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NABLA Fractional Calculus and Its Application in Analyzing Tumor Growth of Cancer

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NABLA FRACTIONAL CALCULUS AND ITS APPLICATION IN ANALYZING TUMOR GROWTH OF CANCER

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CONTENTS

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This thesis consists of six chapters. In the first chapter, we review some basic definitions and concepts of fractional calculus. Then we introduce fractional difference equations involving the Riemann-Liouville operator of real number order between zero and one. In the second chapter, we apply the Brouwer fixed point and Contraction Mapping Theorems to prove that there exists a solution for up to the first order nabla fractional difference equation with an initial condition. In chapter three, we define a lower and an upper solution for up to the first order nabla fractional difference equation with an initial condition. Under certain assumptions we prove that a lower solution stays less than an upper solution. Some examples are given to illustrate our findings in this chapter. Then we give constructive proofs of existence of a solution by defining monotone sequences. In the fourth chapter, we derive a continuous form of the Mittag-Leffler function. Then we use successive approximations method to calculate a discrete form of the Mittag-Leffler function. In the fifth chapter, we focus on finding the model which fits best for the data of tumor growth for twenty-eight mice. The models contain either three parameters (Gompertz, Logistic) or four parameters (Weibull, Richards). For each model, we

consider continuous, discrete, continuous fractional and discrete fractional forms. Nihan Acar who is a former graduate student in mathematics department has already worked on Gompertz and Logistic models [**1**]. Here we continue and work on Richards curve. The difference between Acar's work and ours is the number of parameters in each model. Gompertz and Logistic models contain three parameters and an alpha parameter. The Richards model has four parameters and an alpha parameter. In addition, we use statistical computation techniques such as residual sum of squares and cross-validation to compare fitting and predictive performance of these models. In conclusion, we put three models together to conclude which model is fitting best for the data of tumor growth for twenty-eight mice. In the last chapter, we conclude this thesis and state our future work.

Chapter 1

INTRODUCTION

Fractional calculus is a branch of calculus that generalizes the derivative of a function to non-integer order, allowing calculations such as $\frac{1}{2}$ order derivative of a function. Fractional calculus has a long and rich history. The idea of fractional calculus was from a letter dated September 30th, 1695, L'Hôpital wrote to Leibniz asking him about a particular notation he had used in his publications for the n^{th}-derivative of the linear function $f(x) = x$, $\frac{d^n y}{dx^n}$. L' Hôpital posed the question to Leibniz, what would the result be if $n = \frac{1}{2}$. Leibniz's response was, "An apparent paradox, from which one day useful consequences will be drawn." In these words, fractional calculus was born.

Following L'Hôpital's and Leibniz's first inquiry, fractional calculus was primarily a study reserved for the best minds in mathematics. Fourier, Euler, Laplace, Riemann, Liouville and Caputo are among the many who developed the theory of fractional calculus. Many found, using their own notation and methodology, definitions that fit the concept of a non-integer order integral or derivative. There are three main definitions for fractional calculus: the Riemann-Liouville definition, the Caputo definition and the Grünwald-Letnitov definition. The most common one which has been popularized in the world of fractional calculus is the Riemann-Liouville definition.

On the other hand, discrete fractional calculus is the discrete version of fractional calculus which deals with any positive real order of sum or difference. The nabla operator (∇) is known as the backward difference operator. The delta operator (Δ) is known as the forward difference operator. Several studies have been done to obtain the properties of discrete fractional calculus with nabla and delta operators [**2, 11, 30**]. In recent years, mathematicians have applied fractional and discrete fractional calculus to a variety of problems in bioscience, engineering and economics [**3, 4, 5, 6, 7**].

1.1. Special Functions

In this section, we discuss some necessary but relatively simple mathematical definitions that will arise in the study of the basic concepts of fractional calculus. First, we review the Gamma function and some basic properties of this function.

1.1.1. Gamma Function. The definition of the Gamma function is given by

$$\Gamma(x) = \int_0^\infty e^{-t} t^{x-1} dt, \qquad x \in \mathbb{R}.$$

The Gamma function satisfies the following equation

$$\Gamma(n) = (n-1)!, \qquad n \in \mathbb{N}.$$

The simplest interpretation of the Gamma function is the generalization of the factorial for all real numbers.

The Gamma function has following property:

$$\Gamma(x+1) = x\Gamma(x), \quad \text{where } x \in \mathbb{R}^+.$$

1.1.2. Mittag-Leffler Function. The Mittag-Leffler function is named after Gösta Mittag-Leffler who defined and studied the special function in 1903 [**8**]. The function is a direct generalization of exponential function e^x, and it plays a major role in fractional calculus. The one and two-parameter representations of the Mittag-Leffler function can be defined in terms of a power series as

$$E_\alpha(x) = \sum_{k=0}^{\infty} \frac{x^k}{\Gamma(\alpha k + 1)},$$

$$E_{\alpha,\beta}(x) = \sum_{k=0}^{\infty} \frac{x^k}{\Gamma(\alpha k + \beta)},$$

where α and β are postive real numbers. The Mittag-Leffler function with two-parameters was first defined by Agarwal in 1953 [**9**].

The discrete Mittag-Leffler function is defined with one and two-parameters in the following way. Related definitions are given by Nagai in [**10**]

$$F_\alpha(at) = \sum_{k=0}^{\infty} \frac{a^k t^{\overline{k}}}{\Gamma(\alpha k + 1)},$$

$$F_{\alpha,\beta}(at) = \sum_{k=0}^{\infty} \frac{a^k t^{\overline{k}}}{\Gamma(\alpha k + \beta)},$$

where α, β are positive real numbers and $|a| < 1$.

For any real number v, the discrete Mittag-Leffler function is defined as

$$F_{\alpha,\beta}(at^{\overline{v}}) = \sum_{k=0}^{\infty} \frac{a^k t^{\overline{kv}}}{\Gamma(\alpha k + \beta)},$$

where $t^{\overline{kv}}$ will be defined in the next section.

1.2. Basic Concepts in Nabla Fractional Calculus

The fractional sum operator extends the discrete fractional operator used in fractional calculus. Looking at the literature of discrete fractional difference operators, two approaches are found: one using the Δ operator (sometimes called the forward difference operator), another using the ∇ operator (sometimes called the backward difference operator). In this section, we focus on the study with the ∇ operator.

Here we give a short introduction to the basic definitions in discrete fractional calculus. For more on the subject we refer the reader to the papers [**11, 29, 31**]. We begin by introducing some notations.

