**NEAR EAST UNIVERSITY**

**INSTITUTE OF GRADUATE STUDIES**

**DEPARTMENT OF MATHEMATICS**

# A FRACTIONAL-ORDER ALCOHOLIC CARDIOMYOPATHY EPIDEMIC MODEL WITH NEURAL NETWORK TIME SERIES

**Ph.D. THESIS**

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**Nicosia**

**September, 2023**

## Approval

We certify that we have read the thesis submitted by David Ikechukwu Amilo, titled **"A FRACTIONAL-ORDER ALCOHOLIC CARDIOMYOPATHY EPIDEMIC MODEL WITH NEURAL NETWORK TIME SERIES"** and that in our combined opinion it is fully adequate, in scope and in quality, as a thesis for the award of the degree of Doctor of Philosophy in Mathematics.

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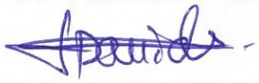
## Declaration

I hereby affirm that all the information presented in this document has been gathered and presented in compliance with the established academic guidelines and ethical principles. Furthermore, I confirm that, in line with these guidelines and principles, I have appropriately cited and referenced all sources of information and data that are not originally from this study.



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David Ikechukwu Amilo

19/09/2023

**Acknowledgements**

My distinct gratitude goes to the One who gives all wisdom. Incomparable appreciation to my friends and family for supporting me all through this journey; I love you all. Special thanks to my supervisors and other lecturers for overseeing and bringing out the best in me.

**David Ikechukwu Amilo**

## Abstract

**A Fractional-Order Alcoholic Cardiomyopathy Epidemic Model with Neural Network Time Series**

**Amilo, David Ikechukwu**

**Supervisor: Assoc. Prof. Dr Bilgen Kaymakamzade**

**PhD, Department of Mathematics**

**September, 2023, 95 pages**

Alcohol consumption is a global problem with associated health risks. This study presents an extended fractional-order Alcoholic Cardiomyopathy (ACM) model incorporating optimal control and sensitivity analysis to understand disease dynamics and parameters for effective control measures. The numerical scheme used Levenberg Marquardt Algorithm (LMA) and Nelder-Mean Algorithm (NMA) with the predictor-corrector method. Results showed effective control measures and sensitive parameters using the fractional operator approach. The proposed Caputo-type fractional-order mathematical model integrates a Neural Network time series for simulations with the world population classified into five categories. The model's existence and uniqueness were investigated through the Laplace transform approach, revealing locally and globally asymptotically stable equilibrium solutions. The Levenberg Marquardt Algorithm (LMA) Neural Network (NN) time series provided enhanced memory effect for possible prognosis. Simulations predicted an upsurge in the coming years with sensitive parameters revealed. Results suggest slowing down the recruitment rate of the alcoholic susceptible as the best approach to slow down disease spread. The ACM-LMA model provides a more realistic disease dynamics with high predictive accuracy when contrasted with other models in the literature.

***Key Words*:** mathematical modeling, Fractional Caputo Derivative, neural network, alcoholic cardiomyopathy, optimal control, sensitivity analysis.

# Özet

**A Fractional-Order Alcoholic Cardiomyopathy Epidemic Model with Neural Network Time Series**

**Amilo, David Ikechukwu**

**Danışman: Assoc. Prof. Dr Bilgen Kaymakamzade**

**PhD, Matematik Ana Bilim Dalı**

**Eylül, 2023, 95 pages**

Tez, uzun süreli alkol kullanımına bağlı olarak kalp kaslarını etkileyen bir durum olan alkolik kardiyomiyopatinin yayılmasının modellenmesine yönelik yeni bir yaklaşım sunmaktadır. Çalışma, alkol tüketiminin vücut üzerindeki uzun vadeli etkilerini dikkate alarak, hastalığın yayılmasının karmaşık dinamiklerini yakalayan kesirli dereceli bir diferansiyel denklem modeli önermektedir.

Önerilen model, geleneksel hesabı tam sayı olmayan derecelere genişleten bir matematik aracı olan kesirli hesap kullanılarak formüle edilmiştir. Kesirli dereceli model, hastalığın hafıza etkisini yakalar ve alkol bağımlılığının kalp üzerindeki uzun vadeli etkilerinin daha doğru bir şekilde temsil edilmesine olanak tanır. Çalışma aynı zamanda geçmiş verilere dayanarak hastalığın gelecekteki görülme sıklığını tahmin etmek için sinir ağı zaman serisi yaklaşımını da içeriyor.

Önerilen model, belirli bir popülasyonda alkolik kardiyomiyopati görülme sıklığına ilişkin gerçek dünya verileri kullanılarak değerlendirilmektedir. Sonuçlar, modelin, gelecekteki insidans oranlarını tahmin etmede yüksek derecede doğrulukla, hastalık yayılımının doğru bir temsilini sağladığını göstermektedir. Çalışma aynı zamanda alkolik kardiyomiyopatinin yayılmasına katkıda bulunan önemli faktörleri ve bunların hastalık dinamikleri üzerindeki etkilerini de tanımlamaktadır.

Genel olarak tez, salgın modellemeye ilişkin mevcut literatüre katkıda bulunmakta ve alkolik kardiyomiyopatinin yayılmasına ilişkin yeni bir bakış açısı sunmaktadır. Önerilen model, hastalığın altında yatan dinamiklere dair içgörü sağlıyor ve politika yapıcılara alkolik kardiyomiyopati görülme sıklığını azaltmaya yönelik etkili stratejiler geliştirmeleri için bir araç sunuyor. Çalışma aynı zamanda kesirli hesabın ve sinir ağı zaman serilerinin sağlık hizmetleri ve diğer alanlardaki karmaşık olayları modellemedeki potansiyelini de vurguluyor.

***Anahtar Kelimeler:*** matematiksel modelleme, Kesirli Caputo Türevi, sinir ağı, alkolik kardiyomiyopati, optimal control, duyarlılık analizi.

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## List of Abbreviations

| | |
|---|---|
| **ACM:** | Alcoholic Cardiomyopathy |
| **LMA:** | Levenberg Marquardt Algorithm |
| **NMA:** | Nelder-Mean Algorithm |
| **FOMCON:** | Fractional-order Control Toolbox |
| **MATLAB:** | Matrix Laboratory |
| **NN:** | Neural Network |
| **S:** | Susceptible |
| **A:** | Alcoholics |
| **C:** | ACM Diseased |
| **T:** | ACM Diseased in Treatment |
| **R:** | Recovered population |
| **ODEs:** | Ordinary Differential Equations |
| **PDEs:** | Partial Differential Equations |
| **FDE:** | Fractional Differential Equations |
| **PDF:** | Probability Density Function |
| **MSE:** | Mean Squared Error |
| **RMSE:** | Root Mean Squared Error |
| **MAE:** | Mean Absolute Error |
| **BIC:** | Bayesian Information Criterion |
| **SIR:** | Susceptible-Infected-Recovered |
| **PSO:** | Particle Swarm Optimization |
| **GA:** | Genetic Algorithm |
| **EOSA:** | Ebola Optimization Search Algorithm |
| **ANN:** | Artificial Neural Network |
| **LMA:** | Levenberg Marquardt Algorithm |

| | |
|---|---|
| **MLP:** | Multi-Layer Perceptron |
| **AI:** | Artificial Intelligence |
| **ML:** | Machine Learning |
| **NN:** | Neural Network |
| **MLP:** | Multi-Layer Perceptron |
| **GA:** | Genetic Algorithm |
| **PSO:** | Particle Swarm Optimization |
| **EOSA:** | Ebola Optimization Search Algorithm |
| **LSTM:** | Long Short-Term Memory |
| **HBO-LSTM:** | Heap-based Optimizer Long Short-Term Memory |
| **RMSE:** | Root Mean Square Error |
| **VAF:** | Variance Accounted For |
| **FOCP:** | Fractional-Order Control Problem |

# CHAPTER I
# Introduction

## Statement of the Problem

Alcoholic cardiomyopathy (ACM) is a severe health condition that occurs due to excessive alcohol consumption. It is a form of dilated cardiomyopathy that affects the heart's pumping ability and can lead to heart failure, arrhythmias, and death (Lacovoni et.al 2010). Although the pathophysiology of ACM is not yet fully understood, recent studies have suggested that fractional calculus and neural network time series models could be useful in modeling the disease's spread and predicting its future trends (Heidari et.al 2022).

Therefore, the problem addressed in this thesis is to develop a fractional-order alcoholic cardiomyopathy epidemic model with a neural network time series approach to investigate the dynamics of ACM in a population. The proposed model aims to incorporate the fractional-order calculus concept, which provides a more accurate representation of the disease's transmission dynamics, and the neural network time series approach, which can capture complex nonlinear relationships among variables and improve model accuracy.

The thesis aims to answer the following research questions:

1. How can fractional calculus concepts be used to develop an alcoholic cardiomyopathy epidemic model that captures the disease's transmission dynamics accurately?

2. How can neural network time series models be incorporated into the proposed epidemic model to improve its predictive accuracy?

3. What are the main factors that contribute to the spread of ACM, and how do they affect the disease's transmission dynamics?

4. How effective is the proposed model in predicting the future trends of ACM, and how does it compare with existing models?

By addressing these research questions, the thesis aims to provide valuable insights into the spread of ACM and develop an accurate model that can help healthcare professionals in developing appropriate intervention strategies to control and prevent the disease's spread.

## Purpose of the Study

The purpose of this thesis is to develop a novel mathematical model for alcoholic cardiomyopathy (ACM) transmission dynamics that incorporates fractional-order calculus and neural network time series techniques. The proposed model aims to provide a more accurate representation of the disease's spread and to predict its future trends.

The specific objectives of the study are as follows:

1. To review the literature on ACM, fractional calculus, and neural network time series models to identify relevant concepts, theories, and methods for developing the proposed model.

2. To develop a fractional-order alcoholic cardiomyopathy epidemic model that incorporates neural network time series techniques.

3. To validate the proposed model using real-world ACM data and compare its performance with existing models.

4. To identify the main factors that contribute to the spread of ACM and their impact on the disease's transmission dynamics.

5. To evaluate the effectiveness of the proposed model in predicting the future trends of ACM and its potential applications for public health policy.

The study's goal is to contribute to the understanding of ACM's transmission dynamics and to provide healthcare professionals with a more accurate tool for predicting and controlling the disease's spread. The proposed model's potential applications include informing public health policies, developing effective prevention strategies, and improving patient care.

## Research Questions/ Hypothesis

### *Research Questions*

1. What are the key factors that influence the transmission dynamics of alcoholic cardiomyopathy (ACM)?

2. Can the incorporation of fractional calculus concepts into an ACM epidemic model provide a more accurate representation of the disease's transmission dynamics?
3. Can a neural network time series approach improve the predictive accuracy of the proposed ACM epidemic model?

4. How does the proposed fractional-order ACM epidemic model with neural network time series compare with existing models in predicting the future trends of ACM?

5. What are the potential public health policy implications of the proposed model for controlling and preventing ACM?

6. Is the proposed model generalizable to other diseases with similar transmission dynamics, and can it be used to inform public health policies for those diseases?

***Hypotheses***

1. The transmission dynamics of ACM are influenced by several key factors, including the frequency and intensity of alcohol consumption, the population size, and the effectiveness of control measures.

2. The incorporation of fractional calculus concepts into an ACM epidemic model can improve its accuracy in representing the disease's transmission dynamics.

3. The use of a neural network time series approach can improve the predictive accuracy of the proposed ACM epidemic model.

4. The proposed fractional-order ACM epidemic model with neural network time series will outperform existing models in predicting the future trends of ACM.

5. The proposed model can inform public health policies for controlling and preventing ACM by identifying effective control measures and intervention strategies.

6. The proposed model is generalizable to other diseases with similar transmission dynamics, and it can be used to inform public health policies for those diseases.

**Significance of the Study**

Alcoholic cardiomyopathy (ACM) is a severe health condition that affects individuals with a history of excessive alcohol consumption, and it can lead to heart failure, arrhythmias, and death. Understanding the transmission dynamics of ACM is essential for developing effective prevention strategies, controlling the spread of the disease, and improving patient care.

The proposed study's significance is threefold:

Firstly, the study proposes a novel approach to model the spread of ACM by incorporating fractional-order calculus and neural network time series techniques. This model can provide a more accurate representation of the disease's transmission dynamics and improve the predictive accuracy of the model. The proposed model can be used as a tool to develop effective intervention strategies to control and prevent the spread of ACM.

Secondly, the proposed model can provide valuable insights into the dynamics of the ACM, identifying the main factors that contribute to the disease's transmission dynamics, and predicting future trends. These insights can help healthcare professionals develop appropriate intervention strategies and public health policies to control and prevent the spread of ACM. Furthermore, the model can be extended to other diseases with similar transmission dynamics, improving our understanding of these diseases and their spread.

Lastly, the proposed model can provide clinicians with a more accurate tool for predicting the progression of ACM and improving patient care. The model can help clinicians identify individuals at high risk of developing ACM and develop personalized treatment plans to manage the disease's progression.

In summary, the proposed study's significance lies in its potential to improve our understanding of the transmission dynamics of ACM, develop effective intervention strategies to control and prevent its spread, and improve patient care. The study's findings could have broader implications beyond ACM, as the proposed model's generalizability to other diseases with similar transmission dynamics could provide a valuable tool for healthcare professionals worldwide. Additionally, the study's insights into the main factors influencing ACM transmission dynamics can help inform public health policies and interventions aimed at reducing the disease's prevalence and improving patient outcomes.

**Limitations**

As with any research study, there are limitations to the proposed fractional-order alcoholic cardiomyopathy epidemic model with neural network time series. Some of the potential limitations of this study include:

1. Data Availability: Data availability is a significant challenge for any disease modeling study. In this study, data availability and quality could impact the accuracy and reliability of the proposed model.

2. Model Assumptions: The proposed model relies on certain assumptions about the underlying transmission dynamics of alcoholic cardiomyopathy, which may not fully capture the complexity of the disease.

3. Parameter Estimation: The model's parameter estimation could be affected by the lack of precise data and uncertainties in the available data, which could limit the model's accuracy and applicability.

4. Generalizability: Although the proposed model has potential applications for other diseases with similar transmission dynamics, its generalizability to other populations or settings may be limited.

5. Ethical Considerations: The proposed model's potential applications in predicting the progression of alcoholic cardiomyopathy raise ethical concerns regarding patient privacy and informed consent.

   Despite these limitations, the proposed model represents a significant contribution to the understanding of alcoholic cardiomyopathy transmission dynamics and provides a valuable tool for healthcare professionals to improve patient care and control the spread of the disease. Future research should address these limitations to further improve the accuracy and applicability of the proposed model.

# CHAPTER II

# Literature Review

## Theoretical Framework

Alcoholic Cardiomyopathy (ACM) is an alarming heart disease caused by excessive alcohol consumption throughout communities worldwide. To study and forecast this deadly ailment's spread behavior, this research implements Fractional Calculus & Mathematical Modeling methods while keeping precision at its core.

The primary goal of our rigorous approach remains focused on building a dependable model explicitly designed for simulating ACM dynamics. Such a system will help us comprehend complex epidemic interactions that play out non-locally and have prolonged interaction periods between individuals across various stages of patient symptom timelines. We aim to achieve this by using an equation-based methodology formulated around Fractional-Order Differential Equations tuned towards long-term memory effects seen in ACM patients as compared against traditional short-memory mechanisms.

Our proposed model also incorporates neural-network time-series application capable enough of improving the accuracy rate whilst representing the complex nature surrounding such a widespread outbreak like ACM accurately. Using historical data collected regarding ACM incidence & mortality rates allows us to train our neural network systematically while providing insights into future trends while assessing different prevention/intervention tactics' impact.

Additionally, analyzing existing literature on fractional calculus coupled with previous research on epidemic modeling will further enrich our theoretical framework development process in terms of Stability Analysis, Numerical Analysis Concepts suited for epidemiology studies and more. Successfully combining mathematical modeling procedures with data-driven methodologies will lead to a comprehensively rigorous approach. Our future endeavors aim to inform effective intervention strategies focused on curbing ACM incidence & solving all related challenges associated with the disease.

## Definition of Terms

### *Mathematical Models*

Mathematical modeling refers to the process of creating a mathematically based abstract description of a physical system. There are various types of mathematical models, including dynamical systems, statistical models, differential equations, and game theoretic models, among others. These different model categories may overlap, and a particular model may have various abstract structures. (Bender, E. A. 2000).

notes that mathematical models can be categorized as linear or nonlinear, static or dynamic, explicit or implicit, discreet or continuous, deterministic or probabilistic (stochastic), strategic or non-strategic, and deductive, inductive, or floating.

***SIR Models***

The SIR model is a fundamental mathematical model used to illustrate the spread of an infection within a population. It is a basic and widely used model that has served as a foundation for other models in epidemiological analysis. Initially proposed by Ronald Ross and William Hammer in the early 1900s, the model was later refined and developed by Kermack and Anderson Gray McKendrick between 1927 and 1933 (Murray, 2003). The SIR model partitions the population into three compartments: Susceptible, Infected, and Removed, thus giving the model its name. This model is particularly useful for predicting the spread of infectious diseases transmitted from human to human and where recovery is limited (Earn et al., 2000).

Recently, the application of the SIR model has expanded beyond traditional health epidemiology and into other fields such as marketing, informatics, sociology, and the economy (Rodrigues, 2016).

The SIR model is given by:

$$\frac{ds}{dt} = -\mathrm{rsI}\ ,$$

$$\frac{dI}{dt} = \mathrm{rsI} - \mathrm{aI}\ ,$$

$$\frac{dR}{dt} = \mathrm{aI}\ ,$$

$$\frac{ds}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0,$$

where,

S(t) is the susceptible population, I(t) is the Infected population, R(t) is the Recovered population, $r > 0$ is the rate of gain in the infective class, $a > 0$ is the rate of removal of infective to the removed class,

with the condition:

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

The classical SIR model has been a foundation for the development of numerous other models, including but not limited to Susceptible-Infected-Susceptible (SIS) model (Harko, 2014), Maternally Derived Immunity-Susceptible-Infectious-Recovered (MSIC) model, and Susceptible-Exposed-Infectious-Recovered (SEIR) model (Brauer, F. and Castillo-Chávez, C, 2001).

***Fractional Calculus***

The concept of fractional calculus can be traced back to 1695 when Leibniz, a renowned German mathematician and early contributor to classical calculus, first proposed it. Later, in 1730, L. Euler further developed this idea (J.Tenreiro Machado et al, 2011). Fractional calculus is an extension of traditional calculus that allows for fractional, irrational, or complex numbers to be used as orders of derivatives and integrals (I Podlubny, 1999). A well-known example of this is Legendre's symbol for the generalized factorial.

$$D^{\alpha}(x^n) = \frac{\Gamma(n+1)}{\Gamma(n+1-\alpha)} x^{n-\alpha},$$

where α is the order of the derivative.

***Fractional Integral***

The fractional integral of order $\alpha > 0$ of a function f: $\mathbb{R}^+ \to \mathbb{R}$ is defined by

$$I^{\alpha}\mathrm{F}\ (\mathrm{t}) = \frac{1}{\Gamma(\alpha)} \int_0^t (t-s)^{\alpha-1} \mathrm{g(s)},$$

where $\Gamma(.)$ is the gamma function.

***Caputo Derivative***

The general definition of the caputo derivative ıs defined as:

$$D^{\alpha}{}_t f(t) = \begin{cases} \frac{1}{\Gamma(\mathrm{n}-\alpha)} \int_0^t (t-s)^{n-\alpha-1} \frac{d^n f(s)}{ds^n} ds, \text{if } \mathrm{n}-1 < \alpha < n, n \epsilon \mathbb{N} \\ \frac{d^n f(t)}{dt^n}, \quad \imath f \alpha = n, \mathrm{n} \epsilon \mathbb{N} \end{cases}$$

where α is the order of the derivative and it's allowed to be a real or complex number.

***Riemann-Liouville Derivative***

The general definition of the Riemann-Liouville derivative ıs defıned as:

$$D^{\alpha}{}_{t} f(t) =$$
$$\begin{cases} \frac{1}{\Gamma(\mathrm{n}-\alpha)} \frac{d^n f(t)}{dt^n} \int_0^t (t-s)^{n-\alpha-1} f(s) ds, & \text{if } \mathrm{n}-1 < \alpha < n, n \epsilon \mathbb{N} \\ \frac{d^n f(t)}{dt^n}, & \imath f\ \alpha = n, \mathrm{n} \epsilon \mathbb{N} \end{cases}$$

The Laplace transform (LT) of the Caputo fractional derivative is given by:

$$\mathcal{L}\{{}_0^c \mathrm{D}_t^{\alpha} N(t)\} = S^{\alpha} N(S) \sum_{m=0}^{n-1} S^{\alpha-m-1} N^{(m)}(0), \qquad 0 < n-1 < \alpha \leq n \in \mathbb{Z}^{+}$$

where $\alpha$ is the order of the derivative and it's allowed to be a real or complex number (Santanu Saha Ray and subhadashan Sahoo, 2019).

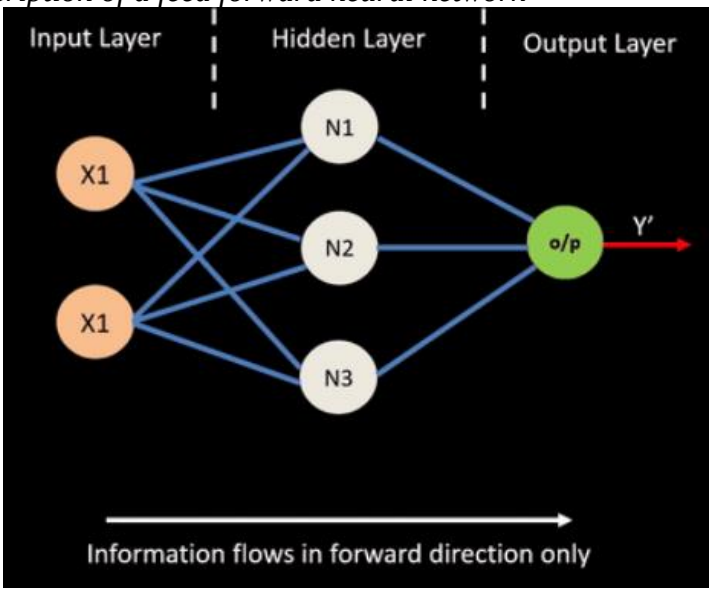
Caputo's fractional derivative formula has proven to be more applicable in practical situations compared to Riemann-Liouville's derivative, as the latter yields a zero derivative for a constant function. Many scientists, including Sardar et al. (2015) and Dumitru Baleanu et al. (2010), have found fractional-order derivatives to be essential in developing models for analyzing dynamical systems. Recent research has also demonstrated the significance of fractional calculus in controlling and synchronizing chaotic systems (Ahmad Taher et al., 2017) as well as other engineering fields. A plethora of research findings support the notion that modeling real-life phenomena with fractional-order derivatives is the most accurate and reliable approach (Naik, P. A et al., 2020).

***Neural Network***

Artificial Neural Networks (ANNs) are a robust tool of artificial intelligence that can solve complex problems by mimicking human intelligence. Unlike traditional statistical and probabilistic methods that rely on nonlinear regression, ANNs excel in solving nonlinear regression problems with high precision, owing to their architecture similar to the human brain (Pavlenko et al., 2018). ANNs process information from observations and convert them into hidden layers. Hidden neurons within the hidden layer(s) compute weights, which are transmitted through the transfer characteristic using neurons within the inner layer. Recurrent and feedforward neural networks are

widely used deep learning techniques for time-domain forecasting, enabling accurate predictions of time series across diverse applications.

Figure 1
*Schematic description of a feed forward neural network*




***Next Generation Matrix***

The concept of next-generation matrix pertains to a square matrix denoted by G, where the element at the i-th row and j-th column represents the expected count of secondary infections of type i initiated by a solitary infected individual of type j, given the assumption that the population of type i is entirely susceptible (Levin et.al 2017).

***Basic Reproduction***

The fundamental reproduction number, commonly denoted as $R_0$, is mathematically defined as the principal Eigen value of the next generation matrix G, expressed as (Diekmann et.al 2010):

$$\mathrm{G} = \mathrm{F}V^{-1}\ ,\ F = \left[\frac{\partial f_{\iota(x_0)}}{\partial x_j}\right], \quad V = \left[\frac{\partial v_{\iota(x_0)}}{\partial x_j}\right],$$

where,

$f_\iota$ are new infections,

$v_\iota$ are transferred infections from one compartment to another,

$x_0$ is the disease-free equilibrium state.

