b}_{13} & \mathfrak{b}_{14} & \mathfrak{b}_{15} \\ \mathfrak{b}_{21} & \mathfrak{b}_{22} & \mathfrak{b}_{23} & \mathfrak{b}_{24} & \mathfrak{b}_{25} \\ \mathfrak{b}_{31} & \mathfrak{b}_{32} & \mathfrak{b}_{33} & \mathfrak{b}_{34} & \mathfrak{b}_{35} \\ \mathfrak{b}_{41} & \mathfrak{b}_{42} & \mathfrak{b}_{43} & \mathfrak{b}_{44} & \mathfrak{b}_{45} \\ \mathfrak{b}_{51} & \mathfrak{b}_{52} & \mathfrak{b}_{53} & \mathfrak{b}_{54} & \mathfrak{b}_{55} \end{bmatrix} = \quad (3.87)$$

$$[lk_j],$$

$$\mathfrak{b}_{12}\mathbb{K}_{21} + \mathfrak{b}_{11}\mathbb{K}_{11} = c_{11}, \quad \mathfrak{b}_{12}\mathbb{K}_{22} + \mathfrak{b}_{13}\mathbb{K}_{32} = c_{12}, \quad (3.88)$$

$$\mathfrak{b}_{11}\mathbb{K}_{13} + \mathbb{K}_{23}\mathfrak{b}_{12} + \mathfrak{b}_{13}\mathbb{K}_{33} + \mathbb{K}_{43}\mathfrak{b}_{14} + \mathfrak{b}_{15}\mathbb{K}_{1n} = c_{13}, \quad (3.89)$$

$$\mathfrak{b}_{11}\mathbb{K}_{14} + \mathbb{K}_{24}\mathfrak{b}_{12} + \mathfrak{b}_{14}\mathbb{K}_{44} = c_{14}, \quad (3.90)$$

$$c_{15} = \mathbb{K}_{15}\mathfrak{b}_{22} - c\mathfrak{b}_{15}, c_{21} = \mathfrak{b}_{22}\mathbb{K}_{21} + \mathfrak{b}_{21}\mathbb{K}_{11}, c_{22} = \mathbb{K}_{22}\mathfrak{b}_{22} + \mathbb{K}_{32}\mathfrak{b}_{23}, \quad (3.91)$$

$$c_{23} = \mathbb{K}_{13}\mathfrak{b}_{21} + \mathbb{K}_{23}\mathfrak{b}_{22} + \mathbb{K}_{33}\mathfrak{b}_{23} + \mathbb{K}_{43}\mathfrak{b}_{24} + \mathbb{K}_{1n}\mathfrak{b}_{25}, \quad \mathfrak{b}_{21}\mathbb{K}_{14} + \mathbb{K}_{24}\mathfrak{b}_{22} \quad (3.92)$$

$$+ \mathfrak{b}_{24}\mathbb{K}_{44} = c_{24},$$

$$c_{25} = \mathbb{K}_{15}\mathfrak{b}_{21} - c\mathfrak{b}_{25}, c_{31} = \mathbb{K}_{11}\mathfrak{b}_{31} + \mathbb{K}_{21}\mathfrak{b}_{32}, c_{32} = \mathbb{K}_{22}\mathfrak{b}_{32} + \mathbb{K}_{32}\mathfrak{b}_{33}, \quad (3.93)$$

$$c_{33} = \mathbb{K}_{13}\mathfrak{b}_{31} + \mathbb{K}_{23}\mathfrak{b}_{32} + \mathbb{K}_{33}\mathfrak{b}_{33} + \mathbb{K}_{43}\mathfrak{b}_{34} + \mathbb{K}_{1n}\mathfrak{b}_{35} \quad (3.94)$$

$$c_{34} = \mathbb{K}_{14}\mathfrak{b}_{31} + \mathbb{K}_{24}\mathfrak{b}_{32} + \mathbb{K}_{44}\mathfrak{b}_{34}, c_{35} = \mathbb{K}_{15}\mathfrak{b}_{31} - c\mathfrak{b}_{35}, \quad (3.95)$$

$$c_{41} = \mathbb{K}_{11}\mathfrak{b}_{41} + \mathbb{K}_{21}\mathfrak{b}_{42}, c_{42} = \mathbb{K}_{22}\mathfrak{b}_{42} + \mathbb{K}_{32}\mathfrak{b}_{43}, \quad (3.96)$$

$$c_{43} = \mathbb{K}_{13}\mathfrak{b}_{41} + \mathbb{K}_{23}\mathfrak{b}_{42} + \mathbb{K}_{33}\mathfrak{b}_{43} + \mathbb{K}_{43}\mathfrak{b}_{44} + \mathbb{K}_{1n}\mathfrak{b}_{45}, \quad (3.97)$$

$$c_{44} = \mathbb{K}_{14}\mathfrak{b}_{41} + \mathbb{K}_{24}\mathfrak{b}_{42} + \mathbb{K}_{44}\mathfrak{b}_{44}, c_{45} = \mathbb{K}_{15}\mathfrak{b}_{51} - c\mathfrak{b}_{55}, \quad (3.98)$$

$$c_{51} = \mathbb{K}_{11}\mathfrak{b}_{51} + \mathbb{K}_{21}\mathfrak{b}_{52}, c_{52} = \mathbb{K}_{22}\mathfrak{b}_{52} + \mathbb{K}_{32}\mathfrak{b}_{53}, \quad (3.99)$$

$$c_{51} = \mathbb{K}_{11}\mathfrak{b}_{51} + \mathbb{K}_{21}\mathfrak{b}_{52}, c_{52} = \mathbb{K}_{22}\mathfrak{b}_{52} + \mathbb{K}_{32}\mathfrak{b}_{53}, \quad (3.100)$$

$$c_{53} = \mathbb{K}_{13}\mathfrak{b}_{51} + \mathbb{K}_{23}\mathfrak{b}_{52} + \mathbb{K}_{33}\mathfrak{b}_{53} + \mathbb{K}_{43}\mathfrak{b}_{54} + \mathbb{K}_{1n}\mathfrak{b}_{55}, \quad (3.101)$$

$$c_{54} = \mathbb{K}_{14}\mathfrak{b}_{51} + \mathbb{K}_{24}\mathfrak{b}_{52} + \mathbb{K}_{44}\mathfrak{b}_{54}, c_{55} = \mathbb{K}_{15}\mathfrak{b}_{51} - c\mathfrak{b}_{55}, \quad (3.102)$$

$$l_{11} = \mathbb{K}_{11}\mathfrak{b}_{11} + \mathbb{K}_{12}\mathfrak{b}_{21}, l_{12} = \mathbb{K}_{11}\mathfrak{b}_{12} + \mathbb{K}_{21}\mathfrak{b}_{22}, \quad (3.103)$$

$$l_{13} = \mathbb{K}_{11}\mathfrak{b}_{13} + \mathbb{K}_{21}\mathfrak{b}_{23}, l_{14} = \mathbb{K}_{11}\mathfrak{b}_{14} + \mathbb{K}_{21}\mathfrak{b}_{24}, \quad (3.104)$$

$$l_{15} = \mathbb{K}_{11}\mathfrak{b}_{15} + \mathbb{K}_{21}\mathfrak{b}_{25}, l_{21} = \mathbb{K}_{22}\mathfrak{b}_{21} + \mathbb{K}_{32}\mathfrak{b}_{31}, \quad (3.105)$$

$$l_{22} = \mathbb{K}_{22}\mathfrak{b}_{22} + \mathbb{K}_{32}\mathfrak{b}_{32}, l_{23} = \mathbb{K}_{22}\mathfrak{b}_{23} + \mathbb{K}_{32}\mathfrak{b}_{33}, \quad (3.106)$$

$$l_{24} = \mathbb{K}_{22}\mathfrak{b}_{24} + \mathbb{K}_{32}\mathfrak{b}_{34}, l_{25} = \mathbb{K}_{22}\mathfrak{b}_{25} + \mathbb{K}_{32}\mathfrak{b}_{35}, \quad (3.107)$$

$$l_{31} = \mathbb{K}_{13}\mathfrak{b}_{11} + \mathbb{K}_{23}\mathfrak{b}_{21} + \mathbb{K}_{33}\mathfrak{b}_{31} + \mathbb{K}_{43}\mathfrak{b}_{41} + \mathbb{K}_{1n}\mathfrak{b}_{51}, \quad (3.108)$$

$$l_{32} = \mathbb{K}_{13}\mathfrak{b}_{12} + \mathbb{K}_{23}\mathfrak{b}_{22} + \mathbb{K}_{33}\mathfrak{b}_{32} + \mathbb{K}_{43}\mathfrak{b}_{42} + \mathbb{K}_{1n}\mathfrak{b}_{52}, \quad (3.109)$$

$$l_{33} = \mathbb{K}_{13}\mathfrak{b}_{13} + \mathbb{K}_{23}\mathfrak{b}_{23} + \mathbb{K}_{33}\mathfrak{b}_{33} + \mathbb{K}_{43}\mathfrak{b}_{43} + \mathbb{K}_{1n}\mathfrak{b}_{53}, \quad (3.110)$$

$$l_{34} = \mathbb{K}_{13}\mathfrak{b}_{14} + \mathbb{K}_{23}\mathfrak{b}_{24} + \mathbb{K}_{33}\mathfrak{b}_{34} + \mathbb{K}_{43}\mathfrak{b}_{44} + \mathbb{K}_{1n}\mathfrak{b}_{54}, \quad (3.111)$$

$$l_{35} = \mathbb{K}_{13}\mathfrak{b}_{15} + \mathbb{K}_{23}\mathfrak{b}_{25} + \mathbb{K}_{33}\mathfrak{b}_{35} + \mathbb{K}_{43}\mathfrak{b}_{45} + \mathbb{K}_{1n}\mathfrak{b}_{55}, \quad (3.112)$$

$$l_{41} = \mathbb{K}_{14}\mathfrak{b}_{11} + \mathbb{K}_{24}\mathfrak{b}_{21} + \mathbb{K}_{44}\mathfrak{b}_{41}, l_{42} = \mathbb{K}_{14}\mathfrak{b}_{12} + \mathbb{K}_{24}\mathfrak{b}_{22} + \mathbb{K}_{44}\mathfrak{b}_{42}, \quad (3.113)$$

$$l_{43} = \mathbb{K}_{14}\mathfrak{b}_{13} + \mathbb{K}_{24}\mathfrak{b}_{23} + \mathbb{K}_{44}\mathfrak{b}_{43}, l_{44} = \mathbb{K}_{14}\mathfrak{b}_{14} + \mathbb{K}_{24}\mathfrak{b}_{24} + \mathbb{K}_{44}\mathfrak{b}_{44}, \quad (3.114)$$

$$l_{45} = \mathbb{K}_{14}\mathfrak{b}_{15} + \mathbb{K}_{24}\mathfrak{b}_{25} + \mathbb{K}_{44}\mathfrak{b}_{45}, l_{51} = \mathbb{K}_{15}\mathfrak{b}_{11} - c\mathfrak{b}_{51}, \quad (3.115)$$

$$l_{52} = \mathbb{K}_{15}\mathfrak{b}_{12} - c\mathfrak{b}_{52}, l_{53} = \mathbb{K}_{15}\mathfrak{b}_{13} - c\mathfrak{b}_{53}, \quad (3.116)$$

$$l_{54} = \mathbb{K}_{15}\mathfrak{b}_{14} - c\mathfrak{b}_{54}, l_{55} = \mathbb{K}_{15}\mathfrak{b}_{15} - c\mathfrak{b}_{55}, \quad (3.117)$$

