AMILO DAVID IKECHUKWU
A FRACTIONAL-ORDER TWO-STRAIN EPIDEMIC MODEL WITH TWO VACCINATIONS
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A FRACTIONAL-ORDER TWO-STRAIN EPIDEMIC MODEL WITH TWO VACCINATIONS

A THESIS SUBMITTED TO THE GRADUATE SCHOOL OF APPLIED SCIENCES

OF

NEAR EAST UNIVERSITY

By

AMILO DAVID IKECHUKWU

In Partial Fulfillment of the Requirements for the Degree of Master of Science

In

Applied Mathematics

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Approval of Director of Graduate School of Applied Sciences

Prof. Dr. Nadire ÇAVUŞ

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I hereby declare that all information in this document has been obtained and presented in accordance with academic rules and ethical conduct. I also declare that as required by these rules and conduct, I have fully cited and referenced all materials and result that are not original to this work.

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ABSTRACT

In this research paper, we extended an existing SIR epidemic integer model containing two strains and two vaccinations by using a system of fractional ordinary differential equations in the sense of Caputo derivative of order $\sigma \in (0,1]$. Four equilibrium points were established: disease free equilibrium, strain1 disease free equilibrium, strain2 disease free equilibrium and endemic equilibrium. Detailed analysis of the equilibrium points of the model was given applying fractional calculus and Routh-Hurwitz criterion.

Analytically, the threshold value of the basic reproduction number was obtained and the description of the existence of the equilibrium points established. It was shown that when the two reproduction number R_1 and R_2 are less than one, the disease die out over time and when either of them are greater than one, the pandemic persist in relation to the thriving strain. In addition, the strain with the higher reproduction number thrives and outshines the other with smaller magnitude. Stability analysis of the equilibrium points was carried out employing the Jacobian matrix. Numerical simulations were iterated to support the analytic results adopting real life data from the Global Influenza Surveillance and Response System (GISRS) of the World Health Organization. It was further discovered that the less presence of vaccine of a given strain in the population, the more the populace of infective in the other strain compartment. Finally, with the fractional order technique, the memory effect of the system is made visible and easy for prognosis.

***Keywords**:* Epidemic model; two strain; two vaccine; fractional calculus; fractional-order model; Routh-Hurwitz criterion; basic reproduction number; stability

ÖZET

Bu araştırmamızda, $\sigma \in (0,1]$ dereceli Caputo türevi anlamında bir kesirli adi diferansiyel denklem sistemi kullanılarak iki tür ve iki aşılama içeren mevcut bir SIR epidemik model genişletilmiştir. Hastalığın olmadığı, 1. türde hastalığın olmadığı, 2. türde hastalığın olmadığı ve endemik durum olmak üzere 4 tane denge noktası oluşturulmuştur. Modelin denge noktalarının detaylı analizinde kesirli kalkülüs ve Routh-Hurwitz kriteri uygulanmıştır.

Analitik olarak, temel üreme sayısının eşik değeri hesaplanmış ve denge noktalarının varlığının açıklaması verilmiştir. Temel üreme sayısı R_1 ve R_2 birden küçük olduğunda, hastalığın zamanla yok olduğu ve herhangi biri birden büyük olduğunda ise pandeminin gelişen türle ilişkili olarak devam ettiği gösterilmiştir. Buna ek olarak, daha büyük çoğalma sayısına sahip tür, küçük bir büyüklüklede olsa, diğerini geçer ve gölgede bırakır. Denge noktalarının stabilite analizi Jacobian matrisi ile yapılmıştır. Dünya Sağlık Örgütü'nün Küresel Grip Gözetim ve Müdahale Sisteminden gerçek hayat verilerini benimseyen analitik sonuçları desteklemekiçin sayısal simülasyonlar yinelenmiştir. Ayrıca, popülasyonda belirli bir türde aşı varlığı ne kadar az olursa, diğer tür bölmesindeki enfeksiyonlu popülasyonun o kadar fazla olduğu keşfedilmiştir. Son olarak, kesirli mertebe tekniği ile, sistemin hafıza etkisi görünür ve prognoz için kolay hale getirilmiştir.

Anahtar Kelimeler: Salgın modeli; iki tür; aşı; kesirli kalkülüs; kesirli-mertebe modeli; Routh-Hurwitz kriteri; temel üreme sayısı; stabilite

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CHAPTER 1

INTRODUCTION

1.1. Fractional Calculus

The notion of fractional calculus was first conceptualized by Leibniz, a German mathematician and early founder of classical calculus in 1695, and was further developed by L. Euler in 1730 (J.Tenreiro Machado et al, 2011).

Fractional calculus is a generalization of the integer calculus such that the order of the derivatives and integrals could be allowed to be fractions, irrational or complex numbers (I Podlubny, 1999).

For example, Legendre's symbol for the generalized factorial is:

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

where α is the order of the derivative.

1.1.1. Definition

The fractional integral of order $\alpha > 0$ of a function f: $\mathbb{R}^{+} \rightarrow \mathbb{R}$ 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.

1.1.2. Definition

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.

1.1.3. Definition

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

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

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

Caputo's fractional derivative formula has shown to be more applicable in real life scenario since the derivative of a constant is zero as in the case of Riemann-Liouville's derivative.

Many Scientists like (Sardar et al, 2015) and (Dumitru Baleanu et al, 2010) have found fractional-order derivatives to be imperative and integrative in formulating models for analyzing dynamical systems. Recent research also has shown fractional calculus to be essential and applicable in control and synchronization of chaotic systems (Ahmad Taher et al, 2017) and many other fields of engineering.

1.2. SIR Model

The SIR model is a mathematical model that depicts how an infection is spread over a population. It is one of the simplest compartments and generic model that birthed other models, often applied in epidemiological analysis. It was first idealized by Ronald Ross and William Hammer in the early twentieth century before been developed and theorized by Kermack and Anderson Gray McKendrick between 1927 and 1933 (Murray, 2003). It consists of three partitions: Susceptible, Infected and Removed population, hence the name SIR model. The model is plausibly prognostic for infective diseases that are transmitted from human to human and where recovery poses resistive limitations (Earn et a, 2000).

New trends have it that the application of SIR model have gone beyond health epidemiological apprehension to conditions pertaining to marketing, informatics, sociology and economy (Rodrigues, 2016).

The SIR model is given by:

$$S \longrightarrow I \longrightarrow R$$

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

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

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

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

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:

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

Many other models like Susceptible-İnfected-susceptible (SIS) (Harko, 2014), Maternally Derived Immunity-Susceptible-Infectious-Recovered (MSIC) and the susceptible-Exposed-Infectious-Recovered (SEIR) have been derived from the classical SIR model (Brauer, F. and Castillo-Chávez, C, 2001).

1.3. Influenza

Influenza also known as "flu" is a communicable disease caused by the influenza virus that is transmitted via airborne droplets and attacks the respiratory system (WHO 2018). Some of its common symptoms include: fevers sore throat, coughing, running noses and headache etc. There are four types of seasonal influenzas virus: Type A, B, C and D. Type A and B virus spread and cause seasonal epidemics however A is known to be more rampant than the others. Influenza virus is substantiated by testing the sputum or mucus from the nose.

Vaccines and antiviral drugs have been formulated and recommended by the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) for curbing and controlling the disease. It is estimated that over 35 million people living in the United State of America (USA) have shown related symptomatic illness from the influenza virus between 2018 and 2019.