The basic reproduction number, denoted as $R_0$, is commonly understood to represent the expected number of secondary cases arising from a single infection in a population that is completely susceptible (Murray, 2003).

$$R_0 \propto \left(\frac{infection}{constant}\right) x \left(\frac{constant}{time}\right) x \left(\frac{time}{infection}\right) = \alpha\beta\gamma$$

where,

$\alpha$ represents the transmissibility,

$\beta$ represents the average rate of constant between susceptible and infected individuals.

$\gamma$ represents the duration of infectiousness.

Empirical research has demonstrated that if the basic reproduction number $R_0$ is less than 1, there will be no epidemic, and the disease will eventually extinguish. Conversely, if $R_0$ is greater than 1, the likelihood of a pandemic outbreak is high. In the case of influenza, the average $R_0$ ranges from 2 to 3, as reported by Mills (2004), a level of contagion consistent with observed transmission patterns.

***Dynamical System***

Let X be a metric space with metric d. Let I be an additive semi-group of real numbers. A dynamical system on X (also known as flow) is defined by a continuous mapping (Sternberg et.al 2010):

$$\pi: X \times I \to X ,$$

with the following properties:

I. $\pi(x, 0) = x, \ for\ all\ x \in X,$

II. $\pi(\pi(x, t), s) = \pi(x, t + s), \quad for\ all\ t \in I.$

***Equilibrium Point***

A point $x^* \in X$ is called an equilibrium or rest point of a dynamical system (Feldman et. al 2011):

$$\pi: X \times \mathbb{R} \to X, \quad \text{if}$$

$$\pi(x,t) = x^* \ for\ all\ t \in \mathbb{R}.$$

***Stability***

An equilibrium point $x^* \in X$ of a dynamical system (Verhulst. F, 2006):

$$\pi: X \times \mathbb{R} \to X,$$

is called stable if for every $\mathcal{E} > 0$ there exist a $\delta = \delta_{\mathcal{E}}$ such that

$$d(x,\mathrm{y}) \leq \delta \ implies\ that\ d\big(x,\pi(x,t)\big) \leq \mathcal{E}\ for\ all\ t \geq 0$$

and asymptotically stable if $x^*$ is stable and there exist a $\delta$ such that

$$\lim_{t\to\infty} \pi(y,t) = x, \qquad for\ all\ y \in X\ \ with\ \ d(x,\mathrm{y}) \leq \delta.$$

***Lyapunov function***

A function $V \in C^1(X)$ is called a Lyapunov function with respect to $f$ if

$V^{\cdot}(x) = grad\,V(x)\,T\,f(x) \leq 0\ for\ all\ x \in X.$

With this definition the following proposition was formulated (Ames et.al 2019):

If there exists a Lyapunov function $V \in C^1(X)$ with respect to $f$ which is positive definite with respect to some rest point $\overline{x} \in$ X, which satisfies the condition:

$V(\bar{x}) =$ 0 and V (x) $>$ 0 $for\ all\ x \in X,$ x $\neq \bar{x}$ ,

then $x$ is stable. If in addition

$\dot{V}$ ($\bar{x}$) = 0 and $\dot{V}$ (x) $<$ 0 $for\ all\ x \in X,$ x $\neq \bar{x},$ then x is asymptotically stable.

***Local Asymptotic Stability***

Let

$$\frac{d^a f(t)}{dt^a} = f(x),\ \ x(0) = x_0\ ,$$

be an autonomous nonlinear fractional-order system with

$$0 < a < 1\ and\ x \in \mathbb{R}^n,$$

and the equilibrium points of the above system are solutions to the equation:

$f(x) = 0.$

An equilibrium is locally asymptotically stable if all Eigenvalues $\lambda_{ij}$ of the Jacobian matrix $J = \frac{\partial f}{\partial x}$ evaluated at the equilibrium satisfy $\left|\arg \lambda_{ij}\right| > \alpha \frac{\pi}{2}$ (Hammouch et.al 2021).

***Routh- Hurwitz Stability Criterion***

The Routh-Hurwitz criterion is a crucial tool for determining the stability of a linear system. It offers a necessary and sufficient condition for the roots of a polynomial to be negative, without requiring direct solution for these roots.

Specifically, the Routh-Hurwitz stability criterion applies to second-order polynomials, and can be expressed as follows (Patil, A. 2021):

$\mathrm{P(s)} = s^2 + a_1 s + a_0$ , $\mathrm{P(s)} = 0$ is stable if and only if $a_1, a_0 > 0$.

Routh- Hurwitz stability Criterion for third order polynomials:

$\mathrm{P(s)} = s^3 + a_2 s^2 + a_1$ , $\mathrm{P(s)} = 0$ ,

is stable if and only if:

$a_2, a_0 > 0 \; and \; a_2 \, a_1 > 0$,

Routh-Hurwitz stability Criterion for higher order polynomials:

Let $\mathrm{D(s)} = a_n s^n + a_{n-1} s^{n-1} + \cdots + a_1 s + a_0$ .

We construct the Routh array as follows:

$$\begin{pmatrix} a_n & a_{n-2} & a_{n-4} & \dots \\ a_{n-1} & a_{n-3} & a_{n-5} & \dots \\ b_1 & b_2 & b_3 & \dots \\ c_1 & c_2 & c_3 & \dots \\ \vdots & \vdots & \vdots & \vdots \cdots \end{pmatrix}$$

$$b_\iota = \frac{a_{n-1} \times a_{n-2\iota} - a_n \times a_{n-(2\iota+1)}}{a_{n-1}},$$

$$c_\iota = \frac{b_\iota \times a_{n-(2\iota+1)} - a_{n-1} \times b_{\iota+1}}{b_1},$$

The polynomial $\mathrm{D(s)}$ has all negative roots if and only if all first-column elements of the Routh array have the same sign.

***Alcoholic Cardiomyopathy***

Alcohol is a widely consumed toxic substance worldwide, with high consumption shown to adversely affect the cardiovascular system and is a major contributor to non-ischemic enlarged cardiomyopathy (Mirijello et al., 2017). Prolonged excessive alcohol consumption can result in cardiovascular breakdown and the development of alcoholic cardiomyopathy (ACM) (Maisch, 2016). Although ACM was first described by Hippocrates in Greece during the 4th century B.C., modern clinical reports were officially released in the 19th century in England and Germany, with the pathophysiological basis for ACM recognized in the 20th century (Klatsky, 2002; Fernández-Solà & Estruch, 2017). Research has established a strong correlation between heavy alcohol consumption and ACM, with common symptoms including chest pain, dizziness, heart palpitations, increased pressure, swelling of veins in the neck, breathing difficulties, edema (fluid buildup and swelling),

particularly in the feet and lower legs, weight loss, and liver swelling (George & Figureueredo, 2011). Treatment for ACM involves reducing alcohol intake while managing withdrawal symptoms, which is better administered in therapy. Statistical research reveals an estimated 25,997 deaths globally from ACM in 2015 (Manthey et al., 2018; H, 2013), and the severity of the condition has led to its classification as an epidemic.

***Optimal Control***

Optimal control in mathematical modeling is a problem that involves finding a control strategy that maximizes or minimizes an objective function, given a set of constraints (Lenhart et.al 2007). The objective function represents a measure of performance, while the control strategy represents the inputs or actions chosen to achieve this performance. The constraints may represent physical or operational limits on the system being controlled.

Mathematically, the optimal control problem can be represented by a set of equations. The dynamical system is described by a set of differential equations, where the state of the system at time t is represented by x(t), the control input at time t is represented by u(t), and the dynamics of the system are described by the function f(x(t), u(t), t). The initial state of the system is x0.

The goal of the optimal control problem is to minimize or maximize a cost functional, represented by the equation:

$$J(x(t), u(t), t) = \int L(x(t), u(t), t)dt + M\big(x(tf)\big).$$

The instantaneous cost function L represents the cost associated with the state and control inputs at each time point, while the terminal cost function M represents the cost associated with the final state of the system. The control input u(t) is subject to constraints represented by the set U, while the state x(t) is subject to constraints represented by the set X.

The optimal control problem is to find the control input u*(t) that minimizes or maximizes the cost functional, subject to the system dynamics and constraints, represented by the equations:

$$u*(t) = argmin_u \in U\, J(x(t), u(t), t),$$

subject to:

$$x'(t) = f(x(t), u(t), t), x(0) = x_0,$$

$$u(t) \in U,$$
$$x(t) \in X.$$

The solution to the optimal control problem provides the optimal control input u*(t) that minimizes or maximizes the cost functional subject to the system dynamics and constraints. This solution can be used to design control systems for various applications, such as robotics, aerospace, chemical engineering, and finance.

**Related Research**

The study of Alcoholic Cardiomyopathy (ACM) and its spread has received significant attention in recent years, resulting in a range of related research. This section provides a comprehensive review of the literature on ACM and its epidemiology, as well as previous research on mathematical modeling and data analysis of ACM.

One of the early studies on ACM was conducted by Klatsky (2002), who identified a strong correlation between heavy alcohol consumption and the development of the disease. Other studies have since confirmed this correlation and investigated the underlying physiological mechanisms that lead to ACM (George & Figureueredo, 2011; Maisch, 2016). In terms of modeling the spread of ACM, a range of approaches have been proposed. For example, a compartmental model was developed by Fernández-Solà and Estruch (2017) to simulate the transmission dynamics of ACM in a population. The model incorporated both the direct effects of alcohol consumption on heart function and the indirect effects on lifestyle factors that increase the risk of the disease.

Fractional calculus has also been applied in previous studies to model the spread of chronic diseases. For example, Caputo et al. (2015) developed a fractional-order epidemic model to simulate the spread of Ebola virus disease in a population. The model incorporated the memory effects observed in disease transmission and was able to capture the long-term dynamics of the epidemic. In recent years, machine learning techniques such as neural networks have been increasingly applied in epidemiological modeling to improve the predictive accuracy of models. For example, Huang et al. (2020) developed a neural network model to predict the incidence of dengue fever in Taiwan. The model was able to outperform traditional statistical models and provide accurate forecasts of the disease.

Mathematical models have long demonstrated their usefulness in the investigation of all forms of epidemics as they satisfactorily depict the transmission elements of the illness. There are fascinating phenomena that have what are termed memory effects, meaning their state does not depend solely on time and position but also on the previous state. Such a system can be very difficult to model and analyze with classical differential equations, but nonlocality gives fractional derivative built-in ability to incorporate memory effects. (Baba, I. A., et al. 2021, Kaymakamzade et al. 2021; GOKBULUT, N., et al. 2021). Mathematical modeling based on enhanced rheological models naturally leads to differential equations of fractional order and to the necessity of the formulation of initial conditions to such equations Caputo derivative is used in this work because it allows the utilization of physically interpretable initial conditions and provides an interpolation between integer-order derivatives. The main properties and advantage of the Caputo operator are that the Laplace transform, interpolation, non-commutation, and linearity of the Caputo fractional derivative which is a generalization of properties the of integer order derivative, where n is replaced by $\alpha$. This is not the case for the Riemann-Liouville operator. The Caputo derivative is more relevant to real-life problems when contrasted with the Reiman-Liouville type since it takes into consideration integer-order initial conditions for fractional differential equations and maintains basic calculus principles.

(Ewees et, al. 2022) proposed a Heap-based optimizer long short-term memory (HBO-LSTM) to forecast wind power from different wind turbines which uses optimization algorithms to train the LSTM and to boost its performance by optimizing its parameters. Their results showed that the HBO-LSTM outpaced other alternative models like particle swam optimization (PSO) etc. However, HBO came 3$^{rd}$ in rank in computational cost using time, when compared with other models. (Oyelade, O. et al, 2022) presented another novel metaheuristic algorithm, Ebola Optimization Search Algorithm (EOSA) incorporating the SIR model on a system of first-order differential equation. Their result showed that EOSA performed better than Genetic Algorithm (GA) and PSO in terms of scalability, convergence, and sensitivity analysis. (Lawal, A. I., & Idris, M. A. 2020) developed an artificial neural network-based mathematical model for the prediction of blast-induced ground vibrations employing the Levenberg Marquardt Algorithm (LMA) and the feed-forward back-propagation Multi-Layer Perceptron (MLP). The proposed ANN-based mathematical model outperformed the other existing models as it gave the lowest time-computational cost, the lowest Mean

Absolute Error (MAE) and Root Mean Square Error (RMSE), with the highest Variance Accounted For (VAF) among the equations compared with higher correlation. Also, the predicted values using the proposed model were closer to the field-measured data when compared with other models, hence its superiority.

Many authors in literature have studied alcohol epidemics, mostly with the conventional classical system of differential equations (Khajji, B., et.al. 2020; Adu et.al. 2017; Sánchez, F., et.al. 2007; Santonja, F. J., et.al. 2010; Guzzo-Merello, et al 2014; Walters et.al. 2013). Some have also studied the evolution of the fractional-order model for studying alcohol epidemics (Rahman, M., et.al. 2021; Singh, J. 2020). (Gómez-Aguilar, J. F. 2018) analyzed an alcoholism model using Liouville–Caputo, and Atangana–Baleanu–Caputo fractional derivatives with constant and variable order, in which two fractional mathematical models are considered; with and without delay combined with analytical and numerical solutions of a nonlinear alcoholism model via variable-order fractional differential equations to develop a completer and more realistic model. (Weaver, M. A. 2020) developed an alcohol fractional model and proved the existence and uniqueness of the solution, with basic computational numerical solutions using fixed point theorem to show that fractional models via Caputo Fabrizio have good applications. Also, (Mayengo et al. 2020) studied alcohol-related health risks with changing behaviors via cultural beliefs employing fuzzy modeling, with optimal control centered on increasing the resistance of susceptible individuals and curbing their chances of becoming alcoholics.

However, no author to our knowledge narrowed the fractional-order technique to analyzing the dynamics of Alcoholic cardiomyopathy (ACM), as an epidemy while integrating Neural Networks time series; simulating and comparing with real-life data (Manthey, J. J. 2020; Zou, H. W., 2014; Manthey., J. 2019; Bardach, A. E., et al. 2017; Statista 2016; Setti, M. O., et al. 2021) to predict future outcomes. In this research, the Caputo type of the fractional-order approach combined with a Levenberg Marquardt Algorithm (LMA) Neural Network time series is employed to study the dynamics of the ACM, having both analytic solutions and numerical simulations to buttress the findings. Firstly, the ACM is described schematically and transformed into a system of fractional differential equations, by following the basic mechanism of the classical order but in addition, replacing the classical order n with the fractional order $\alpha$. The existence, uniqueness, and stability of the system are carried out amongst other analytic computations. Finally, numerical simulations are performed integrating the

LMA to the ACM model (which implements the predictor-corrector method) using real-life data sets (Manthey, J. J. 2020). The resulting model stands out from other models in the literature as it combines all the advantages of Caputo fractional derivatives and the LMA Neural Network time series, realistically describing the disease dynamics while providing high accuracy in prediction with memory effects, hence its novelty and superiority. The related research on ACM and its epidemiology provides a solid foundation for the proposed research. By combining the insights from existing literature with fractional calculus and neural network time series, the proposed model is expected to contribute to the understanding of ACM transmission dynamics and inform the development of effective intervention strategies.

# CHAPTER III
## Methodology

The objective of this study is to develop a fractional-order alcoholic cardiomyopathy epidemic model with neural network time series to examine the dynamics of ACM while integrating neural networks time series and simulating and comparing with real-life data to predict future outcomes. To accomplish this objective, a mixed-methods research design that incorporates both qualitative and quantitative research methods will be used to investigate the dynamics of alcoholic cardiomyopathy using a fractional-order model with neural network time series. The research design will consist of preliminary literature review, theoretical development, model development, neural network time series, data collection, simulation and analysis, and a conclusion.

The preliminary literature review will be conducted to determine the current research status in alcoholic cardiomyopathy and the application of fractional-order models with neural network time series. After the preliminary literature review, a theoretical framework will be created for the study. In this section, a fractional-order model for alcoholic cardiomyopathy will be developed using the Caputo derivative. The neural network time series will be incorporated into the fractional-order model in the next section using the Levenberg Marquardt Algorithm (LMA) to simulate and compare with real-life data.

To validate the model, data on alcoholic cardiomyopathy will be collected from relevant sources, including hospitals and medical records. The data will be analyzed to determine the model parameters, and the model will be calibrated based on the data. The simulation and analysis section will simulate the model and analyze the outcomes. The outcomes will be compared to real-life data and analyzed to determine the effectiveness of the model.

Finally, the conclusion section will discuss the results' implications, and suggest areas for future research. In conclusion, the mixed-methods research design proposed in this study will provide a comprehensive approach to developing a fractional-order alcoholic cardiomyopathy epidemic model with neural network time series. The research design will allow us to analyze the dynamics of alcoholic cardiomyopathy

while integrating neural networks time series and simulating and comparing with real-life data to predict future outcomes.

**Dynamics of the ACM-LMA Model**

The evaluation of fractional-order alcoholic cardiomyopathy (ACM) epidemic models with neural network time series is incomplete without a comprehensive understanding of their dynamic nature hence, introducing us to one vital aspect: The Dynamics of the ACM-LMA Model within this field of study. This section offers insights into said aspects. By combining both fractional-order derivatives and neural network time series skillfully in creating our models- specifically relying on Caputo fractional derivative modeling for covering more nuanced complexities associated with disease progression while employing Levenberg Marquardt Algorithm (LMA) optimization techniques for superior data processing accuracy - we gain an unparalleled ability for developing highly predictive models capable of exploring even more intricate aspects under examination surrounding Alzheimer's. Additionally, we conduct stability analysis to determine where the equilibrium points lie, while also checking for any conflicting solutions with our unique analysis in hopes of creating as precise a model as possible that can aid in better predictions for ACM's dynamic changes.

To simulate the dynamics of the ACM-LMA model, numerical methods such as the Predictor Corrector method will be employed. The model's outputs can then be analyzed using statistical methods such as regression analysis and goodness-of-fit tests to validate the accuracy of the model's predictions.

In summary, the dynamics of the ACM-LMA model in the proposed fractional-order ACM epidemic model with neural network time series as shown in Figures 2 and 3, is crucial to the model's accuracy and reliability. The incorporation of fractional-order derivatives and neural network time series allows for a more comprehensive and realistic modeling of the complex and anomalous dynamics of ACM. The stability and uniqueness of the model are essential aspects of the dynamics, and numerical and statistical methods can be used to simulate and analyze the model's outputs. Descriptions of variables and parameters are shown in Tables 2 and 3.

Figure 2

*Schematic diagram of the ACM-LMA model*

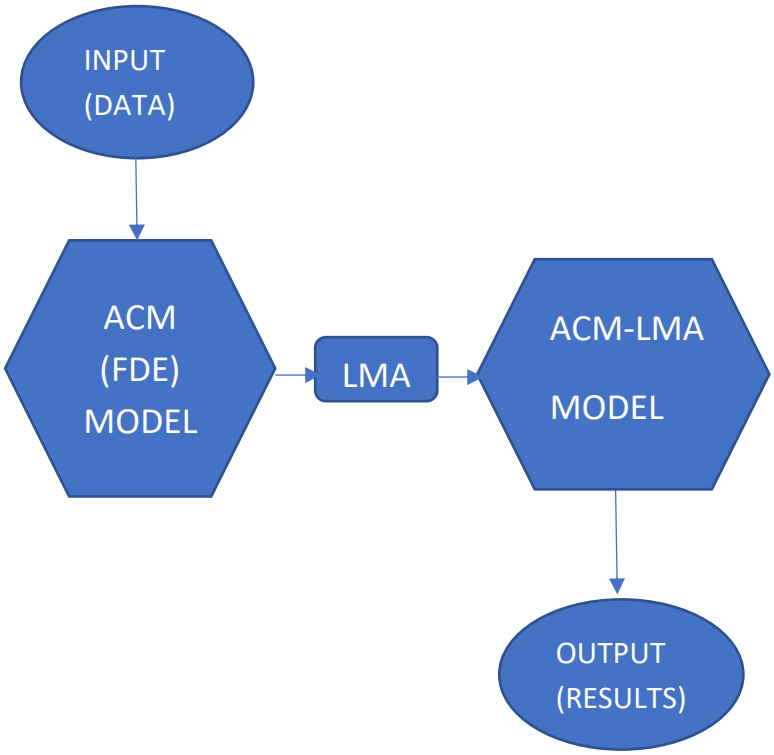


Figure 3

*Schematic diagram of the ACM (FDE) model*

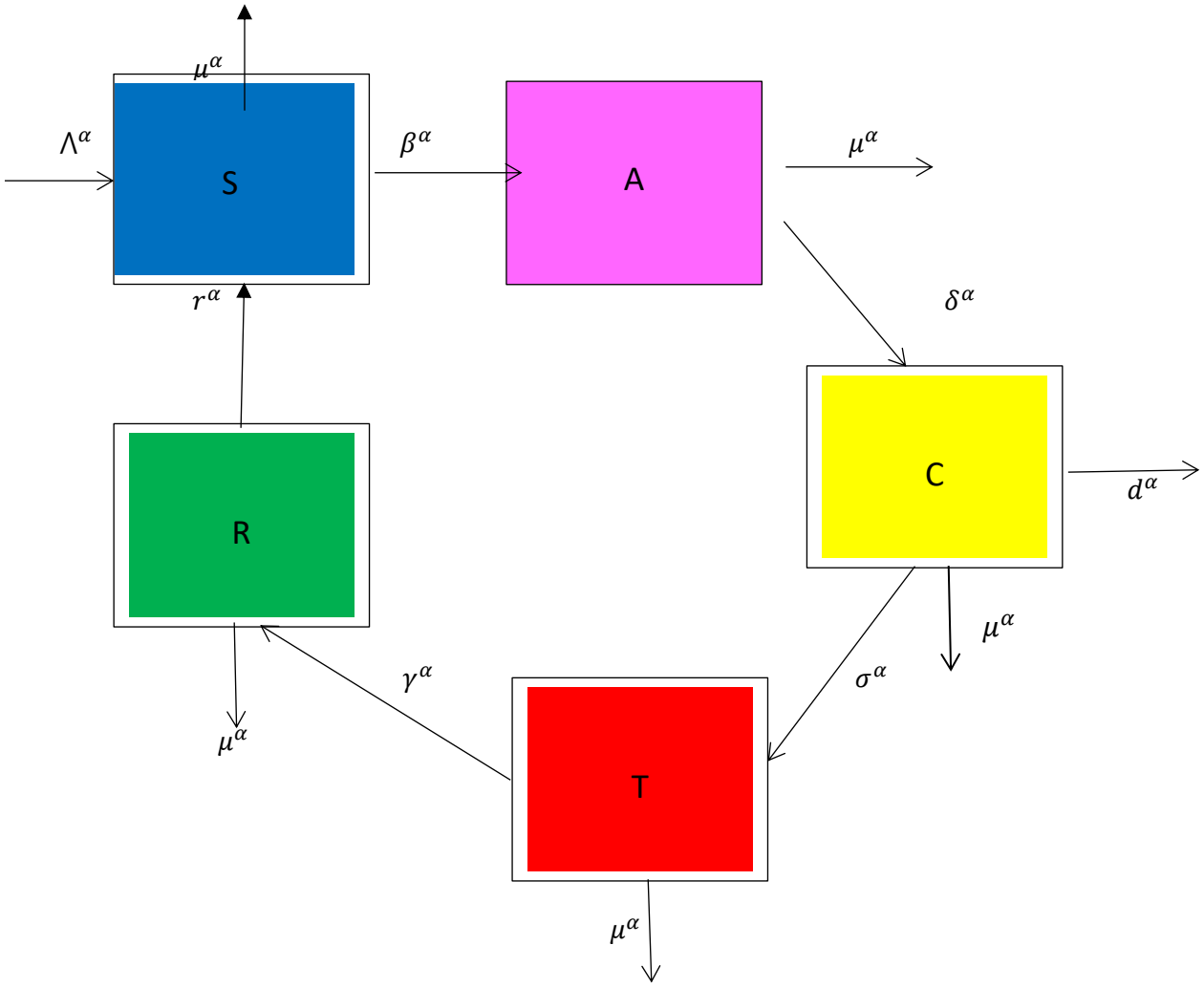



Table 1

*Description of variables of the model.*

| Variable | Description |
|---|---|
| $S$ | Susceptible alcohol drinkers (moderate consumers) |
| $A$ | Alcoholic addicts |
| $C$ | Alcoholic cardiomyopathy diseased population |

| | |
|---|---|
| $T$ | Alcoholic cardiomyopathy diseased individuals under treatment |
| $R$ | Recovered population |