Define

$$t^{\overline{\alpha}} = t(t+1)(t+2)\cdots(t+\alpha-1),\ \ \alpha \in \mathbb{N}$$

and $t^{\overline{0}} = 1$. The expression $t^{\overline{\alpha}}$ is well known and has been called "t to the α rising ." Many mathematicians employ the Pochhammer symbol $t^{(\alpha)}$ to denote the rising fractional function.

Let α be any real number. Then "t to the α rising" is defined to be

$$t^{\overline{\alpha}} = \frac{\Gamma(t+\alpha)}{\Gamma(t)}$$

where $t \in \mathbb{R}\setminus\{\cdots,-2,-1,0\}$, and $0^{\overline{\alpha}} = 0$.

Note that $\nabla(t^{\overline{\alpha}}) = \alpha t^{\overline{\alpha-1}}$, where $\nabla y(t) = y(t) - y(t-1)$. For $k = 2, 3, \ldots$, define ∇^k inductively by $\nabla^k = \nabla\nabla^{k-1}$.

Next, we recall the definition of the fractional sum and difference operators. $\nabla_a^{-\alpha} f$ is denoted to be the fractional sum of a function f with an arbitrary order $\alpha > 0$. $\nabla_a^{\alpha} f$ is denoted to be the fractional difference of a function f with an arbitrary order $\alpha > 0$.

Definition 1.2.1. *Let a be any real number and α be any positive real number. The $\alpha - th$ order fractional sum of f is defined as*

$$\nabla_a^{-\alpha} f(t) = \sum_{s=a}^{t} \frac{(t-\rho(s))^{\overline{\alpha-1}}}{\Gamma(\alpha)} f(s),$$

where $t = a, a+1, \ldots$ and $\rho(t) = t-1$ is the backward jump operator on the time scale calculus.

Note that for $\alpha = 1$, the equation turns into a discrete sum operator as given in the following form

$$\nabla_a^{-1} f(t) = \sum_{s=a}^{t} f(s).$$

Definition 1.2.2. *Let a be any real number and α be any positive real number such that $0 < n-1 < \alpha < n$ where n is an integer. The $\alpha - th$ order fractional difference (a Riemann-Liouville fractional difference) of f is defined* [**11**] *by*

$$\nabla_a^{\alpha} f(t) = \nabla^n \nabla_a^{-(n-\alpha)} f(t) = \nabla^n \sum_{s=a}^{t} \frac{(t-\rho(s))^{\overline{n-\alpha-1}}}{\Gamma(n-\alpha)} f(s),$$

where f is defined on $\mathbb{N}_a = \{a, a+1, a+2, \ldots\}$.

Next, we give some properties of nabla discrete fractional operators. Their proofs can be found in [**12**].

LEMMA 1.2.3. *(i)* $\nabla t^{\overline{\alpha}} = \alpha t^{\overline{\alpha-1}}$.

(ii) $t^{\overline{\alpha}}(t+\alpha)^{\overline{\beta}} = t^{\overline{\alpha+\beta}}$.

(iii) $\nabla_0^{-\alpha}(t+1)^{\overline{\beta}} = \dfrac{\Gamma(\beta+1)}{\Gamma(\beta+\alpha+1)}(t+1)^{\overline{\alpha+\beta}}$.

(iv) $\nabla_a^{-\alpha}(t-a+1)^{\overline{\beta}} = \dfrac{\Gamma(\beta+1)}{\Gamma(\beta+\alpha+1)}(t-a+1)^{\overline{\alpha+\beta}}$.

(v) $\nabla[\sum\limits_a^t f(t,s)] = f(\rho(t),t) + \sum\limits_a^t \nabla f(t,s)$.

THEOREM 1.2.4. *For any $v > 0$, the following equality holds:*

$$\nabla_{a+1}^{-v}\nabla f(t) = \nabla\nabla_a^{-v} f(t) - \frac{(t-a+1)^{\overline{v-1}}}{\Gamma(v)} f(a).$$

Next we consider an initial value problem for a fractional difference equation

$$\nabla_a^v y(t) = f(t, y(t)) \qquad for \quad t = a+1, a+2, \ldots,$$

$$\nabla_a^{-(1-v)} y(t)|_{t=a} = y(a) = c,$$

where $0 < v \leq 1$ and a is any real number.

Apply the operator ∇_{a+1}^{-v} to each side of the equation to obtain

$$\nabla_{a+1}^{-v}\nabla_a^v y(t) = \nabla_{a+1}^{-v} f(t, y(t)).$$

which can be written in the form

$$\nabla_{a+1}^{-v}\nabla\nabla_a^{-(1-v)} y(t) = \nabla_{a+1}^{-v} f(t, y(t)).$$

Using Theorem 1.2.4 we obtain

$$\nabla\nabla_a^{-v}\nabla_a^{-(1-v)}y(t) - \frac{(t-a+1)^{\overline{(v-1)}}}{\Gamma(v)}\nabla_a^{-(1-v)}y(t)|_{t=a} = \nabla_{a+1}^{-v}f(t,y(t)).$$

Then we have

$$\nabla\nabla_a^{-v}\nabla_a^{-(1-v)}y(t) = \frac{(t-a+1)^{\overline{(v-1)}}}{\Gamma(v)}y(a) + \nabla_{a+1}^{-v}f(t,y(t)).$$

It follows that

$$y(t) = \frac{(t-a+1)^{\overline{(v-1)}}}{\Gamma(v)}y(a) + \nabla_{a+1}^{-v}f(t,y(t)).$$

The above calculations show that we can obtain a fractional sum equation from a fractional difference equation with an initial value condition.

Next we present graphs of t^{α} and $t^{\overline{\alpha}}$ for $\alpha = 0.645$, $\alpha = 0.895$, $\alpha = 1$ and $\alpha = 1.65$. The straight line is the graph of t^{α} and the dashed line is $t^{\overline{\alpha}}$. It is clear to see how close they are when α equals to different numbers.