To which

$$c_{kj} + l_{kj}, \quad (3.118)$$

$$c_{11} + l_{11} = \mathbb{K}_{11}\mathfrak{b}_{11} + \mathbb{K}_{21}\mathfrak{b}_{12} + \mathbb{K}_{11}\mathfrak{b}_{11} + \mathbb{K}_{12}\mathfrak{b}_{21} = 2(\mathbb{K}_{11}\mathfrak{b}_{11} + \mathbb{K}_{21}\mathfrak{b}_{12}), \quad (3.119)$$

$$c_{12} + l_{12} = \mathbb{K}_{22}\mathfrak{b}_{12} + \mathbb{K}_{32}\mathfrak{b}_{13} + \mathbb{K}_{11}\mathfrak{b}_{12} + \mathbb{K}_{21}\mathfrak{b}_{22}, \quad (3.120)$$

$$c_{12} + l_{12} = \mathbb{K}_{21}\mathfrak{b}_{22} + \mathbb{K}_{32}\mathfrak{b}_{13} + (\mathbb{K}_{11} + \mathbb{K}_{22})\mathfrak{b}_{12}, \quad (3.121)$$

$$c_{13} + l_{13} = \mathbb{K}_{13}\mathfrak{b}_{11} + \mathbb{K}_{23}\mathfrak{b}_{12} + \mathbb{K}_{33}\mathfrak{b}_{13} + \mathbb{K}_{43}\mathfrak{b}_{14} + \mathbb{K}_{1n}\mathfrak{b}_{15} + \mathbb{K}_{11}\mathfrak{b}_{13} \quad (3.122)$$

$$+ \mathbb{K}_{21}\mathfrak{b}_{23},$$

$$c_{13} + l_{13} = \mathbb{K}_{13}\mathfrak{b}_{11} + \mathbb{K}_{23}\mathfrak{b}_{12} + (\mathbb{K}_{11} + \mathbb{K}_{33})\mathfrak{b}_{13} + \mathbb{K}_{43}\mathfrak{b}_{14} + \mathbb{K}_{1n}\mathfrak{b}_{15} \quad (3.123)$$

$$+ \mathbb{K}_{21}\mathfrak{b}_{23},$$

$$c_{14} + l_{14} = \mathbb{K}_{14}\mathfrak{b}_{11} + \mathbb{K}_{24}\mathfrak{b}_{12} + \mathbb{K}_{44}\mathfrak{b}_{14} + \mathbb{K}_{11}\mathfrak{b}_{14} + \mathbb{K}_{21}\mathfrak{b}_{24}, \quad (3.124)$$

$$c_{14} + l_{14} = \mathbb{K}_{14}\mathfrak{b}_{11} + \mathbb{K}_{24}\mathfrak{b}_{12} + (\mathbb{K}_{11} + \mathbb{K}_{44})\mathfrak{b}_{14} + \mathbb{K}_{21}\mathfrak{b}_{24}, \quad (3.125)$$

$$c_{15} + l_{15} = \mathbb{K}_{15}\mathfrak{b}_{22} - c\mathfrak{b}_{15} + \mathbb{K}_{11}\mathfrak{b}_{15} + \mathbb{K}_{21}\mathfrak{b}_{25}, \quad (3.126)$$

$$c_{15} + l_{15} = \mathbb{K}_{15}\mathfrak{b}_{22} + (\mathbb{K}_{11} - c)\mathfrak{b}_{15} + \mathbb{K}_{21}\mathfrak{b}_{25}, \quad (3.127)$$

$$c_{21} + l_{21} = \mathbb{K}_{11}\mathfrak{b}_{21} + \mathbb{K}_{21}\mathfrak{b}_{22} + \mathbb{K}_{22}\mathfrak{b}_{21} + \mathbb{K}_{32}\mathfrak{b}_{31}, \quad (3.128)$$

$$c_{21} + l_{21} = (\mathbb{K}_{11} + \mathbb{K}_{22})\mathfrak{b}_{21} + \mathbb{K}_{21}\mathfrak{b}_{22} + \mathbb{K}_{32}\mathfrak{b}_{31}, \quad (3.129)$$

$$c_{22} + l_{22} = \mathbb{K}_{22}\mathfrak{b}_{22} + \mathbb{K}_{32}\mathfrak{b}_{23} + \mathbb{K}_{22}\mathfrak{b}_{22} + \mathbb{K}_{32}, \quad (3.130)$$

$$c_{22} + l_{22} = 2(\mathbb{K}_{22}\mathfrak{b}_{22} + \mathbb{K}_{32}\mathfrak{b}_{23}), \quad (3.131)$$

$$\begin{aligned} c_{23} + l_{23} = & \mathbb{K}_{13}\mathfrak{b}_{21} + \mathbb{K}_{23}\mathfrak{b}_{22} + \mathbb{K}_{33}\mathfrak{b}_{23} + \mathbb{K}_{43}\mathfrak{b}_{24} + \mathbb{K}_{1n}\mathfrak{b}_{25} + \mathbb{K}_{22}\mathfrak{b}_{23} \\ & + \mathbb{K}_{32}\mathfrak{b}_{33}, \end{aligned} \quad (3.132)$$

$$\begin{aligned} c_{23} + l_{23} = & \mathbb{K}_{13}\mathfrak{b}_{21} + \mathbb{K}_{23}\mathfrak{b}_{22} + (\mathbb{K}_{22} + \mathbb{K}_{33})\mathfrak{b}_{23} + \mathbb{K}_{43}\mathfrak{b}_{24} + \mathbb{K}_{1n}\mathfrak{b}_{25} \\ & + \mathbb{K}_{32}\mathfrak{b}_{33}, \end{aligned} \quad (3.133)$$

$$c_{24} + l_{24} = \mathbb{K}_{14}\mathfrak{b}_{21} + \mathbb{K}_{24}\mathfrak{b}_{22} + \mathbb{K}_{44}\mathfrak{b}_{24} + \mathbb{K}_{22}\mathfrak{b}_{24} + \mathbb{K}_{32}\mathfrak{b}_{34}, \quad (3.134)$$

$$c_{24} + l_{24} = \mathbb{K}_{14}\mathfrak{b}_{21} + \mathbb{K}_{24}\mathfrak{b}_{22} + (\mathbb{K}_{22} + \mathbb{K}_{44})\mathfrak{b}_{24} + \mathbb{K}_{32}\mathfrak{b}_{34}, \quad (3.135)$$

$$c_{25} + l_{25} = \mathbb{K}_{15}\mathfrak{b}_{21} + (\mathbb{K}_{22} - c)\mathfrak{b}_{25} + \mathbb{K}_{32}\mathfrak{b}_{35}, \quad (3.136)$$

$$c_{25} + l_{25} = \mathbb{K}_{15}\mathfrak{b}_{21} - c\mathfrak{b}_{25} + \mathbb{K}_{22}\mathfrak{b}_{25} + \mathbb{K}_{32}\mathfrak{b}_{35}, \quad (3.137)$$

$$c_{25} + l_{25} = \mathbb{K}_{15}\mathfrak{b}_{21} - c\mathfrak{b}_{25} + \mathbb{K}_{22}\mathfrak{b}_{25} + \mathbb{K}_{32}\mathfrak{b}_{35}, \quad (3.138)$$

$$c_{25} + l_{25} = \mathbb{K}_{15}\mathfrak{b}_{21} + (\mathbb{K}_{22} - c)\mathfrak{b}_{25} + \mathbb{K}_{32}\mathfrak{b}_{35}, \quad (3.139)$$

$$\begin{aligned} c_{31} + l_{31} = & \mathbb{K}_{11}\mathfrak{b}_{31} + \mathbb{K}_{21}\mathfrak{b}_{32} + \mathbb{K}_{13}\mathfrak{b}_{11} + \mathbb{K}_{23}\mathfrak{b}_{21} + \mathbb{K}_{33}\mathfrak{b}_{31} + \mathbb{K}_{43}\mathfrak{b}_{41} \\ & + \mathbb{K}_{1n}\mathfrak{b}_{51}, \end{aligned} \quad (3.140)$$

$$\begin{aligned} c_{31} + l_{31} = & (\mathbb{K}_{11} + \mathbb{K}_{33})\mathfrak{b}_{31} + \mathbb{K}_{21}\mathfrak{b}_{32} + \mathbb{K}_{13}\mathfrak{b}_{11} + \mathbb{K}_{23}\mathfrak{b}_{21} + \mathbb{K}_{43}\mathfrak{b}_{41} \\ & + \mathbb{K}_{1n}\mathfrak{b}_{51}, \end{aligned} \quad (3.141)$$

$$\begin{aligned} c_{32} + l_{32} = & \mathbb{K}_{22}\mathfrak{b}_{32} + \mathbb{K}_{32}\mathfrak{b}_{33} + \mathbb{K}_{13}\mathfrak{b}_{12} + \mathbb{K}_{23}\mathfrak{b}_{22} + \mathbb{K}_{33}\mathfrak{b}_{32} + \mathbb{K}_{43}\mathfrak{b}_{42} \\ & + \mathbb{K}_{1n}\mathfrak{b}_{52}, \end{aligned} \quad (3.142)$$

$$\begin{aligned} c_{32} + l_{32} = & (\mathbb{K}_{22} + \mathbb{K}_{33})\mathfrak{b}_{32} + \mathbb{K}_{32}\mathfrak{b}_{33} + \mathbb{K}_{13}\mathfrak{b}_{12} + \mathbb{K}_{23}\mathfrak{b}_{22} + \mathbb{K}_{43}\mathfrak{b}_{42} \\ & + \mathbb{K}_{1n}\mathfrak{b}_{52}, \end{aligned} \quad (3.143)$$

$$c_{33} + l_{33} = \mathbb{K}_{13}\mathfrak{b}_{31} + \mathbb{K}_{23}\mathfrak{b}_{32} + \mathbb{K}_{33}\mathfrak{b}_{33} + \mathbb{K}_{43}\mathfrak{b}_{34} + \mathbb{K}_{43}\mathfrak{b}_{42} + \mathbb{K}_{1n}\mathfrak{b}_{35} \\ + \mathbb{K}_{13}\mathfrak{b}_{13} + \mathbb{K}_{23}\mathfrak{b}_{13} + \mathbb{K}_{33}\mathfrak{b}_{33} + \mathbb{K}_{43}\mathfrak{b}_{43} + \mathbb{K}_{1n}\mathfrak{b}_{53} \quad (3.144)$$