Table 2

*Description of parameters of the model*

| Parameter | Description |
|---|---|
| $\Lambda^{\alpha}$ | Recruitment rate |
| $\beta^{\alpha}$ | The rate at which alcoholics susceptible become addicted |
| $d^{\alpha}$ | The rate at which an alcoholic cardiomyopathy diseased individual die |
| $\mu^{\alpha}$ | Natural death rate |
| $\delta^{\alpha}$ | The rate at which addictive develop alcoholic cardiomyopathy disease |
| $\gamma^{\alpha}$ | Recovery rate |
| $\sigma^{\alpha}$ | Rate at which alcoholic cardiomyopathy diseased receive treatment. |
| $r^{\alpha}$ | Rate at which a recovered individual return to the susceptible compartment |

From Fig 3.2, we obtain the Caputo type fractional order system of equations:

$$
\begin{aligned}
{}_{0}^{c}\mathrm{D}_{t}^{\alpha} S(t) &= \Lambda^{\alpha} + r^{\alpha} R(t) \; - \frac{\beta^{\alpha} S(t)}{N} A(t) - \mu^{\alpha} S(t), \\
{}_{0}^{c}\mathrm{D}_{t}^{\alpha} A(t) &= \frac{\beta^{\alpha} S(t)}{N} A(t) - \mu^{\alpha} A(t) - \delta^{\alpha} A(t) C(t) \; , \\
{}_{0}^{c}\mathrm{D}_{t}^{\alpha} C(t) &= \delta^{\alpha} A(t) C(t) - \mu^{\alpha} C(t) - \sigma^{\alpha} C(t) - d^{\alpha} C(t), \\
{}_{0}^{c}\mathrm{D}_{t}^{\alpha} T(t) &= \sigma^{\alpha} C(t) - \gamma^{\alpha} \, T(t) - \mu^{\alpha} T(t), \\
{}_{0}^{c}\mathrm{D}_{t}^{\alpha} R(t) &= \gamma^{\alpha} \, T(t) - \mu^{\alpha} R(t) - r^{\alpha} R(t).
\end{aligned}
\tag{3.1}
$$

Given that $S(t) + A(t) + C(t) + T(t) + R(t) = N(\mathrm{t})$, $0 < \alpha < 1$

## Existence and Uniqueness of Solution

**Theorem 1.** The solution to system (2.1) exits and is unique.
**Proof.**

$$\begin{aligned} {}_0^c\mathrm{D}_t^{\alpha}\mathrm{N(t)} &= \Lambda^{\alpha} - \mu^{\alpha}S(t) - \mu^{\alpha}A(t) - \mu^{\alpha}C(t) - \mu^{\alpha}T(t) - \mu^{\alpha}R(t) - d^{\alpha}I(t), \\ &= \Lambda^{\alpha} - \mu^{\alpha}\big(S(t) + A(t) + C(t) + T(t) + R(t)\big) - d^{\alpha}I(t), \\ &= \Lambda^{\alpha} - \mu^{\alpha}N(t) - d^{\alpha}C(t), \\ &\leq \Lambda^{\alpha} - \mu^{\alpha}N(t). \end{aligned}$$

Applying the Laplace transform method to solve Gronwall's inequality with initial condition $N(t_0)\geq 0$, we get:

$$\lfloor \mathcal{L}\{{}_0^c\mathrm{D}_t^{\alpha}N(t) + \mu^{\alpha}N(t)\} \leq \mathcal{L}\{\Lambda^{\alpha}\},$$

$$\lfloor \mathcal{L}\{{}_0^c\mathrm{D}_t^{\alpha}N(t)\} + \mu^{\alpha}\mathcal{L}\{N(t)\} \leq \mathcal{L}\{\Lambda^{\alpha}\}.$$

Employing the properties of Laplace transform,

$$S^{\alpha}\mathcal{L}\{N(t)\} - \sum_{m=0}^{n-1} S^{\alpha-m-1}N^{(m)}(t_0) + \mu^{\alpha}\mathcal{L}\{N(t)\} \leq \frac{\Lambda^{\alpha}}{S},$$

$$\mathcal{L}\{N(t)\}(S^{\alpha} + \mu^{\alpha}) \leq \sum_{m=0}^{n-1} S^{\alpha-m-1}N^{(m)}(t_0) + \frac{\Lambda^{\alpha}}{S},$$

$$\mathcal{L}\{N(t)\} \leq \sum_{m=0}^{n-1} \frac{S^{\alpha-m-1}}{(S^{\alpha} + \mu^{\alpha})}N^{(m)}(t_0) + \frac{\Lambda^{\alpha}}{S(S^{\alpha} + \mu^{\alpha})}.$$

Applying partial fractions, we arrive at:

$$\mathcal{L}\{N(t)\} \leq \frac{\Lambda^{\alpha}}{\mu^{\alpha}}\left[\frac{1}{S} - \frac{1}{S\left(1 + \frac{\mu^{\alpha}}{S^{\alpha}}\right)}\right] + \sum_{m=0}^{n-1} \frac{1}{S^{m+1}\left(1 + \frac{\mu^{\alpha}}{S^{\alpha}}\right)}N^{(m)}(t_0). \tag{3.2}$$

Since, $\sum_{n=0}^{\infty}\left(\frac{-\mu^{\alpha}}{s^{\alpha}}\right)^n$ is the is Taylor series expansion for $F(t) = \frac{1}{\left(1+\frac{\mu^{\alpha}}{s^{\alpha}}\right)}$. Then we will have that:

$$\mathcal{L}\{N(t)\} \leq \frac{\Lambda^{\alpha}}{\mu^{\alpha}}\left[\frac{1}{S} - \frac{1}{S}\sum_{n=0}^{\infty}\left(\frac{-\mu^{\alpha}}{s^{\alpha}}\right)^n\right] + \sum_{m=0}^{n-1} \frac{1}{S^{m+1}} \sum_{n=0}^{\infty}\left(\frac{-\mu^{\alpha}}{s^{\alpha}}\right)^n N^{(m)}(t_0),$$

$$= \frac{\Lambda^\alpha}{\mu^\alpha}\left[\frac{1}{S} - \frac{1}{S}\sum_{n=0}^{\infty}\left(\frac{-\mu^\alpha}{s^\alpha}\right)^n\right] + \sum_{m=0}^{n-1}\sum_{n=0}^{\infty}\frac{(-\mu^\alpha)^n}{s^{\alpha n+m+1}}N^{(m)}(t_0).$$

Taking Laplace inverse function, we have

$$N(t) \le \frac{\Lambda^\alpha}{\mu^\alpha}\left\{\mathcal{L}^{-1}\left\{\frac{1}{s}\right\} - \sum_{n=0}^{\infty}(-\mu^\alpha)^n\mathcal{L}^{-1}\left(\frac{1}{s^{\alpha n+1}}\right)\right\} + \sum_{m=0}^{n-1}\sum_{n=0}^{\infty}(-\mu^\alpha)^n N^{(m)}(t_0)\mathcal{L}^{-1}\left\{\frac{1}{s^{\alpha n+m+1}}\right\}.$$

Thus, we have

$$N(t) \le \frac{\Lambda^\alpha}{\mu^\alpha}\left\{1 - \frac{\sum_{n=0}^{\infty}(-\mu^\alpha t^\alpha)^n}{\Gamma(\alpha n+1)}\right\} + \sum_{m=0}^{n-1}\sum_{n=0}^{\infty}\frac{(-\mu^\alpha t^\alpha)^n}{\Gamma(\alpha n+m+1)}t^m N^{(m)}(t_0).$$

Employing the Mittag-leffler function:

$E_{a,b}(z) = \Sigma_{n=0}^{\infty}\frac{z^m}{\Gamma(am+b)}$, $a > 0,\ b > 0$, and $E_a(z) = E_{a,1}(z) = \Sigma_{n=0}^{\infty}\frac{z^m}{\Gamma(am+1)}$,

we get:

$$N(t) \le \frac{\Lambda^\alpha}{\mu^\alpha}[1 - E_\alpha(-\mu^\alpha t^\alpha)] + \sum_{m=0}^{n-1}E_{\alpha,m+1}(-\mu^\alpha t^\alpha)N^{(m)}(t_0)t^m,$$

where the series of the Mittag-leffler functions $E_\alpha(-\mu^\alpha t^\alpha)$ and $E_{\alpha,m+1}(-\mu^\alpha t^\alpha)$ are converge.

Therefore, the system (1) has a bounded solution, and hence solution exit.

Each equation of the system (1) can be represented by

$$\begin{aligned} {}_0^c\mathrm{D}_t^\alpha y(t) &= G(t,y), \quad y(0) = y_0 \\ G(t,y) &= P(y) + Q(y) + r, y = y(t). \end{aligned} \tag{3.3}$$

We now show that the system (iv) is Lipschitz continuous.

$$\begin{aligned} |G(t,y) - G(t,y^*)| &= |P(y) + Q(y) + r - (P(y^*) + Q(y^*) + r)|, \\ &= \left|P\big((y(t) - y^*(t)\big) + Q(y(t) - y^*(t))\right|, \\ &\le \left\|P\big((y(t) - y^*(t)\big)\right\| + \|Q(y(t) - Q(y^*(t))\|, \\ &= \|P\|.\|(y(t) - y^*(t)\| + \|Q(y(t) - Q(y^*(t))\|, \\ &\le \|P\|.\|y(t) - y^*(t)\| + \|(y(t) - y^*(t)\|, \\ &= (\|P\| + 1)\|y(t) - y^*(t)\|, \\ &= M\|y(t) - y^*(t)\|. \end{aligned}$$

Where $M = (\|P\| + 1)$, and $M\|y(t) - y^{\alpha}(t)\| < \infty$ .

Hence $G$ is uniformly Lipschitz continuous and bounded.

To complete the proof for uniqueness of the system (1).

Let $0 < \alpha < 1$, $\varphi = [0, h^*] \subseteq \mathbb{R}$ and $\psi = \|y(t) - y(0)\| \leq K$, and $g: \varphi \times \psi \to \mathbb{R}$ be a continuous bounded function, that is there exist $L > 0$ such that $|g(t, y)| \leq L$, since $G$ is Lipschitz continuous.

Let $MK < L$, then $\exists$ a unique $y \in C^{\alpha}[0, h^*]$ for the initial value problem (iv), where $h^* = \{h, (\frac{K\Gamma(\alpha+1)}{L})^{\frac{1}{\alpha}}\}$

Let $E = \{y \in C^{\alpha}[0, h^*]: \|y(t) - y(0)\| \leq K\}$, observe that $E \subseteq \mathbb{R}$ is closed and hence a complete metric space. Transforming the system (iv) to the equivalent Volterra integral equation:

$$
\begin{aligned}
{}_0^c\mathrm{D}_t^{-\alpha}[{}_0^c\mathrm{D}_t^{\alpha} y(t)] &= {}_0^c\mathrm{D}_t^{\alpha} g(t, y), \\
y(t) - y(0) &= \frac{1}{\Gamma(\alpha)} \int_0^t (t - \emptyset)^{\alpha - 1} g\big(\emptyset, y(\emptyset)\big) d\emptyset, \\
y(t) &= y(0) + \tfrac{1}{\Gamma(\alpha)} \textstyle\int_0^t (t - \emptyset)^{\alpha - 1} g\big(\emptyset, y(\emptyset)\big) d\emptyset. \qquad (3.4)
\end{aligned}
$$

Defining an operator $G$ in $E$, with $G: E \to E$ such that:

$$
G[y](t) = y_0 + \tfrac{1}{\Gamma(\alpha)} \textstyle\int_0^t (t - \emptyset)^{\alpha - 1} g\big(\emptyset, y(\emptyset)\big) d\emptyset.
$$

It follows that,

$$
\begin{aligned}
|G[y(t)] - y(0)| &= \left| \tfrac{1}{\Gamma(\alpha)} \textstyle\int_0^t (t - \emptyset)^{\alpha - 1} g\big(\emptyset, y(\emptyset)\big) d\emptyset \right|, \\
&\leq \frac{1}{\Gamma(\alpha)} \int_0^t (t - \emptyset)^{\alpha - 1} L d\emptyset, \\
&\leq \frac{L}{\Gamma(\alpha + 1)} (h^*)^{\alpha}, \\
&\leq \frac{L}{\Gamma(\alpha + 1)} \frac{K\Gamma(\alpha + 1)}{L}, \\
&\leq K.
\end{aligned}
$$

So, $G$ is well defined.

Next;

$$
\begin{aligned}
&|G[y](t) - G[y^*](t)| \\
&= \left| \frac{1}{\Gamma(\alpha)} \int_0^t (t - \emptyset)^{\alpha - 1} [g\big(\emptyset, y(\emptyset)\big) - g\big(\emptyset, y^*(\emptyset)\big)] d\emptyset \right|,
\end{aligned}
$$

$$\leq \frac{1}{\Gamma(\alpha)}\int_0^t (t-\emptyset)^{\alpha-1} M\|y-y^*\| d\emptyset,$$

$$\leq \frac{M}{\Gamma(\alpha)}\|y-y^*\|\frac{\Gamma(\alpha)}{\Gamma(\alpha+1)}t^{\alpha},$$

$$\leq \frac{M}{\Gamma(\alpha+1)}\|y-y^*\|(h^*)^{\alpha},$$

$$\leq \frac{M}{\Gamma(\alpha+1)}\|y-y^*\|\frac{K\Gamma(\alpha+1)}{L},$$

So, $|G[y]-G[y^*]| \leq \frac{MK}{\mathrm{L}}\|y-y^*\|$, and from hypothesis $\frac{MK}{\mathrm{L}} < 1$.

Therefore, as a consequence of Banach contraction principle, $E$ is a contraction and has a unique fixed point (Hincal et.al. 2021). Hence, from Picard-lindelof theorem (Delavari, H.,et al. 2012), the system (iv) has a unique solution and a biological feasible region as:

$$\Omega = \left\{\left(S(t), E(t), I(t), I_{s(t)}, R(t)\right) \in \mathbb{R}_+^5 : N(t) \leq \frac{\Lambda^{\alpha}}{\mu^{\alpha}}[1-E_{\alpha}(-\mu^{\alpha}t^{\alpha})] + \sum_{m=0}^{n-1} E_{\alpha,m+1}(-\mu^{\alpha}t^{\alpha})N^{(m)}(t_0)t^m\right\}. \qquad (3.5)$$

**Basic Reproduction Number**

The reproduction number is computed by engaging the new generation matrix method. Considering the addiction and infected compartment the Jacobian matrices $F$ and $V$ representing the new infectivity and the transfer of persons connecting the compartments respectively we get:

$$F = \begin{bmatrix} \frac{\beta^{\alpha}S(t)}{N} & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix},$$

$$V = \begin{bmatrix} \mu^{\alpha}+\delta^{\alpha}C(t) & \delta^{\alpha}A(t) & 0 \\ -\delta^{\alpha}C(t) & -\delta^{\alpha}A(t)+\mu^{\alpha}+\sigma^{\alpha}+d^{\alpha} & 0 \\ 0 & -\sigma^{\alpha} & \gamma^{\alpha}+\mu^{\alpha} \end{bmatrix},$$

evaluating at $E_0 = \left(\frac{\Lambda^{\alpha}}{\mu^{\alpha}}, 0,0,0,0\right)$ gives:

$$FV^{-1} = \begin{bmatrix} \frac{\beta^{\alpha} s^{0}}{N^{0}} & 0 & 0 \\ \mu^{\alpha} & & \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix},$$

So,

$$R_0 = \frac{\beta^{\alpha}}{\mu^{\alpha}}.$$

**Stability Analysis**

**Theorem 2.** The system (1) is locally asymptotically stable at $\boldsymbol{E_0} = \left(\frac{\wedge^{\boldsymbol{\alpha}}}{\boldsymbol{\mu^{\alpha}}}, \mathbf{0}, \mathbf{0}, \mathbf{0}, \mathbf{0}\right)$ if and only if $\boldsymbol{R_0 < 1}$.

**Proof.** Evaluating the Jacobian at $E^0$, we get:

$$\begin{pmatrix} -\mu^{\alpha} & -\beta^{\alpha} & 0 & 0 & r^{\alpha} \\ 0 & -\beta^{\alpha} - \mu^{\alpha} & 0 & 0 & 0 \\ 0 & 0 & -(\mu^{\alpha} + \sigma^{\alpha} + d^{\alpha}) & 0 & 0 \\ 0 & 0 & \sigma^{\alpha} & -(\gamma^{\alpha} + \mu^{\alpha}) & 0 \\ 0 & 0 & 0 & \gamma^{\alpha} & -\mu^{\alpha} \end{pmatrix}.$$

After computation we get the characteristic equation to be:

$(-\mu^{\alpha} - \lambda)(-\beta^{\alpha} - \mu^{\alpha} - \lambda)(-\mu^{\alpha} - \sigma^{\alpha} - d^{\alpha} - \lambda)\ (-\gamma^{\alpha} - \mu^{\alpha} - \lambda)(-\mu^{\alpha} - \lambda) = 0$ .

Hence,

$\lambda_1 = \lambda_2 = -\mu^{\alpha}$,

$\lambda_3 = -[\beta^{\alpha} + \mu^{\alpha}]$,

$\lambda_4 = -[\mu^{\alpha} + \sigma^{\alpha} + d^{\alpha}]$,

$\lambda_5 = -[\gamma^{\alpha} + \mu^{\alpha}]$,

We see that all eigen values are negative $\left(\left|\arg \lambda_j\right| = \pi > \frac{\sigma\pi}{2}, j = 1,2, \ldots, 5\right)$.

So, if $R_0 < 1$ i.e. $0 > -2\beta^{\alpha} > -\beta^{\alpha} - \mu^{\alpha}$.

Then the system is locally asymptotically stable at $E_0$ If and only if $R_0 < 1$.

Proof complete.

**Endemic Equilibrium**

$E_1 = (S^1, A^1, C^1, T^1, R^1)$

$S^1 = \frac{[\Lambda^\alpha + r^\alpha R^1]\,[\Lambda^\alpha - d^\alpha C^1]\mu^\alpha}{\mu^{2\alpha}\beta^\alpha A^1 - [\Lambda^\alpha - d^\alpha C^1]}$,

$A^1 = \frac{[\Lambda^\alpha + r^\alpha R^1]}{\mu^\alpha + \delta^\alpha C^1} + \frac{\Lambda^\alpha - d^\alpha C^1}{\beta^\alpha}$,

$C^1 = \frac{\sqrt{4\delta^\alpha d^\alpha[\beta^\alpha(\Lambda^\alpha + r^\alpha R^1)] + [\beta^\alpha(\mu^\alpha + \sigma^\alpha + d^\alpha)]^2 - 2\beta^\alpha(\mu^\alpha + \sigma^\alpha + d^\alpha)\delta^\alpha \Lambda^\alpha + \delta^{2\alpha}\Lambda^{2\alpha}} - \beta^\alpha(\mu^\alpha + \sigma^\alpha + d^\alpha) + \delta^\alpha\Lambda^\alpha}{2\delta^\alpha d^\alpha}$

,

$T^1 = \left(\frac{\sigma^\alpha}{\gamma^\alpha + \mu^\alpha}\right)\left[\frac{\beta^\alpha[\Lambda^\alpha + r^\alpha R^1]}{\beta^\alpha[\mu^\alpha + \sigma^\alpha + d^\alpha] - \delta^\alpha[\Lambda^\alpha - d^\alpha C^1]} - \frac{\mu^\alpha}{\delta^\alpha}\right]$,

$R^1 = \frac{\gamma^\alpha\sigma^\alpha\mu^\alpha[\beta^\alpha[\mu^\alpha + \sigma^\alpha + d^\alpha] - \delta^\alpha[\Lambda^\alpha - d^\alpha C^1]\,] - \delta^\alpha\gamma^\alpha\sigma^\alpha\beta^\alpha\Lambda^\alpha}{\delta^\alpha[\gamma^\alpha\sigma^\alpha\beta^\alpha r^\alpha - (\mu^\alpha + r^\alpha)(\gamma^\alpha + \mu^\alpha)(\beta^\alpha[\mu^\alpha + \sigma^\alpha + d^\alpha] - \delta^\alpha(\Lambda^\alpha - d^\alpha C^1))]}$,

$E_1$ is biologically meaningful if $[\beta^\alpha[\mu^\alpha + \sigma^\alpha + d^\alpha] - \delta^\alpha[\Lambda^\alpha - d^\alpha C^1]] < 1$, and hence $C^1 > 0$.

**Theorem 3.** The system (1) is locally asymptotically stable at $E_1 = (S^1, A^1, C^1, T^1, R^1)$ if and only if $R_0 > 1$.

**Proof**. Evaluating the Jacobian at $E^1$, we get:

$$\begin{pmatrix} -\frac{\beta^\alpha A^1}{N^1} - \mu^\alpha & -\frac{\beta^\alpha S^1}{N^1} & 0 & 0 & r^\alpha \\ \frac{\beta^\alpha A^1}{N^1} & -\frac{\beta^\alpha S^1}{N^1} - \mu^\alpha - \delta^\alpha C^1 & -\delta^\alpha A^1 & 0 & 0 \\ 0 & \delta^\alpha C^1 & \delta^\alpha A^1 - (\mu^\alpha + \sigma^\alpha + d^\alpha) & 0 & 0 \\ 0 & 0 & \sigma^\alpha & -(\gamma^\alpha + \mu^\alpha) & 0 \\ 0 & 0 & 0 & \gamma^\alpha & -\mu^\alpha - r^\alpha \end{pmatrix}.$$

After computation we get the characteristic equation to be:

$\Big[(-\mu^\alpha - \gamma^\alpha - \lambda)(-\mu^\alpha - r^\alpha - \lambda)(\lambda^2 + \lambda(\frac{\beta^\alpha A^1}{N^1} + \delta^\alpha C^1 + 2\mu^\alpha - \frac{\beta^\alpha S^1}{N^1}) + \mu^{2\alpha} +$

$\frac{\beta^\alpha A^1}{N^1}(\delta^\alpha C^1 + \mu^\alpha) - \mu^\alpha(\frac{\beta^\alpha S^1}{N^1} + \delta^\alpha C^1)((\delta^\alpha A^1 - (\mu^\alpha + \sigma^\alpha + d^\alpha) -$

$\delta^\alpha C^1(\frac{\beta^\alpha A^1}{N^1}\delta^\alpha A^1 + \delta^\alpha A^1\lambda + \delta^\alpha A^1\mu^\alpha) + \frac{\beta^\alpha A^1}{N^1}\delta^\alpha C^1\sigma^\alpha\gamma^\alpha r^\alpha)\Big] = 0.$

And,

$\lambda_1 = -(\mu^\alpha + \gamma^\alpha)$,

$\lambda_2 = -(\mu^\alpha + r^\alpha)$,

$$\lambda_3 = -\frac{\left(\delta^{2\alpha}C^1A^1+\frac{\beta^\alpha A^1}{N^1}\delta^\alpha C^1\sigma^\alpha\gamma^\alpha r^\alpha-(\delta^\alpha A^1+d^\alpha+\sigma^\alpha+\mu^\alpha+\frac{\beta^\alpha A^1}{N^1}\delta^{2\alpha}A^1)\right)}{\delta^{2\alpha}C^1A^1-1},$$

And the quadratic: $A\lambda^2 + B\lambda + C$.

Where:

$A = 1,$

$B = (\frac{\beta^\alpha A^1}{N^1} + \delta^\alpha C^1 + 2\mu^\alpha - \frac{\beta^\alpha S^1}{N^1}),$

$C = \mu^{2\alpha} + \frac{\beta^\alpha A^1}{N^1}(\delta^\alpha C^1 + \mu^\alpha) - \mu^\alpha(\frac{\beta^\alpha S^1}{N^1} + \delta^\alpha C^1),$

Employing the Routh-Hurwitz criterion, we have that $B > 0$ and $C < 0$, if $R_0$>1.

Then all eigen values will be negative $\left(\left|\arg\lambda_j\right| = \pi > \frac{\sigma\pi}{2}, j = 1,2,\dots,5\right)$,

and hence the system is locally asymptotically stable at $E_1$ if and only if $R_0 > 1$.