Xingyang (XuXingyang et al 2018) and many others have tried to work on a fractional order epidemic model for influenza dynamics applying the reimbursements of the fractional-order

concept to influenza dynamic in order to postulate conditions under which the epidemic can be contained. Other scientists like Moustafa-Elshahed (Moustafa-Elshahed et al, 2011) have adopted the fractional-order unification on influenza dynamics and have even extended it to an SIRC model.

1.4. Basic Reproduction

1.4.1. Definition

The next generation matrix is defined as the square matrix G in which the ijth element of G is the expected number of secondary infections of type i caused by a single infected individuals of type j assuming that the population of type i is completely susceptible.

1.4.2. Definition

The basic reproduction number is defined as the dominant Eigen value of the new generation matrix G such that:

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

where,

f_ι are new infections,

v_ι are transferred infections from one compartment to another,

x_0 is the disease free equilibrium state.

The basic reproduction R_0 is informally connoted as the likely number of secondary cases originated by a single infection in an entirely susceptible populace (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,

α represents the transmissibility,

β represents the average rate of constant between susceptible and infected individuals.

γ represents the duration of infectiousness

Studies have shown that if $R_0 < 1$ then there will not be an epidemic and the disease will die out naturally. However, if $R_0 > 1$ it implies that the odds of a pandemic are high.

Influenza is known to have an average reproduction number, R_0 of 2 to 3 (Mills, 2004), plausible enough to explain its contagion.

1.5. Stability

Stability in general sense is a state in which something isn't prone to a significant alteration. In dynamics, the concept of stability hypothesizes a system capable of returning (or at least approaching) its original state after perturbation.

A system is said to be stable if all the roots of the characteristic equation lie on the left half plane; i.e. are negative.

1.5.1. Definition

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:

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

with the following properties:

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

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

1.5.2. Definition

A point $x^* \in X$ is called an equilibrium or rest point of a dynamical system

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

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

1.5.3. Definition

An equilibrium point $x^* \in X$ of a dynamical system

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

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 δ such that

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

1.5.4. Definition

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 and proven.

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

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

then x is stable.

If in addition

$$\dot{V}(\bar{x}) = 0 \text{ and } \dot{V}(\mathrm{x}) < 0\ for\ all\ x \in X,\ \mathrm{x} \neq \bar{x},$$

then x is asymptotically stable.

1.5.5. Theorem

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 Eigen values λ_{ij} of the Jacobian matrix $J = \frac{\partial f}{\partial x}$ evaluated at the equilibrium satisfy $\left|\arg \lambda_{ij}\right| > \alpha \frac{\pi}{2}$.

1.6. Routh- Hurwitz Stability Criterion

The Routh-Hurwitz criterion provides the necessary and sufficient condition for stability of a linear system. It used to ascertain if the roots of a polynomial will be negative without directly solving for them.

Routh- Hurwitz stability Criterion for second order polynomials:

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

Routh- Hurwitz stability Criterion for third order polynomials:

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

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:

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

We construct the Routh array as follows:

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

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

$$c_l = \frac{b_l \times a_{n-(2l+1)} - a_{n-1} \times b_{l+1}}{b_1},$$

$$\vdots$$

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

CHAPTER 2

A TWO-STRAIN EPIDEMIC MODEL WITH TWO VACCINATIONS

2.1. Description of the Integer Model

Many authors like (Yukihiko Nakata et al, 2014) and (Rahman A, Zou X, 2011) have proposed several epidemic models and carried out stability research. One of such is the two-strain epidemic model with two vaccinations proposed by (Bilgen Kaymakamzade et al, 2017) as follows:

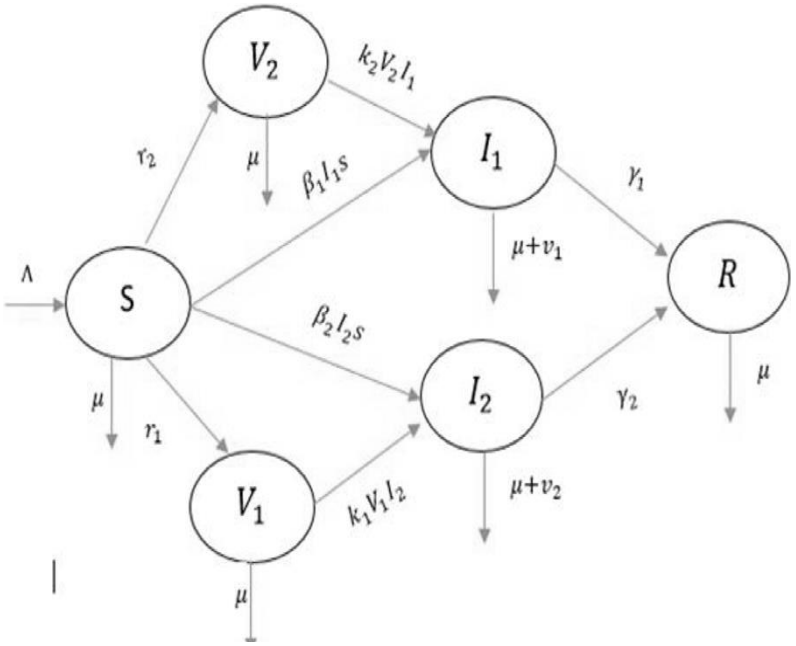

Figure 1.1: Transmission diagram

Fig1.1 illustrates the flow and transfer of the disease dynamics of influenza with two strain and two vaccinations. Arrows pointing to a compartment represent an addition of population while an arrow pointing away from compartment signifies removal of population from the compartment.

The model is derived as follows:

$$\frac{dS}{dt} = \Lambda - (\beta_1 I_1 + \beta_2 I_2 + \lambda)S,$$

$$\frac{dV_1}{dt} = r_1 S - (k_2 I_2 + \mu)V_1,$$

$$\frac{dV_2}{dt} = r_2 S - (k_2 I_1 + \mu) V_2, \quad (2.1)$$

$$\frac{dI_1}{dt} = (k_2 V_2 + \beta_1 S) I_1 - \alpha_1 I_1,$$

$$\frac{dI_2}{dt} = (k_1 V_1 + \beta_2 S) I_2 - \alpha_2 I_2,$$

$$\frac{dR}{dt} = \gamma_1 I_1 + \gamma_2 I_2 - \mu R$$

Where,

$$\lambda = r_1 + r_2 + \mu, \ \alpha_1 = \mu + V_1 + \gamma_1, \ \alpha_2 = \mu + V_2 + \gamma_2.$$

With the condition that:

$$S + V_1 + V_2 + I_1 + I_2 + R = N.$$

The population $N(t)$ is separated into six partitions: S, V_1, V_2, I_1, I_2 and R which represent the dimension of susceptible, inoculated with the vaccination for strain 1, inoculated with the vaccination for strain 2, infected with strain 1, infected with strain 2 and recovered cubicle respectively. Equal birth and death in the population without dual infection were assumed with respect to all variables and constraint.

Table 2.1: Variables and Parameter.

Parameter	Description
N	total population
Λ	recruitment rate of individuals

$\frac{1}{\mu}$	average time of life expectancy
r_1	rate of vaccination with strain 1
r_2	rate of vaccination with strain 2
k_1	transmission coefficient of vaccinated individuals V_1 to strain 2
k_2	transmission coefficient of vaccinated individuals V_2 to strain 1
β_1	transmission coefficient of susceptible individuals to strain 2
β_2	transmission coefficient of susceptible individuals to strain 1
$\frac{1}{\gamma_1}$	average infection period of strain 1
$\frac{1}{\gamma_2}$	average infection period of strain 2
V_1	infection induced death rate of strain 1
V_2	infection induced death rate of strain 2

The authors carried out an integer order stability analysis on the model employing Lyapunov functions, with influenza as the epidemic disease. Numerical analysis was carried out to further buttress the analytic outcomes. Without conflict of interest they concluded that the system was globally stable if the reproduction coefficients were less than one. They further discovered that the strain with higher reproduction ratio dominates the other with less and the recruitment parameter as the most significant factor influencing the reproduction ratio and hence the global stability of each boundary equilibrium.