$$c_{33} + l_{33} = 2(\mathbb{K}_{13}\mathfrak{b}_{31} + \mathbb{K}_{23}\mathfrak{b}_{32} + \mathbb{K}_{33}\mathfrak{b}_{33} + \mathbb{K}_{43}\mathfrak{b}_{34} + \mathbb{K}_{1n}\mathfrak{b}_{35} + \mathbb{K}_{13}\mathfrak{b}_{13} \\ + \mathbb{K}_{23}\mathfrak{b}_{13} + \mathbb{K}_{33}\mathfrak{b}_{33} + \mathbb{K}_{43}\mathfrak{b}_{43} + \mathbb{K}_{1n}\mathfrak{b}_{53}), \quad (3.145)$$

$$c_{34} + l_{34} = \mathbb{K}_{14}\mathfrak{b}_{31} + \mathbb{K}_{24}\mathfrak{b}_{32} + \mathbb{K}_{44}\mathfrak{b}_{34} + \mathbb{K}_{13}\mathfrak{b}_{14} + \mathbb{K}_{23}\mathfrak{b}_{24} + \mathbb{K}_{33}\mathfrak{b}_{34} \\ + \mathbb{K}_{43}\mathfrak{b}_{54}, \quad (3.146)$$

$$c_{34} + l_{34} = \mathbb{K}_{14}\mathfrak{b}_{31} + \mathbb{K}_{24}\mathfrak{b}_{32} + (\mathbb{K}_{33} + \mathbb{K}_{44})\mathfrak{b}_{34} + \mathbb{K}_{13}\mathfrak{b}_{14} + \mathbb{K}_{23}\mathfrak{b}_{24} \\ + \mathbb{K}_{43}\mathfrak{b}_{44} + \mathbb{K}_{1n}\mathfrak{b}_{54}, \quad (3.147)$$

$$c_{35} + l_{35} = \mathbb{K}_{15}\mathfrak{b}_{31} - c\mathfrak{b}_{35} + \mathbb{K}_{13}\mathfrak{b}_{15} + \mathbb{K}_{23}\mathfrak{b}_{25} + \mathbb{K}_{33}\mathfrak{b}_{35} + \mathbb{K}_{43}\mathfrak{b}_{45} \\ + \mathbb{K}_{1n}\mathfrak{b}_{55}, \quad (3.148)$$

$$c_{35} + l_{35} = \mathbb{K}_{15}\mathfrak{b}_{31} + (\mathbb{K}_{33} - c)\mathfrak{b}_{35} + \mathbb{K}_{13}\mathfrak{b}_{15} + \mathbb{K}_{23}\mathfrak{b}_{25} + \mathbb{K}_{43}\mathfrak{b}_{45} \\ + \mathbb{K}_{1n}\mathfrak{b}_{55}, \quad (3.149)$$

$$c_{41} + l_{41} = \mathbb{K}_{11}\mathfrak{b}_{41} + \mathbb{K}_{21}\mathfrak{b}_{42} + \mathbb{K}_{14}\mathfrak{b}_{11} + \mathbb{K}_{24}\mathfrak{b}_{21} + \mathbb{K}_{44}\mathfrak{b}_{41}, \quad (3.150)$$

$$c_{41} + l_{41} = (\mathbb{K}_{11} + \mathbb{K}_{44})\mathfrak{b}_{41} + \mathbb{K}_{21}\mathfrak{b}_{42} + \mathbb{K}_{14}\mathfrak{b}_{11} + \mathbb{K}_{24}\mathfrak{b}_{21}, \quad (3.151)$$

$$c_{42} + l_{42} = \mathbb{K}_{22}\mathfrak{b}_{42} + \mathbb{K}_{32}\mathfrak{b}_{43} + \mathbb{K}_{14}\mathfrak{b}_{12} + \mathbb{K}_{24}\mathfrak{b}_{22} + \mathbb{K}_{44}\mathfrak{b}_{42}, \quad (3.152)$$

$$c_{42} + l_{42} = (\mathbb{K}_{22} + \mathbb{K}_{44})\mathfrak{b}_{42} + \mathbb{K}_{32}\mathfrak{b}_{43} + \mathbb{K}_{14}\mathfrak{b}_{12} + \mathbb{K}_{24}\mathfrak{b}_{22}, \quad (3.153)$$

$$c_{43} + l_{43} = \mathbb{K}_{13}\mathfrak{b}_{41} + \mathbb{K}_{23}\mathfrak{b}_{42} + \mathbb{K}_{33}\mathfrak{b}_{43} + \mathbb{K}_{43}\mathfrak{b}_{44} + \mathbb{K}_{1n}\mathfrak{b}_{45} + \mathbb{K}_{14}\mathfrak{b}_{13} \\ + \mathbb{K}_{24}\mathfrak{b}_{23} + \mathbb{K}_{44}\mathfrak{b}_{43}, \quad (3.154)$$

$$c_{43} + l_{43} = \mathbb{K}_{13}\mathfrak{b}_{41} + \mathbb{K}_{23}\mathfrak{b}_{42} + (\mathbb{K}_{33} + \mathbb{K}_{44})\mathfrak{b}_{43} + \mathbb{K}_{43}\mathfrak{b}_{44} + \mathbb{K}_{1n}\mathfrak{b}_{45} \\ + \mathbb{K}_{14}\mathfrak{b}_{13} + \mathbb{K}_{24}\mathfrak{b}_{23}, \quad (3.155)$$

$$c_{44} + l_{44} = \mathbb{K}_{14}\mathfrak{b}_{41} + \mathbb{K}_{24}\mathfrak{b}_{42} + \mathbb{K}_{44}\mathfrak{b}_{44} + \mathbb{K}_{14}\mathfrak{b}_{14} + \mathbb{K}_{24}\mathfrak{b}_{24} + \mathbb{K}_{44}\mathfrak{b}_{44}, \quad (3.156)$$

$$c_{44} + l_{44} = 2(\mathbb{K}_{14}\mathfrak{b}_{41} + \mathbb{K}_{24}\mathfrak{b}_{42} + \mathbb{K}_{44}\mathfrak{b}_{44} + \mathbb{K}_{14}\mathfrak{b}_{14} + \mathbb{K}_{24}\mathfrak{b}_{24} + \mathbb{K}_{44}\mathfrak{b}_{44}), \quad (3.157)$$

$$c_{45} + l_{45} = \mathbb{K}_{15}\mathfrak{b}_{51} - c\mathfrak{b}_{55} + \mathbb{K}_{14}\mathfrak{b}_{15} + \mathbb{K}_{24}\mathfrak{b}_{25} + \mathbb{K}_{44}\mathfrak{b}_{45}, \quad (3.158)$$

$$c_{45} + l_{45} = (\mathbb{K}_{14} + \mathbb{K}_{15})\mathfrak{b}_{15} - c\mathfrak{b}_{55} + \mathbb{K}_{24}\mathfrak{b}_{25} + \mathbb{K}_{44}\mathfrak{b}_{45}, \quad (3.159)$$

$$c_{51} + l_{51} = \mathbb{K}_{11}\mathfrak{b}_{51} + \mathbb{K}_{21}\mathfrak{b}_{52} + \mathbb{K}_{15}\mathfrak{b}_{11} - c\mathfrak{b}_{51}, \quad (3.160)$$

$$c_{51} + l_{51} = (\mathbb{K}_{11} - c)\mathfrak{b}_{51} + \mathbb{K}_{21}\mathfrak{b}_{52} + \mathbb{K}_{15}\mathfrak{b}_{11}, \quad (3.161)$$

$$c_{52} + l_{52} = \mathbb{K}_{22}\mathfrak{b}_{52} + \mathbb{K}_{32}\mathfrak{b}_{53} + \mathbb{K}_{15}\mathfrak{b}_{12} - c\mathfrak{b}_{52}, \quad (3.162)$$

$$c_{52} + l_{52} = (\mathbb{K}_{22} - c)\mathfrak{b}_{52} + \mathbb{K}_{32}\mathfrak{b}_{53} + \mathbb{K}_{15}\mathfrak{b}_{12}, \quad (3.163)$$

$$\begin{aligned} c_{53} + l_{53} &= \mathbb{K}_{13}\mathfrak{b}_{51} + \mathbb{K}_{23}\mathfrak{b}_{52} + \mathbb{K}_{33}\mathfrak{b}_{53} + \mathbb{K}_{43}\mathfrak{b}_{54} + \mathbb{K}_{1n}\mathfrak{b}_{55} + \mathbb{K}_{15}\mathfrak{b}_{13} \\ &\quad - c\mathfrak{b}_{53}, \end{aligned} \quad (3.164)$$

$$\begin{aligned} c_{53} + l_{53} &= \mathbb{K}_{13}\mathfrak{b}_{51} + \mathbb{K}_{23}\mathfrak{b}_{52} + (\mathbb{K}_{33} - c)\mathfrak{b}_{53} + \mathbb{K}_{43}\mathfrak{b}_{54} + \mathbb{K}_{1n}\mathfrak{b}_{55} \\ &\quad + \mathbb{K}_{15}\mathfrak{b}_{13}, \end{aligned} \quad (3.165)$$

$$c_{54} + l_{54} = \mathbb{K}_{14}\mathfrak{b}_{51} + \mathbb{K}_{24}\mathfrak{b}_{52} + \mathbb{K}_{44}\mathfrak{b}_{54} + \mathbb{K}_{15}\mathfrak{b}_{14} - c\mathfrak{b}_{54}, \quad (3.166)$$

$$c_{54} + l_{54} = \mathbb{K}_{14}\mathfrak{b}_{51} + \mathbb{K}_{24}\mathfrak{b}_{52} + (\mathbb{K}_{44} - c)\mathfrak{b}_{54} + \mathbb{K}_{15}\mathfrak{b}_{14}, \quad (3.167)$$

$$c_{55} + l_{55} = \mathbb{K}_{15}\mathfrak{b}_{51} - c\mathfrak{b}_{55} + \mathbb{K}_{15}\mathfrak{b}_{15} - c\mathfrak{b}_{55}, \quad (3.168)$$

$$c_{55} + l_{55} = 2(\mathbb{K}_{15}\mathfrak{b}_{51} - c\mathfrak{b}_{55} + \mathbb{K}_{15}\mathfrak{b}_{15} - c\mathfrak{b}_{55}). \quad (3.169)$$

Since $\mathfrak{b}_{kj} = \mathfrak{b}_{jk}$, matrix equation is reduced to following system of equations with

$\mathfrak{b}_{kj}$:

$$c_{kj} + l_{kj} = \begin{cases} -1 & \text{for } k = j \\ 0 & \text{for } k \neq j \end{cases} \quad (3.170)$$