**Theorem 4.** The system (1) is globally asymptotically stable at the given positive equilibriums.

**Proof**. Consider the Lyapunov function:

$V(x_1, x_2, x_3, \dots, x_n) = \sum_{i=1}^{n}(x_i(t)x^*)^{\frac{1}{2}}$,

$$V(S(t), A(t), C(t), T(t), R(t)) = (S(t)S^*)^{\frac{1}{2}} + (A(t)S^*)^{\frac{1}{2}} + (C(t)C^*)^{\frac{1}{2}} + (T(t)T^*)^{\frac{1}{2}} + (R(t)R^*)^{\frac{1}{2}}.$$

Applying the linearity of Caputo operator, and the relation $(ab)^{\frac{1}{2}} \leq \frac{(a+b)}{2}$, we get:

$$\begin{aligned}
{}_0^c\mathrm{D}_t^\alpha V(S(t), A(t), C(t), T(t), R(t)) &= {}_0^c\mathrm{D}_t^\alpha\left((S(t)S^*)^{\frac{1}{2}} + (A(t)S^*)^{\frac{1}{2}} + (C(t)C^*)^{\frac{1}{2}} + (T(t)T^*)^{\frac{1}{2}} + (R(t)R^*)^{\frac{1}{2}}\right),\\
&\leq \frac{1}{2}({}_0^c\mathrm{D}_t^\alpha(S(t)+S^*) + {}_0^c\mathrm{D}_t^\alpha(A(t)+A^*) + {}_0^c\mathrm{D}_t^\alpha(C(t)+C^*) + {}_0^c\mathrm{D}_t^\alpha(T(t)+T^*) + {}_0^c\mathrm{D}_t^\alpha(R(t)+R^*)),\\
&= \frac{1}{2}({}_0^c\mathrm{D}_t^\alpha(N(t)+N^*),\\
&= \frac{1}{2}[\Lambda^\alpha - \mu^\alpha(N(t)+N^*) - (d^\alpha(C(t)+C^*))].
\end{aligned}$$

Case 1: Substituting the disease-free equilibrium $E_0(N^0) = \left(\frac{\Lambda^\alpha}{\mu^\alpha}\right)$ we get:

$$\begin{aligned}
{}_0^c\mathrm{D}_t^\alpha V(S(t), A(t), C(t), T(t), R(t)) &\leq \frac{1}{2}[\Lambda^\alpha - \mu^\alpha(N(t)+\frac{\Lambda^{\alpha^*}}{\mu^\alpha}) - (d^\alpha(C(t)+C^*))],\\
&= -\frac{1}{2}[\mu^\alpha\big(N(t)\big) + d^\alpha\big(C(t)\big)],
\end{aligned}$$

$$= -M(x(t)).$$

Where $M\big(x(t)\big) = \frac{1}{2}[\mu^{\alpha}\big(N(t)\big) + d^{\alpha}\big(C(t)\big)]$.

Next;

Case 2: At the endemic equilibrium $E_1(N^1)$, we arrive at:

$$ {}_0^C\mathrm{D}_t^{\alpha} V(S(t), A(t), C(t), T(t), R(t)) \leq \frac{1}{2}[\Lambda^{\alpha} - \mu^{\alpha}(N(t)+N^*) - (d^{\alpha}(C(t)+C^*))],$$

$$\leq -\tfrac{1}{2}[\mu^{\alpha}\big(N(t)\big) + d^{\alpha}\big(C(t)\big),$$

$$= -M(x(t)).$$

Since $N^1 > 0$,

Where $M\big(x(t)\big) = \frac{1}{2}[\mu^{\alpha}\big(N(t)\big) + d^{\alpha}\big(C(t)\big)]$.

Hence by the theorem of global stability of non-autonomous fractional order systems (Delavari, H., et. al 2012), the system (2.1) is globally stable at the equilibriums.

**Numerical Simulations**

In this section, numerical simulations are carried out to support the analytical results using the Matlab code fde12.m, which implements the Predictor Corrector method proposed by (Diethelm, K. and Freed, A.D. 1998; Garrappa, R. 2014). Real-life data and parameters were adopted and calculated from worldometer- real time world statistics, summaries of alcoholic cardiomyopathy and previous studies (Manthey, J. J. 2020; Manthey, J. 2019; Manthey, J. P. 2018; Manthey, J., et al. 2017, Manthey, J. I. 2013; Worldometer-real time wolrd statistics; results and gbd summaries of alcoholic cardiomyopathy level 4, 2019; Reich, O., et al. 2020).

Neural Network time series was integrated and employed to train the model in making predictions by randomizing data using Levenberg Marquardt algorithm and analyzing performance using Mean Square Error (MSE) approach. The Artificial Neural Network employed can be summarized with the formular:

$$Y_i = f\left(\emptyset_i + \sum_{j}^{m} w_{ij}\, X_j\right),$$

Where $\emptyset_i$ is the bias at the hidden layer, $m$ is the number of neurons in the hidden layer, $w_{ij}$ is the connection weight between the hidden layer and the input variable $X_j$, $f$ is the transfer function and $Y_i$ is the output variable.

Figure 3

*ACM dynamics with all compartments when* $R_0 < 1$

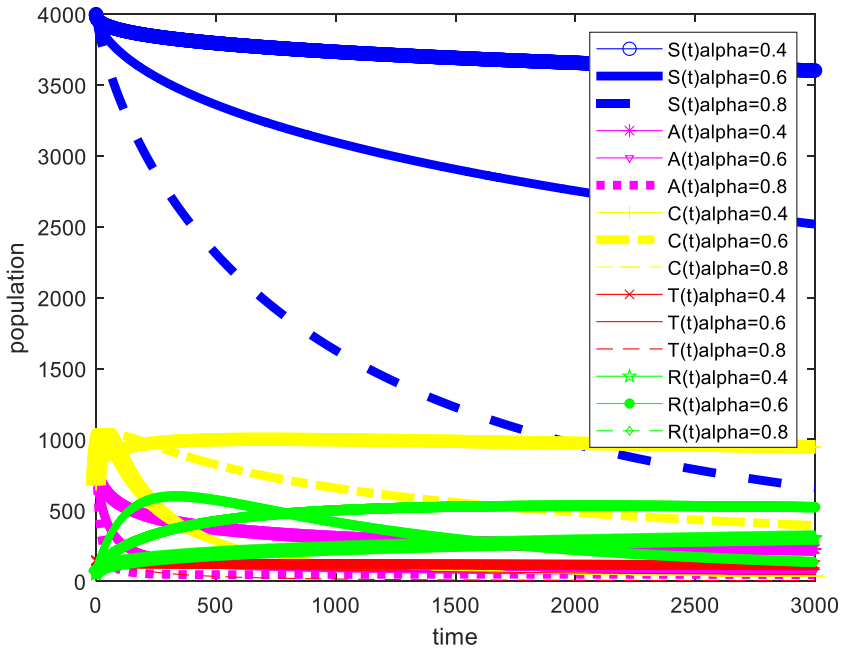



Figure 4

*ACM dynamics with all compartments when* $R_0 > 1$

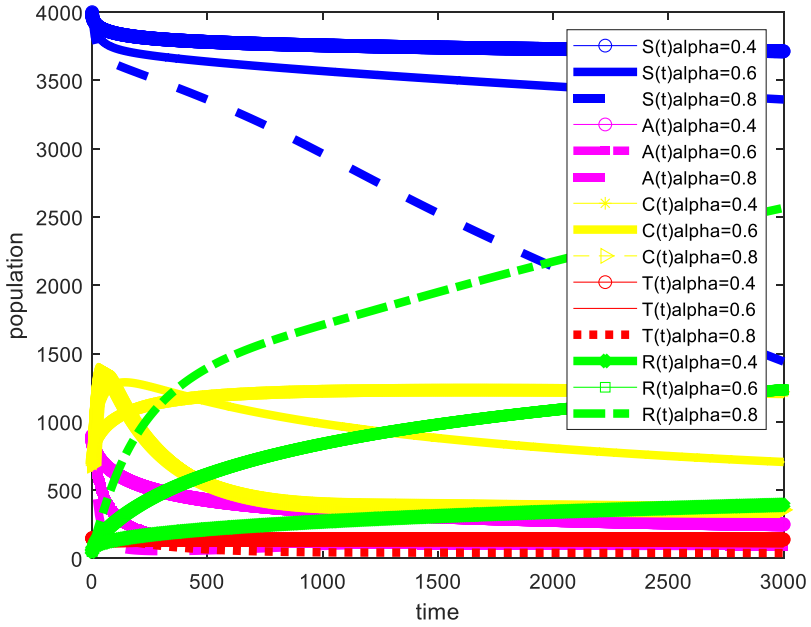


Figure 5

*Comparison of the Susceptible alcoholics against the ACM compartment when* $R_0 < 1$.

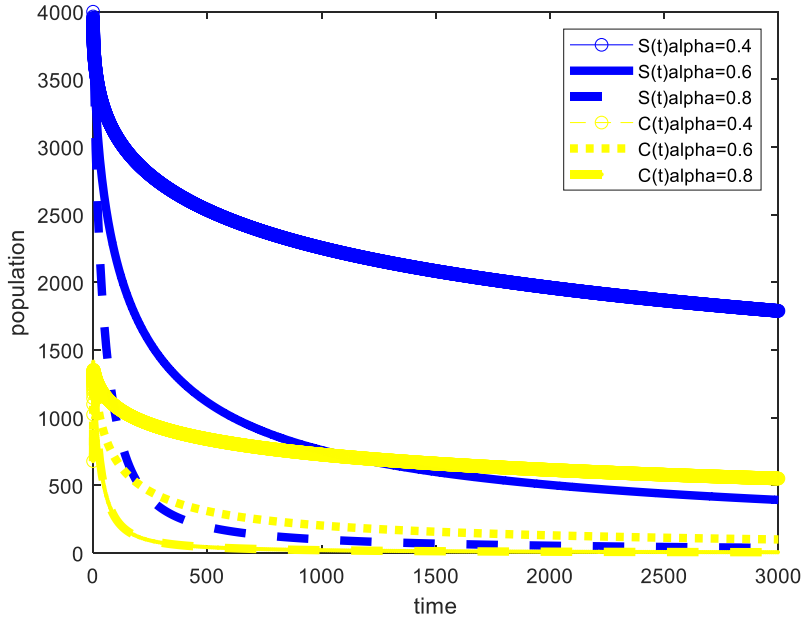



Figure 6

*Comparison of the Susceptible alcoholics against the ACM compartment when* $R_0 > 1$

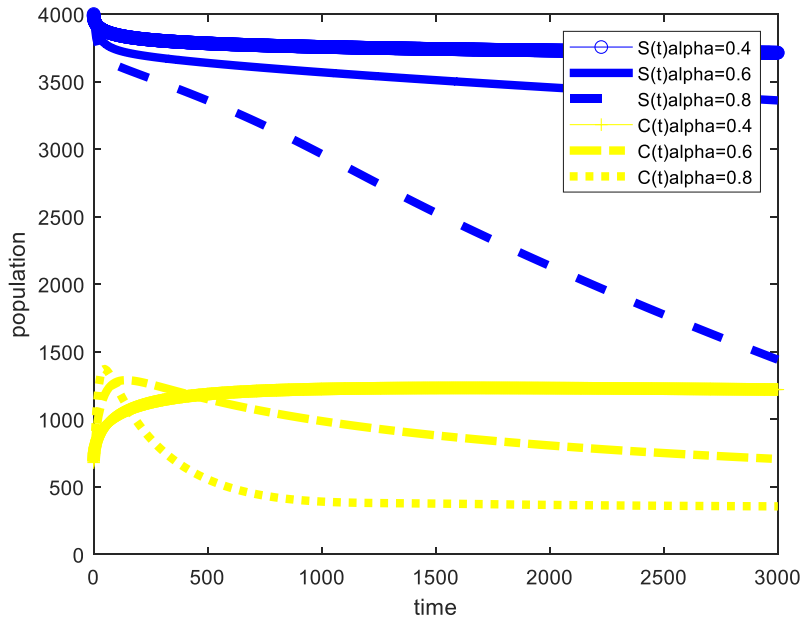


Figure 7

*Dynamics of the Addicted alcoholics against the ACM compartment when* $R_0 < 1$

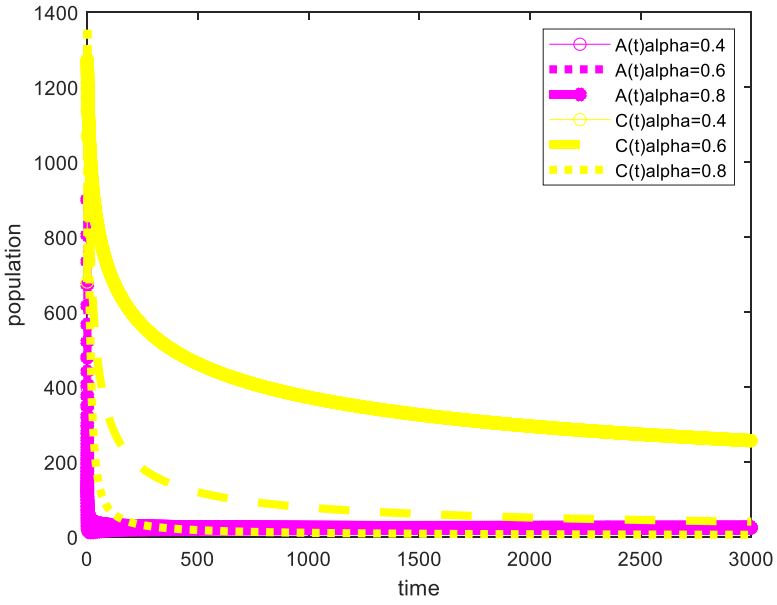



Figure 8

*Dynamics of the Addicted alcoholics against the ACM compartment when* $R_0 > 1$

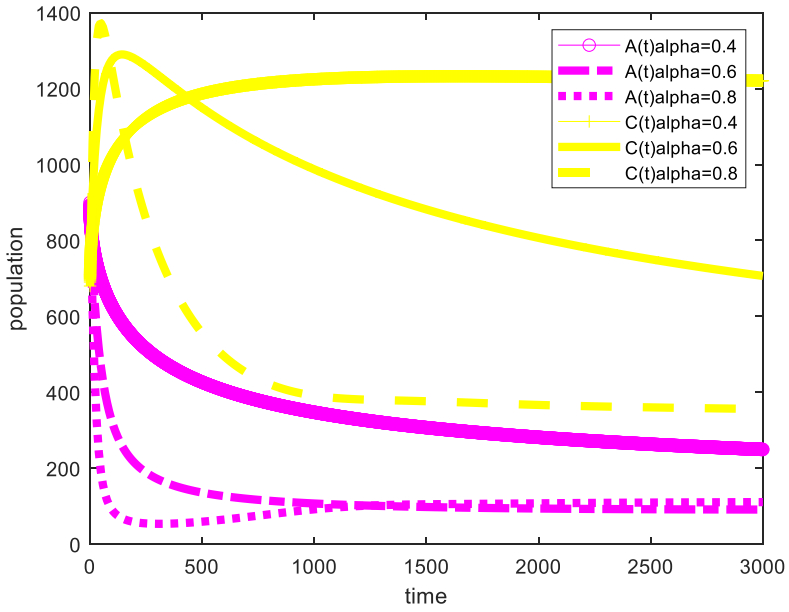


Figure 9

*Comparison of the ACM against the Treatment compartment when* $R_0 < 1$

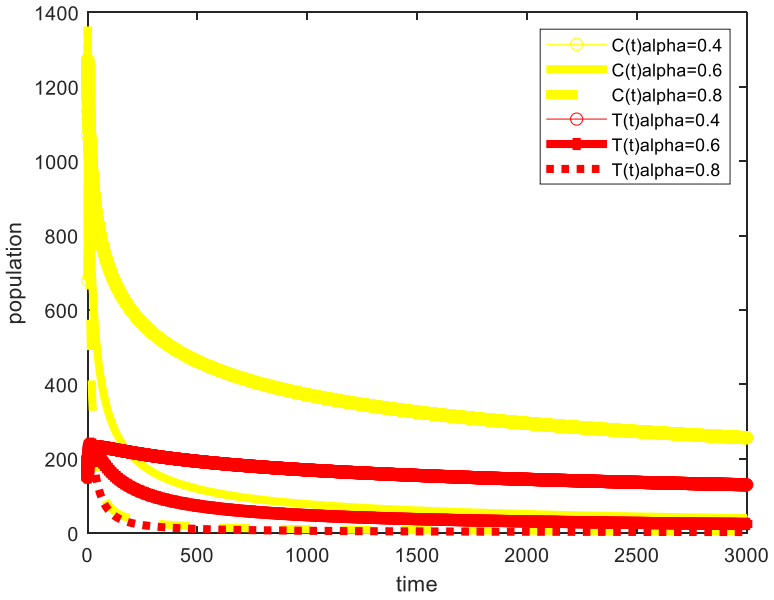



Figure 10

*Comparison of the ACM against the Treatment compartment when* $R_0 > 1$

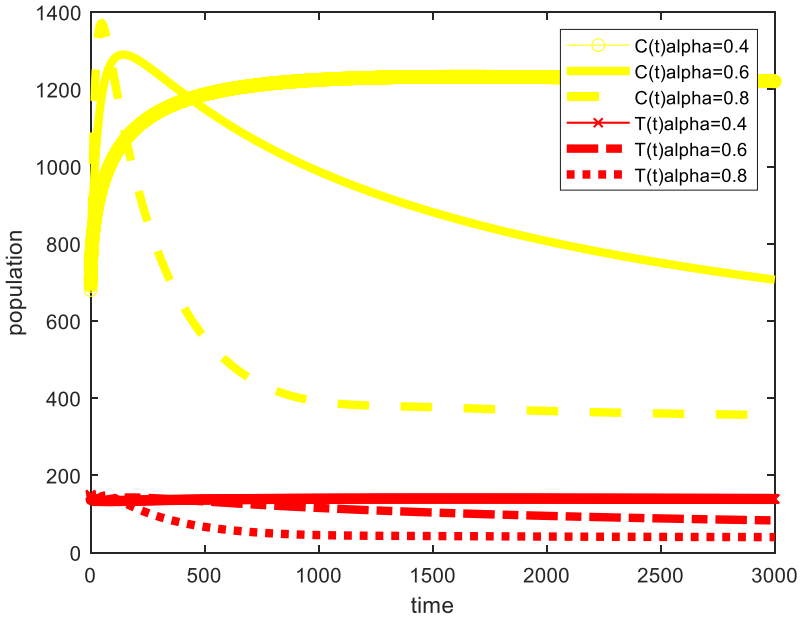


Figure 11

*Comparison of the ACM against the recovered compartment when* $R_0 < 1$.