CHAPTER 3

THE FRACTIONAL TWO-STRAIN EPIDEMIC MODEL WITH TWO VACCINATIONS

3.1. The Fractional Model

Integrating fractional order on model (2.1) with same parameters, and σ as the order of the differential equation we arrive at the following:

$$\begin{aligned}
\frac{d^{\sigma}S(t)}{dt^{\sigma}} &= \Lambda - (\beta_1 I_1 + \beta_2 I_2 + \lambda) S, \\
\frac{d^{\sigma}V_1(t)}{dt^{\sigma}} &= r_1 S - (k_1 I_2 + \mu) V_1, \\
\frac{d^{\sigma}V_2(t)}{dt^{\sigma}} &= r_2 S - (k_2 I_1 + \mu) V_2, \\
\frac{d^{\sigma}I_1(t)}{dt^{\sigma}} &= (k_2 V_2 + \beta_1 S) I_1 - \alpha_1 I_1, \\
\frac{d^{\sigma}I_2(t)}{dt^{\sigma}} &= (k_1 V_1 + \beta_2 S) I_2 - \alpha_2 I_2, \\
\frac{d^{\sigma}R(t)}{dt^{\sigma}} &= \gamma_1 I_1 + \gamma_2 I_2 - \mu R,
\end{aligned} \tag{3.1}$$

Where $\sigma \in (0,1]$ is the order of the fractional derivative.

The fractional derivative of model (2.1) is in the sense of Caputo as Caputo technique is often used in real life application as it allows initial values for the fractional differential equations with Caputo derivatives similar to the integer order differential equations.

Theorem 3.1: The biological feasible region of model (3.1) is

$$\varphi = \left\{ (S, V_1, V_2, I_1, I_2, R \in \mathbb{R}_+^6 : 0 \leq N \leq \frac{\Lambda}{\mu} \right\}$$

and positively invariant.

Proof:

$$0 \leq \frac{d^{\sigma}S(t)}{dt^{\sigma}} + \frac{d^{\sigma}V_1(t)}{dt^{\sigma}} + \frac{d^{\sigma}V_2(t)}{dt^{\sigma}} + \frac{d^{\sigma}I_1(t)}{dt^{\sigma}} + \frac{d^{\sigma}I_2(t)}{dt^{\sigma}} + \frac{d^{\sigma}R(t)}{dt^{\sigma}}$$

$$= \Lambda - \mu(S + V_1 + V_2 + I_1 + I_2 + R) - V_1 I_1 - V_2 I_2$$

$$< \Lambda - \mu(N)$$

$$\Rightarrow \ 0 \leq \Lambda - \mu N$$

$$\Rightarrow \ N \leq \frac{\Lambda}{\mu}$$

Observe that all parameters used are nonnegative. So, since the system is bounded given any initial condition the solution is defined for any time $t \geq 0$ and remains in the region. Therefore, the region φ is positively invariant.

3.2. Model Analysis

Instead of analyzing system (3.1), owing to non-existence of the recovered compartment, we investigate the behavior of the following system:

$$\begin{aligned}
\frac{d^{\sigma}S(t)}{dt^{\sigma}} &= \Lambda - (\beta_1 I_1 + \beta_2 I_2 + \lambda) S, \\
\frac{d^{\sigma}V_1(t)}{dt^{\sigma}} &= r_1 S - (k_1 I_2 + \mu) V_1, \\
\frac{d^{\sigma}V_2(t)}{dt^{\sigma}} &= r_2 S - (k_2 I_1 + \mu) V_2, \\
\frac{d^{\sigma}I_1(t)}{dt^{\sigma}} &= (k_2 V_2 + \beta_1 S) I_1 - \alpha_1 I_1, \\
\frac{d^{\sigma}I_2(t)}{dt^{\sigma}} &= (k_1 V_1 + \beta_2 S) I_2 - \alpha_2 I_2.
\end{aligned} \tag{3.2}$$

3.2.1. Equilibria

The equilibrium points are computed by equating system (3.2) to zero and solving concurrently. The following equilibria are therefore gotten:

I. Disease free equilibrium point E_0 to the coordinates $(S^0(t), V^0{}_1(t), V^0{}_2(t), I^0{}_1(t), I^0{}_2(t))$ is given by $E_0 = \left(\frac{\Lambda}{\lambda}, \frac{\Lambda r_1}{\mu\lambda}, \frac{\Lambda r_2}{\mu\lambda}, 0, 0\right)$.

II. Strain1 disease free equilibrium E_1 to the coordinates

$(\bar{S}(t), \bar{V}_1(t), \bar{V}_2(t), \bar{I}_1(t), \bar{I}_2(t))$ is given by

$$\bar{S}(t) = \frac{\Lambda}{\beta_2 I_2 + \lambda},$$

$$\bar{V}_1(t) = \frac{\Lambda r_1}{(k_1 I_2 + \mu)(\beta_2 I_2 + \lambda)}, \quad \bar{V}_2(t) = \frac{\Lambda r_2}{\mu(\beta_2 I_2 + \lambda)}, \quad \bar{I}_1(t) = 0.$$

and $\bar{I}_2(t)$ is the root of the quadratic

$$A\bar{I}_2^{\,2} + B\bar{I}_2 + C = 0, \tag{3.3}$$

where,

$$A = \alpha_2 k_1 \beta_2, \; B = \alpha_2 k_1 \lambda + \alpha_2 \mu \beta_2 - \Lambda k_1 \beta_2,$$

$$C = \alpha_2 \mu \lambda - \Lambda r_1 k_1 - \Lambda \mu \beta_2.$$

E_1 will only be biologically meaningful and hence exist if $\bar{I}_2(t)$ is positive.

We can see this by employing the Routh-Hurwitz criterion and so the polynomial (3.3) which can also be expressed in this form:

$$\bar{I}_2^{\,2} + \frac{B}{A}\bar{I}_2 + \frac{C}{A} = 0$$

will have positive roots if $\frac{B}{A} < 0 \; and \; \frac{C}{A} > 0 \;\; or \;\; \frac{B}{A} > 0 \; and \; \frac{C}{A} < 0$. Since A is clearly positive it suffices to consider if $B < 0 \; and \; C > 0 \;\; or \;\; B > 0 \; and \; C < 0$.

Suppose for contradiction that $B < 0 \; and \; C > 0$.

$$B < 0 \Rightarrow \alpha_2 k_1 \lambda + \alpha_2 \mu \beta_2 - \Lambda k_1 \beta_2 < 0$$

$$\Rightarrow \alpha_2 < \frac{\Lambda k_1 \beta_2}{k_1 \lambda + \mu \beta_2} \tag{3.4}$$

$$C > 0 \Rightarrow \alpha_2 \mu \lambda - \Lambda r_1 k_1 - \Lambda \mu \beta_2 > 0$$

$$\Rightarrow \alpha_2 > \frac{\Lambda r_1 k_1 + \Lambda \mu \beta_2}{\mu \lambda} \tag{3.5}$$

Simplifying (3.4) and (3.5) we get that,

$$\frac{\Lambda r_1 k_1 + \Lambda \mu \beta_2}{\mu \lambda} < \alpha_2 < \frac{\Lambda k_1 \beta_2}{k_1 \lambda + \mu \beta_2}$$

and therefore

$$\frac{\Lambda r_1 k_1+\Lambda\mu\beta_2}{\mu\lambda} - \frac{\Lambda k_1\beta_2}{k_1\,\lambda+\,\mu\beta_2} < 0,$$

it follows that

$$\frac{\Lambda r_1 {k_1}^2+\Lambda\mu\beta_2 r_1 k_1+\Lambda\mu^2{\beta_2}^2}{\mu\lambda(k_1\,\lambda+\,\mu\beta_2)} < 0,$$

contradiction since all parameters are non-negative. Hence, $B > 0\ and\ C < 0$.