Specifically, we obtain the system of algebraic equations with regard

to $\mathfrak{b}_{11}, \mathfrak{b}_{12}, \mathfrak{b}_{13}, \mathfrak{b}_{14}, \mathfrak{b}_{15}, \mathfrak{b}_{22}, \mathfrak{b}_{23}, \mathfrak{b}_{24}, \mathfrak{b}_{25}, \mathfrak{b}_{33}, \mathfrak{b}_{34}, \mathfrak{b}_{35}, \mathfrak{b}_{44}, \mathfrak{b}_{45}$, and $\mathfrak{b}_{55}$.

$$\mathbb{K}_{11}\mathfrak{b}_{11} + \mathbb{K}_{21}\mathfrak{b}_{12} = -\frac{1}{2}, \mathbb{K}_{21}\mathfrak{b}_{22} + \mathbb{K}_{32}\mathfrak{b}_{13} + (\mathbb{K}_{11} + \mathbb{K}_{22})\mathfrak{b}_{12} = 0, \quad (3.171)$$

$$\mathbb{K}_{13}\mathfrak{b}_{11} + \mathbb{K}_{23}\mathfrak{b}_{12} + (\mathbb{K}_{11} + \mathbb{K}_{33})\mathfrak{b}_{12} + \mathbb{K}_{43}\mathfrak{b}_{14} + \mathbb{K}_{1n}\mathfrak{b}_{15} + \mathbb{K}_{21}\mathfrak{b}_{23} = 0, \quad (3.172)$$

$$\mathbb{K}_{14}\mathfrak{b}_{11} + \mathbb{K}_{24}\mathfrak{b}_{12} + (\mathbb{K}_{11} + \mathbb{K}_{44})\mathfrak{b}_{14} + \mathbb{K}_{21}\mathfrak{b}_{24} \quad (3.173)$$

$$= 0, \mathbb{K}_{15}\mathfrak{b}_{22} + (\mathbb{K}_{11} - c)\mathfrak{b}_{15} + \mathbb{K}_{21}\mathfrak{b}_{25} = 0,$$

$$\begin{aligned}
& \mathbb{K}_{22}\mathfrak{b}_{22} + \mathbb{K}_{32}\mathfrak{b}_{23} \\
& = -\frac{1}{2}, \mathbb{K}_{13}\mathfrak{b}_{21} + \mathbb{K}_{23}\mathfrak{b}_{22} + (\mathbb{K}_{22} + \mathbb{K}_{33})\mathfrak{b}_{23} + \mathbb{K}_{43}\mathfrak{b}_{24} \quad (3.174)
\end{aligned}$$

$$+ \mathbb{K}_{1n}\mathfrak{b}_{25} + \mathbb{K}_{32}\mathfrak{b}_{33} = 0,$$

$$\mathbb{K}_{14}\mathfrak{b}_{21} + \mathbb{K}_{24}\mathfrak{b}_{22} + (\mathbb{K}_{22} + \mathbb{K}_{44})\mathfrak{b}_{24} + \mathbb{K}_{32}\mathfrak{b}_{34} \quad (3.175)$$

$$= 0, \mathbb{K}_{15}\mathfrak{b}_{21} + (\mathbb{K}_{22} - c)\mathfrak{b}_{25} + \mathbb{K}_{32}\mathfrak{b}_{35} = 0,$$

$$\mathbb{K}_{13}\mathfrak{b}_{31} + \mathbb{K}_{23}\mathfrak{b}_{32} + \mathbb{K}_{33}\mathfrak{b}_{33} + \mathbb{K}_{43}\mathfrak{b}_{34} + \mathbb{K}_{1n}\mathfrak{b}_{35} = -\frac{1}{2}, \quad (3.176)$$

$$\mathbb{K}_{14}\mathfrak{b}_{31} + \mathbb{K}_{24}\mathfrak{b}_{32} + (\mathbb{K}_{33} + \mathbb{K}_{44})\mathfrak{b}_{34} + \mathbb{K}_{13}\mathfrak{b}_{14} + \mathbb{K}_{23}\mathfrak{b}_{24} + \mathbb{K}_{43}\mathfrak{b}_{44} \quad (3.177)$$

$$+ \mathbb{K}_{1n}\mathfrak{b}_{54} = 0,$$

$$\mathbb{K}_{15}\mathfrak{b}_{31} + (\mathbb{K}_{33} - c)\mathfrak{b}_{35} + \mathbb{K}_{13}\mathfrak{b}_{15} + \mathbb{K}_{23}\mathfrak{b}_{25} + \mathbb{K}_{43}\mathfrak{b}_{45} + \mathbb{K}_{1n}\mathfrak{b}_{55} = 0, \quad (3.178)$$

$$\mathbb{K}_{14}\mathfrak{b}_{41} + \mathbb{K}_{24}\mathfrak{b}_{42} + \mathbb{K}_{44}\mathfrak{b}_{44} = -\frac{1}{2}, \quad (3.179)$$

$$(\mathbb{K}_{14} + \mathbb{K}_{15})\mathfrak{b}_{15} - c\mathfrak{b}_{55} + d_{24}\mathfrak{b}_{25} + d_{44}\mathfrak{b}_{45} = 0, d_{15}\mathfrak{b}_{51} - c\mathfrak{b}_{55} = -\frac{1}{2} \quad (3.180)$$

We get the following matrix equation.

$$GB = -\frac{1}{2}J, G = G(i). \quad (3.181)$$

$$\begin{aligned}
& \begin{bmatrix} \mathbb{K}_{11} & \mathbb{K}_{21} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \mathbb{K}_{11} + \mathbb{K}_{22} & \mathbb{K}_{32} & 0 & \mathbb{K}_{21} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \mathbb{K}_{31} & \mathbb{K}_{23} & \mathbb{K}_{11} + \mathbb{K}_{33} & \mathbb{K}_{43} & \mathbb{K}_{1n} & 0 & \mathbb{K}_{21} & 0 & 0 & 0 & 0 & 0 & 0 \\ \mathbb{K}_{14} & \mathbb{K}_{24} & 0 & \mathbb{K}_{11} + \mathbb{K}_{44} & 0 & \mathbb{K}_{21} & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \mathbb{K}_{15} & 0 & 0 & 0 & \mathbb{K}_{11} - c & 0 & \mathbb{K}_{21} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \mathbb{K}_{22} & 0 & \mathbb{K}_{32} & 0 & 0 & 0 & 0 & 0 \\ 0 & \mathbb{K}_{13} & 0 & 0 & 0 & \mathbb{K}_{23} & \mathbb{K}_{22} + \mathbb{K}_{33} & d_{43} & \mathbb{K}_{1n} & 0 & \mathbb{K}_{32} & 0 & 0 \\ G = & 0 & \mathbb{K}_{14} & 0 & 0 & \mathbb{K}_{24} & 0 & \mathbb{K}_{22} + \mathbb{K}_{44} & 0 & \mathbb{K}_{32} & 0 & 0 & 0 \\ 0 & \mathbb{K}_{15} & 0 & 0 & 0 & 0 & 0 & 0 & \mathbb{K}_{22} - c & 0 & \mathbb{K}_{32} & 0 & 0 \\ 0 & 0 & \mathbb{K}_{13} & 0 & 0 & 0 & 0 & \mathbb{K}_{23} & 0 & \mathbb{K}_{33} & \mathbb{K}_{43} & 0 & 0 \\ 0 & 0 & \mathbb{K}_{14} & \mathbb{K}_{13} & 0 & 0 & 0 & \mathbb{K}_{24} & d_{23} & 0 & \mathbb{K}_{33} + \mathbb{K}_{44} & 0 & \mathbb{K}_{43} \\ 0 & 0 & \mathbb{K}_{15} & 0 & \mathbb{K}_{13} & 0 & \mathbb{K}_{23} & 0 & 0 & 0 & \mathbb{K}_{33} - c & 0 & \mathbb{K}_{43} \mathbb{K}_{1n} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \mathbb{K}_{14} & \mathbb{K}_{24} & \mathbb{K}_{44} & 0 \\ 0 & 0 & 0 & 0 & \mathbb{K}_{15} + \mathbb{K}_{14} & 0 & \mathbb{K}_{24} & \mathbb{K}_{24} & 0 & 0 & 0 & \mathbb{K}_{44} & -c \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \mathbb{K}_{15} & 0 & 0 & -c \end{bmatrix}
\end{aligned}$$

(3.182)

3.3 Research Methodology

The present study uses the Physics-Informed Neural Network (PINN) architecture as a hybrid modeling approach that combines deep learning with a system's governing physical rules, which are commonly stated as partial differential equations (PDEs). The major objective for this methodology is to overcome the limits of solely data-driven models, especially in cases where data is few, noisy, or expensive to gather. PINNs incorporate the underlying physics into the learning process by embedding the differential equations, boundary conditions, and initial conditions directly into a neural network's loss functions. In this way, it enables the model not only to learn from existing data but also to respect the structural and causal linkages imposed by physical laws for improved accuracy and generalizability in its predictions. The first thing to do when using the PINN technique is to define mathematically the problem in physics. Consider a system of ODE. The space-time coordinates are taken as input by the neural network's input layer, and the approximate solution is given out by the output layer of the neural network. The network consists of several hidden layers with nonlinear tangent hyperbolic activation functions $\tanh$ to express complicated patterns in solution space.

3.4 Results and Discussion

3.4.1 SEIJR Model Simulation

The fig.3.1 illustrates the Population vs Time plot graphically for SEIJR model representation graphically with PINNs for total number of Population. The graph illustrates the SEIJR model simulation over 200 days using a Physics-Informed Neural Network with a population of about 100,000, divided into the Susceptible (S), Exposed (E), Infected (I), Isolation (J), and Recovered (R) compartments. At the outset, nearly everyone is susceptible, while this number plummets between days 75 and 125 due to fast transmission. The exposed class, E, surges and peaks around day 120 before going

on a decline as individuals either get infected or recover. J, the Isolation class, grows rather slowly, peaking at approximately day 130 and showing treatment failure in certain situations. The recovered population, R, increases steadily after day 100, peaking at day 175 to indicate successful containment. Overall, the simulation results show major epidemic phases, including transmission, resistance emergence, and recovery, using the SEIJR-PINN architecture.