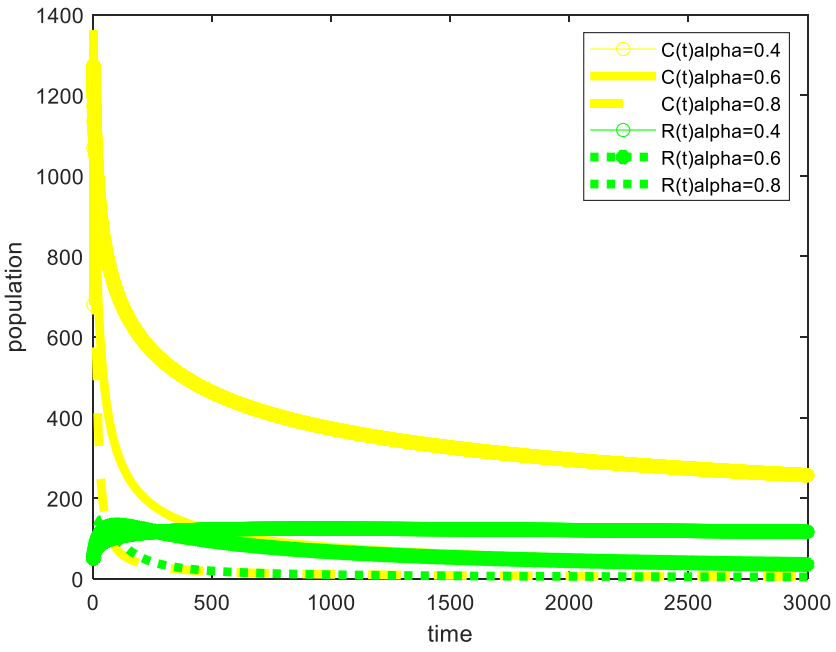



Figure 12

*Comparison of the ACM against the recovered compartment when* $R_0 > 1$

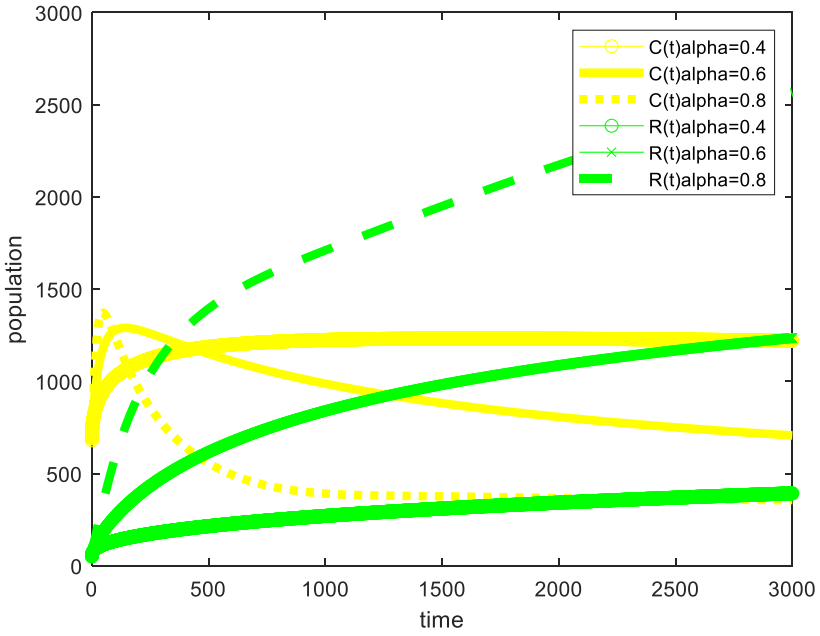


Figure 13

*Neural Network Regression Model-Data Fit*

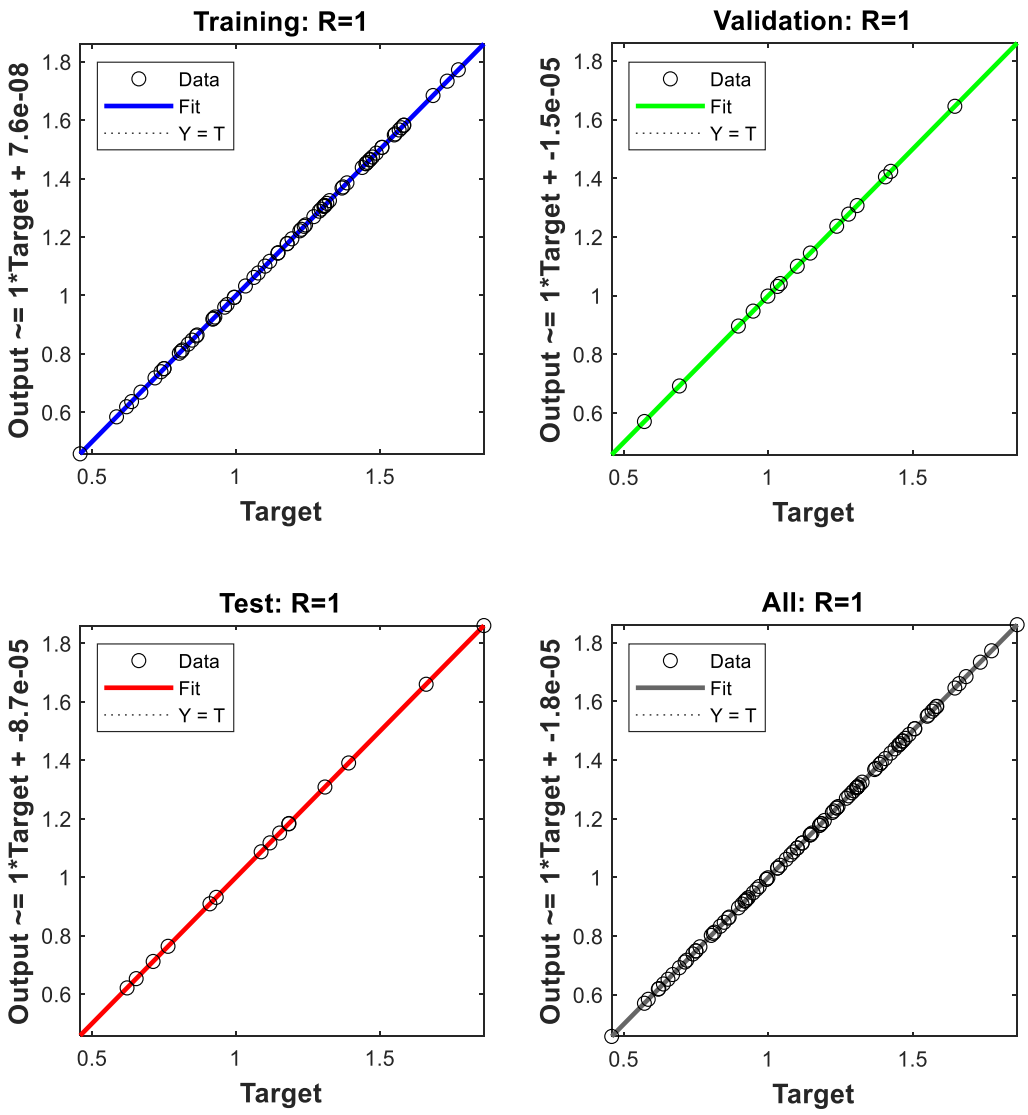


Figure 14

*Response of Output Element*

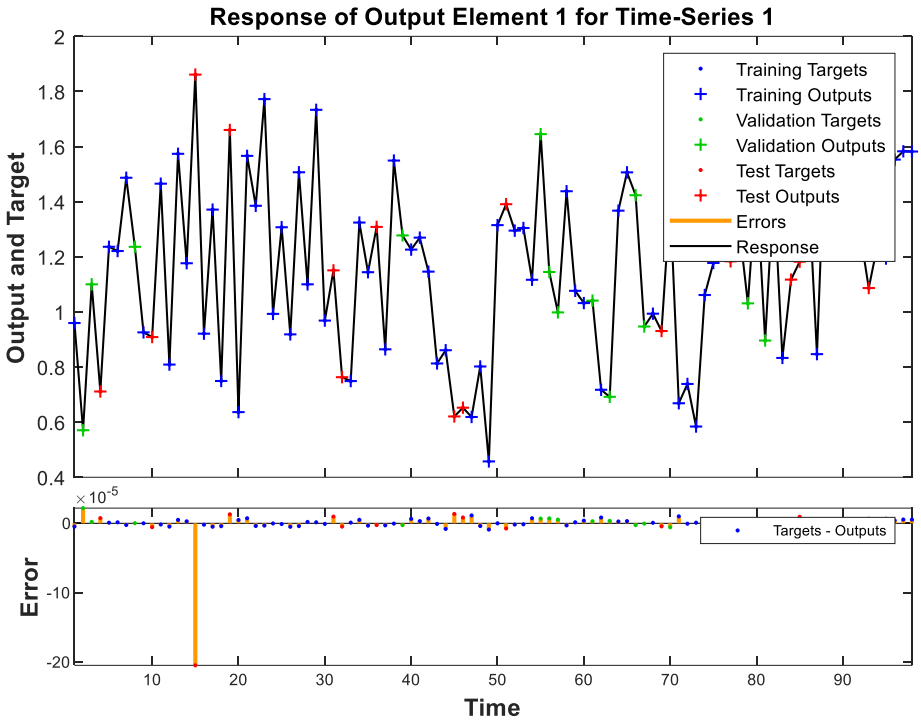



Figure 15

*Neural Network Model Training State*

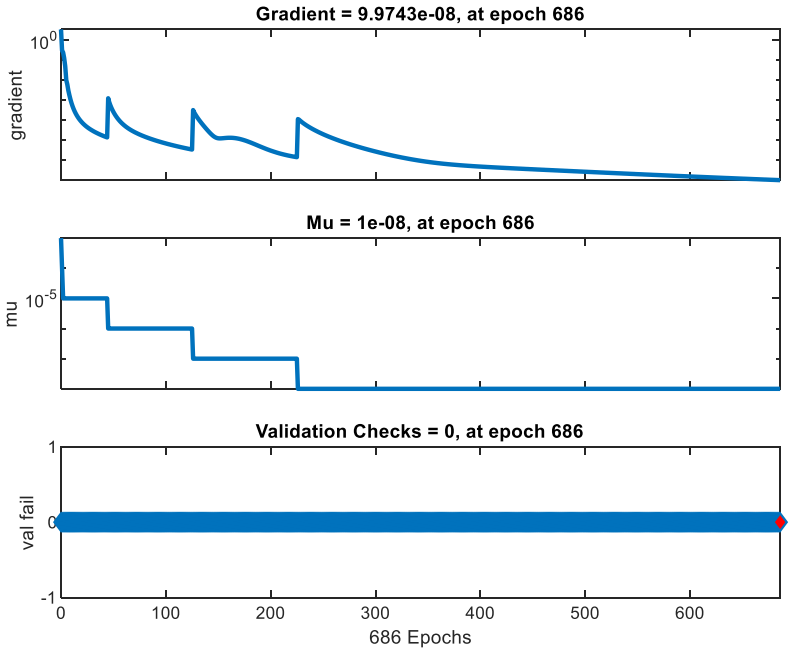


Figure 16

*Performance Validation Neural Network Model*

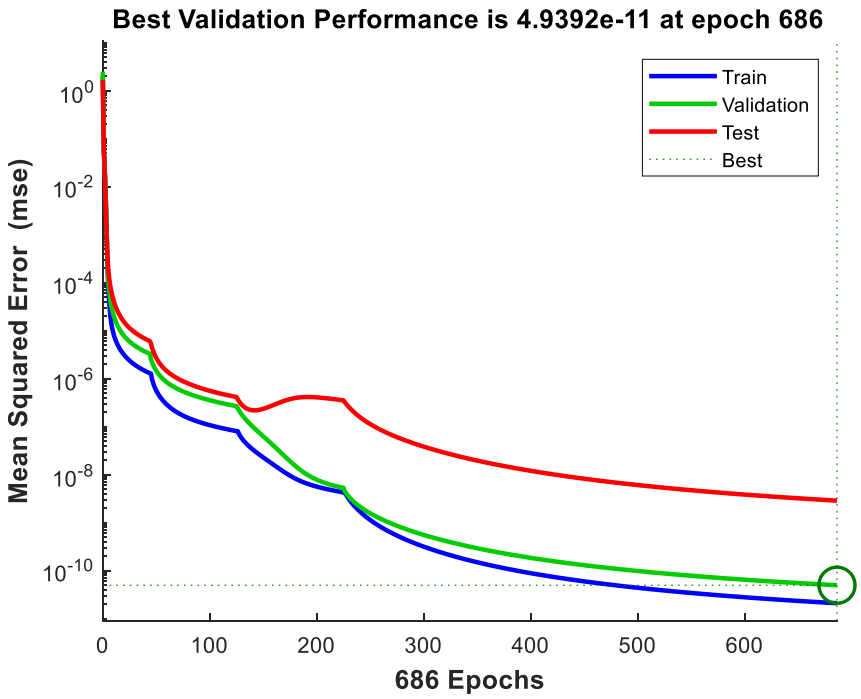
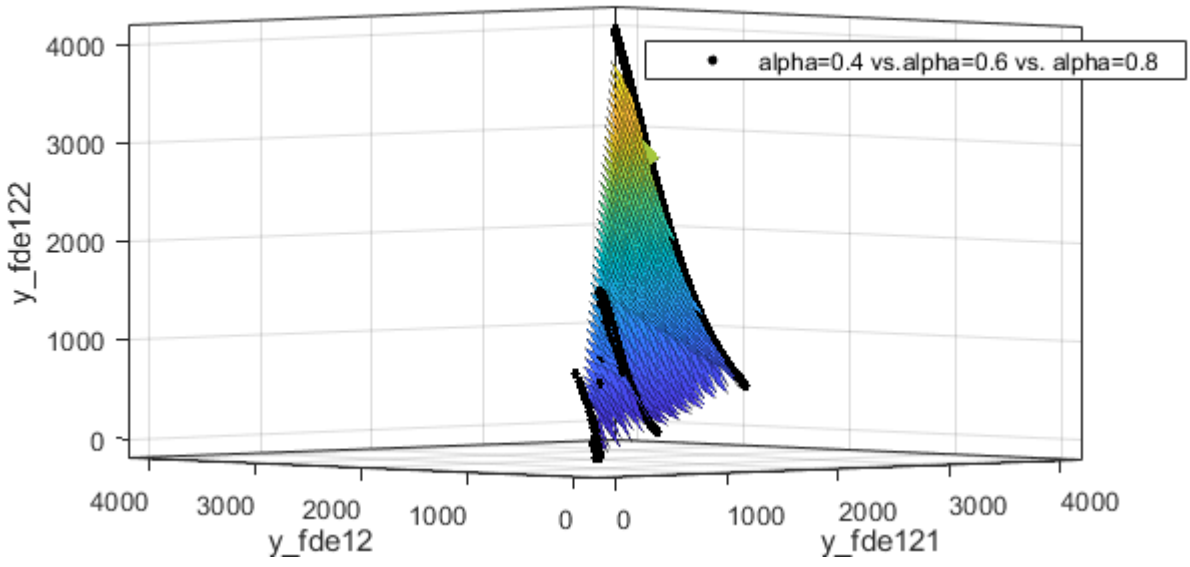



Figure 17

*Comparison of Various Alpha Values in Curve Fitting*



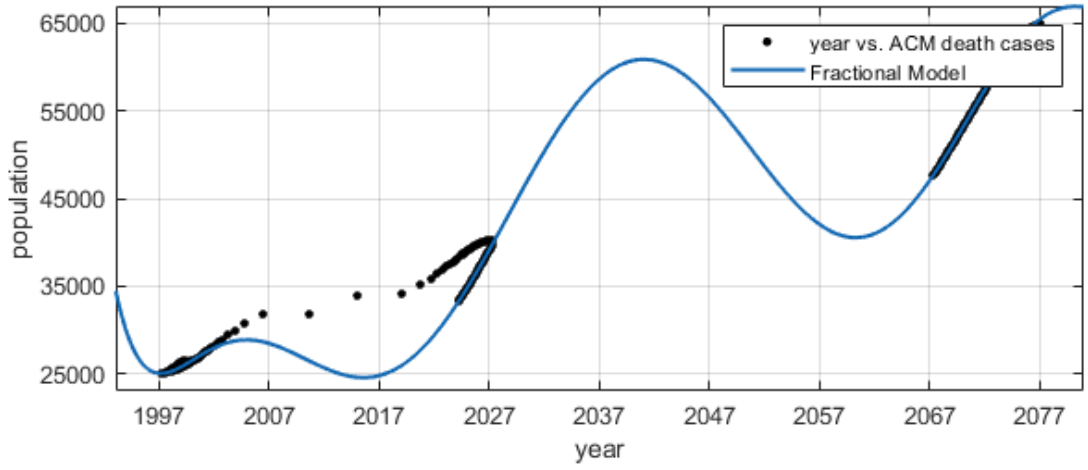
Nearest neighbor interpolant:

$f(x, y)$ = piecewise constant surface computed from p where x is normalized by mean 1051 and std 1400 and where y is normalized by mean 796.6 and std 1088

Coefficients: p = coefficient structure

Goodness of fit: SSE: 4874, R-square: 1.

Figure 18
*Model Prediction*




Linear model Poly9:

$$f(x) = p_1 * x^9 + p_2 * x^8 + p_3 * x^7 + p_4 * x^6 + p_5 * x^5 + p_6 * x^4 + p_7 * x^3 + p_8 * x^2 + p_9 * x + p_{10}$$

Coefficients (with 95% confidence bounds):

$p_1 = -1.057e-28$ $(-4.971e-28, 2.856e-28)$

$p_2 = 7.012e-23$ $(6.31e-23, 7.714e-23)$

$p_3 = -1.199e-18$ $(-1.25e-18, -1.147e-18)$

$p_4 = 8.191e-15$ $(7.995e-15, 8.386e-15)$

$p_5 = -2.8e-11$ $(-2.841e-11, -2.759e-11)$

$p_6 = 4.939e-08$ $(4.893e-08, 4.985e-08)$

$p_7 = -4.151e-05$ $(-4.175e-05, -4.126e-05)$

$p_8 = 0.01326$ $(0.01322, 0.01331)$

$p_9 = -0.2284$ $(-0.2318, -0.225)$

$p_{10} = 1.225$ $(1.159, 1.292)$

Goodness of fit:

SSE: 1.314e+08, R-square: 0.9999, Adjusted R-square: 0.9999, RMSE: 11.7.

**Results**

Upon examining both numerical and analytical solutions, it was found that the behavior of the ACM epidemic depended heavily on the reproduction coefficient $R_0$. Specifically, when $R_0$ is less than one, there is a stable disease-free equilibrium; this leads to a rapid reduction in disease spread as indicated by Figure 4 and Figure 6. Conversely, if the value of $R_0$ exceeds one, then an unstable endemic equilibrium occurs instead leading to increased epidemic thrivency observed in Figure 5 and Figure 7. Figures between (i.e., including) 4 through to (i.e., including) 7 demonstrate that alcohol use greatly increases susceptibility to ACM disease; over time, most individuals from within the addicts' compartment transition into the ACM compartments shown in Figures 6 and Figure 3. Figure between (inclusive of) Figures from--8 & --9 elucidate how treatment effectiveness can speed up recovery among those affected by an ACM population during periods where outbreaks occur. As illustrated via Figures between (i.e., including) Figures --17 & --18 shows how different alpha values affect model goodness via reflected accuracy shown SSE displays at -1 .314 e+08 with R-square displaying rough significance around .9999 indicating fine-curve fitting with commensurate level accuracy preceded by noteworthy correlation demonstrated across training data along testing validating datasets all reflecting maximum accuracy.

With decreasing alpha values reflected across different compartments showcased through Figure--12 sets which observed smoother convergence outpacing corresponding results similarly observed with respect to neural network time series training models featured between inclusive of figures from Figures--13 through to--16 showcasing performance levels besides overall ability according to regression functions juxtaposed against response algorithms following data input from various sources. The statistical evidence suggests a robust relationship among variables. Our predictive model forecasts an approximate spike of sixty million cases relating to ACM-caused mortalities during twenty-forty-one and twenty-forty-two. Notably, countries across the world could witness more than sixty-five thousand such demises by two-thousand seventy-seven based on our analyses.

**Conclusion and Discussion**

The analytical and numerical solutions of the ACM-LMA model provide guidance on how to mitigate an ACM pandemic. It has been observed that reducing the reproduction coefficients to less than one results in a healthy population over time. The numerical simulations support this assertion by revealing specific parameters that can be targeted. As alpha approaches zero, faster convergence is observed, providing insights into the memory effect and the tendency of a compartment size irrespective of time. Also, minimizing the transmission infectivity rate can slow down the disease explosion. Additionally, reducing recruitment rate onto the alcoholic susceptible and improving the rate of recovery can lead to a healthy population. However, failure to control the epidemic may lead to a significant reduction in the population. An ACM pandemic is only feasible if there is a massive recruitment of susceptible individuals over time, a colossal reduction in the recovery rate, and a lack of effective and widely available treatment. Hence, better treatment and low recruitment rate onto the alcoholic susceptible can quickly mitigate the ACM pandemic, while reducing recruitment is the most ideal.

The Neural Network (NN) time series integrated into the fractional model demonstrates expediency by training the model with 70% of data, validating with 15%, and testing with 15%. The ACM-LMA fractional model provides insights into the disease dynamics from previous years into the future. Based on historical data, the model predicts an additional surge in the epidemic in the year 2027 if the dynamics of the epidemic persist at the same rate. It predicts a first peak of over 60,000,000 prevalent cases across North and Central America, North Africa, the Caribbean, Central and Eastern Europe, Australia, and Asia between the years 2040-2042 and a decline below 45,000,000 in the coming years. These predictions may suggest degenerative immunity over time, unpreparedness and unawareness, unresponsive ACM cases, overwhelmed health professionals and limited clinical facilities, and sudden responsiveness and control measures after the surge, respectively.

The ACM-LMA model's foresight reveals the epidemic in circles, like a sine wave with a progressing amplitude, period, and range. A future study for regulatory measures and optimal control is imperative to provide a closer look at the solution and deploy a control strategy to contain the dynamical system by revealing the conditions for optimality and then optimizing the objective function to prevent an explosion of the epidemic. However, the research on the dynamics of the ACM as projected by the

ACM-LMA model indicates that the epidemic may linger in a progressive trend in subsequent years to come as long as heavy alcohol consumption persists.

# CHAPTER IV

## Sensitivity Analysis and Optimization of the ACM-LMA Model

Fractional calculus is a powerful tool for modeling biological and mechanical phenomena due to its advantages of non-locality and memory effects. Many research findings suggest that modeling real-life phenomena with fractional-order derivatives is the most accurate and reliable. Among the types of fractional derivative operators, the Caputo type is more realistic, as it allows for the inclusion of traditional initial boundary conditions.

Optimal control involves determining a control approach to either minimize or maximize the objective function or a specific performance index subject to constraints. The control parameterization technique involves approximating the control function by a linear combination of basic functions, where the coefficients in the linear combination are decision variables to be chosen optimally. Solving optimal control problems for a particular model can reveal insights that may not be easily obtained otherwise and can be used to appraise past policies with respect to the objective function and to suggest improved strategies.

Various optimization approaches and algorithms have been proposed, and their applications are determined by the intended problem to be solved. For instance, the Heap-based optimizer long short-term memory (HBO-LSTM) was proposed to forecast wind power from different wind turbines, and it outperformed other alternative models like particle swam optimization (PSO), although it came third in rank in computational cost using time. The Ebola Optimization Search Algorithm (EOSA) incorporating the SIR model on a system of a first-order differential equation performed better than the Genetic Algorithm (GA) and PSO in terms of scalability, convergence, and sensitivity analysis. However, the Levenberg Marquardt Algorithm (LMA) has been shown to have more advantages over the above-mentioned algorithms.

Alcoholic cardiomyopathy is a leading cause of global mortality, and many authors in literature have employed fractional-order systems to study alcoholism, its related diseases, and dynamics. In this chapter, we consider a fractional-order Alcoholic Cardiomyopathy (ACM) epidemic model of the Caputo type, with the aim of studying the dynamics of the ACM by performing sensitivity analysis to predict

outcomes as parameters vary and to narrow down control measures to this epidemic and slope down the curves. We combine the Nelder-Mean algorithm and Levenberg Marquardt Algorithm (LMA) alongside the predictor-corrector scheme to support the sensitivity analysis of the system in reaching specific optimized parameters and optimally control the disease dynamics. The model divides the world population into five categories: susceptible (S), alcoholics (A), ACM diseased (C), ACM diseased in treatment (T), and recovered population (R). We begin by carrying out sensitivity analysis, followed by optimal control analysis with some numerical simulations, and finally, present our results and conclusions. Our approach is novel and superior, as it combines the advantages of the memory effect, scalability, convergence, and commensurate accuracy with less time computational cost in finding the global optimal solution.

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$$
\begin{aligned}
{}_0^C\mathrm{D}_t^{\alpha} S(t) &= \Lambda^{\alpha} + r^{\alpha} R(t) \; - \frac{\beta^{\alpha} S(t)}{N} A(t) - \mu^{\alpha} S(t), \\
{}_0^C\mathrm{D}_t^{\alpha} A(t) &= \frac{\beta^{\alpha} S(t)}{N} A(t) - \mu^{\alpha} A(t) - \delta^{\alpha} A(t) C(t) \; , \\
{}_0^C\mathrm{D}_t^{\alpha} C(t) &= \delta^{\alpha} A(t) C(t) - \mu^{\alpha} C(t) - \sigma^{\alpha} C(t) - d^{\alpha} C(t), \\
{}_0^C\mathrm{D}_t^{\alpha} T(t) &= \sigma^{\alpha} C(t) - \gamma^{\alpha} \, T(t) - \mu^{\alpha} T(t), \\
{}_0^C\mathrm{D}_t^{\alpha} R(t) &= \gamma^{\alpha} \, T(t) - \mu^{\alpha} R(t) - r^{\alpha} R(t).
\end{aligned}
\tag{4.1}
$$

Where, $S(t) + A(t) + C(t) + T(t) + R(t) = N(\mathrm{t})$.

Observe that the solution to the system (4.1) exists and is unique, as shown in Chapter III, and well detailed in (David Amilo et al. 2022). Hence, the nominal equation for the system (1) has a unique solution and it is close to the exact solution (Guo, Y., et al 2016).

**Sensitivity Analysis**

Given $v = (\Lambda, r, \beta, \mu, \delta, \sigma, d, \gamma)^T$ and $N_s = (S, A, C, T, R)$ and setting $S(t) = x_1(t), A(t) = x_2(t), C(t) = x_3(t), T(t) = x_4(t)$ and $R(t) = x_5(t)$.

The sensitivity function is given by:

$$W = \frac{\partial x}{\partial v} = \begin{bmatrix} \frac{\partial S(t)}{\partial \Lambda} & \frac{\partial S(t)}{\partial \mathrm{r}} & \frac{\partial S(t)}{\partial \beta} & \frac{\partial S(t)}{\partial \mu} & \frac{\partial S(t)}{\partial \delta} & \frac{\partial S(t)}{\partial \sigma} & \frac{\partial S(t)}{\partial d} & \frac{\partial S(t)}{\partial \gamma} \\ \frac{\partial A(t)}{\partial \Lambda} & \frac{\partial A(t)}{\partial \mathrm{r}} & \frac{\partial A(t)}{\partial \beta} & \frac{\partial A(t)}{\partial \mu} & \frac{\partial A(t)}{\partial \delta} & \frac{\partial A(t)}{\partial \sigma} & \frac{\partial A(t)}{\partial d} & \frac{\partial A(t)}{\partial \gamma} \\ \frac{\partial C(t)}{\partial \Lambda} & \frac{\partial C(t)}{\partial \mathrm{r}} & \frac{\partial C(t)}{\partial \beta} & \frac{\partial C(t)}{\partial \mu} & \frac{\partial C(t)}{\partial \delta} & \frac{\partial C(t)}{\partial \sigma} & \frac{\partial C(t)}{\partial d} & \frac{\partial C(t)}{\partial \gamma} \\ \frac{\partial T(t)}{\partial \Lambda} & \frac{\partial T(t)}{\partial \mathrm{r}} & \frac{\partial T(t)}{\partial \beta} & \frac{\partial T(t)}{\partial \mu} & \frac{\partial T(t)}{\partial \delta} & \frac{\partial T(t)}{\partial \sigma} & \frac{\partial T(t)}{\partial d} & \frac{\partial T(t)}{\partial \gamma} \\ \frac{\partial R(t)}{\partial \Lambda} & \frac{\partial R(t)}{\partial \mathrm{r}} & \frac{\partial R(t)}{\partial \beta} & \frac{\partial R(t)}{\partial \mu} & \frac{\partial R(t)}{\partial \delta} & \frac{\partial R(t)}{\partial \sigma} & \frac{\partial R(t)}{\partial d} & \frac{\partial R(t)}{\partial \gamma} \end{bmatrix},$$

$$\triangleq \begin{bmatrix} x_6(t) & x_8(t) & x_{10}(t) & x_{12}(t) & x_{14}(t) & x_{16}(t) & x_{18}(t) & x_{20}(t) \\ x_7(t) & x_9(t) & x_{11}(t) & x_{13}(t) & x_{15}(t) & x_{17}(t) & x_{19}(t) & x_{21}(t) \\ x_{22}(t) & x_{23}(t) & x_{24}(t) & x_{25}(t) & x_{26}(t) & x_{27}(t) & x_{28}(t) & x_{29}(t) \\ x_{30}(t) & x_{32}(t) & x_{34}(t) & x_{36}(t) & x_{38}(t) & x_{40}(t) & x_{42}(t) & x_{44}(t) \\ x_{31}(t) & x_{33}(t) & x_{35}(t) & x_{37}(t) & x_{39}(t) & x_{41}(t) & x_{43}(t) & x_{45}(t) \end{bmatrix}$$

$$P(v) = \frac{\partial N_s}{\partial x} =$$

$$\begin{pmatrix} -\mu^\alpha & -\beta^\alpha & 0 & 0 & r^\alpha \\ 0 & -\beta^\alpha - \mu^\alpha - \delta c(t) & -\delta A(t) & 0 & 0 \\ 0 & \delta C(t) & \delta A(t) - (\mu^\alpha + \sigma^\alpha + d^\alpha) & 0 & 0 \\ 0 & 0 & \sigma^\alpha & -(\gamma^\alpha + \mu^\alpha) & 0 \\ 0 & 0 & 0 & \gamma^\alpha & -(\mu^\alpha + r^\alpha) \end{pmatrix},$$

$$Q(v) = \frac{\partial N_s}{\partial v} = \begin{bmatrix} 1 & R(t) & -A(t) & -S(t) & 0 & 0 & 0 & 0 \\ 0 & 0 & A(t) & -A(t) & -A(t)C(t) & 0 & 0 & 0 \\ 0 & 0 & 0 & -C(t) & A(t)C(t) & -C(t) & -C(t) & 0 \\ 0 & 0 & 0 & -T(t) & 0 & C(t) & 0 & -T(t) \\ 0 & -R(t) & 0 & -R(t) & 0 & 0 & 0 & T(t) \end{bmatrix},$$

At the nominal values $v_0 = (0.1, 0.01, 0.02, 0.03, 0.01, 0.01, 0.01, 0.03)^T, \alpha = 0.8$

The sensitivity equation is then given by:

$${}_0^C\mathrm{D}_t^{0.8} W = P(v_0)W + Q(v_0)$$

$$= \begin{pmatrix} -0.03 & -0.02 & 0 & 0 & 0.01 \\ 0 & -0.02 & -0.01x_2(t) & 0 & 0 \\ 0 & 0.01x_3(t) & 0.01x_2(t) - 0.05 & 0 & 0 \\ 0 & 0 & 0.01 & -0.06 & 0 \\ 0 & 0 & 0 & 0.03 & -0.04 \end{pmatrix} \begin{bmatrix} x_6(t) & x_8(t) & x_{10}(t) & x_{12}(t) & x_{14}(t) & x_{16}(t) & x_{18}(t) & x_{20}(t) \\ x_7(t) & x_9(t) & x_{11}(t) & x_{13}(t) & x_{15}(t) & x_{17}(t) & x_{19}(t) & x_{21}(t) \\ x_{22}(t) & x_{23}(t) & x_{24}(t) & x_{25}(t) & x_{26}(t) & x_{27}(t) & x_{28}(t) & x_{29}(t) \\ x_{30}(t) & x_{32}(t) & x_{34}(t) & x_{36}(t) & x_{38}(t) & x_{40}(t) & x_{42}(t) & x_{44}(t) \\ x_{31}(t) & x_{33}(t) & x_{35}(t) & x_{37}(t) & x_{39}(t) & x_{41}(t) & x_{43}(t) & x_{45}(t) \end{bmatrix}$$

$$+ \begin{bmatrix} 1 & x_5(t) & -x_2(t) & -x_1(t) & 0 & 0 & 0 & 0 \\ 0 & 0 & x_2(t) & -x_2(t) & -x_2(t)x_3(t) & 0 & 0 & 0 \\ 0 & 0 & 0 & -x_3(t) & x_2(t)x_3(t) & -x_3(t) & -x_3(t) & 0 \\ 0 & 0 & 0 & -x_4(t) & 0 & x_3(t) & 0 & -x_4(t) \\ 0 & -x_5(t) & 0 & -x_5(t) & 0 & 0 & 0 & x_4(t) \end{bmatrix} \quad (3.2)$$

Combining equation (ii) and (iii), we get:

$$\begin{cases} {}_0^C\mathrm{D}_t^{0.8} x_1(t) = 0.1 + 0.01x_6(t) - 0.02x_2(t) - 0.03x_1(t) & x_1(0) = x_{10} \\ {}_0^C\mathrm{D}_t^{0.8} x_2(t) = -0.01x_2(t) - 0.01x_2(t)x_3(t) & x_2(0) = x_{20} \\ {}_0^C\mathrm{D}_t^{0.8} x_3(t) = 0.01x_2(t)x_3(t) - 0.05x_3(t) & x_3(0) = x_{30} \\ {}_0^C\mathrm{D}_t^{0.8} x_4(t) = 0.01x_3(t) - 0.06x_4(t) & x_4(0) = x_{40} \\ {}_0^C\mathrm{D}_t^{0.8} x_5(t) = 0.03x_4(t) - 0.04x_5(t) & x_5(0) = x_{50} \\ {}_0^C\mathrm{D}_t^{0.8} x_6(t) = -0.03x_6(t) - 0.02x_7(t) + 0.01x_{31}(t) + 1 & x_6(0) = 0 \\ {}_0^C\mathrm{D}_t^{0.8} x_7(t) = -0.03x_7(t) - 0.02x_2(t)x_{22}(t) & x_7(0) = 0 \\ {}_0^C\mathrm{D}_t^{0.8} x_8(t) = -0.03x_8(t) - 0.02x_9(t) + 0.01x_{33}(t) & x_8(0) = 0 \\ \vdots & \\ {}_0^C\mathrm{D}_t^{0.8} x_{45}(t) = 0.03x_{44}(t) - 0.04x_{45}(t) & x_{45}(0) = 0 \end{cases}$$

Figure 19.