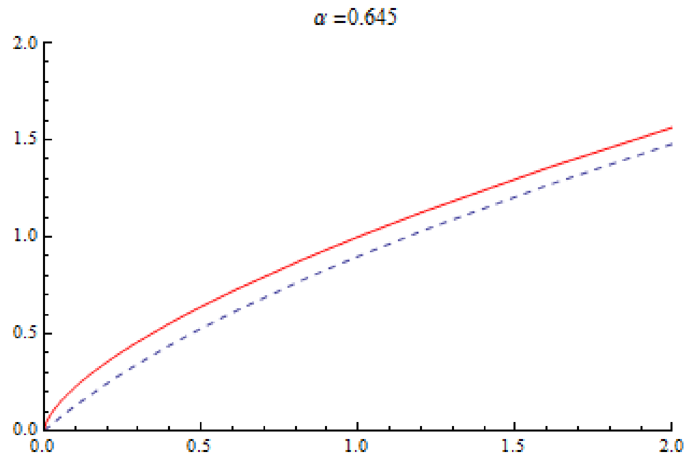

FIGURE 1.2.1. t^{α}, $t^{\overline{\alpha}}$ for $\alpha = 0.645$

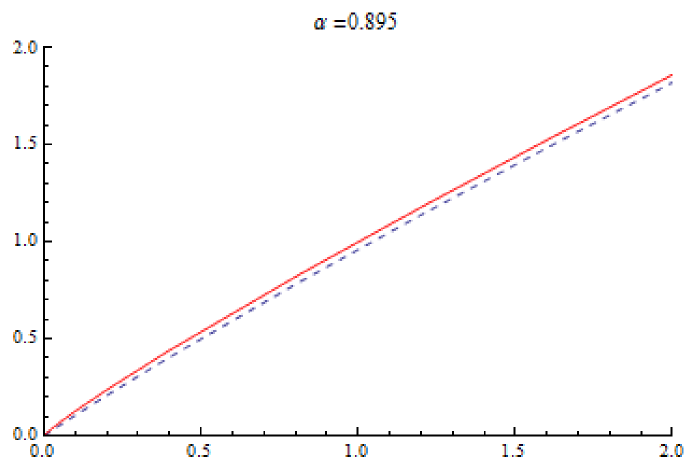

FIGURE 1.2.2. t^{α}, $t^{\overline{\alpha}}$ for $\alpha = 0.895$

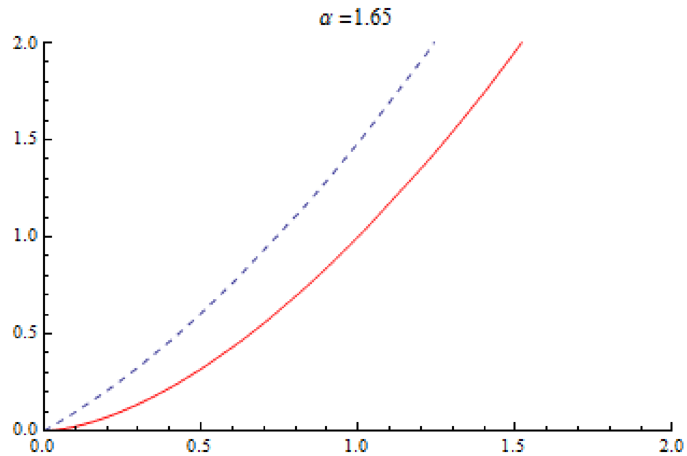

FIGURE 1.2.3. t^{α}, $t^{\overline{\alpha}}$ for $\alpha = 1.65$

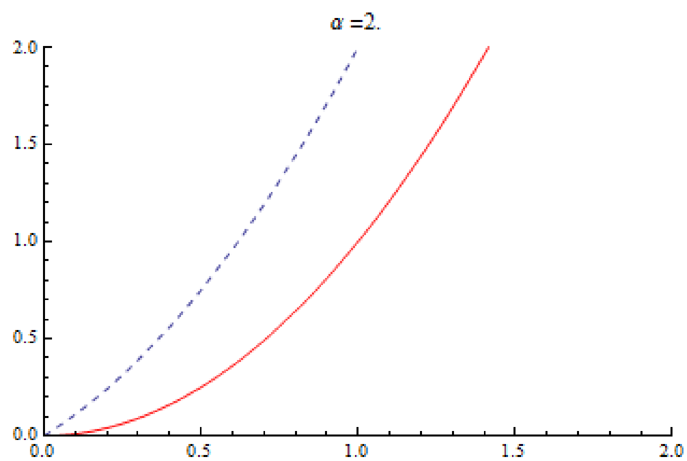

FIGURE 1.2.4. t^{α}, $t^{\overline{\alpha}}$ for $\alpha = 2$

Chapter 2

APPLICATIONS OF FIXED POINT THEOREMS

Before we search for methods of solving a fractional equation, we want to know whether there exists a solution. Fixed point theorems are some of the most important theorems in mathematics. Among other applications, they are used to show the existence of solutions to differential equations, as well as of equilibria in game theory [**27, 28**]. In this chapter, we apply the Brouwer fixed point theorem and the Contraction Mapping Theorem to prove the existence of a solution for up to the first order nabla fractional difference equation with an initial condition.

2.1. Existence of Solution by the Brouwer Fixed Point Theorem

The Brouwer fixed point theorem is one of the early achievements of algebraic topology, named after Luitzen Brouwer. It serves as a basis of many fixed point theorems which are important in functional analysis. Among hundreds of fixed point theorems, Brouwer's is particularly well known. The theorem is also used for providing deep results about differential equations and is covered in most introductory courses on differential geometry. In economics, Brouwer's fixed-point theorem and its extension, the Kakutani fixed-point theorem, play a central role in proof of existence of general equilibrium in market economics as developed in the 1950s [**36**].

At first, we discuss some definitions of fixed point theory. It would be helpful to get some ideas and results of the theory before entering the detailed proofs.

Definition 2.1.1. *Let $\mathbb{X}$ be any space and f be a map of $\mathbb{X}$, or a subset of X, into X. A point $x \in \mathbb{X}$ is called a fixed point for f if $x = f(x)$.*

Theorem 2.1.2. *(Brouwer fixed point theorem [**13**]) Let $K \subseteq \mathbb{R}^n$ and $K = \{(x_1, x_2, \ldots, x_n) : c_i \le x_i \le d_i, i = 1, 2, \ldots, n\}$. Suppose $T : K \to K$ is continuous. Then T has a fixed point in K.*

We consider the initial value problem

$$\begin{cases} \nabla_{t_0}^{\alpha} y(t) = f(t, y(t)), 0 < \alpha < 1 \\ \nabla_{t_0}^{-(1-\alpha)} y(t) \mid_{t=t_0} = y(t_0) = y_0. \end{cases} \tag{2.1}$$

Let $f(t, y)$ be a continuous function in y for each t in $[t_0, b]$ and be bounded on $[t_0, b] \times \mathbb{R}$, where $[t_0, b] = \{t_0, t_0 + 1, t_0 + 2, \cdots, b\}$. The following questions arise for problem (2.1). Does a solution exist? Is it unique? How can solutions be approximated? We will try to answer to all these questions in next few sections.