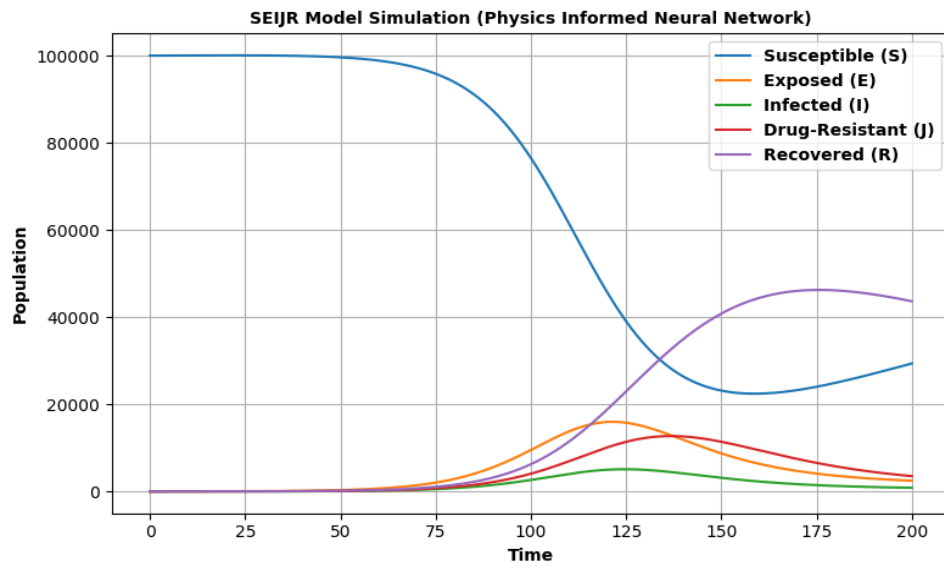


Fig 3.1: SEIJR Model Representation Graphically with PINNs for total Number of Population.

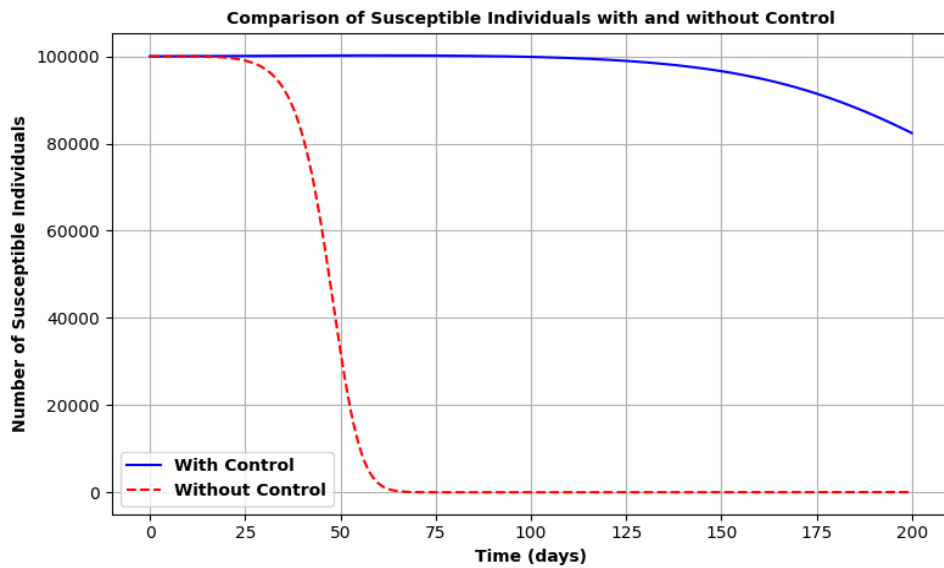


Fig 3.2: Susceptible Population over Time.

3.4.2 Susceptible populations over Time

The fig.3.2 illustrates the Number of susceptible individual's vs Time plot graphically for Susceptible Population over Time. The graph depicts the pattern of change in the susceptible population during 200 days under two different conditions-with and without control. Under control, the susceptible remains consistent for the first 50 days and then gradually decreases due to limited transmission, treatment, and recovery; there is a slight increase beyond day 150 due to reinfection (ϕ). In contrast, without management, the vulnerable population declines sharply after day 30 and is completely depleted by day 60, indicating rapid, uncontrolled spread. The comparison emphasizes the need of action in maintaining a section of the susceptible population while averting widespread infection.

3.4.3 Exposed Population over Time

The fig.3.3 depicts the Number of Exposed Individuals vs Time plot graphically for Exposed population over Time. The graph compares the exposed population over time in two different scenarios: with and without control measures. Interventions, such as treatment (μ), isolated infection dropout (ϵ), and immunity loss (ϕ), result in a gradual rise in the exposed count, a low peak around day 120, and a steady reduction, indicating effective control in delaying and minimizing the epidemic's effects. Without management, the exposed population grows quickly, peaking around day 70, indicating rapid and broad transmission. This contrast highlights the importance of prompt and sustained public health initiatives in flattening the curve, lowering illness burden, and avoiding healthcare system overburden.

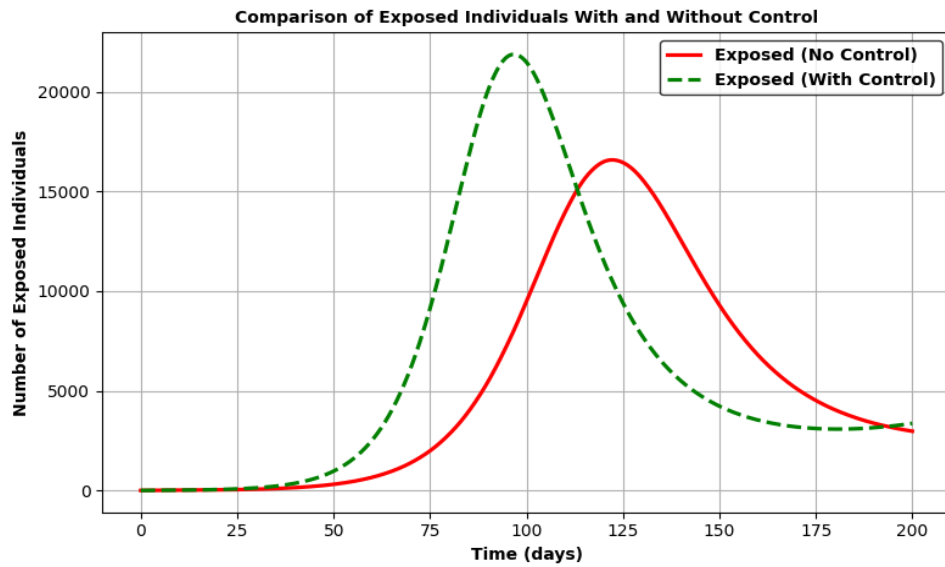


Fig 3.3: Exposed population over Time.

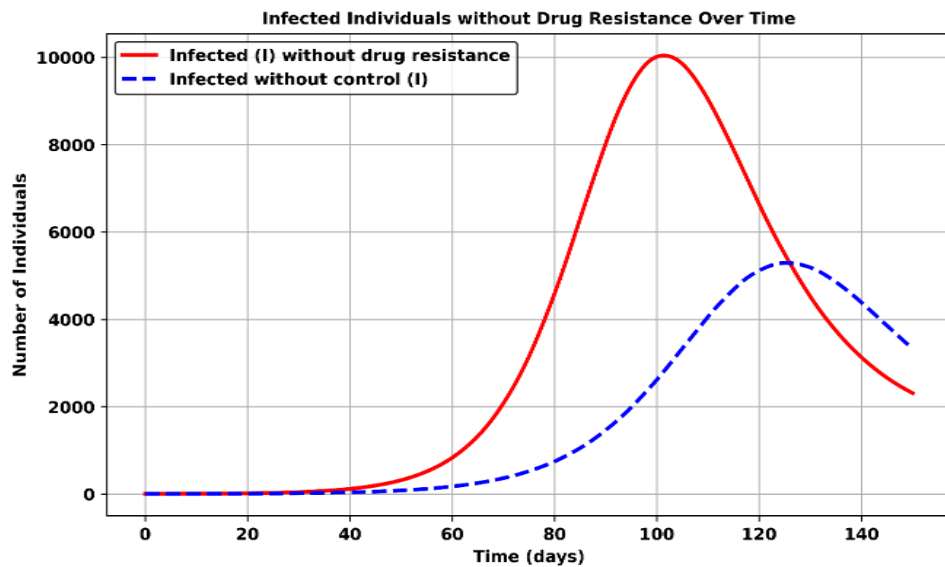


Fig 3.4: Infected Individuals without Drug Resistance over Time.

3.4.4 Infected Individuals Without Drug Resistance over Time

The fig.3.4 demonstrates the Number of Individuals vs Time plot graphically for Infected Individuals without Drug Resistance over Time. The graph shows the number of infected people who do not have isolated over time under baseline settings. Infections begin with just three instances in a 100,000-person population and climb steadily due to high transmission, peaking at roughly 820 on day 30, then dropping due to recovery, treatment, mortality, and isolated. By day 160, infections have stabilized at 300,

indicating an endemic state managed by spontaneous recovery and therapy. Although the infection persists, it is controllable. Introducing additional controls, such as greater treatment or vaccination, would most likely minimize the peak and speed the decline, emphasizing the need of early and sustained interventions to reduce long-term illness burden.

3.4.5 Infected Individuals with Drug Resistance over Time

The fig.3.5 illustrates the Number of Drug-Resistant vs Time plot graphically for Infected Individuals with Drug Resistance over Time. The graph shows the number of drug-resistant sick persons over time in two scenarios: with and without control. Without intervention, the population steadily rises, reaching 145 by day 45 before gradually stabilizing at 110 by day 160, demonstrating chronic drug resistance. Controlling for increased treatment rate ($\mu = 0.3$) and higher dropout rate ($\varepsilon = 0.08$) results in slower growth, peaking earlier at 120 on day 35 and stabilizing at 80. The controlled curve continuously remains lower than the uncontrolled one, demonstrating the efficacy of timely, focused treatments in lowering isolated patients. These findings highlight the necessity of improving medication efficacy and clearance in order to manage resistance and guide public health measures.

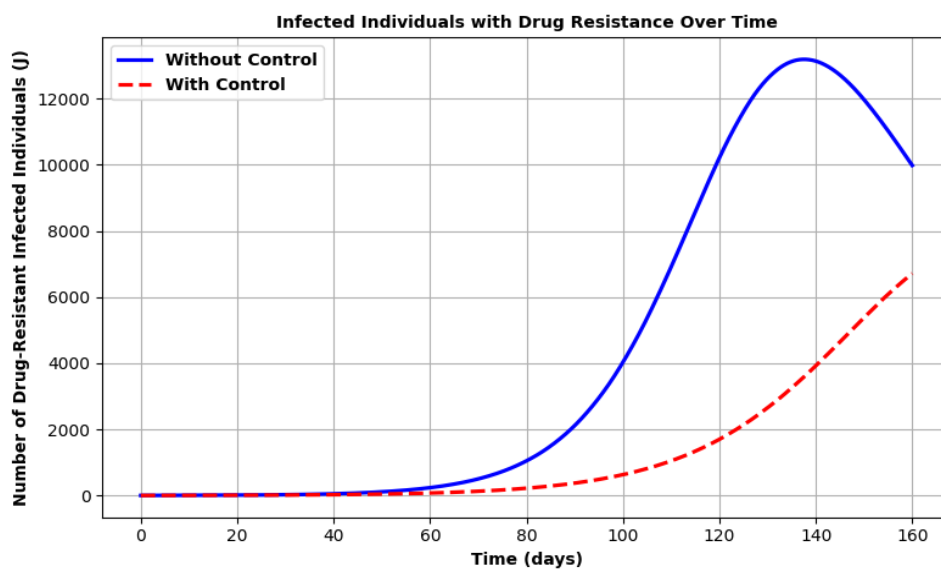


Fig 3.5: Infected Individuals with Drug Resistance over Time.