*Sensitivity of $x_1(t)$ to $x_5(t)$ on parameters*

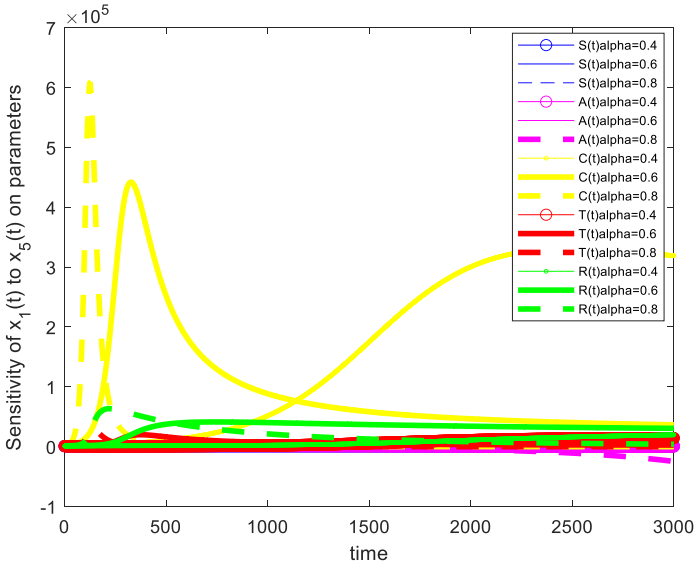
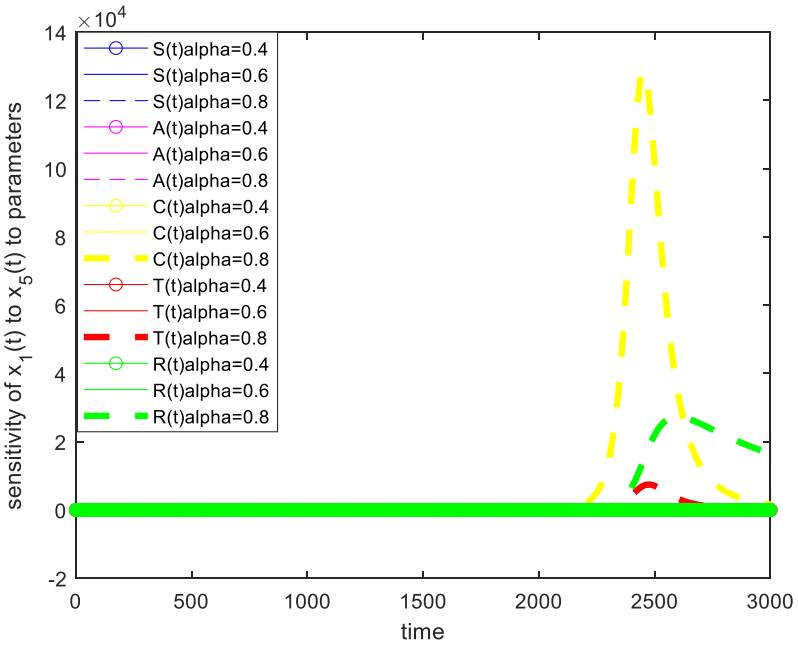


Figure 20.

*Sensitivity of $x_1(t)$ to $x_5(t)$ on parameters*




**Optimal Control Analysis**

In view of optimality for the system (1), we would employ two control variables: creating awareness and sensitization to reduce the propaganda of susceptible contacting with alcohol users and abusers; "infection" $u_1(t)$, and reduction of alcohol consumption $u_2(t)$.

The objective function is given by:

$$J(u_1, u_2) = min \int_0^L [G_1 S(t) + G_2 A(t) + G_3 C(t) + \frac{1}{2}(Z_1 {u_1}^2(t) + Z_2 {u_2}^2(t))]dt,$$

Subject to the state system

$$\begin{aligned}
{}_0^C\mathrm{D}_t^\alpha S(t) &= \Lambda^\alpha + r^\alpha R(t) - \frac{\beta^\alpha S(t)}{N} A(t) - (\mu^\alpha + u_1(t))S(t), \\
{}_0^C\mathrm{D}_t^\alpha A(t) &= \frac{\beta^\alpha S(t)}{N} A(t) - (\mu^\alpha + u_2(t))A(t) - (\delta^\alpha + u_2(t))A(t)C(t), \\
{}_0^C\mathrm{D}_t^\alpha C(t) &= (\delta^\alpha + u_2(t))A(t)C(t) - (\mu^\alpha + \sigma^\alpha + d^\alpha + u_2(t))C(t), \\
{}_0^C\mathrm{D}_t^\alpha T(t) &= (\sigma^\alpha + u_2(t))C(t) - \gamma^\alpha T(t) - \mu^\alpha T(t), \\
{}_0^C\mathrm{D}_t^\alpha R(t) &= \gamma^\alpha T(t) - \mu^\alpha R(t) - r^\alpha R(t).
\end{aligned} \tag{3.3}$$

Such that $S(t) \geq 0, A(t) \geq 0, C(t) \geq 0, T(t) \geq 0, R(t) \geq 0,$

where $G_1, G_2, G_3$ are relative weights and $Z_1$ and $Z_2$ measure the associated cost of creating awareness and sensitization and reduction of alcohol consumption respectively.

Our aim is to find the control function such that

$$J(u_1^*, u_2^*) = \min \{J(u_1, u_2), u_1, u_2 \in U\},$$

Subject to the state system, where the control set is defined as

$$U = \{(u_1, u_2): u_i(t), 0 \leq u_i(t) \leq 1, i = 1,2\},$$

Employing the Pontryagin's maximum principle to ascertain the condition for optimality, we get the following Hamiltonian $H$ with respect to control variables:

$$\begin{aligned} H = {} & G_1 S(t) + G_2 A(t) + G_3 C(t) + \frac{1}{2}\left(Z_1 {u_1}^2(t) + Z_2 {u_2}^2(t)\right) + \lambda_1[\Lambda^\alpha + r^\alpha R(t) - \\ & \frac{\beta^\alpha S(t)}{N} A(t) - (\mu^\alpha + u_1(t))S(t)] + \lambda_2\left[\frac{\beta^\alpha S(t)}{N} A(t) - (\mu^\alpha + u_2(t))A(t) - (\delta^\alpha + \right. \\ & \left. u_2(t))A(t)C(t)\right] + \lambda_3[(\delta^\alpha + u_2(t))A(t)C(t) - (\mu^\alpha + \sigma^\alpha + d^\alpha + u_2(t))C(t)] + \\ & \lambda_4[(\sigma^\alpha + u_2(t))C(t) - \gamma^\alpha T(t) - \mu^\alpha T(t)] + \lambda_5[\gamma^\alpha T(t) - \mu^\alpha R(t) - r^\alpha R(t)], \end{aligned} \tag{3.4}$$

where $\lambda_1(t), \lambda_2(t), \lambda_3(t), \lambda_4(t)$ and $\lambda_5(t)$ are made up of the adjoint variables.

The solution of the resulting system is determined by taking the partial derivatives of Hamiltonian in (v) with respect to the associated variables. We obtain the necessary optimality conditions for the system of equation:

$$\begin{cases} {}_0^c\mathrm{D}_t^\alpha S(t) = \dfrac{\partial H}{\partial \lambda_s}(t), & {}_0^c\mathrm{D}_t^\alpha A(t) = \dfrac{\partial H}{\partial \lambda_A}(t), \\ {}_0^c\mathrm{D}_t^\alpha C(t) = \dfrac{\partial H}{\partial \lambda_c}(t), & {}_0^c\mathrm{D}_t^\alpha T(t) = \dfrac{\partial H}{\partial \lambda_T}(t), \\ & {}_0^c\mathrm{D}_t^\alpha R(t) = \dfrac{\partial H}{\partial \lambda_R}(t), \end{cases} \tag{3.5}$$

$$\begin{cases} {}_0^c\mathrm{D}_L^\alpha \lambda_S(t) = -\dfrac{\partial H}{\partial S}(t), & {}_0^c\mathrm{D}_L^\alpha \lambda_A(t) = -\dfrac{\partial H}{\partial A}(t), \\ {}_0^c\mathrm{D}_L^\alpha \lambda_C(t) = -\dfrac{\partial H}{\partial C}(t), & {}_0^c\mathrm{D}_L^\alpha \lambda_T(t) = -\dfrac{\partial H}{\partial T}(t), \\ {}_0^c\mathrm{D}_L^\alpha \lambda_R(t) = -\dfrac{\partial H}{\partial R}(t), & \dfrac{\partial H}{\partial u}(t) = 0, \end{cases} \tag{3.6}$$

**Theorem 5.** Given the optimal controls, $(u_1{}^*, u_2{}^*)$ is the solution of the above control system, and we can find the adjoint variables $\lambda_i(t)$ for $i = S, A, C, T, R$ satisfying:

$$ {}_0^C\mathrm{D}_L^\alpha \lambda_i(t) = \frac{\partial H}{\partial i}. $$

Where $\lambda_i(L)$=0, for $i = S, A, C, T, R$.

then the optimal control variables $u_1{}^*(t), u_2{}^*(t)$ is given as:

$$ u_1{}^*(t) = \max\left\{min\left\{\frac{\lambda_S(t)S^*(t)}{Z_1}, 1\right\}, 0\right\}, $$

$$ u_2{}^*(t) = \max\left\{min\left\{\frac{X}{Z_2}, 1\right\}, 0\right\}. $$

Where,

$$ X = \lambda_A(t)A^*(t) - A^*(t)C^*(t)[1 + \lambda_C(t)] + C^*(t)[1 - \lambda_T(t)]. $$

**Proof:** Evaluating the adjoint system:

$$ {}_0^C\mathrm{D}_L^\alpha \lambda_S(t) = -G_1 + \lambda_S(t)(\mu^\alpha + u_1(t)), $$

$$ {}_0^C\mathrm{D}_L^\alpha \lambda_A(t) = -G_2 + \lambda_S(t)\left[\frac{\beta^\alpha S}{N}\right] - \lambda_A(t)\left[\frac{\beta^\alpha S}{N} - (\mu^\alpha + u_2(t)) - (\delta^\alpha + u_2(t))C(t)\right] - \lambda_C(t)(\delta^\alpha + u_2(t))C(t), $$

$$ {}_0^C\mathrm{D}_L^\alpha \lambda_C(t) = -G_3 + \lambda_A(t)[(\delta^\alpha + u_2(t))A(t)] - \lambda_C(t)[(\delta^\alpha + u_2(t))A(t)] + (\mu^\alpha + \sigma^\alpha + d^\alpha + u_2(t)) - \lambda_T(t)[(\sigma^\alpha + u_2(t))A(t)], $$

$$ {}_0^C\mathrm{D}_L^\alpha \lambda_T(t) = \lambda_T(t)[\gamma^\alpha + \mu^\alpha] - \lambda_R(t)\gamma^\alpha, $$

$$ {}_0^C\mathrm{D}_L^\alpha \lambda_R(t) = -\lambda_S(t)[r^\alpha] - \lambda_R(t)[\gamma^\alpha + \mu^\alpha], $$

Next, we apply $\frac{\partial H}{\partial u_i}(t) = 0$,

$$ \frac{\partial H}{\partial u_1}(t) = u_1 Z_1 - \lambda_S(t)S(t), $$

$$ \frac{\partial H}{\partial u_1}(t) = u_2 Z_2 - \lambda_A(t)A(t) - A(t)C(t) + \lambda_C(t)A(t)C(t) - C(t) + \lambda_T(t)C(t). $$

So, $u_1 = \frac{\lambda_S(t)S(t)}{Z_1}$, $u_2 = \frac{\lambda_A(t)A^*(t) - A^*(t)C^*(t)[1+\lambda_C(t)] + C^*(t)[1-\lambda_T(t)]}{Z_2}$.

Hence,

$$u_1{}^*(t) = \max\left\{min\left\{\frac{\lambda_S(t)S^*(t)}{Z_1}, 1\right\}, 0\right\},$$

$$u_2{}^*(t) = \max\left\{min\left\{\frac{X}{Z_2}, 1\right\}, 0\right\},$$

Proof complete.

**FOCP Scheme**

We incorporate the new scheme motivated by the fundamental theorem of calculus well detailed in (Khan, A., et. al. (2021) alongside FOMCON Toolbox and fde12.m in MATLAB, for modeling fractional control problems as it implements the Predictor Corrector method proposed by (Aleksei Tepljakov 2022) and (Diethelm, K. and Freed, A.D. 1998; Garrappa, R. 2014) respectively.

Figure 21.

*Optimization of sensitivity analysis on system $x_i(t)$*

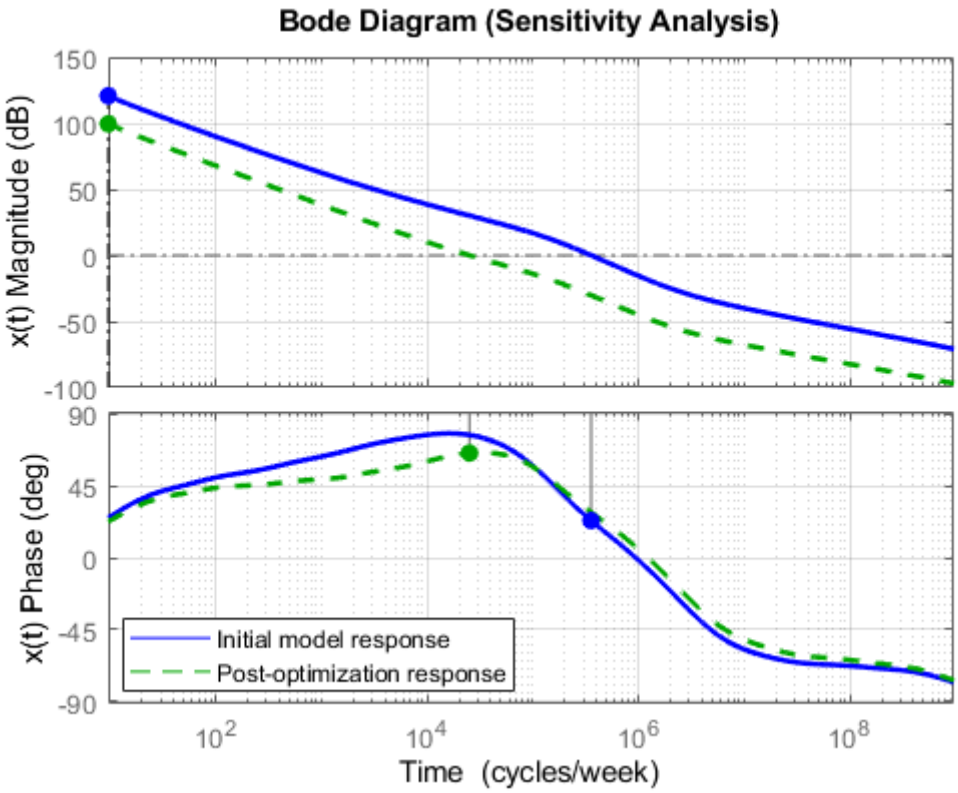


Figure 22.

*Optimization control of ACM compartment*

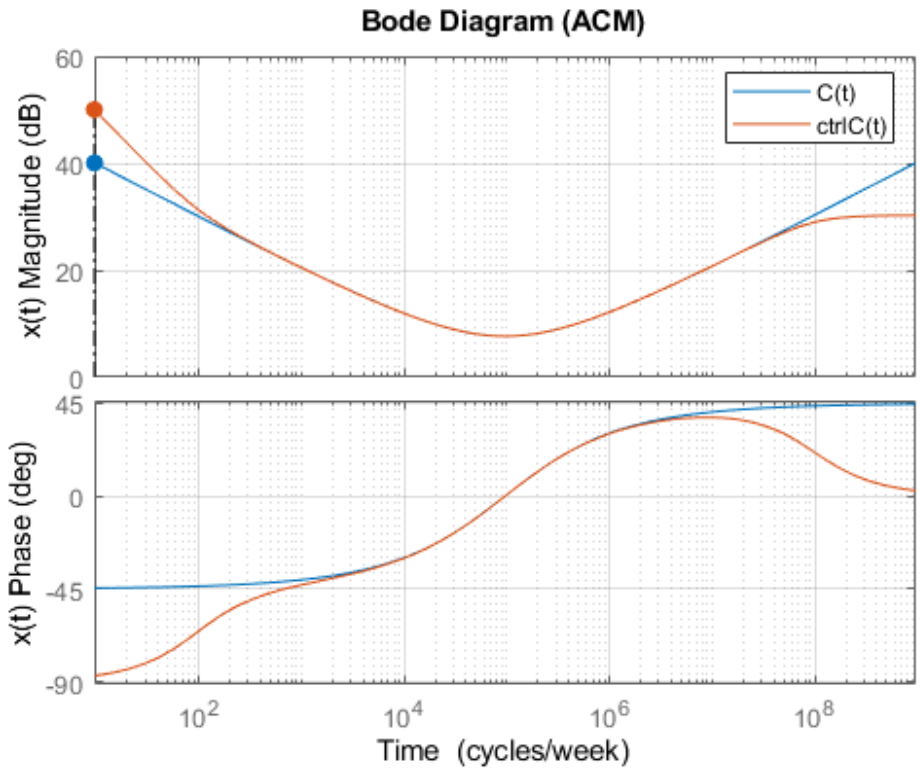



Figure 23.

*Progress information and control parameters of* $x_i(t)$

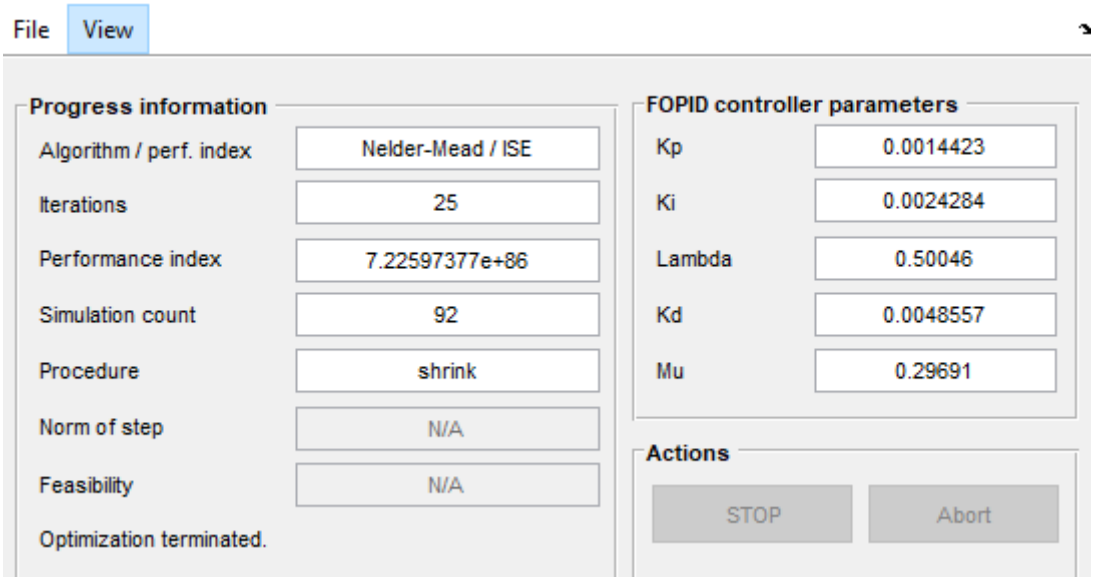


Figure 24

*$S(t)$ compartment with and without control*

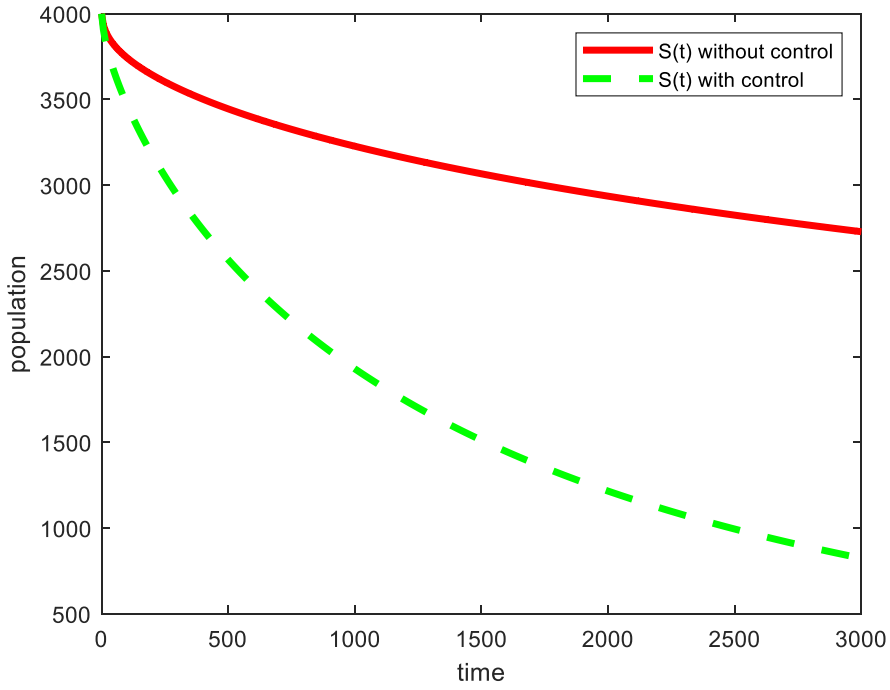



Figure 25.