And so E_1 exist if

$$\frac{\Lambda r_1 k_1+\Lambda\mu\beta_2}{\alpha_{\,2}\mu\lambda} > 1. \qquad (3.6)$$

III. Strain2 disease free equilibrium E_2 to the coordinates $(\hat{S}(t)\,, \hat{V}_{\,1}(t), \hat{V}_{\,2}(t), \hat{I}_1(t), \hat{I}_2(t))$ is given by

$$\hat{S}(t) = \frac{\Lambda}{\beta_1 I_1+\,\lambda}, \quad \hat{V}_{\,1}(t) = \frac{\Lambda r_1}{\mu(\beta_1 I_1+\lambda)}$$

$$\hat{V}_{\,2}(t) = \frac{\Lambda r_2}{(k_2\,I_1+\mu)(\beta_1 I_1+\,\lambda)}, \quad \hat{I}_2(t) = 0.$$

and $\hat{I}_1(t)$ is the root of the quadratic

$$A\,\hat{I}_1^{\,2} + B\hat{I}_1 + C = 0\,,$$

where,

$$A = \alpha_{\,2}k_1\beta_2,\ B = \alpha_{\,1}k_2\,\lambda + \alpha_{\,1}\mu\beta_1 - \Lambda k_1\beta_2,$$

$$C = \alpha_{\,1}\mu\lambda - \Lambda r_2 k_2 - \Lambda\mu\beta_1\,.$$

Similarly E_2 will only be biologically meaningful and hence exist if $\hat{I}_2(t)$ is positive. And therefore $C < 0$ so

$$\frac{\Lambda r_2 k_2+\Lambda\mu\beta_1}{\alpha_{\,1}\mu\lambda} > 1 \qquad (3.7)$$

IV. Double strain infection equilibrium E_3 to the coordinates $(\check{S}(t), \check{V}_1(t), \check{V}_2(t), \check{I}_1(t), \check{I}_2(t))$ is given by

$$\check{S}(t) = \frac{\Lambda}{\beta_1 I_1 + \beta_2 I_2 + \lambda}, \quad \check{V}_1(t) = \frac{\Lambda r_1}{(k_1 I_2 + \mu)(\beta_1 I_1 + \beta_2 I_2 + \lambda)},$$

$$\check{V}_2(t) = \frac{\Lambda r_2}{(k_2 I_1 + \mu)(\beta_1 I_1 + \beta_2 I_2 + \lambda)}.$$

$\check{I}_1(t)$ is the root of the equation

$$A_1 I_1^2 + B_1 I_1 I_2 + C_1 I_1 + D_1 I_2 + E_1 = 0,$$

where,

$$A_1 = -\alpha_1 k_2 \beta_1, \; B_1 = -\alpha_1 \beta_2 k_2 \quad C_1 = \Lambda k_2 \beta_1 - \alpha_1 \lambda k_2 - \alpha_1 \mu \beta_1,$$
$$D_1 = -\alpha_1 \mu \beta_2 \quad E_1 = \Lambda k_2 r_2 - \alpha_1 \mu \lambda + \Lambda \mu \beta_1.$$

And

$\check{I}_2(t)$ is the root of the equation

$$A_2 I_2^2 + B_2 I_1 I_2 + C_2 I_1 + D_2 I_2 + E_2 = 0,$$

where,

$$A_2 = -\alpha_2 k_1 \beta_2, \; B_2 = -\alpha_2 \beta_1 k_1 \; C_2 = -\alpha_2 \mu \beta_1,$$
$$D_2 = \Lambda k_1 \beta_2 - \alpha_2 \lambda k_1 - \alpha_2 \mu \beta_2 \; E_1 = \Lambda k_1 r_1 - \alpha_2 \mu \lambda + \Lambda \mu \beta_2,$$

The equilibrium E_3 exist and would be biologically meaningful if $\check{I}_1(t)$ and $\check{I}_2(t)$ are positive.

3.2.2. Reproduction Number

We proceed by computing the reproduction number by employing the new generation matrix method discussed in chapter 2. Considering the infected compartment $(I_1(t), I_2(t))$, the jacobian matrices F and V representing the new infectivity and the transfer of persons connecting the compartments respectively, evaluated at E_0 are given by

$$\partial F = \begin{pmatrix} k_2 V_2 + \beta_1 S \\ k_1 V_1 + \beta_2 S \end{pmatrix}, \partial V = \begin{pmatrix} \alpha_1 I_1 \\ \alpha_2 I_2 \end{pmatrix}$$

$$F = \begin{pmatrix} k_2 V^0{}_2 + \beta_1 S^0 & 0 \\ 0 & k_1 V^0{}_1 + \beta_2 S^0 \end{pmatrix},$$

$$V = \begin{pmatrix} \alpha_1 & 0 \\ 0 & \alpha_2 \end{pmatrix},$$

$$G = FV^{-1} = \begin{pmatrix} \frac{k_2 V^0{}_2 + \beta_1 S^0}{\alpha_1} & 0 \\ 0 & \frac{k_1 V^0{}_1 + \beta_2 S^0}{\alpha_2} \end{pmatrix}.$$

The Jacobian matrix of G will be:

$$|G - Ip| = \begin{pmatrix} \frac{k_2 V^0{}_2 + \beta_1 S^0}{\alpha_1} - p & 0 \\ 0 & \frac{k_1 V^0{}_1 + \beta_2 S^0}{\alpha_2} - p \end{pmatrix},$$

$$\Rightarrow \left(\frac{k_2 V^0{}_2 + \beta_1 S^0}{\alpha_1} - p\right)\left(\frac{k_1 V^0{}_1 + \beta_2 S^0}{\alpha_2} - p\right) = 0$$

$$\Rightarrow p_1 = \frac{k_2 V^0{}_2 + \beta_1 S^0}{\alpha_1},\ p_2 = \frac{k_1 V^0{}_1 + \beta_2 S^0}{\alpha_2}$$

$$\Rightarrow p_1 = \frac{k_2 r_2 \Lambda}{\alpha_1 \mu\lambda} + \frac{\beta_1 \Lambda}{\alpha_1 \lambda},\ p_2 = \frac{k_1 r_1 \Lambda}{\alpha_2 \mu\lambda} + \frac{\beta_2 \Lambda}{\alpha_2 \lambda}.$$

Since the basic reproduction number is the dominant eigen value, then

$$R_0 = \max\{R_1, R_2\},$$

where

$$R_1 = \frac{k_2 r_2 \Lambda}{\alpha_1 \mu\lambda} + \frac{\beta_1 \Lambda}{\alpha_1 \lambda},$$

and

$R_2 = \frac{k_1 r_1 \Lambda}{\alpha_2 \mu \lambda} + \frac{\beta_2 \Lambda}{\alpha_2 \lambda}$.