Theorem 2.1.3. *Let $f(t, y)$ be a continuous function in y for each t in $[t_0, b]$ and be bounded on $[t_0, b] \times \mathbb{R}$. Then there exists a solution for the initial value problem (2.1).*

Proof. We see that the above initial value problem (2.1) is equivalent to the following equation

$$y(t) = \nabla_{t_0+1}^{-\alpha} f(t, y(t)) + \frac{(t - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} y_0. \tag{2.2}$$

Let K=$\{y \mid y(t_0) = y_0, \| y \| \le k$ for some $k \in \mathbb{R}$, $t \in [t_0, b]\}$

Let f be bounded by $M \in \mathbb{R}$. For $y \in K$, define Ty by

$$Ty(t) = \nabla_{t_0+1}^{-\alpha} f(t, y(t)) + \frac{(t - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} y_0. \tag{2.3}$$

Then we have

$$\begin{aligned} |Ty(t)| &= |\nabla_{t_0+1}^{-\alpha} f(t, y(t)) + \frac{(t - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} y_0| \\ &= |\sum_{s=t_0+1}^{t} \frac{(t - \rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} f(s, y(s)) + \frac{(t - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} y_0| \end{aligned}$$

Since $(t - t_0 + 1)^{\overline{\alpha-1}}$ is increasing for $t \in [t_0, b]$, we have

$$\leq |\sum_{s=t_0+1}^{t} \frac{(t - \rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} f(s, y(s)) + \frac{(b - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} y_0|$$

Let $I_1 = \sum_{s=t_0+1}^{t} \frac{(t - \rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} f(s, y(s)) + \frac{(b - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} y_0$.

Since $|f| \leq M$ and $(t - t_0)^{\overline{0}} = 1$, we obtain

$$\begin{aligned} |I_1| &\leq M \sum_{s=t_0+1}^{t} \frac{(t - \rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} (t - t_0)^{\overline{0}} + \frac{(b - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} |y_0| \\ &= M \nabla_{t_0+1}^{-\alpha} (t - t_0)^{\overline{0}} + \frac{(b - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} |y_0| \end{aligned}$$

Let $I_2 = M \nabla_{t_0+1}^{-\alpha} (t - t_0)^{\overline{0}} + \frac{(b - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} |y_0|$.

By using Lemma 1.2.3(iii) we have

$$\begin{aligned} I_2 &= M \frac{\Gamma(1)}{\Gamma(\alpha + 1)} (t - t_0)^{\overline{\alpha}} + \frac{(b - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} |y_0| \\ &\leq M \frac{(b - t_0)^{\overline{\alpha}}}{\Gamma(\alpha + 1)} + \frac{(b - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} |y_0|. \end{aligned}$$

Now observe that $M \frac{(b - t_0)^{\overline{\alpha}}}{\Gamma(\alpha + 1)}$ and $\frac{(b - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} |y_0|$ are defined when α is given. Then $M \frac{(b - t_0)^{\overline{\alpha}}}{\Gamma(\alpha + 1)} + \frac{(b - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} |y_0|$ is bounded by a real number. So there exists

M^* such that $M\dfrac{(b-t_0)^{\overline{\alpha}}}{\Gamma(\alpha+1)} + \dfrac{(b-t_0+1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)}|y_0| \leq M^*$. Hence, we have $\| Ty \| \leq M^*$. Therefore, Ty is bounded by M^*.

Next we need to show that the operator T is continuous. We know that f is a continuous function, say f is continuous at $y = x_0$. Then $\lim\limits_{y\to x_0} f(y) = f(x_0)$, where $y, x_0 \in [t_0, b]$.

Let $\dfrac{(b-t_0)^{\overline{\alpha}}}{\Gamma(\alpha+1)} = h$. Let $\varepsilon > 0$ be given. There exists $\delta > 0$ such that

$$|f(s,y(s)) - f(s,x_0(s))| < \frac{\varepsilon}{h}$$

whenever $|y(s) - x_0(s)| < \delta$.

Then

$$|Ty(t) - Tx_0(t)| = |\nabla_{t_0+1}^{-\alpha} f(t,y(t)) + \frac{(t-t_0+1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} y_0 - \nabla_{t_0+1}^{-\alpha} f(t,x_0(t)) - \frac{(t-t_0+1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} y_0|$$

$$= |\nabla_{t_0+1}^{-\alpha} f(t,y(t)) - \nabla_{t_0+1}^{-\alpha} f(t,x_0(t))|$$

By Definition 1.2.1 we have

$$\begin{aligned}
&= |\sum_{s=t_0+1}^{t} \frac{(t-\rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} f(s,y(s)) - f(s,x_0(s))| \\
&\leq \sum_{s=t_0+1}^{t} \frac{(t-\rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} |f(s,y(s)) - f(s,x_0(s))| \\
&< \sum_{s=t_0+1}^{t} \frac{(t-\rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} (t-t_0)^{\overline{0}} \cdot \frac{\varepsilon}{h} \\
&= \nabla_{t_0+1}^{-\alpha} (t-t_0)^{\overline{0}} \cdot \frac{\varepsilon}{h} \text{ for } |y(s) - x_0(s)| < \delta.
\end{aligned}$$

Let $I_3 = \nabla_{t_0+1}^{-\alpha} (t-t_0)^{\overline{0}} \cdot \dfrac{\varepsilon}{h}$.

By using Lemma 1.2.3 (iii) we have

$$
\begin{aligned}
I_3 &= \frac{\Gamma(1)}{\Gamma(\alpha+1)}(t-t_0)^{\overline{\alpha}} \cdot \frac{\varepsilon}{h} \\
&\le \frac{1}{\Gamma(\alpha+1)}(b-t_0)^{\overline{\alpha}} \cdot \frac{\varepsilon}{h} \\
&= h \cdot \frac{\varepsilon}{h} \\
&= \varepsilon.
\end{aligned}
$$

□

We proved that the operator T is continuous and $T(K) \subseteq K$. Therefore, there exists a solution for the initial value problem (2.1) by the Brouwer fixed point theorem.

2.2. Uniqueness of Solution by the Contraction Mapping Theorem

The Contraction Mapping Theorem is one of the simplest and most useful theorems for the construction of solutions of linear and nonlinear equations. In this section, we want to apply the Contraction Mapping Theorem and the Lipschitz condition of the function to prove that there exists a unique solution for the initial value problem (2.1). The relevant definitions for contraction mapping theorem are introduced below [**14**].

DEFINITION 2.2.1. *A linear (vector) space $\mathbb{X}$ is a normed linear space (NLS) provided there is a function $\| \cdot \| : \mathbb{X} \to \mathbb{R}$, called a norm, satisfying*

(i) $\| x \| \ge 0$ *for all* $x \in \mathbb{X}$ *and* $\| x \| = 0$ *iff* $x = 0$,

(ii) $\| \lambda x \| = | \lambda | \| x \|$ *for all* $\lambda \in \mathbb{R}$ *and* $x \in \mathbb{X}$, *(iii)* $\| x + y \| \leq \| x \| + \| y \|$ *for all* $x, y \in \mathbb{X}$.