*$A(t)$ compartment with and without control*

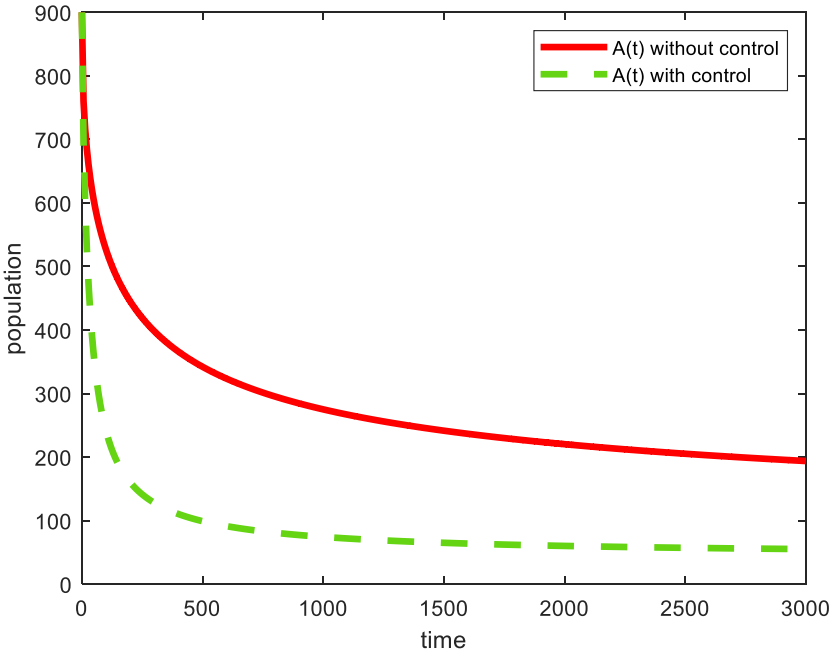


Figure 26.

*$C(t)$ compartment with and without control*

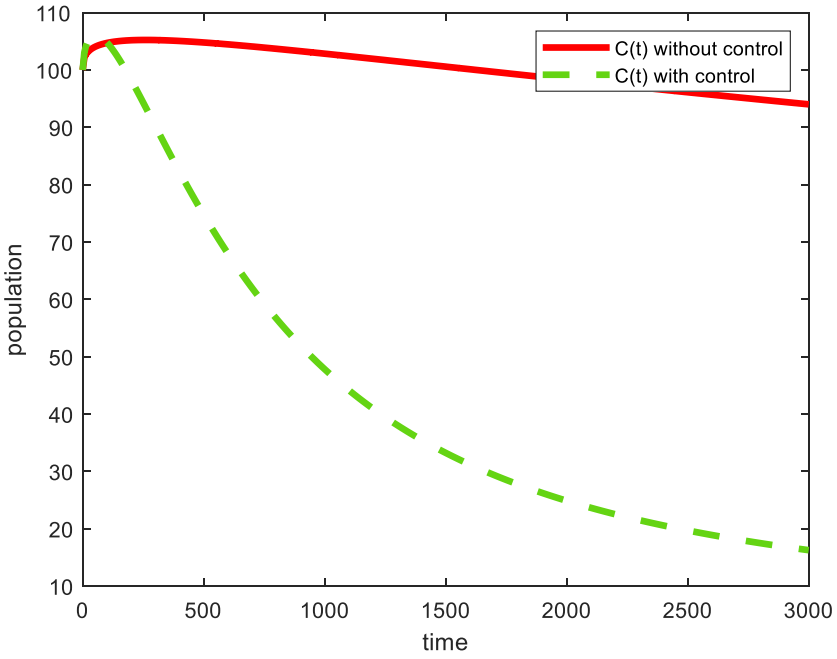



Figure 27.

*$R(t)$ compartment with and without control*

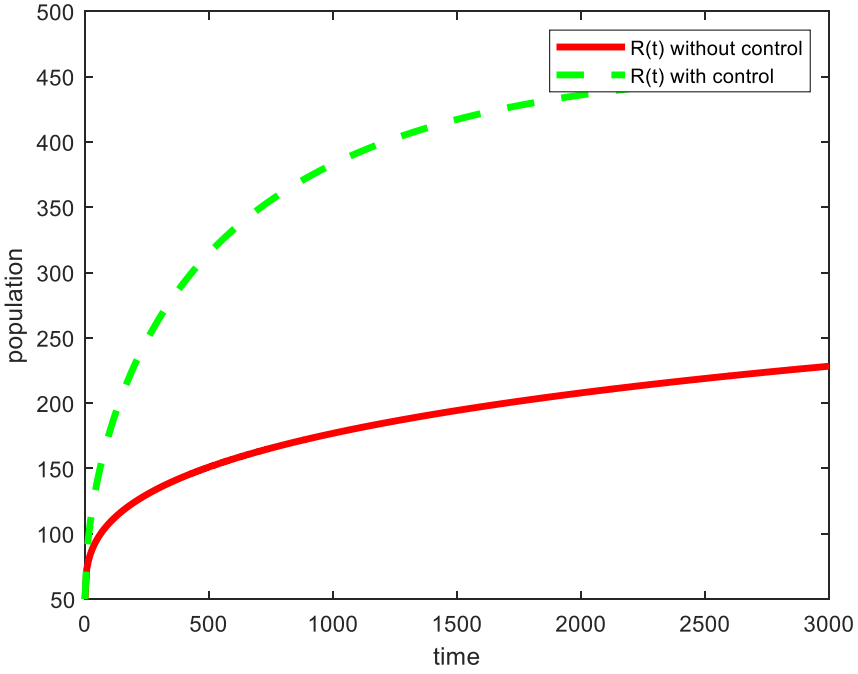


Figure 28.

*Control analysis*

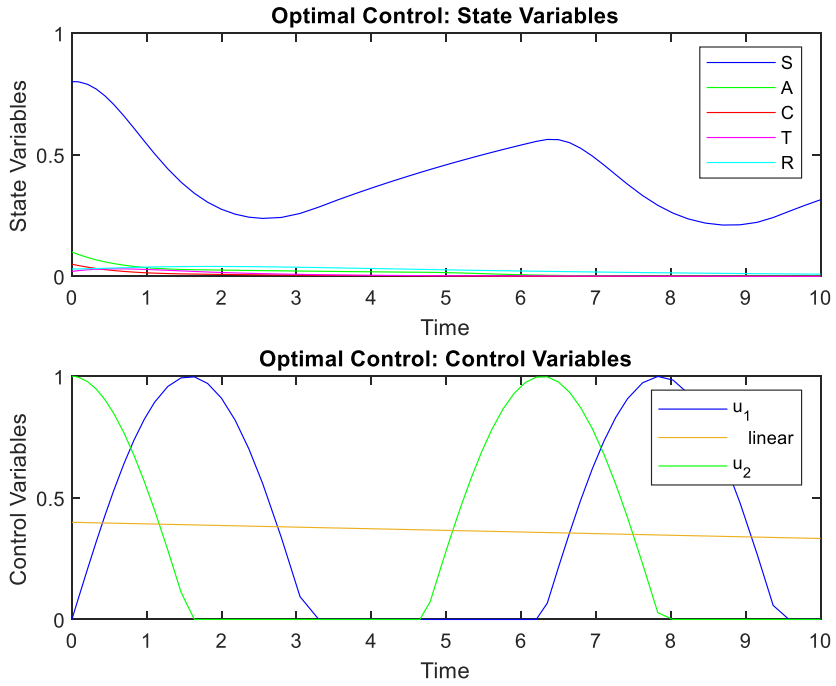



Figure 29.

*Phase space plot of A(t), $u_1$ (t) & J*

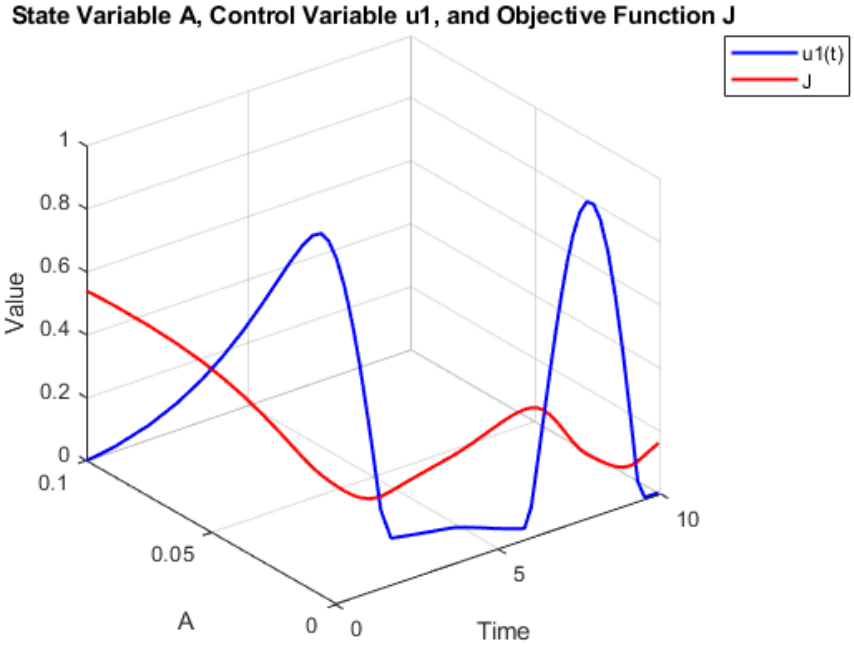


Figure 30.

*Phase space plot of A(t), $u_2$ (t) & J*

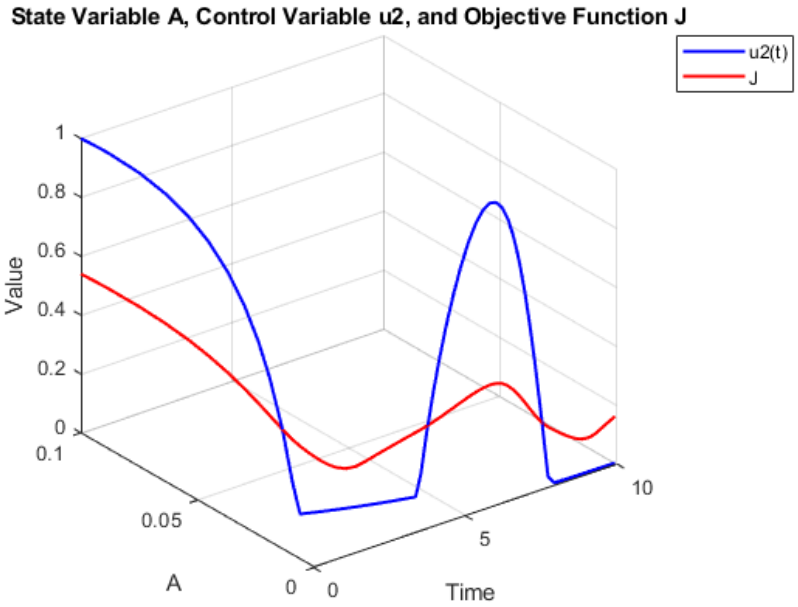



Figure 31.

*Effect of control variables on state variables*

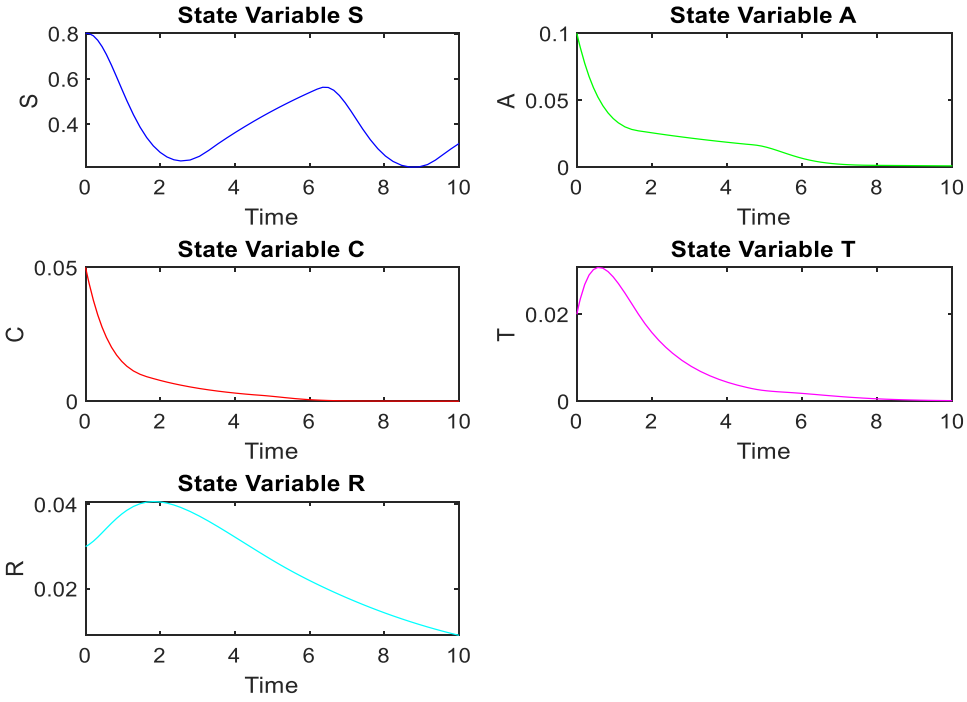


Figure 32.

*Objective function trajectory*

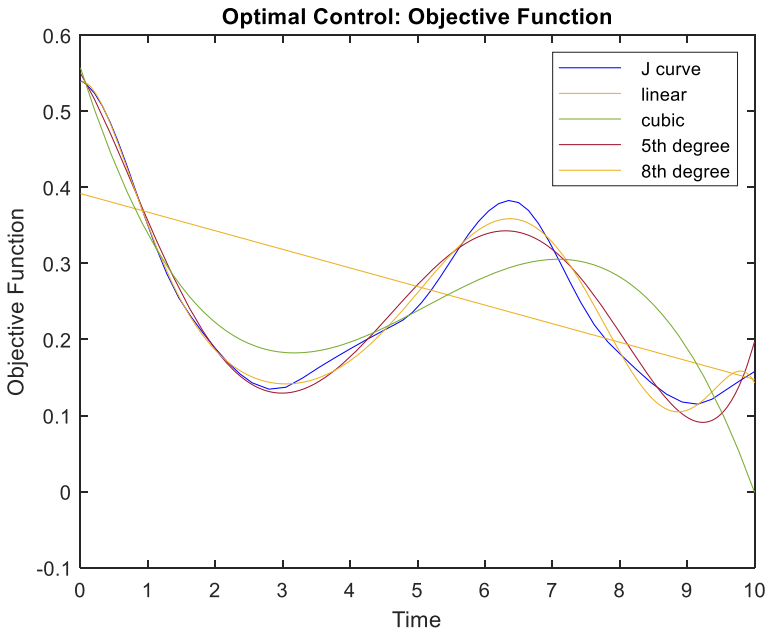



Figure 33.

*Control variables $u_1$ (t), $u_2$ (t)*

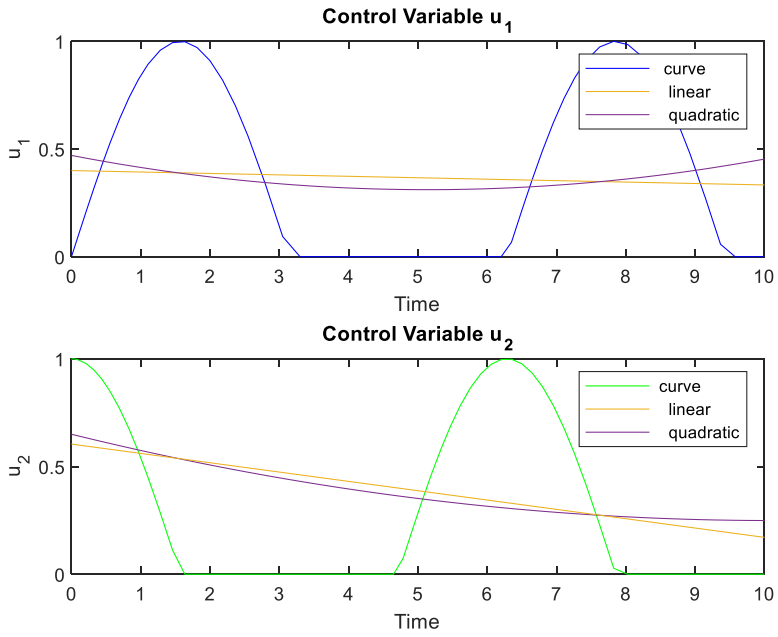


Figure 34.

*Surface plots of S, $u_1$ (t), $u_2$ (t) and J*

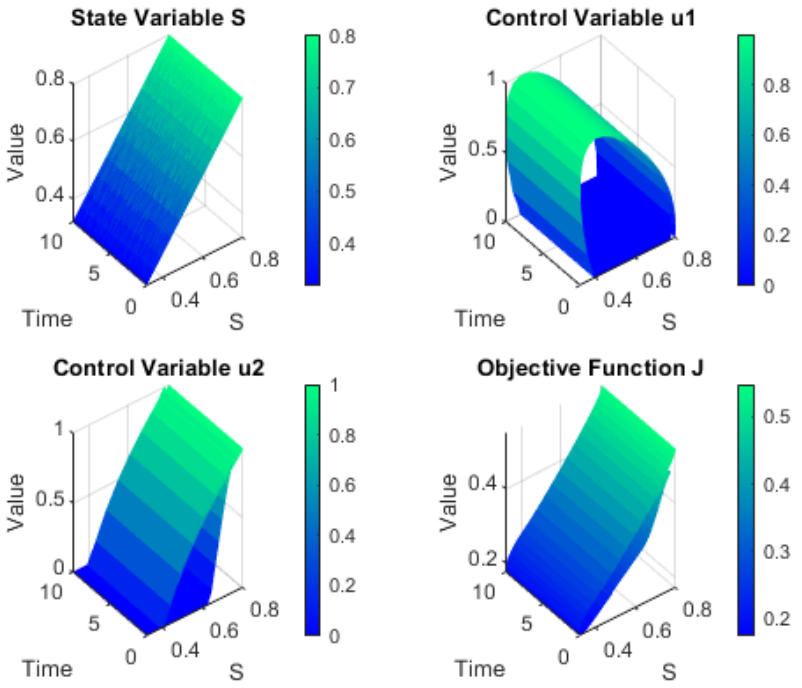



Figure 35.

*Surface plots of A, $u_1$ (t), $u_2$ (t) and J*

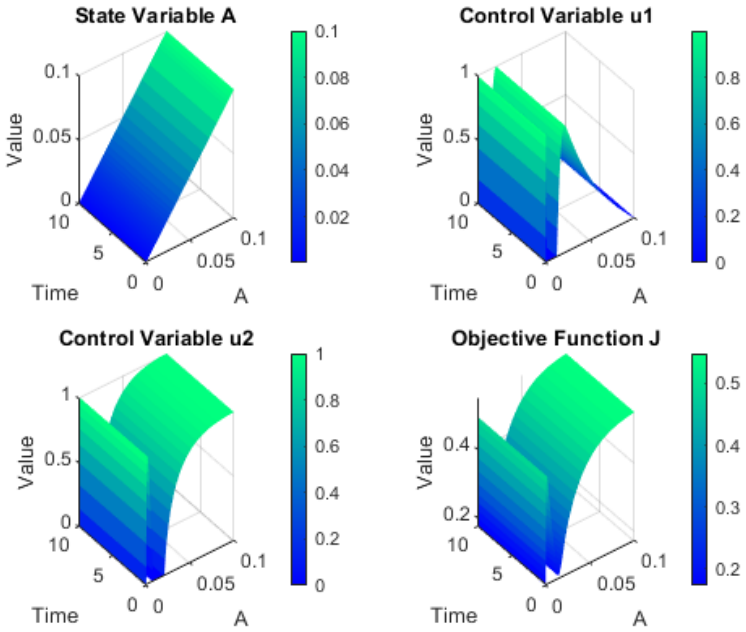


Figure 36.

*Surface plots of $C$, $u_1$ (t), $u_2$ (t) and J*

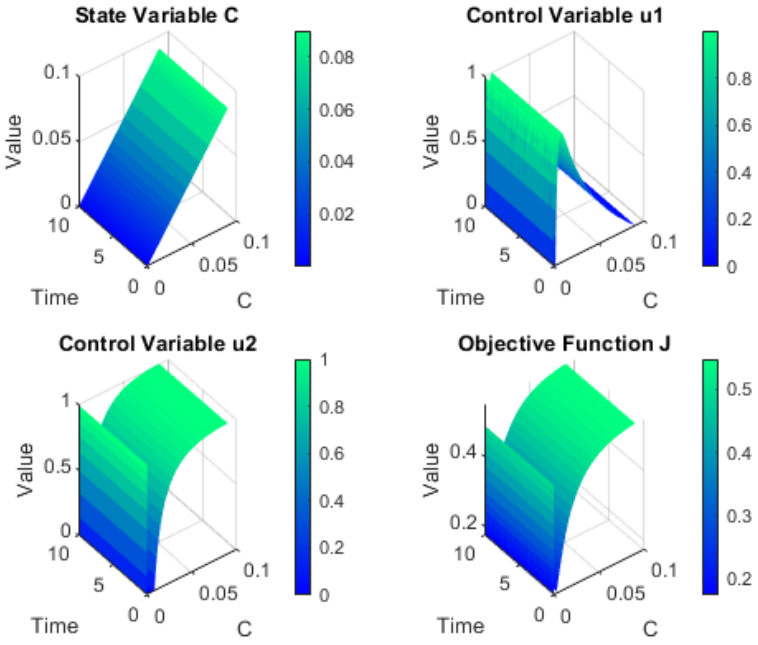



Figure 37.

*Surface plots of $T$, $u_1$ (t), $u_2$ (t) and J*

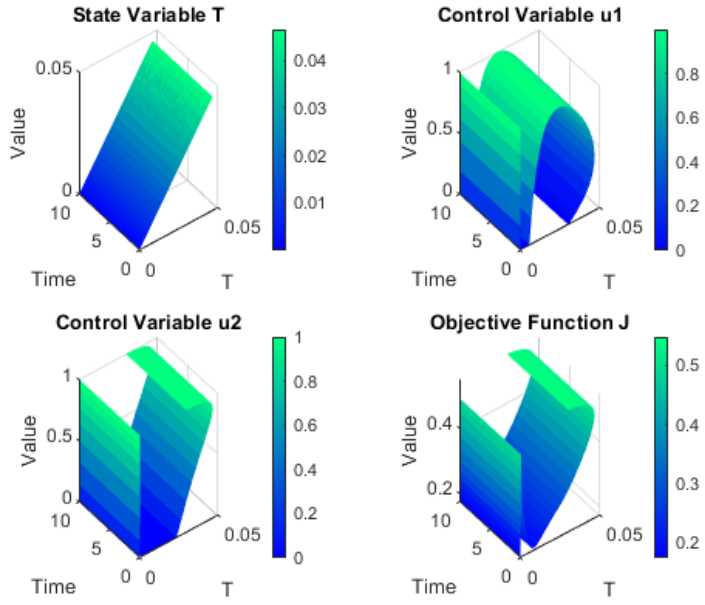
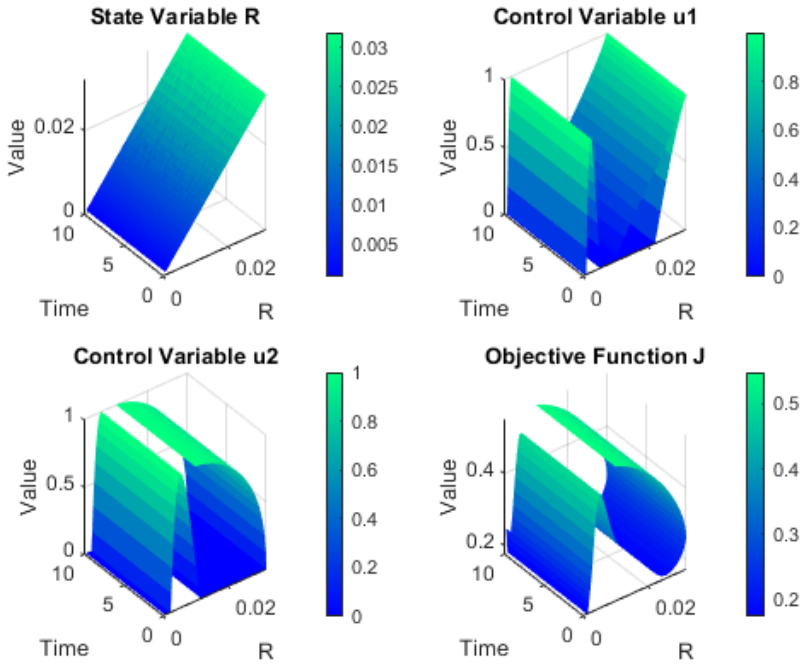


Figure 38.