3.2.3. Stability Analysis

The Jacobian matrix of model (3.2) is given by

$$\begin{pmatrix} -(\beta_1 I_1 + \beta_2 I_2 + \lambda) & 0 & 0 & -\beta_1 S & -\beta_2 S \\ r_1 & -(k_1 I_2 + \mu) & 0 & 0 & -k_1 V_1 \\ r_2 & 0 & -(k_2 I_1 + \mu) & -k_2 V_2 & 0 \\ \beta_1 I_1 & 0 & k_2 I_1 & k_2 V_2 + \beta_1 S - \alpha_1 & 0 \\ \beta_2 I_2 & k_1 I_2 & 0 & 0 & k_1 V_1 + \beta_2 S - \alpha_2 \end{pmatrix} \quad (3.8)$$

Theorem 3.2: The disease-free equilibrium E_0 is locally asymptotically stable if $R_1 < 1$ and $R_2 < 1$.

Proof:

Evaluating the Jacobian matrix (3.6) of model (3.2) at E_0 we get,

$$\begin{pmatrix} -\lambda & 0 & 0 & \frac{-\beta_1 \Lambda}{\lambda} & \frac{-\beta_2 S}{\lambda} \\ r_1 & -\mu & 0 & 0 & \frac{-k_1 r_1 \Lambda}{\mu\lambda} \\ r_2 & 0 & -\mu & \frac{-k_2 r_2 \Lambda}{\mu\lambda} & 0 \\ 0 & 0 & 0 & \frac{k_2 r_2 \Lambda}{\mu\lambda} + \frac{\beta_1 \Lambda}{\lambda} - \alpha_1 & 0 \\ 0 & 0 & 0 & 0 & \frac{k_1 r_1 \Lambda}{\mu\lambda} + \frac{\beta_2 \Lambda}{\lambda} - \alpha_2 \end{pmatrix}$$

Solving for the Eigen values we arrive at

$$(-\lambda - p)(-\mu - p)(-\mu - p)\left[\left(\frac{k_2 r_2 \wedge}{\mu\lambda} + \frac{\beta_1 \wedge}{\lambda} - \alpha_1\right) - p\right]\left[\left(\frac{k_1 r_1 \wedge}{\mu\lambda} + \frac{\beta_2 \wedge}{\lambda} - \alpha_2\right) - p\right]=0.$$

Further solving and simplifying, we get that

$$p_1 = -\lambda, p_2 = p_3 = -\mu$$

and the quadratic

$$p^2 + a_1 p + a_2 = 0\ ,$$

where

$$a_1 = (\alpha_1(-R_1 + 1) + \alpha_2(-R_2 + 1))\ ,$$

$$a_2 = \left(\alpha_1(R_1 - 1)\alpha_2(R_2 - 1)\right).$$

Observe that a_1 and a_2 will only be positive when $R_1 < 1$ and $R_2 < 1$.

So, by Routh-Hurwitz criterion all eigenvalues are negative $\left(\left|\arg\lambda_j\right| = \pi > \frac{\sigma\pi}{2}, j = 1,2,\ldots,5\right)$ if

$$R_1 < 1 \text{ and } R_2 < 1.$$

Therefore, the disease-free equilibrium E_0 is locally asymptotically stable for $\sigma \in (0,1]$ if $R_1 < 1$ and $R_2 < 1$.

Theorem 3.2: The Strain1 disease equilibrium E_1 is locally asymptotically stable if $R_1 < 1$.

Proof:

Evaluating the Jacobian matrix (3.8) of model (3.2) at E_1 we get,

$$\begin{pmatrix} -(\beta_2 I_2 + \lambda) & 0 & 0 & \frac{-\beta_1 \wedge}{\beta_2 I_2 + \lambda} & \frac{-\beta_2 \wedge}{\beta_2 I_2 + \lambda} \\ r_1 & -(k_1 I_2 + \mu) & 0 & 0 & \frac{-k_1 r_1 \wedge}{(\beta_2 I_2 + \lambda)(k_1 I_2 + \mu)} \\ r_2 & 0 & -\mu & \frac{-k_2 r_2 \wedge}{(\beta_2 I_2 + \lambda)\mu} & 0 \\ 0 & 0 & 0 & \frac{k_2 r_2 \wedge}{(\beta_2 I_2 + \lambda)\mu} + \frac{\beta_1 \wedge}{\beta_2 I_2 + \lambda} - \alpha_1 & 0 \\ \beta_2 I_2 & k_1 I_2 & 0 & 0 & \frac{k_1 r_1 \wedge}{(\beta_2 I_2 + \lambda)(k_1 I_2 + \mu)} + \frac{\beta_2 \wedge}{\beta_2 I_2 + \lambda} - \alpha_2 \end{pmatrix}$$

Solving the matrix for the Eigen values we arrive at:

$$[-(\beta_1 I_1 + \lambda) - p][-(k_1 I_2 + \mu) - p][-\mu - p]\left[\left(\frac{k_2 r_2 \wedge}{(\beta_2 I_2 + \lambda)\,\mu} + \frac{\beta_1 \wedge}{\beta_2 I_2 + \lambda} - \alpha_1\right) - p\right]\left[\left(\frac{k_1 r_1 \wedge}{(\beta_2 I_2 + \lambda)\,(k_1 I_2 + \mu)} + \frac{\beta_2 \wedge}{\beta_2 I_2 + \lambda} - \alpha_2\right) - p\right] = 0.$$

Further solving and simplifying previous equation, we get that

$$p_1 = -(\beta_1 I_1 + \lambda), \qquad p_2 = -(k_1 I_2 + \mu), \qquad p_3 = -\mu,$$

and the quadratic:

$$p^2 + a_1 p + a_2 = 0,$$

where

$$a_1 = \left(\frac{-\alpha_2 \lambda}{\beta_2 I_2 + \lambda}\left(\frac{k_1 r_1 \wedge}{\alpha_2 \lambda (k_1 I_2 + \mu)} + \frac{\beta_2 \wedge}{\alpha_2 \lambda} - 1 - \frac{\beta_2 I_2}{\lambda}\right)\right) + \left(\frac{-\alpha_1 \lambda}{\beta_2 I_2 + \lambda}\left(R_1 - 1 - \frac{\beta_2 I_2}{\lambda}\right)\right),$$

$$a_2 = \left(\frac{\alpha_2 \lambda}{\beta_2 I_2 + \lambda}\left(\frac{k_1 r_1 \wedge}{\alpha_2 \lambda (k_1 I_2 + \mu)} + \frac{\beta_2 \wedge}{\alpha_2 \lambda} - 1 - \frac{\beta_2 I_2}{\lambda}\right)\right)\left(\frac{\alpha_1 \lambda}{\beta_2 I_2 + \lambda}\left(R_1 - 1 - \frac{\beta_2 I_2}{\lambda}\right)\right).$$

Applying equation (3.6), a_1 and a_2 will only be positive when $R_1 < 1$. So, by Routh-Hurwitz criterion, all eigenvalues are negative $\left(|\arg \lambda_j| = \pi > \frac{\sigma\pi}{2}, j = 1,2,\dots,5\right)$ if $R_1 < 1$. Therefore, the strain 1 disease equilibrium E_1 is locally asymptotically stable for $\sigma \in (0,1]$ if $R_1 < 1$.

Theorem 3.3: The Strain2 disease equilibrium E_2 is locally asymptotically stable if $R_2 < 1$.