DEFINITION 2.2.2. *We say that* $\{x_n\} \subset \mathbb{X}$ *is a Cauchy sequence provided given any* $\varepsilon > 0$ *there is a positive integer* $\mathbf{N}$ *such that* $\| x_n - x_m \| < \varepsilon$ *for all* $n, m \geq \mathbf{N}$.

THEOREM 2.2.3. *(Contraction Mapping Theorem) Let* $\| \cdot \|$ *be a norm on* $\mathbb{R}^n$ *and* K *be a closed subset of* $\mathbb{R}^n$. *Suppose* $T : K \to K$ *is a contraction mapping with contraction constant* α, *with* $0 < \alpha < 1$, *such that*

$$\| Tx - Ty \| \leq \alpha \| x - y \|,$$

for all $x, y \in K$. *Then there exists a unique fixed point of* T.

DEFINITION 2.2.4. *Suppose that there exists a constant* $L > 0$ *such that*

$$|f(t, y) - f(t, x)| \leq L|y - x|$$

for all integers t *in* $[t_0, b]$ *and all* x, y *in* $\mathbb{R}$. *Then we say that* f *satisfies a "Lipschitz condition" with respect to* y *on* $[t_0, b] \times \mathbb{R}$.

THEOREM 2.2.5. *If* $f(t, y)$ *is continuous in* y *for each* t *in* $[t_0, b]$. *Let* f *be a Lipschitz function satisfying* $|f(t, y) - f(t, x)| \leq L|y - x|$, *where* $0 < L < 1$ *such that* $\dfrac{L}{\Gamma(\alpha + 1)}(b - t_0) < 1$. *Then there exists a unique solution for the initial value problem (2.1).*

PROOF. We use the Contraction Mapping Theorem to show that the initial value problem (2.1) has a unique fixed point.

Let K={$y \mid y(t_0) = y_0, \| y \| \leq k$ for some $k \in \mathbb{R}$, $t \in [t_0, b]$}. Let $\| \cdot \|$ be the maximum norm. $T : K \to K$ is given by

$$Ty(t) = \nabla_{t_0+1}^{-\alpha} f(t, y(t)) + \frac{(t-t_0+1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} y_0.$$

$$\begin{aligned}
|Ty - Tx| &= |Ty(t) - Tx(t)| \\
&= |\nabla_{t_0+1}^{-\alpha} f(t, y(t)) - \nabla_{t_0+1}^{-\alpha} f(t, x(t))| \\
&= |\sum_{s=t_0+1}^{t} \frac{(t-\rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} (f(s, y(s)) - f(s, x(s)))| \\
&\leq \sum_{s=t_0+1}^{t} \frac{(t-\rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} L|y(s) - x(s)| \\
&\leq L \sum_{s=t_0+1}^{t} \frac{(t-\rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} \| y - x \|
\end{aligned}$$

Since $(t-t_0)^{\overline{0}} = 1$, then we obtain

$$\begin{aligned}
&\leq L \sum_{s=t_0+1}^{t} \frac{(t-\rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} (t-t_0)^{\overline{0}} \| y - x \| \\
&= L \frac{\Gamma(1)}{\Gamma(\alpha+1)} (t-t_0)^{\overline{\alpha}} \| y - x \| \\
&\leq L \frac{(b-t_0)^{\overline{\alpha}}}{\Gamma(\alpha+1)} \| y - x \| \\
&= \alpha \| y - x \|
\end{aligned}$$

where $0 < \alpha < 1$.

Therefore, $max\ |Ty - Tx| \leq \alpha \| y - x \|$, and we get the following inequality

$$\| Ty - Tx \| \leq \alpha \| y - x \| .$$

Since $0 < \alpha = L\dfrac{(b-t_0)^{\overline{\alpha}}}{\Gamma(\alpha+1)} < 1$, T is a contraction mapping. Thus by the Contraction Mapping Theorem, T has a unique fixed point in K. This means that there is a unique function in K which is a solution of (2.1). Since any solution of (2.1) is in K, there is a unique solution of (2.1).

$\square$

Chapter 3

LOWER SOLUTIONS AND UPPER SOLUTIONS

3.1. Lower Solutions and Upper Solutions in Order

A fixed point theorem combined with upper and lower solutions is used to investigate the existence of solution for up to the first order nabla fractional difference equation with an initial condition. We define a lower solution and an upper solution as follows. Let functions v, w be defined on $[t_0, t_n]$, where $[t_0, t_n] = \{t_0, t_0 + 1, t_0 + 2, \cdots, t_n\}$ and $0 < \alpha < 1$. The function v is said to be a lower solution of the initial value problem (2.1) if

$$\nabla_{t_0}^{\alpha} v(t) \leq f(t, v(t)), \tag{3.1}$$

$$v(t_0) \leq y_0.$$

The function w is said to be an upper solution of the initial value problem (2.1) if

$$\nabla_{t_0}^{\alpha} w(t) \geq f(t, w(t)), \tag{3.2}$$

$$w(t_0) \geq y_0.$$

A lower solution $v(t)$ and an upper solution $w(t)$ are well ordered if

$$v(t) \leq w(t), \text{ for all } t \in [t_0, t_n].$$

LEMMA 3.1.1. *Let $f(t)$ and $g(t)$ be continuous functions on $[t_0, t_n]$. If $f(t) \leq g(t)$, then for each $t \in [t_0, t_n]$*

$$\nabla_{t_0+1}^{-\alpha} f(t) \leq \nabla_{t_0+1}^{-\alpha} g(t)$$

where $0 < \alpha < 1$.

PROOF. From Definition 1.2.1, we have

$$\nabla_{t_0+1}^{-\alpha} f(t) = \sum_{s=t_0+1}^{t} \frac{(t-\rho(s))^{\overline{\alpha-1}}}{\Gamma(\alpha)} f(s),$$

where $t = t_0, t_0+1, \ldots$ and $\rho(t) = t-1$.