*Surface plots of R, $u_1$ (t), $u_2$ (t) and J*




## Result and Conclusion

The sensitivity analysis simulations indicate that the parameters exhibit higher sensitivity in the ACM compartment, followed by the recovery compartment and then the alcoholic compartment, as depicted in Figure 19 and Figure 20 Among these parameters, the five most sensitive ones, in their order, are the rate at which alcoholics develop alcoholic cardiomyopathy disease, the rate at which alcoholic cardiomyopathy diseased individuals receive treatment, the rate at which susceptible individuals become alcoholics, death rate from ACM, and the recovery rate from ACM. The subsequent sensitive parameters are the rate at which recovered individuals return to the susceptible state and the natural death rate. The optimality of the sensitivity analysis of the system is demonstrated in Figure 21 and Figure 22. Additionally, Figure 23 outlines the optimal control of the top five most sensitive and controllable parameters, including the corresponding procedure and performance index, while Figures 24 to 28 illustrate the impact of the control on the system at various compartments.

The plot for the state variable S as shown in Figures 24 and 31 revealed the trend of susceptibility to alcohol over time. The control strategies aimed at creating awareness and sensitization were found to have the potential to reduce susceptibility to alcohol

by informing and educating the population. The state variable A represented the population of alcoholics, and the corresponding plot depicted the dynamics of individuals affected by alcoholism. The control strategies, if effective, could contribute to a reduction in the number of individuals struggling with alcoholism, as depicted in Figures 24, 25, 26 and 27. The plot for the state variable C illustrated the occurrence of alcoholic cardiomyopathy within the population. The control strategies were expected to have an impact on reducing the occurrence of this condition by targeting alcohol consumption and associated risk factors. The state variable T represented the population in treatment for alcoholism, and its plot showcased the number of individuals seeking and undergoing treatment. The control strategies had the potential to influence individuals' decisions to seek treatment and increase the overall treatment uptake. Lastly, the state variable R indicated individuals who successfully recovered from alcoholism. The plot for this variable highlighted the impact of the control strategies in enhancing the recovery process and contributing to a higher number of individuals achieving recovery.

In addition to the state variables, the analysis considered two control variables: u1(t) and u2(t) as illustrated in Figure 28. The plot for u1(t) demonstrated the effect of creating awareness and sensitization to reduce the propagation of susceptible individuals contacting alcohol users and abusers. It reflected the efforts put into awareness campaigns and measures aimed at preventing contact with alcohol-related environments. On the other hand, the plot for u2(t) represented the reduction of alcohol consumption, indicating the measures taken to decrease alcohol consumption in the population. These are depicted in Figures 29 to 33.

The objective function J was formulated by combining the state variables and control variables into a single measure, with its trajectory shown in Figure 32, and all corresponding surface plots shown through Figures 34-38. This function aimed to optimize the system's behavior over time, taking into account the weighted coefficients and regularization terms. By minimizing the objective function, the control strategies aimed to achieve desired outcomes such as reducing susceptibility, alcoholism prevalence, alcoholic cardiomyopathy, and increasing treatment and recovery rates.

The optimal control analysis provided a mathematical framework for understanding the potential impact of implementing control strategies involving awareness and sensitization, as well as reducing alcohol consumption, in the dynamics of alcoholism.

The interpretation of the results suggested that these control strategies had the potential to influence the system's behavior and contribute to the prevention and treatment of alcoholism.

The use of the fractional operator has been demonstrated as particularly suitable for studying the transmission dynamics of ACM disease, particularly its optimal control via the implicit finite difference and transversality conditions. The findings suggest that raising awareness and reducing alcohol consumption can significantly reduce the incidence of ACM and its associated mortality. However, relying solely on treatment may not be sufficient to prevent a potential pandemic. Notably, if the rate at which alcoholics develop ACM is kept below 0.0015, assuming that other parameters remain nominal and moderate, the epidemic would easily die out, implying a negligible number of ACM cases and reduced mortality. This underscores the importance of minimizing alcohol consumption and enhancing awareness. Future research involving other prominent fractional control schemes is welcomed to compare results.

# CHAPTER V

## Findings and Discussion

The study findings suggest that the spread of alcoholic cardiomyopathy (ACM) can be mitigated by maintaining a reproduction coefficient ($R_0$) below one, resulting in a stable disease-free equilibrium. Conversely, an $R_0$ above one leads to an unstable endemic equilibrium, resulting in a thriving epidemic. As the population becomes more susceptible to alcohol use, there is a higher likelihood of developing ACM, and most addicts eventually move into the ACM compartments over time.

The study also demonstrates the impact of treatment and recovery on the ACM population, with treatment effectiveness determining the speed of recovery. Additionally, increasing the susceptible and addicted population leads to a rise in the ACM compartments and vice versa. Lower alpha values lead to more rapid convergence of the different compartments.

The model's neural network time series training using data demonstrates a strong correlation between variables, with an R value of 1 for training, testing, and validation. The model fits over different alpha values with maximum accuracy, with an overall goodness of fit SSE: 1.314e+08 and R-square: 0.9999. The p-values further indicate a strong correlation between variables.

Based on the model's predictions, there will be a surge of approximately 60,000,000 ACM death cases between 2041-2042, with death cases surpassing 65,000 in 2077 globally. The study highlights the importance of reducing alcohol consumption and raising awareness to prevent the spread of ACM and its associated mortality.

The sensitivity analysis simulations reveal that the ACM compartment exhibits higher parameter sensitivity, followed by the recovery compartment and the alcoholic compartment. The five most sensitive parameters include the rate at which alcoholics develop ACM disease, the rate at which ACM patients receive treatment, the rate at which susceptible individuals become alcoholics, death rate from ACM, and the recovery rate from ACM. The study outlines the optimal control of these parameters, including the corresponding procedure and performance index. The effect of the control on the system is illustrated in various compartments.

The use of the fractional operator is highly suitable for studying the transmission dynamics of ACM, particularly in terms of optimal control via implicit finite difference and transversality conditions. The study suggests that reducing alcohol consumption and raising awareness can significantly reduce the incidence of ACM and its associated

mortality. However, relying solely on treatment may not be sufficient to prevent a potential pandemic. The research also suggests that keeping the rate at which alcoholics develop ACM below 0.0015, assuming other parameters remain nominal and moderate, could lead to the epidemic's easy extinction, with minimal ACM cases and reduced mortality. These findings highlight the significance of minimizing alcohol consumption and enhancing awareness. Future studies employing other leading fractional control schemes are encouraged to compare results.

The findings suggest that the ACM-LMA model can be used to guide efforts in mitigating an ACM pandemic. One effective strategy is to reduce the reproduction coefficients to less than one, which leads to a healthy population over time. The numerical simulations show that reducing the transmission infectivity rate, minimizing recruitment rate onto the alcoholic susceptible, and improving the rate of recovery can also help prevent an outbreak. However, failure to control the epidemic may lead to a significant reduction in the population.

The NN time series integrated into the fractional model shows that the ACM-LMA model provides insights into the disease dynamics from previous years into the future. The model predicts an additional surge in the epidemic in the year 2027 if the dynamics of the epidemic persist at the same rate. It also predicts a first peak of over 60,000,000 prevalent cases between 2040-2042, followed by a decline below 45,000,000 in the coming years. These predictions may suggest degenerative immunity over time, unpreparedness and unawareness, unresponsive ACM cases, overwhelmed health professionals and limited clinical facilities, and sudden responsiveness and control measures after the surge, respectively.

The ACM-LMA model's foresight reveals the epidemic in circles, like a sine wave with a progressing amplitude, period, and range. However, the research suggests that the epidemic may continue in a progressive trend in subsequent years to come as long as heavy alcohol consumption persists. Therefore, future research on the dynamics of the ACM and the implementation of regulatory measures and optimal control strategies are necessary to prevent an explosion of the epidemic.

# CHAPTER VI
# Conclusion and Recommendations

## Recommendations

This research has demonstrated the impact of alcohol consumption on the spread of alcoholic cardiomyopathy (ACM) and its associated mortality. The findings suggest that the reproduction coefficient ($R_0$) plays a crucial role in determining the epidemic's stability or instability, and reducing alcohol consumption and raising awareness are vital to preventing its spread. Treatment and recovery also play a significant role in mitigating the epidemic, and the study highlights the importance of controlling the five most sensitive parameters, including the rate at which alcoholics develop ACM disease, the rate at which ACM patients receive treatment, the rate at which susceptible individuals become alcoholics, death rate from ACM, and the recovery rate from ACM.

The fractional-order model with neural network time series training used in this study is highly suitable for studying the transmission dynamics of ACM, particularly in terms of optimal control via implicit finite difference and transversality conditions. The model provides insights into the disease dynamics from previous years into the future and predicts a surge in the epidemic in the year 2027, followed by a first peak of over 60,000,000 prevalent cases between 2040-2042, and a subsequent decline below 45,000,000 in the coming years.

The study recommends that future research should focus on the implementation of regulatory measures and optimal control strategies to prevent an explosion of the epidemic. These strategies could include reducing the transmission infectivity rate, minimizing recruitment rate onto the alcoholic susceptible, and improving the rate of recovery. Furthermore, reducing the rate at which alcoholics develop ACM below 0.0015, assuming other parameters remain nominal and moderate, could lead to the epidemic's easy extinction, with minimal ACM cases and reduced mortality. The study's findings have significant implications for policymakers and healthcare providers globally, as it highlights the need for proactive measures to reduce alcohol consumption and raise awareness of the risks associated with alcohol abuse. Additionally, it emphasizes the importance of prioritizing treatment and recovery for

individuals with ACM and implementing optimal control strategies to prevent the spread of the disease.

The prevention of spreading ACM requires educational programs emphasizing government collaboration with relevant stakeholders for effective implementation directed towards increasing public awareness about heavy alcohol use dangers: risks of developing signs or symptoms along managing treatment options appropriately from nearby care facilities until being referred if needed by trained primary-care physicians such as having adequate equipment like echocardiography or electrocardiography knowledgeably applied timely diagnosed results accurately among caring patients experiencing symptoms before it worsens into a severe condition requiring specialist attention from an informed cadre which may not thoroughly reflect real-life scenarios complexities due to inherent limitation in model dynamics being subject to additional research validation.

**Recommendations According to Findings**

After perusing our recent study's findings mitigating alcoholic cardiomyopathy's (ACM) spread whilst reducing mortality levels relies on adopting these recommendations:

1. Reduce Alcohol Consumption: High alcohol intake contributes significantly to increased ACM prevalent occurrences. Hence government bodies working together with public health organizations should educate the masses by running effective campaigns in line with promoting responsible drinking behavior.

2. Increase Treatment & Recovery: Treatment interventions have a significant impact on reducing ACM incidence while recovery programs for recovering patients relapse prevention should be prioritized and easily accessed by healthcare providers.

3. Optimize Control Strategies-Optimizing the top-five most sensitive parameters is essential in lowering ACM prevalence rates. Thus, efficient procedures alongside optimal control strategies set up accordingly are necessary for reducing incidences.

4.Enhance Surveillance and Monitoring: Keeping alcoholics' rate of developing ACM at minimal levels requires accurate monitoring mechanisms put in place for early identification of volatile epidemics

5.Invest in Research & Development-Implementing regulatory measures based on knowledgeable dynamics of implementing an effective fractional control scheme aimed at prioritizing prevention mechanisms against epidemic explosions becoming much deadlier again highlights regulators need investments to yield beneficial results.

Achieving maximum potential toward reducing mortality levels rests wholly on government organizations, public health sectors, healthcare providers & affected individuals working collectively towards achieving shared goals resulting in an action-driven approach. No doubt exists regarding the necessity for significant reform within our current educational framework.

The structure which has been erected does not supply learners with critical knowledge or abilities necessary for triumph in contemporary society. To rectify this situation there are many moving parts which must be addressed including financial insufficiencies, outdated teaching methods and anachronistic coursework materials.

**Recommendations for Future Research**

Based on the findings of this study, several recommendations for future research are suggested:

1. The use of other leading fractional control schemes should be considered to compare results with the current study's fractional operator. The comparison will provide a comprehensive view of the most effective control schemes in mitigating the spread of ACM.

2. Future studies should explore the impact of various behavioral interventions such as counseling, behavioral therapy, and other therapeutic interventions in preventing ACM's spread. These studies should evaluate the effectiveness of these interventions in reducing alcohol consumption and its associated risks.

3. Future studies should investigate the role of genetic factors in ACM susceptibility. The study of genetic risk factors could help identify individuals who are more vulnerable to ACM development and provide insight into the disease's underlying mechanisms.

4. There is a need for more research on the impact of comorbidities on ACM development and mortality. This research could help in the identification of at-risk populations and the development of tailored interventions.

5. The use of machine learning techniques such as deep learning and reinforcement learning could be explored in future studies to improve the accuracy and precision of the ACM epidemic predictions.

6. Future research should investigate the impact of environmental factors such as pollution and other occupational hazards on the incidence and mortality of ACM.

7. There is a need for more research on the long-term effects of ACM treatment and recovery. This research could provide insight into the effectiveness of treatment and the long-term outcomes of individuals who have recovered from ACM.

8. Finally, the implementation of regulatory measures and optimal control strategies should be investigated in future studies. The investigation will provide insight into the most effective policies and measures in mitigating the spread of ACM and reducing its associated mortality.

   In summary, future research should aim to develop more effective prevention strategies, improve our understanding of the disease's underlying mechanisms, and identify the most effective treatment and control measures. These efforts will be critical in reducing the incidence and mortality associated with ACM and improving the health outcomes of individuals affected by this disease.

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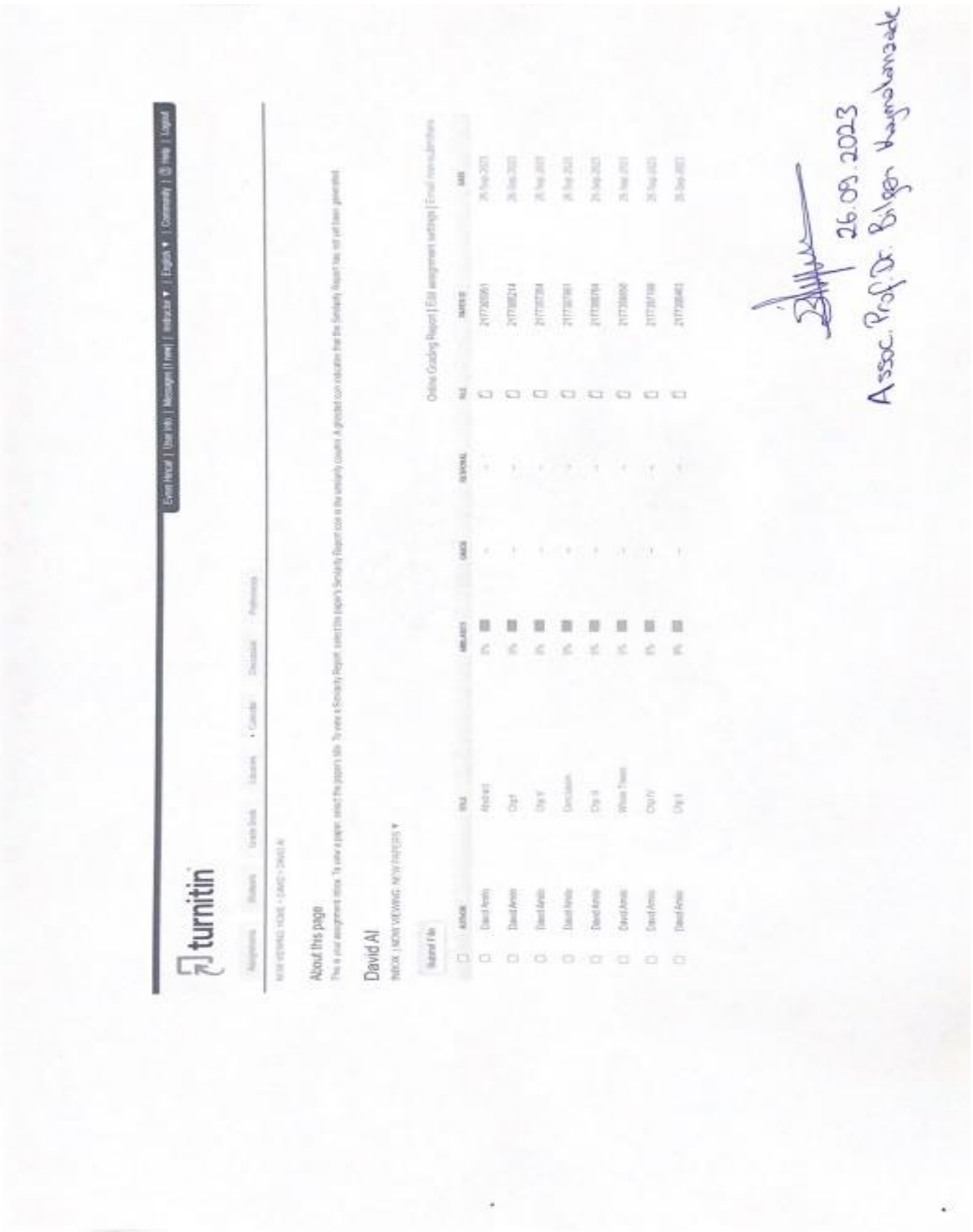
# APPENDICES
## Appendix A



# CURRICULUM VITAE

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Nationality : Nigerian


## EDUCATION

| Degree | Institution | Year of Graduation |
|---|---|---|
| MSc. | Near East University Cyprus<br>Department of Mathematics | 2020 |
| B.Sc. | Ebonyi State University<br>Abakaliki, Nigeria<br>Department of Mathematics | 2014 |

## WORK EXPERIENCE

| Year | Place | Enrollment |
|---|---|---|
| 2021 – date | Near East University,<br>Department of Mathematics | Lecturer |
| 2015 – 2016 | Eko Electricity Distribution<br>Company (EKEDC) | IT Operator |
| 2016 – 2017 | Jhopiego for Mother and Child<br>Survival Program (MCSP) | Statistician (Intern) |
| 2017 – 2018 | NPower | Mathematics Teacher |
| 2013 – 2014 | Ministry of works, Abakaliki | Statistician (intern) |

## FOREIGN LANGUAGE

- English, fluently spoken and written.

## TECHNICAL SKILL

- Network Administration
- Programming Research software (Python, MATLAB, Wolfram Mathematica, SPSS)
- Data Science and Machine Learning

## THESIS

- **MSc**: IKECHUKWU, A. D. (2020). A FRACTIONAL-ORDER TWO-STRAIN EPIDEMIC MODEL WITH TWO VACCINATIONS (Doctoral dissertation, NEAR EAST UNIVERSITY).
- **Ph.D.**: DAVID IKECHUKWU AMILO (2023). A FRACTIONAL-ORDER ALCOHOLIC CARDIOMYOPATHY EPIDEMIC MODEL WITH NETWORK TIME SERIES (Doctoral dissertation, NEAR EAST UNIVERSITY).

## SCIENTIFIC TALKS AND WORKSHOP

- Fifth International Conference on Analysis and Applied Mathematics (ICAAM) Sept 2020
- Numerical Functional Analysis (ICAAM) Nov 2021

## RESEARCH INTEREST

- Mathematical Modelling
- Epidemiology
- Optimization
- Machine Learning
- Data Science

## HONOURS AND AWARDS

- Young Researcher Award, Near East University, 2022.
- Best graduating student Applied Mathematics Near East University 2020 session.
- Bronze medal, National Mathematics Competition for University Students (NAMCUS) Abuja 2015.
- 3rd best-graduating student Mathematics/Statistics Department Ebonyi State University 2014 session.

## PUBLICATIONS IN INTERNATIONAL REFERERED JOURANAL (IN COVERAGE OF SCOPUS, SCIE, UGC CARE, SSCI/SCI-EXPANDED, DOAJ AND PUBMED)

- David Amilo, Bilgen Kaymakamzade, Evren Hincal. A fractional-order mathematical model for lung cancer incorporating integrated therapeutic approaches. Sci Rep 13, 12426 (2023). doi.org/10.1038/s41598-023-38814-2 **[published]**
- David Amilo, Bilgen Kaymakamzade, Evren Hincal, (2023). A Fractional-Order Modeling and Sensitivity Analysis in the Investigation of Colorectal Cancer. (REF: PFDA-23-38) Progress in Fractional Differentiation and Applications. **[In press]**
- David Amilo, Bilgen Kaymakamzade, Evren Hincal, Kamyar Hosseini, (2023) Modeling Gene Expression Via Caputo-Type Fractional-Order Calculus. (REF: PFDA-23-31) Progress in Fractional Differentiation and Applications. **[In press]**
- David Amilo, Bilgen Kaymakamzade, Evren Hincal, (2023). A Study on Lung Cancer using Nabla Discrete Fractional-order Model in Mathematica Moravica **[In press]**
- David Amilo, Bilgen Kaymakamzade, Evren Hincal, (2022). An Integrated Therapy Approach for Optimizing Fractional Differential Equation Control Across the Five Stages of Bladder Cancer. Progress in Fractional Differentiation and Applications. **[In press]**
- David Amilo, Bilgen Kaymakamzade, Evren Hincal, (2022). A Fractional Order Alcoholic Cardiomyopathy Epidemic Model with Network Time Series, Computational and Mathematical Methods in Medicine, Volume 2022. Pages 15 doi.org/10.1155/2022/7716514 **[In press]**
- David Amilo, Bilgen Kaymakamzade (2022). A fractional-order super-spreader Covid-19 model using Caputo derivative. Progress in Fractional Differentiation and Applications doi.org/10.19677/pfda/output **[In press]**
- GOKBULUT, N., AMILO, D., & KAYMAKAMZADE, B. (2021). Fractional SVIR model for COVID-19 under Caputo derivative. Journal of Biometry Studies. Journal of Biometry Studies, 1(2), 58-64. doi.org/10.29329/JofBS.2021.349.04 **[published]**
- Kaymakamzade, B., Hincal, E., & Amilo, D. (2021, February). A fractional-order two-strain epidemic model with two vaccinations. In AIP Conference Proceedings (Vol. 2325, No. 1, p. 020048). AIP Publishing LLC. doi.org/10.1063/5.0040309 **[published]**
- David Amilo, Khadijeh Sadri, Bilgen Kaymakamzade, Evren Hincal, (2023). A Mathematical Model with Fractional-Order Dynamics for the Combined Treatment of Metastatic Colorectal Cancer in Communications in Nonlinear Science and Numerical Simulation. **[Under Review]**
- Kaymakamzade, B., Savaşan, A., Kara, B., Tulbentci, T., & Amilo, D. (2023). The Effects of Expansions in Hospitals on the Applicability of Performance Certificate Programme.. Sci Rep (2023). **[Under Review]**
- Hakan Aytaçoğlu; David Amilo; Bilgen Kaymakamzade; Evren Hincal; Onder Coban; Pınar Tulay (2023). Predicting Embryo Quality in ICS. Reproductive Sciences. **[Under Review]**

- Cemile Bagkur; David Amilo; Bilgen Kaymakamzade (2023). A Fractional-Order Model For Nosocomial Infection Caused By Pseudomonas Aeruginosa in Northern Cyprus. Computers in Biology and Medicine. **[Under Review]**

## SEMINARS

- Mathematical Modelling of Breast Cancer via BI-RADS 4 Subcategories, Near East University, Cyprus, 2022.
- A Fractional-Order Alcoholic Cardiomyopathy Epidemic Model with Neural Network Time Series, Near East University, Cyprus, 2022.
- Modeling of Distance-Learning in Mathematics Education, Near East University, Cyprus, 2022.

## COURSES GIVEN (2021-date)

- Foundation Mathematics I
- Foundation Mathematics II
- Mathematics for Business and Economics I
- Mathematics for Business and Economics II
- Probability and Statistics for Engineering
- Probability and Statistics for Business and Economics

## REFERENCES

- Prof. Dr. Evren Hınçal Vice Dean, Faculty of Arts and Sciences Chair, Department of Mathematics. evren.hincal@neu.edu.tr
- Assoc. Prof. Dr. Bilgen Kaymakamzade Chair, Primary and Secondary Education Mathematics Teaching Vice Chair, Department of Mathematics Coordinator, Mathematics Courses Near East University bilgen.kaymakamzade@neu.edu.tr
- Prof. Dr. Ali Efdal Ozkul Dean, Faculty of Arts and Sciences aliefdal.ozkul@neu.edu.tr