Proof:

Evaluating the Jacobian matrix (3.8) of model (3.2) at E_2 we get

$$\begin{pmatrix} -(\beta_1 I_1 + \lambda) & 0 & 0 & \frac{-\beta_1 \wedge}{\beta_1 I_1 + \lambda} & \frac{-\beta_2 \wedge}{\beta_1 I_1 + \lambda} \\ r_1 & -\mu & 0 & 0 & \frac{-k_1 r_1 \wedge}{(\beta_1 I_1 + \lambda)\,\mu} \\ r_2 & 0 & -(k_2 I_1 + \mu) & \frac{k_2 r_2 \wedge}{(\beta_1 I_1 + \lambda)\,(k_2 I_1 + \mu)} & 0 \\ \beta_1 I_1 & 0 & k_2 I_1 & \frac{k_2 r_2 \wedge}{(\beta_1 I_1 + \lambda)(k_2 I_1 + \mu)} + \frac{\beta_1 \wedge}{\beta_1 I_1 + \lambda} - \alpha_1 & 0 \\ 0 & 0 & 0 & 0 & \frac{k_1 r_1 \wedge}{(\beta_1 I_1 + \lambda)\,\mu} + \frac{\beta_2 \wedge}{\beta_1 I_1 + \lambda} - \alpha_2 \end{pmatrix},$$

solving the matrix for the Eigen values we arrive at:

$$[-(\beta_1 I_1 + \lambda) - p][-\mu - p][-(k_2 I_1 + \mu) - p]\left[\left(\frac{k_2 r_2 \wedge}{(\beta_1 I_1 + \lambda)(k_2 I_1 + \mu)} + \frac{\beta_1 \wedge}{\beta_1 I_1 + \lambda} - \alpha_1\right) - p\right]\left[\left(\frac{k_1 r_1 \wedge}{(\beta_1 I_1 + \lambda)\,\mu} + \frac{\beta_2 \wedge}{\beta_1 I_1 + \lambda} - \alpha_2\right) - p\right] = 0.$$

Further solving and simplifying we get that

$$p_1 = -(\beta_1 I_1 + \lambda), \qquad p_2 = -\mu, \qquad p_3 = -(k_2 I_1 + \mu),$$

and the quadratic

$$p^2 + a_1 p + a_2 = 0,$$

where

$$a_1 = \left(\frac{-\alpha_1 \lambda}{\beta_1 I_1 + \lambda}\left(\frac{k_2 r_2 \wedge}{\alpha_1 \lambda (k_2 I_1 + \mu)} + \frac{\beta_1 \wedge}{\alpha_1 \lambda} - 1 - \frac{\beta_1 I_1}{\lambda}\right)\right) + \left(\frac{-\alpha_2 \lambda}{\beta_1 I_1 + \lambda}\left(R_2 - 1 - \frac{\beta_1 I_1}{\lambda}\right)\right),$$

$$a_2 = \left(\frac{\alpha_1 \lambda}{\beta_1 I_1 + \lambda}\left(\frac{k_2 r_2 \wedge}{\alpha_1 \lambda (k_2 I_1 + \mu)} + \frac{\beta_1 \wedge}{\alpha_1 \lambda} - 1 - \frac{\beta_1 I_1}{\lambda}\right)\right)\left(\frac{\alpha_2 \lambda}{\beta_1 I_1 + \lambda}\left(R_2 - 1 - \frac{\beta_1 I_1}{\lambda}\right)\right).$$

Applying equation (3.7), a_1 and a_2 will only be positive when $R_2 < 1$.

So, by Routh-Hurwitz criterion, eigenvalues are negative $\left(\left|\arg \lambda_j\right| = \pi > \frac{\sigma\pi}{2}, j = 1,2,\dots,5\right)$ if $R_2 < 1$.

Therefore, the strain 2 disease equilibrium E_2 is locally asymptotically stable for $\sigma \in (0,1]$ if $R_2 < 1$.

CHAPTER 4

NUMERICAL SIMULATIONS OF THE FRACTIONAL MODEL

In this chapter, numerical simulations were carried out to support the analytic results using the Matlab code fde12.m which implements the Predictor-Corrector Method proposed by (Diethelm, K., & Freed, A. D. 1998).

Parameters were calculated and adopted from previous studies (Ye, X., & Xu, C. 2019). The assumed initial conditions are $\big(S(t), V_1(t), V_2(t), I_1(t), I_2(t)\big) = (200,133,133,2,2)$ with a time prospect of 100 days and varying values of the order of the derivative between 0 and 1.

To further buttress the simulation, real data were collected from the Global Influenza Surveillance and Response System (GISRS) of the World Health Organization (WHO)

(World Health Organization 2020) and analyzed using SPSS.

r

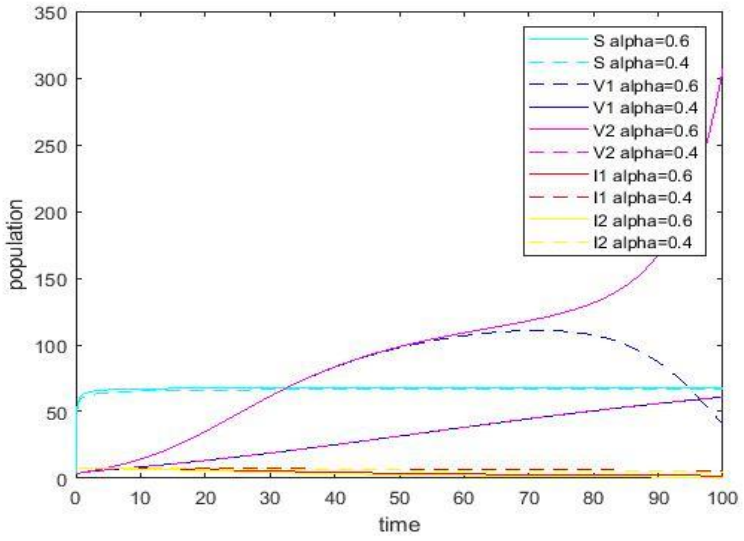

Figure 4.1: Disease free equilibrium E_0

Here both strains die out. Parameter values are: $\wedge = 200,\ \lambda = 0.01,\ r_1 = 0.3,\ r_2 = 0.3\ \mu = 0.02,\ \alpha_1 = 0.0003\ ,\ \alpha_2 = 0.0003, \beta_1 = 0.00001,\ \beta_2 = 0.00001,\ k_1 = 0.007\ k_2 = 0.009$ and order of the derivative 0.6 and 0.4 simultaneously.

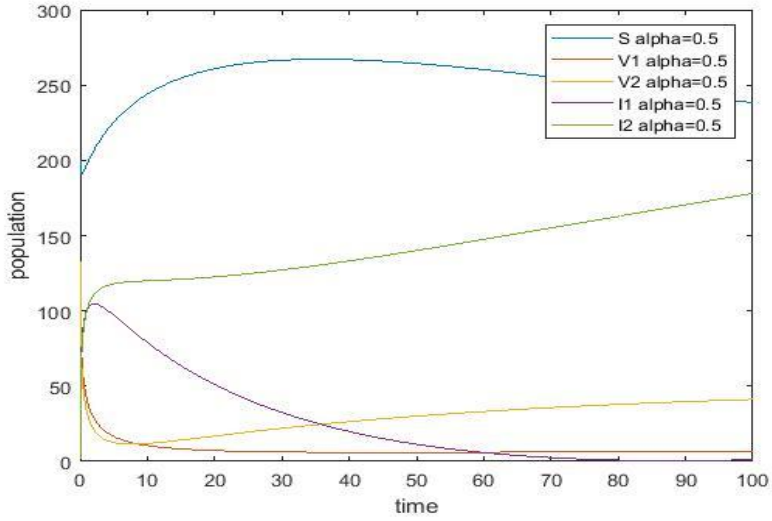

Figure 4.2: Strain 1 disease free equilibrium E_1

Parameter values are: $\wedge = 20,\ \lambda = 0.5,\ r_1 = 0.3,\ r_2 = 0.3\ \mu = 0.02,\ \alpha_1 = 0.0721\ ,\ \alpha_2 = 0.0719,\ \beta_1 = 0.0000001,\ \beta_2 = 0.0000001,\ k_1 = 0.0089,\ k_2 = 0.0099$ and order of the derivative is 0.5.