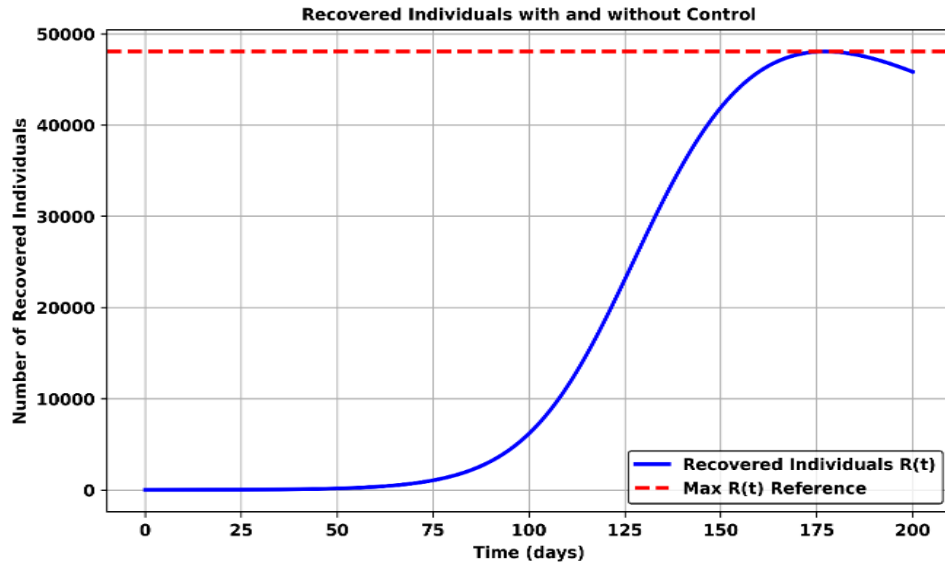


Fig 3.6: Recovered Population over Time.

3.4.6 Recovered Individuals over Time

The fig.3.6 depicts the Number of Recovered Individuals vs Time plot graphically for Recovered Population over Time. The graph shows the progression of the recovered population $R(t)$ over 200 days in a five-compartment model of an infectious disease with drug resistance. Individuals recover from both infected (U) and isolation (V) compartments at rates P and ϵ , respectively, starting at $R(0) = 0$. The solid blue line shows a continuous increase in recoveries, which finally level out as the pandemic stabilizes. The dotted red line represents the model's maximum recovery capacity. The reduction in growth is due to fewer active infections and a balance of recovery, immunity loss, and natural mortality. Overall, the graph highlights recovery's critical role in epidemic control and long-term disease patterns.

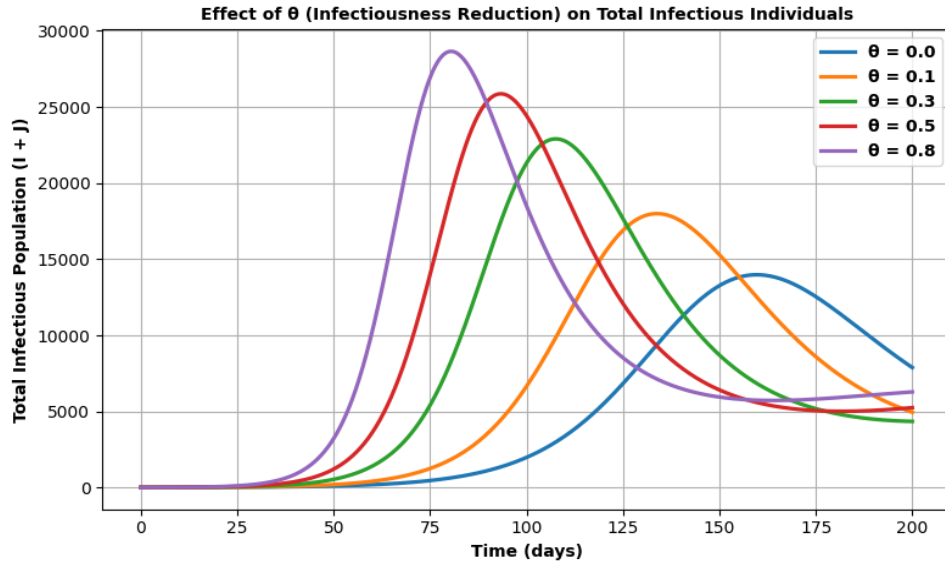


Fig 3.7: Reduction Control Variable over Time.

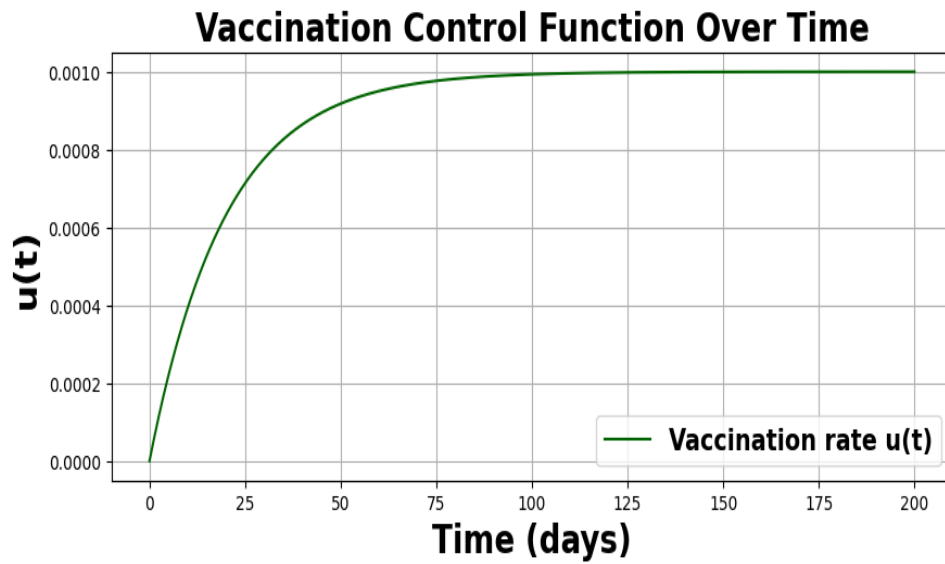


Fig 3.8: Vaccination Control over Time.

3.4.7 Effect of θ (Infectious Reduction) on Total Infectious Individuals

The fig.3.7 illustrates the Total Infected Population($I+J$) vs Time for Reduction Control Variable over Time. The simulation examines how changing the control parameter θ , which decreases the infectiousness of isolation individuals (J), impacts overall infections ($I + V$) ($I + J$) over time. As θ climbs from 0.0 to 0.8, the J class becomes

more infectious, resulting in earlier infection peaks. The lowest illness burden is obtained when $\theta = 0.0$ since the isolation individuals are not infectious. When $\theta = 0.8$ the infectiousness is the same as actively infected individuals (I) and hence hastens the outbreak. The results point to the prevention of drug-resistant transmission as a means of reducing total infections while promoting effective disease management strategies.

3.4.8 Behavior of Vaccination Control over Time

The fig.3.8 depicts the $u(t)$ vs Time plot graphically for Vaccination Control over Time. The graph represents the time evolution of the vaccination control variable $u(t)$. Starting around zero at $t=0$, it indicates early constraints in vaccine supply and infrastructure. The control rises steadily over time, peaking and stabilizing at 0.001, indicating that the system has reached its maximum vaccination capability. Real vaccination rollouts indeed accelerate as resources and public engagement increase, and a steady rise to such a peak reflects this. Biologically, this sustained effort diminishes the susceptible population as it increases immunity. The trend strongly points out that long-term vaccination is necessary for successful disease management.

3.4.9 Behavior of Awareness Control Variable over Time

The fig.3.9 demonstrates the Awareness Level $a(t)$ vs Time plot graphically for Awareness Control Variable over Time. The graph shows the temporal trend for the awareness control variable. The awareness effort starts off at a very low value, close to zero, representing the early stages of an epidemic when the general public is largely unaware of the threat of an illness and no meaningful preventive measures are yet taken. As time progresses, the awareness control variable increases continuously, showing that more and more of the public is responding to the outbreak because the word is spreading, and concern is building. The control value increases rapidly between $t = 0$

and $t = 25$, reaching the peak at $t = 25$. This represents the height of public attention and behavior change-when people are most responsive to health advisories, when awareness-driven treatments like mask-wearing, hand cleanliness, and social distance are most active. After the peak, awareness drops steadily with moderate declines due to psychological exhaustion, social complacency, or a lessened feeling of risk. However, the control remains above zero for an extensive period of time, indicating that while attention declines, a residual degree of awareness persists in the population. The overall pattern in this-low, peaking quite early, and then decreasing steadily-represents a realistic and deliberate behavioral response to illness spread. It reflects a change in character for public attention: urgent and intense in the initial stages of a threat, relaxing as individuals adapt or become tired over time. Its form represents an adaptive method of awareness which is both timely and responsive to actual behavioral developments throughout the course of an epidemic.

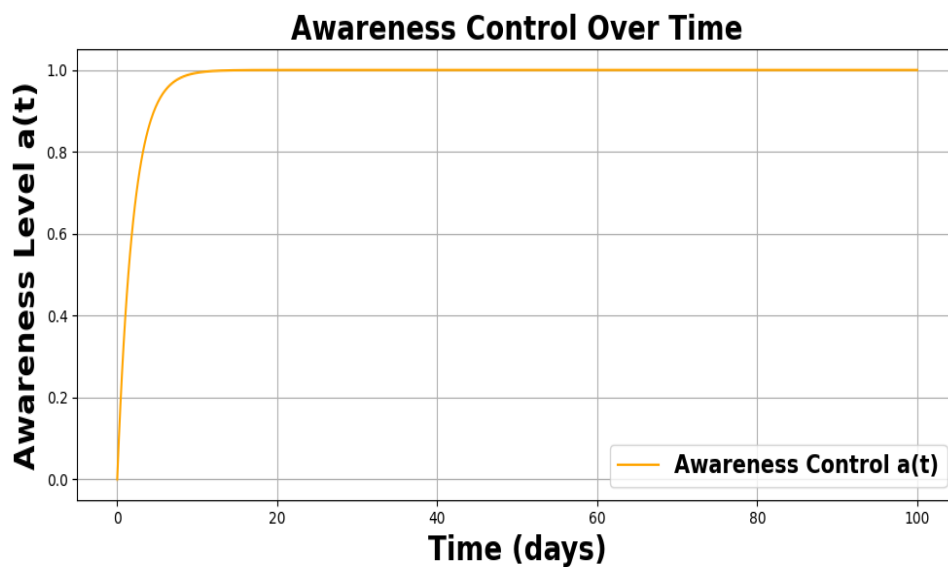


Fig 3.9: Awareness Control Variable over Time.