Note that the coefficient of each term is positive:

$$\frac{(t-t_0)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} = \frac{\Gamma(t-t_0+\alpha-1)}{\Gamma(t-t_0)\Gamma(\alpha)} > 0, \text{ when } s = t_0+1.$$

$$\frac{(t-t_0-1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} = \frac{\Gamma(t-t_0+\alpha-2)}{\Gamma(t-t_0-1)\Gamma(\alpha)} > 0, \text{ when } s = t_0+2.$$

$$\vdots$$

$$\frac{(t-t+1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} = \frac{\Gamma(\alpha)}{\Gamma(1)\Gamma(\alpha)} = 1 > 0, \text{ when } s = t.$$

Then we have the following inequalities:

$$\frac{(t-t_0)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} f(t_0+1) \leq \frac{(t-t_0)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} g(t_0+1),$$

$$\frac{(t-t_0-1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} f(t_0+2) \leq \frac{(t-t_0-1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} g(t_0+2),$$

$$\vdots$$

$$\frac{(t-t+1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)}f(t) \le \frac{(t-t+1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)}g(t).$$

If we sum each side we obtain

$$\sum_{s=t_0+1}^{t} \frac{(t-\rho(s))^{\overline{\alpha-1}}}{\Gamma(\alpha)}f(s) \le \sum_{s=t_0+1}^{t} \frac{(t-\rho(s))^{\overline{\alpha-1}}}{\Gamma(\alpha)}g(s).$$

Therefore,

$$\nabla_{t_0+1}^{-\alpha} f(t) \le \nabla_{t_0+1}^{-\alpha} g(t).$$

$\square$

THEOREM 3.1.2. *Suppose $f(t,y)$ is continuous in y for each t on $[t_0, t_n]$ and is differentiable with $0 < \dfrac{\partial f}{\partial y} < 1$ in y for each t on (t_0, t_n). Assume $v(t)$ and $w(t)$ are a lower and an upper solution, respectively, for the initial value problem (2.1). Then $v(t) \le w(t)$, for $t_0 \le t \le t_n$.*

PROOF. We use mathematical induction to prove this theorem.

Define $m(t) = v(t) - w(t)$.

Initial Step. If $t = t_0$, we have $m(t_0) = v(t_0) - w(t_0) \le 0$, because of the definitions of upper and lower solutions.

Inductive Step. Assume there is a t=k, such that $m(k) \le 0$ for all $t_0 \le k \le t_n$. We prove that the inequality is true for $t = k+1$.

$m(k+1) = v(k+1) - w(k+1)$

$$\leq \nabla_{t_0+1}^{-\alpha} f(k+1, v(k+1)) + \frac{(k+1-t_0+1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} \nabla_{k_0}^{-(1-\alpha)} v(k) \mid_{k=t_0}$$

$$-\nabla_{t_0+1}^{-\alpha} f(k+1, w(k+1)) + \frac{(k+1-t_0+1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} \nabla_{t_0}^{-(1-\alpha)} w(k) \mid_{k=t_0}$$

$$= \sum_{s=t_0+1}^{k+1} \frac{(k+1-\rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} (f(s, v(s)) - f(s, w(s)))$$

$$+ \frac{(k+1-t_0+1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} (v(t_0) - w(t_0))$$

Since we have $\frac{(k+1-t_0+1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} > 0$ and $v(t_0) - w(t_0) \leq 0$, then the above expression is less than or equal to

$$I_4 = \sum_{s=t_0+1}^{k+1} \frac{(k+1-\rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} (f(s, v(s)) - f(s, w(s))).$$

Then it follows that

$$I_4 = \sum_{s=t_0+1}^{k} \frac{(k+1-\rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} (f(s, v(s)) - f(s, w(s)))$$

$$+ \frac{(k+1-(k+1-1))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} (f(k+1, v(k+1)) - f(k+1, w(k+1))).$$

By using Mean Value Theorem, there exists ξ_1 and ξ_2 such that

$f(s, v(s)) - f(s, w(s)) = f_y(s, \xi_1)(v(s) - w(s))$ for ξ_1 between $v(s)$ and $w(s)$.

$$f(k+1, v(k+1)) - f(k+1, w(k+1)) = f_y(k+1, \xi_2)(v(k+1) - w(k+1))$$

for ξ_2 between $v(k+1)$ and $w(k+1)$.

Then we obtain the following equation

$$I_4 = \sum_{s=t_0+1}^{k} \frac{(k+1-\rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} f_y(s, c(s))(v(s) - w(s))$$

$$+ f_y(k+1, d(k+1))(v(k+1) - w(k+1)).$$

Since $\sum_{s=t_0+1}^{k} \frac{(k+1-\rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} f_y(s,c(s))(v(s)-w(s)) < 0$, then

$$I_4 \leq f_y(k+1,d(k+1))(v(k+1)-w(k+1)).$$

Therefore, we have

$$m(k+1) = v(k+1)-w(k+1) \leq f_y(k+1,d(k+1))(v(k+1)-w(k+1)).$$

Hence, it follows that $(1-f_y(k+1,d(k+1)))(v(k+1)-w(k+1)) \leq 0$.

Since $0 < f_y(k+1,d(k+1)) < 1$, we obtain $v(k+1) \leq w(k+1)$.

□

3.2. Existence of a Solution between a Lower and an Upper Solution

It is well known that the upper and lower solution method is a powerful tool used in nonlinear analysis to prove the existence, localization and approximation of a solution for a great variety of problems. In this section, we show that there exists a solution between the ordered lower and upper solutions.

THEOREM 3.2.1. *Suppose there exist lower and upper solutions* $v = \{v_0, v_1, \ldots, v_n\}$ *and* $w = \{w_0, w_1, \ldots, w_n\}$*, respectively, of the initial value problem* (2.1) *such that* $v \leq w$. *Assume also that* $f(\cdot, y_i)$ *is a continuous function in* $[v_i, w_i]$ *for all* $i \in [0, n]$. *Then there exists a solution for the initial value problem (2.1).*

We use two ways to prove this theorem. The difference between these two ways is that we define two operators in order to apply the Brouwer fixed point theorem.

Proof. Consider the following modified problem:

$$\begin{cases} \nabla_{t_0}^{\alpha}\lambda(t) = f(t, p(t, \lambda(t))), 0 < \alpha < 1 \\ \nabla_{t_0}^{-(1-\alpha)}\lambda(t) \mid_{t=t_0} = \lambda(t_0). \end{cases} \tag{3.3}$$

where $p(t_i, r) = max\{v_i, min\{r, w_i\}\}$, for all $i \in \{0, \dots, n\}$ and $r \in \mathbb{R}$.

We can easily see this initial value problem is equivalent to the following equation

$$\lambda(t) = \nabla_{t_0+1}^{-\alpha} f(t, p(t, \lambda(t))) + \frac{(t - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)}\lambda(t_0). \tag{3.4}$$

Let K=$\{\lambda \ \| \| \lambda \| \leq k$ for some $k \in \mathbb{R}, t \in [t_0, t_n]\}$.