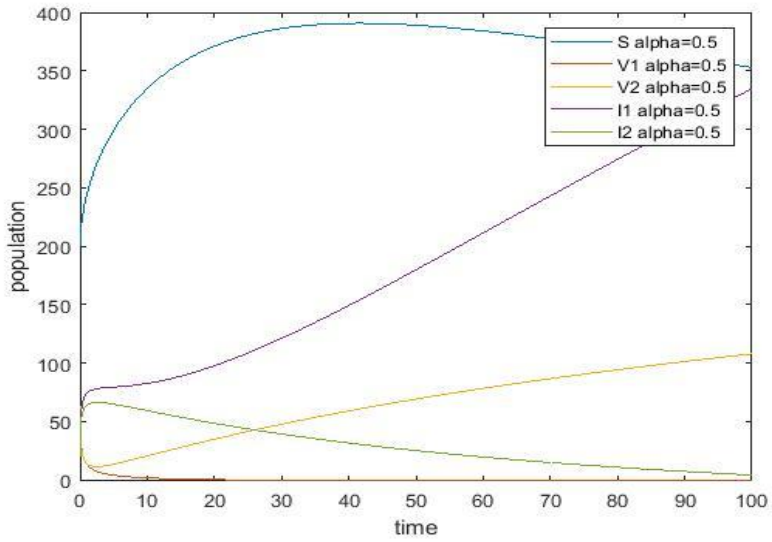

Figure 4.3: Strain 2 disease free equilibrium E_2

Parameter values are: $\wedge = 43,\ \lambda = 0.0001,\ r_1 = 0.03,\ r_2 = 0.003\ \mu = 0.02,\ \alpha_1 = 0.000001\ ,\ \alpha_2 = 0.01,\ \beta_1 = 0.00001,\ \beta_2 = 0.001,\ k_1 = 0.0089,\ k_2 = 0.0099$ and order of the derivative is 0.5

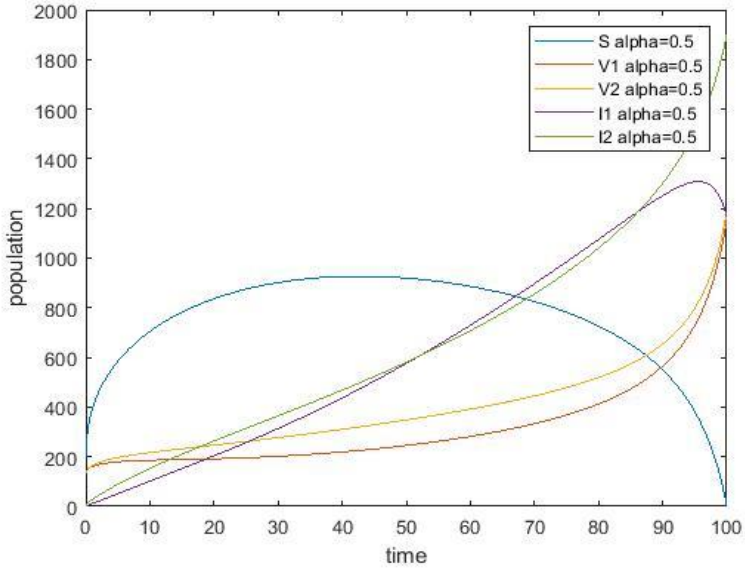

Figure 4.4: Endemic equilibrium E_3

Parameter values are: $\wedge = 200,\ \lambda = 0.01,\ r_1 = 0.3,\ r_2 = 0.3\ \mu = 0.02,\ \alpha_1 = 0.0003$, $\alpha_2 = 0.0003, \beta_1 = 0.001,\ \beta_2 = 0.001, k_1 = 0.0089,\ k_2 = 0.009$ and order of the derivative is 0.5

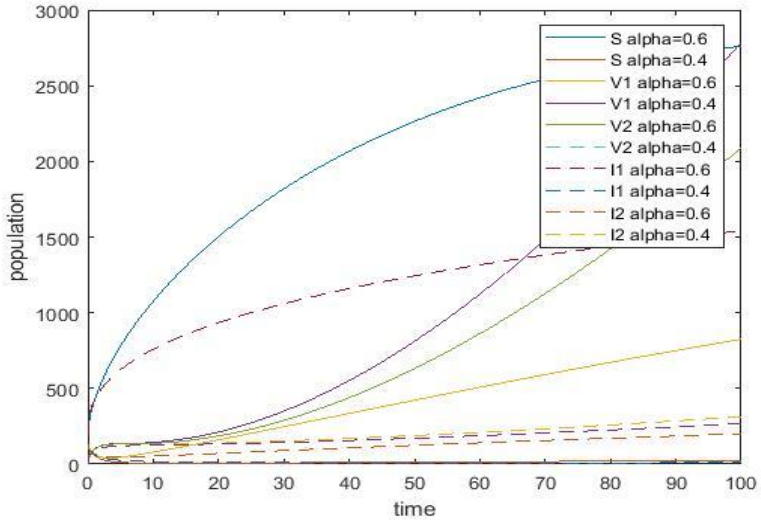

Figure 4.5: Endemic effect of vaccine

$\wedge = 200,\ \lambda = 0.03,\ r_1 = 0.3,\ r_2 = 0.3\ \mu = 0.02,\quad \alpha_1 = 0.0009,\ \alpha_2 = 0.0007,\quad \beta_1 = 0.00003,\ \beta_2 = 0.00003,\ k_1 = 0.003\ k_2 = 0.003$ and order of the derivative 0.6 and 0.4 simultaneously.

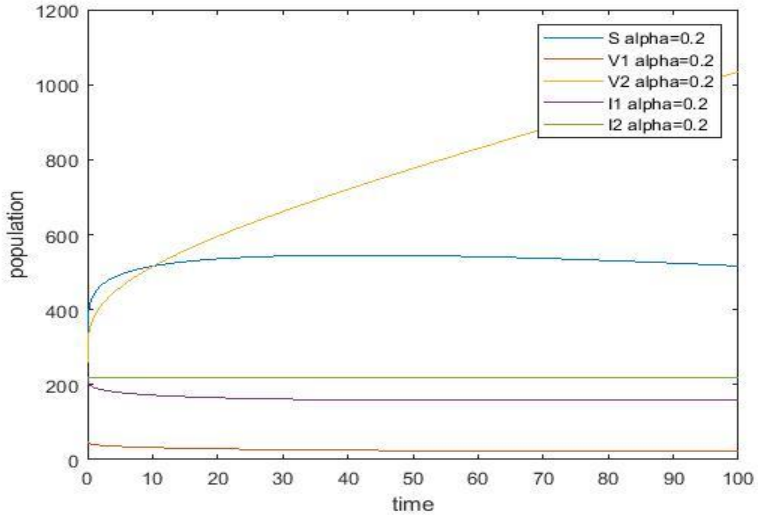

Figure 4.6: Endemic effect of low V_1

$\wedge = 200,\ \lambda = 0.03,\ r_1 = 0.3,\ r_2 = 0.3\ \mu = 0.02,\ \ \alpha_1 = 0.07\ ,\ \alpha_2 = 0.09,\ \beta_1 = 0.00003,$ $\beta_2 = 0.00003,\ k_1 = 0.00001\ k_2 = 0.00001$ and order of the derivative is 0.2.