3.4.10 SEIJR Dynamics under Different Initial Conditions

The fig.3.10 depicts the Populations vs Time plot graphically for SEIJR Dynamic Under Different Initial Conditions over Time. In a compartmental SEIJR model, the five graphs depict various disease progression scenarios according to beginning conditions. The disease rapidly subsides when susceptibility is high and infections are low, indicating that the disease-free equilibrium (DFE) is locally stable since $R_0 < 1$. On the other hand, endemic behavior—where the disease persists at steady levels, suggesting $R_0 > 1$ and endemic equilibrium stability—occurs when initial infections are moderate to high. The system stabilizes with a high recovered and low susceptible population even after a large outbreak. The role of herd immunity and the resilience of DFE are highlighted by scenarios with strong initial immunity or post-outbreak recovery, which demonstrate that the infection swiftly fades out.

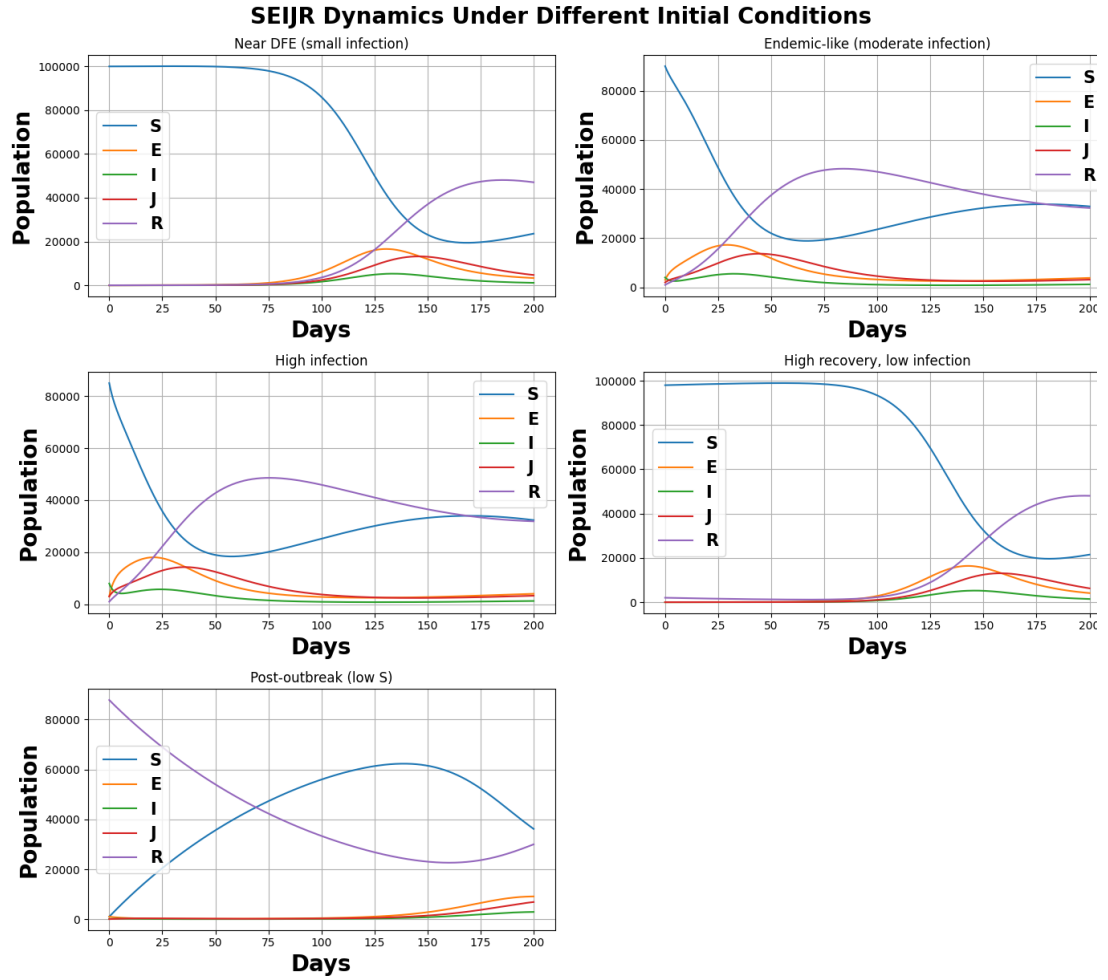


Fig 3.10: SEIJR Dynamic Under Different Initial Conditions over Time.

3.4.11 Lyapunov Function over Time

The fig.3.11 illustrates the $v(t)$ vs Time plot graphically for Lyapunov Function Variable over Time. The dynamics of the Lyapunov function $V(t) = I^2 + J^2$ are demonstrated by the plot, with $I(t)$ and $J(t)$ representing the number of Isolated infected and isolated infected individuals at time t , respectively. The function is a popular technique for the determination of the stability of equilibrium points for dynamical systems, particularly epidemiological models. If $V(t)$ diminishes over time and approaches zero, this indicates that the disease has been eradicated and the system is returning to its state of health. However, this plot is non-monotonic. $V(t)$ begins at a

low point and is a fairly small number of cases. However, over time—particularly after someday 75—the function rises quickly to a peak of around day 140. This sharp increase is reflected in growth in both infected and drug-resistant individuals to indicate that the pandemic is worsening. The peak of the Lyapunov function reflects the peak disease burden of the population. After this point, the function begins to deteriorate, showing that interventions like treatment, recovery, and dropout from isolated class begin to outweigh infection transmission, leading in a gradual decrease in infections. The presence of a peak followed by a drop indicates that the disease-free equilibrium is not Lyapunov stable at the current parameter values. In a Lyapunov-stable system, $V(t)$ drops steadily from the start, indicating that the infection progressively diminishes with no major breakouts. In contrast, this graph portrays a system in which the virus spreads and may become endemic before being controlled. To achieve Lyapunov stability and control an outbreak, adjust parameters such as treatment rate (μ), transmission rate (β), and immunity duration (ϕ).

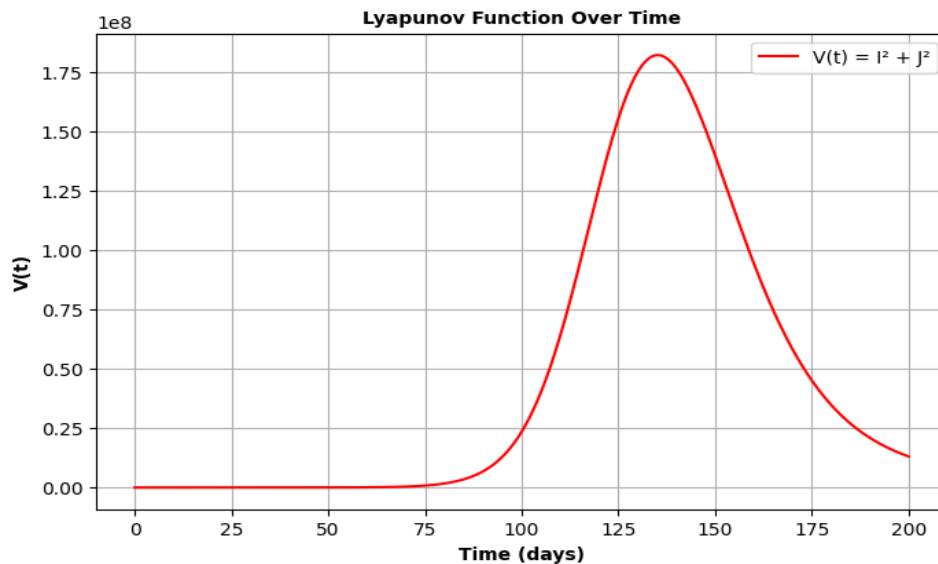


Fig 3.11: Lyapunov Function Variable over Time.

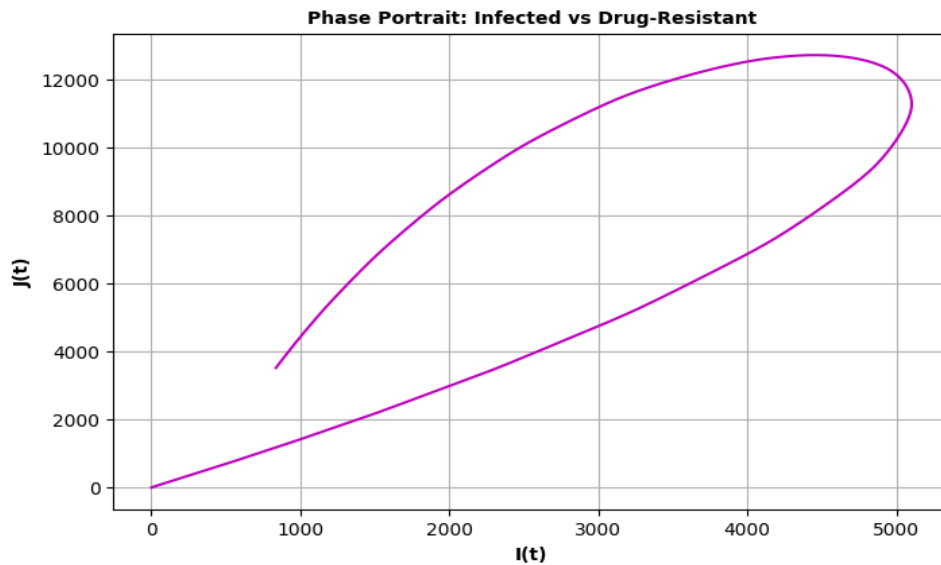


Fig 3.12: Phase Portrait Variable over Time.

3.4.12 Phase Portrait: Infected vs Isolated

The fig.3.12 illustrates the $J(t)$ vs $I(t)$ plot graphically for Phase Portrait Variable over Time. Plotting $J(t)$ (the isolated infected population) vs $I(t)$ (the ordinary infected population) demonstrates disease progression and resistance development in a population. This graph displays the disease's course by demonstrating how the two compartments evolve in relation to one another rather than just across time. Initially, as the number of infected patients increases, the isolated population remains small, indicating that resistance has not spread widely. As the infection develops, the graph shows a delayed but rapid increase in isolated patients, demonstrating how resistance frequently occurs following widespread infection—most likely due to treatment pressure or pathogen genetic mutation. The graph's loop-like trajectory shows an increase and reduction of both infected and isolated individuals, signaling that the system will eventually revert to a stable disease-free or endemic state. This pattern displays a single epidemic wave with no protracted oscillations, meaning that infection and resistance gradually decline over time due to recovery, treatment, or intervention.

approaches. Overall, the graph represents key stages in disease dynamics, such as the early epidemic, peak infection, emergence of drug resistance, and eventual decline. This information is crucial for public health planning because it underscores the importance of early intervention and resistance monitoring in averting outbreaks that last longer or are more severe.