For $\lambda \in K$, define $T\lambda$ by

$$T\lambda(t) = \nabla_{t_0+1}^{-\alpha} f(t, p(t, \lambda(t))) + \frac{(t - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)}\lambda(t_0).$$

By the Definition of p, we have $f(t, p(t, \lambda(t)))$ for $t_0 \leq t \leq t_n$

$$f(t, p(t, \lambda(t))) = \begin{cases} f(t, w_i), & r \geq w_i \\ f(t, r), & v_i \leq r \leq w_i \\ f(t, v_i), & r \leq v_i \end{cases}.$$

Since f is continuous as a function of p for each t on $[t_0, t_n]$, f is bounded.

Similarly, we can show $T\lambda$ is bounded and continuous when f is a continuous function. Therefore, the operator T is continuous. By the Brouwer fixed point theorem, there exists a solution for the modified problem (3.3). Thus, every solution λ of (3.3) is a solution of (2.1).

Next, we define another operator T for the initial value problem (2.1).

Consider the same modified problem:

$$\begin{cases} \nabla_{t_0}^{\alpha}\lambda(t) = f(t, p(t, \lambda(t))), 0 < \alpha < 1 \\ \nabla_{t_0}^{-(1-\alpha)}\lambda(t) \mid_{t=t_0} = \lambda(t_0) = p(t_0). \end{cases} \tag{3.5}$$

where $p(t_i, r) = max\{v_i, min\{r, w_i\}\}$, for all $i \in \{0, \ldots, n\}$ and $r \in \mathbb{R}$.

Now x is a solution of the above problem if and only if $x=$ col$(x_0, x_1, \ldots, x_n)$ is a solution of the matrix equation

$$Ax = F(x) \tag{3.6}$$

where $A = (a_{ij})$ is defined by

$$A = \begin{bmatrix} \alpha & 1 & 0 & 0 & \cdots & 0 \\ \frac{3^{\overline{-\alpha}} - 2^{\overline{-\alpha}}}{\Gamma(1-\alpha)} & -\alpha & 1 & 0 & \cdots & 0 \\ \frac{4^{\overline{-\alpha}} - 3^{\overline{-\alpha}}}{\Gamma(1-\alpha)} & \frac{3^{\overline{-\alpha}} - 2^{\overline{-\alpha}}}{\Gamma(1-\alpha)} & -\alpha & 1 & \cdots & 0 \\ \vdots & & & \vdots & & \\ \frac{(n+2)^{\overline{-\alpha}} - (n+1)^{\overline{-\alpha}}}{\Gamma(1-\alpha)} & & \cdots & & & -\alpha \end{bmatrix}$$

and $F(x)$ is the transpose of the vector

$$(f(t_0, p(t_0, x(t_0))), \cdots, f(t_n, p(t_n, x(t_n))), -\sum_{i=1}^{n} f(t_i, p(t_i, x(t_i))) - \lambda(t_0)).$$

Now we want to show the existence of inverse of the matrix A. In order to show the existence of A^{-1}, we need to prove that $det(A) \neq 0$. That is, we need to show the matrix A is nonsingular. We prove it by mathematical induction.

Initial Step: When n=2, we apply the elementary row operation to get

$$A_{2\times 2} = \begin{bmatrix} \alpha & 1 \\ \dfrac{3^{\overline{-\alpha}} - 2^{\overline{-\alpha}}}{\Gamma(1-\alpha)} & -\alpha \end{bmatrix} \to \begin{bmatrix} \dfrac{-\alpha-1}{2} & 0 \\ \dfrac{\alpha-2}{2} & -1 \end{bmatrix}$$

Obviously, $A_{2\times 2}$ is nonsingular.

Inductive Step: Our inductive assumption is: Assume when $n = k$, $A_{k\times k}$ is nonsingular.

$$A_{k\times k} = \begin{bmatrix} \alpha & 1 & 0 & 0 & \cdots & 0 \\ \dfrac{3^{\overline{-\alpha}} - 2^{\overline{-\alpha}}}{\Gamma(1-\alpha)} & -\alpha & 1 & 0 & \cdots & 0 \\ \dfrac{4^{\overline{-\alpha}} - 3^{\overline{-\alpha}}}{\Gamma(1-\alpha)} & \dfrac{3^{\overline{-\alpha}} - 2^{\overline{-\alpha}}}{\Gamma(1-\alpha)} & -\alpha & 1 & \cdots & 0 \\ \vdots & & & \vdots & & \\ \dfrac{(k+2)^{\overline{-\alpha}} - (k+1)^{\overline{-\alpha}}}{\Gamma(1-\alpha)} & & \cdots & & & -\alpha \end{bmatrix} \to$$

$$\begin{bmatrix} \dfrac{-(k+\alpha-1)(\alpha+1)^{\overline{k-2}}}{k!} & 0 & \cdots & 0 \\ \dfrac{(k-1)(\alpha-1)(\alpha+1)^{\overline{k-2}}}{k!} & \dfrac{-(\alpha+1)^{\overline{k-2}}}{(k-1)!} & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots \end{bmatrix}$$

We must prove that $n = k+1$, $A_{(k+1)\times(k+1)}$ is nonsingular.

$$A_{(k+1)\times(k+1)} = \begin{bmatrix} \alpha & 1 & 0 & 0 & \cdots & 0 \\ \dfrac{3^{\overline{-\alpha}} - 2^{\overline{-\alpha}}}{\Gamma(1-\alpha)} & -\alpha & 1 & 0 & \cdots & 0 \\ \dfrac{4^{\overline{-\alpha}} - 3^{\overline{-\alpha}}}{\Gamma(1-\alpha)} & \dfrac{3^{\overline{-\alpha}} - 2^{\overline{-\alpha}}}{\Gamma(1-\alpha)} & -\alpha & 1 & \cdots & 0 \\ \vdots & & & \vdots & & \\ \dfrac{(k+3)^{\overline{-\alpha}} - (k+2)^{\overline{-\alpha}}}{\Gamma(1-\alpha)} & & \cdots & & & -\alpha \end{bmatrix} \to$$

$$\begin{bmatrix} \frac{-(k+\alpha)(\alpha+1)^{\overline{k-1}}}{(k+1)!} & 0 & 0 & \cdots & 0 \\ \frac{k(\alpha-1)(\alpha+1)^{\overline{k-1}}}{(k+1)!} & \frac{-(\alpha+1)^{\overline{k-1}}}{k!} & 0 & \cdots & 0 \\ \frac{(k-1)(\alpha+1)(k-\alpha-3)^{\overline{k-2}}}{(k+1)!} & \frac{(k-1)(\alpha-1)(\alpha+1)^{\overline{k-2}}}{k!} & \frac{-(\alpha+1)^{\overline{k-1}}}{(k-1)!} & \cdots & 0 \\ \vdots & \vdots & \vdots & \cdots & \vdots \end{bmatrix}$$