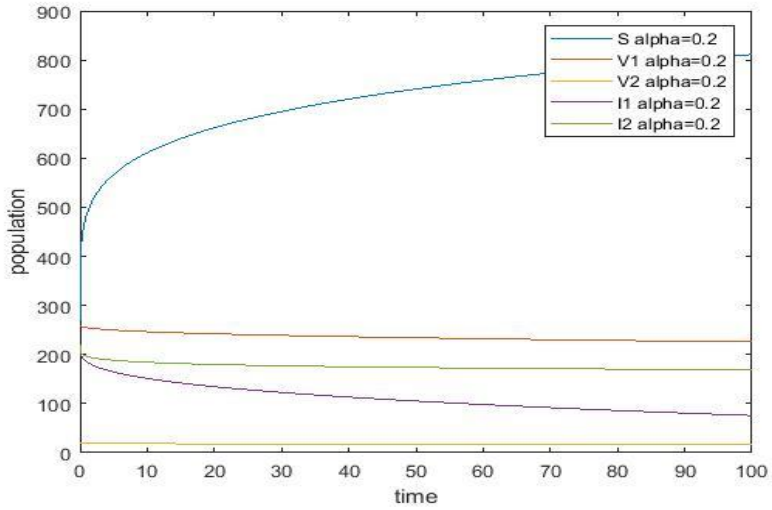

Figure 4.7: Endemic effect of low V_2

$\wedge = 200,\ \lambda = 0.03,\ r_1 = 0.3,\ r_2 = 0.3\ \mu = 0.02,\ \ \alpha_1 = 0.07\ ,\ \alpha_2 = 0.09,\ \beta_1 = 0.00003,$ $\beta_2 = 0.00003,\ k_1 = 0.00001\ k_2 = 0.00001$ and order of the derivative is 0.2.

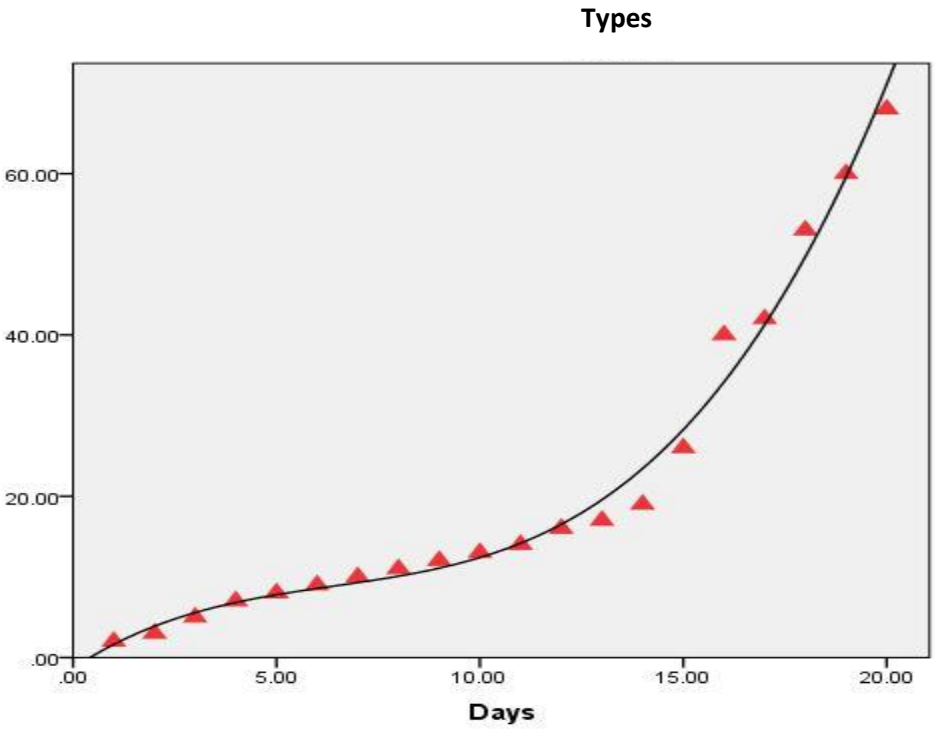

Figure 4.8: Curve fitting of the influenza data

CHAPTER 5

RESULTS AND CONCLUSION

In this paper, we have investigated a fractional order two strain epidemic model with two vaccinations as a generalization of the integer order model proposed by (Baba, I. A., et al 2018). The reproduction number(R_0) has been computed and used to prove the stability at various equilibriums of the fractional-order model of the seasonal influenza disease.

Analytically and numerically, following mathematical analysis, the disease free equilibrium is locally asymptotically stable when $R_1 < 1$ and $R_2 < 1$ which implies that the disease will die out in the population over a period of time. Also, the strain1 disease free equilibrium locally asymptotically stable if $R_1 < 1$ and $R_2 > 1$ while the strain2 disease free equilibrium locally asymptotically stable if $R_1 > 1$ and $R_2 < 1$. This means that one disease strain outperforms the other as it becomes endemic and the other dies out. In other words the strain with a higher reproduction number thrives and the other with a reproduction less than 1 dies out eventually.

Furthermore, the endemic equilibrium tends to be locally asymptotically stable when $R_1 > 1$ and $R_2 > 1$ which means that both strains persist in the population.

It can be seen that the stability of the various equilibrium depends on the degree of the threshold of the reproduction numbers:

$$R_1 = \frac{k_2 r_2 \Lambda}{\alpha_1 \mu \lambda} + \frac{\beta_1 \Lambda}{\alpha_1 \lambda}$$

and

$$R_2 = \frac{k_1 r_1 \Lambda}{\alpha_2 \mu \lambda} + \frac{\beta_2 \Lambda}{\alpha_2 \lambda}.$$

Therefore, to evade a pandemic of the disease, it is sufficient to shrink the threshold value of the reproduction number below 1. The fastest way to accomplish this is by dropping the occurrence of the recruitment rate. We see this from the numerical simulations that as the population increases the magnitude of the infective also increases. Another way would be vaccinating the entire population if possible so long as the vaccinations are effective and safe, as many flu vaccines cause neurological disorder.

More so, from the numerical simulations, the memory effect can clearly be appreciated, deduced from incorporating the fractional order on the system as compared to the integer order; where the values of the fractional order were varied between 0 and 1. It is easy to see from Figure 4.5, Figure 4.6 and Figure 4.7 that when the vaccine for a strain is absent, the strain amplifies as compared to when its vaccine is prevailing. In other words, more infective will join a certain strain compartment when the vaccine for the other outperforms its vaccine but in different magnitude, implying that one strain become stronger than the other.

Fig 4.8 clearly shows that the model predictive accuracy is good with a regression coefficient of 0.988. We see how the predictive line from the curve fitting portends the real data signifying mathematical prognosis and memory effect.

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APPENDICES

APPENDIX 1

TEZ

Assist. Prof. Dr. Bilgen Kaymakamzade

26.07.2020

YAKIN DOĞU ÜNİVERSİTESİ

APPENDIX 2

ETHICAL APROVAL DOCUMENT

Date: 24/07/2020

To the **Graduate School of Applied Sciences**

The research project titled "**A FRACTIONAL-ORDER TWO-STRAIN EPIDEMIC MODEL WITH TWO VACCINATIONS** " has been evaluated. Since the researcher(s) will not collect primary data from humans, animals, plants or earth, this project does not need to go through the ethics committee.

Title: Assist.Prof.Dr.

Name Surname: Bilgen Kaymakamzade

Signature:

Role in the Research Project: Supervisor