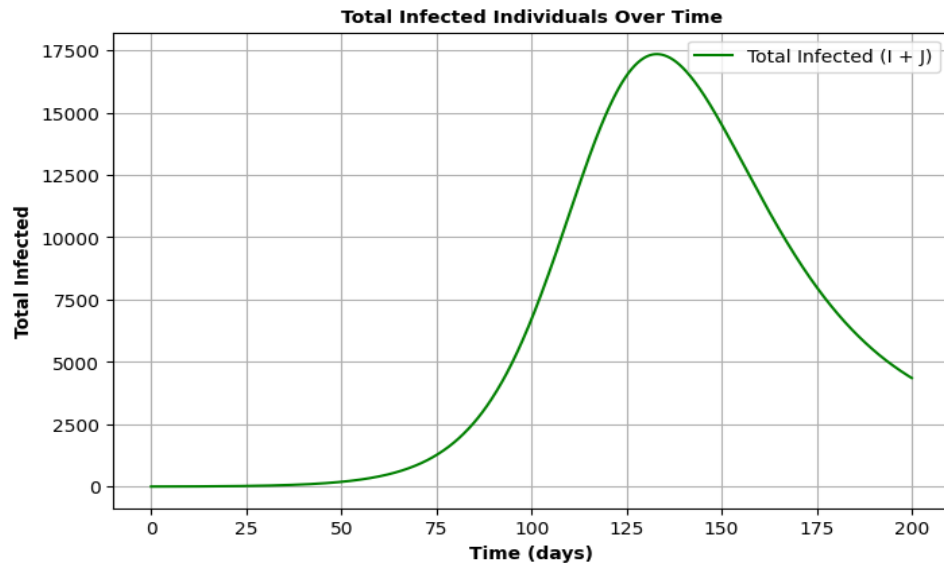


Fig 3.13: Infected Individuals Variable over Time.

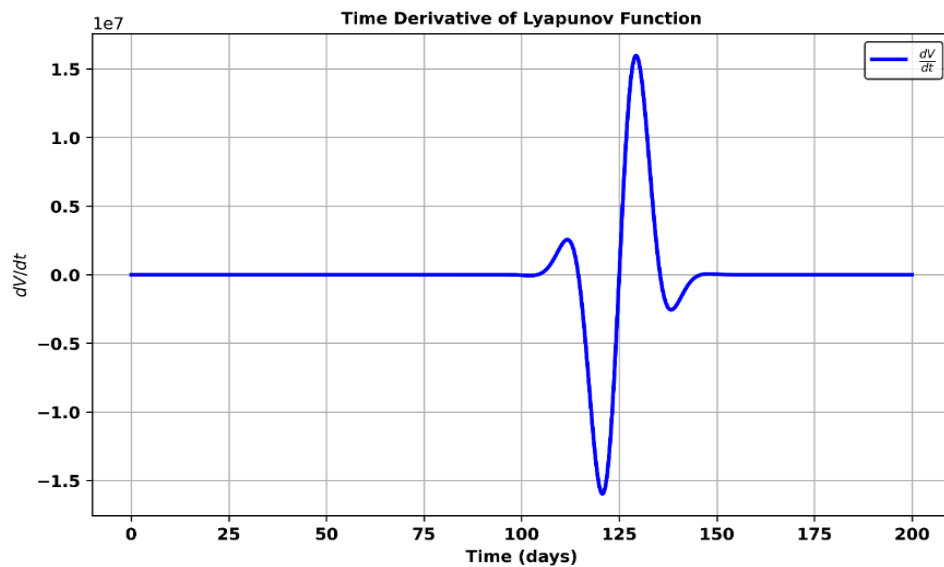


Fig 3.14: Derivative of Lyapunov Function Variable over Time.

3.4.13 Total Infected Individuals over Time

The fig.3.13 illustrates the Total Infected vs Time plot graphically for Infected Individuals Variable over Time. Over a period of 200 days, the graph shows the development of the isolated infected population $j(t)$ and infected population $I(t)$. At first, there almost no afflicted individuals, which suggests that an outbreak has begun or that early detection was successful. Infectious progressively rise over time, then experience a powerful exponential surge around day135 of infection. With about 17500 persons infected overall, this peak reflects the highest disease burden in the population. The graphs obvious decreasing trend after the peak indicates that treatment, isolated, or natural recovery are effective intervention strategies that can cause the infected population to steadily diminish. Epidemic dynamics controlled by the reduction of vulnerable individuals or better control methods are characterized by the symmetric rise and fall pattern. In order prevent peak infections and lessen the overall strain on public health systems, control techniques must be implemented at the right time, as this graph clearly illustrates the temporal behavior of disease outbreak.

3.4.14 Time Derivative of Lyapunov Function

The fig.3.14 demonstrates the dv/dt vs Time plot graphically for Derivative of Lyapunov Function Variable over Time. Over a period 200 days, the shows the evolution of the overall number of infections in a community. There are two compartments within the whole infected population: isolated individuals ($J(t)$ and actively infected individuals $I(t)$). The illness epidemic is in its early stages with limited transmission, as indicated by the curves initial show development in the number of infections. This is probably because there were few initial cases or early intervention efforts. The disease spreads more swiftly with time, leading to notable rise in the total number of afflicted individuals. This sharp increase is common in infectious disease

dynamics during the exponential development phase, when the basic reproduction number (R) is higher than 1. Around day 135, when the infectious load on the population is at its peak, the curve hits its apex. This peak suggests that either the infection has achieved saturation in the susceptible group or that the effects of control measures (immunization, treatment, or isolation) are starting to manifest. The graph indicates a decline in the total number of infected individuals after the peak, suggesting that new infectious are being progressively defeated by recovery or death in conjunction with decreased transmission. This downward trend suggests that the outbreak has stabilized or that illnesses have been contained.

3.4.15 Local Sensitivity Analysis

The fig.3.15 illustrates the Sensitivity index vs sensitivity on peak drug-resistances/ Isolated infectious for Sensitivity Analysis over Time. The results of a local sensitivity analysis on the peak number of infected individuals I in the the SEIJR compartmental model are displayed in the bar graph above. The proportionate change in the infection peak relative to the baseline scenario is indicated by each set of bars, which represents a $\pm 10\%$ perturbation in one of the model parameters. The sensitivity index indicates which parameters have the greatest impact on the disease dynamic by quantifying how responsive the peak infection level is to slight variations in each parameter. The study demonstrates that the transmission rate β has the highest sensitivity index in both directions, suggesting that it has a major influence on the size of the outbreak. Since a $\pm 10\%$ decrease in β results in a lower infection peak and a 10% increase in β results in a higher peak, it is imperative to control transmission through measures including mask use, vaccination, and social distance. Infection burden reduction is significantly impacted by parameters like progression rate K , recovery rate P and the treatment resistance development rate μ . Natural death rate η waning immunity rate ϕ are

examples of parameters with limited sensitivity, meaning they have little impact on the short-term peak of infections. This analysis offers important suggestions for public health officials, highlighting the possibility of significant disease burden reductions and improved epidemic control results through focused change of extremely sensitive parameters.

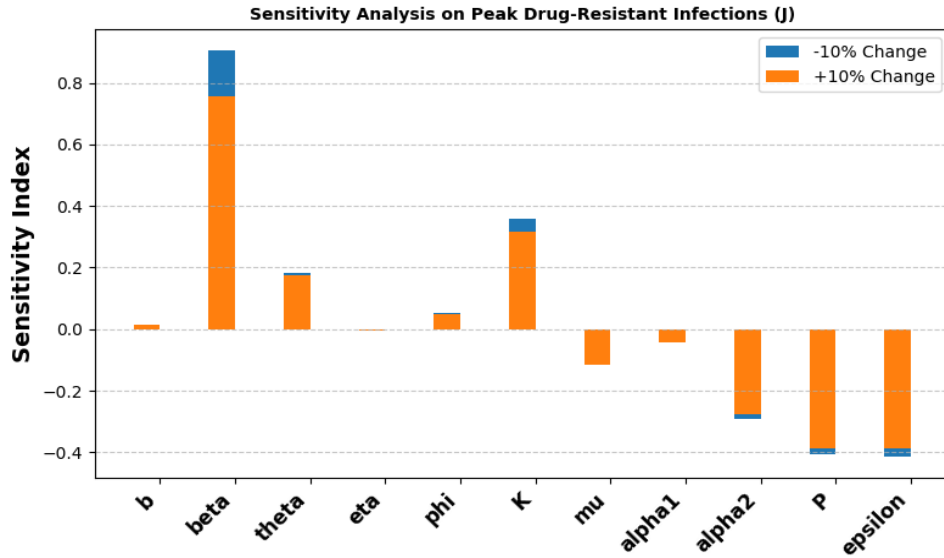


Fig 3.15: Sensitivity Analysis over Time.

3.5 Conclusion

In order to better understand the dynamic of infectious disease included incubation, therapy, isolated, and transient immunity loss, we developed a compartmental SEIJR model in this study. The evolution of susceptible (S), exposed (E), actively infected (I), isolated infected (J) and recovered (R) populations over time is represented by five nonlinear ordinary differential equations in the model.

- The parameter $\theta < 1$ controls the infectiousness in the isolated class, while the term $\frac{\beta S(I+\theta J)}{N}$ controls the infection dynamics, representing disease transmission across both actively infected and isolated individuals. This highlights the dual

importance of infection sources and the role that resistant people play in the transmission of disease.

- The infected class I either transitions to recovery (R), developed isolated class (J), or leaves the community due to disease-induced or natural mortality, while the incubation rate (K) controls the transition from exposure control of infectious disease is the establishment of resistance as a result of therapeutic pressure, which is illustrated by the treatment rate (μ)
- A potentially persistent source of infection, the isolated infected class (J) is affected by mortality, dropout (ε), and limited recovery. People from both the resistant and diseased compartments are obtained by the recovered class, but they also continuously lose their immunity ϕ , which feeds back into the susceptible pool. When simulating reinfection and declining immunity, this mechanism is essential.
- Using Physics-Informed Neural Networks (PINNs), the nonlinear complexity and parameter uncertainty of the model were addressed. PINNs learn system dynamics while maintaining biological rules by combining SEIJR differential equations with epidemic data. This approach offers better parameter estimation, less processing, and more predictive accuracy than conventional techniques.
- The population is constantly increasing through births (b) and decreasing due to natural and disease-related deaths, resulting in a bounded system. The comprehensive model framework enables the study of complicated disease characteristics such as numerous infection waves, persistence, and resistance proliferation.

The model's equilibrium points can be calculated analytically, and their local stability can be explored using the Jacobian matrix and the basic reproduction number (R_0).

Lyapunov stability analysis can provide global insights by determining whether the disease-free or endemic equilibrium is locally attractive under specific parameter circumstances.

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