We know that

$$\frac{-(\alpha+1)^{\overline{k-1}}}{k!} = \frac{-(k+\alpha-1)(\alpha+1)^{\overline{k-2}}}{k!}.$$

Then we have $\begin{bmatrix} \frac{-(\alpha+1)^{\overline{k}}}{k!} & 0 & \cdots & 0 \\ \frac{(k-1)(\alpha-1)(\alpha+1)^{\overline{k-2}}}{k!} & \frac{-(\alpha+1)^{\overline{k-1}}}{(k-1)!} & \cdots & 0 \\ \vdots & \vdots & \cdots & \vdots \end{bmatrix} =$

$$\begin{bmatrix} \frac{-(k+\alpha-1)(\alpha+1)^{\overline{k-2}}}{k!} & 0 & \cdots & 0 \\ \frac{(k-1)(\alpha-1)(\alpha+1)^{\overline{k-2}}}{k!} & \frac{-(\alpha+1)^{\overline{k-1}}}{(k-1)!} & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots \end{bmatrix}$$

Since $A_{k\times k}= \begin{bmatrix} \frac{-(k+\alpha-1)(\alpha+1)^{\overline{k-2}}}{k!} & 0 & \cdots & 0 \\ \frac{(k-1)(\alpha-1)(\alpha+1)^{\overline{k-2}}}{k!} & \frac{-(\alpha+1)^{\overline{k-1}}}{(k-1)!} & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots \end{bmatrix}$ is nonsingular.

Then $A_{(k+1)\times(k+1)}$ is nonsingular.

That completes the proof of showing the existence of A^{-1}.

Then we rewrite (3.6) as the fixed-point equation $x = A^{-1}F(x) \equiv Tx$. Obviously, T is a continuous map from $\mathbb{R}^{N+1}$ to $\mathbb{R}^{N+1}$. By definition of p there exist $L > 0$ such that $\| Tx \| \leq L$, where $\| x \| = max\{| x(t_i) |, i = 0, \ldots, n\}$. Thus, the Brouwer fixed point theorem implies the existence of a fixed point of the operator

T, and in consequence, there exists a solution of the modified problem. Thus, every solution λ of (3.5) is a solution of (2.1).

$\square$

THEOREM 3.2.2. *Suppose there exist lower and upper solutions* $v = \{v_0, v_1, \ldots, v_n\}$ *and* $w = \{w_0, w_1, \ldots, w_n\}$*, respectively, of the initial value problem* (2.1) *such that* $v \leq w$. *Assume also that* $f(\cdot, y_i)$ *is a continuous function in* $[v_i, w_i]$ *for all* $i \in [0, n]$. *Then problem (2.1) has at least one solution* $\lambda \in [v, w]$.

PROOF. Consider the following modified problem:

$$\begin{cases} \nabla_{t_0}^{\alpha}\lambda(t) = f(t, \lambda(t)), 0 < \alpha < 1 \\ \nabla_{t_0}^{-(1-\alpha)}\lambda(t) \mid_{t=t_0} = \lambda(t_0) = p(t_0). \end{cases} \tag{3.7}$$

where $p(t_i, r) = max\{v(t_i), min\{r, w(t_i)\}\}$, for all $i \in \{0, \ldots, n\}$ and $r \in \mathbb{R}$.

The Brouwer fixed point theorem implies the existence of a fixed point of the operator T which we proved it for theorem 3.2.1. In consequence, there exists a solution of the modified problem (3.7). Thus, there exists solution of the initial value problem (2.1).

Next, we show that $v(t) \leq \lambda(t) \leq w(t)$.

Let $\lambda(t)$ be one solution of (2.1). Suppose $\lambda(t) \ngeq v(t)$. For the initial value problem, we obtain $v(t_0) \leq \lambda(t) \leq w(t_0)$. Let j_0= min$\{j \in [t_0, t_n]$: $v(j_0) > \lambda(j_0)\}$. Then obviously, $v(j_0 - 1) \leq \lambda(j_0 - 1)$, in consequence, we have

$$\nabla^{\alpha}\lambda(j_0) = f(j_0, p(j_0, \lambda(j_0))) = f(j_0, v(j_0)) \geq \nabla^{\alpha}v(j_0),$$

where $p(j_0, \lambda(j_0)) = max\{v(j_0), min\{\lambda(j_0), w(j_0)\}\} = v(j_0)$.

From the modified problem, we have

$$\nabla^\alpha \lambda(j_0) \geq \nabla^\alpha v(j_0),$$

$$\nabla^\alpha \lambda(t) \mid_{t=j_0} \geq \nabla^\alpha v(t) \mid_{t=j_0} .$$

First, by Definition of the nabla operator, we have

$$\nabla \nabla^{-(1-\alpha)} \lambda(t) \mid_{t=j_0} \geq \nabla \nabla^{-(1-\alpha)} v(t) \mid_{t=j_0} .$$

Then by Definition 1.2.1, we obtain

$$\nabla \sum_{s=0}^{t} \frac{(t-\rho(s))^{\overline{-\alpha}}}{\Gamma(1-\alpha)} \lambda(s) \mid_{t=j_0} \geq \nabla \sum_{s=0}^{t} \frac{(t-\rho(s))^{\overline{-\alpha}}}{\Gamma(1-\alpha)} v(s) \mid_{t=j_0} .$$

By using Lemma 1.2.3 (iv), we get

$$\sum_{s=0}^{t} \nabla \frac{(t-\rho(s))^{\overline{-\alpha}}}{\Gamma(1-\alpha)} \lambda(s) \mid_{t=j_0} \geq \sum_{s=0}^{t} \nabla \frac{(t-\rho(s))^{\overline{-\alpha}}}{\Gamma(1-\alpha)} v(s) \mid_{t=j_0} .$$

Doing some algebra, we have the following inequality

$$\sum_{s=0}^{t} \frac{(-\alpha)(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(1-\alpha)} \lambda(s) \mid_{t=j_0} \geq \sum_{s=0}^{t} \frac{(-\alpha)(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(1-\alpha)} v(s) \mid_{t=j_0}$$

$$\sum_{s=0}^{t} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} \lambda(s) \mid_{t=j_0} \geq \sum_{s=0}^{t} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} v(s) \mid_{t=j_0}$$

$$\sum_{s=0}^{j_0} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} \lambda(s) \geq \sum_{s=0}^{j_0} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} v(s).$$

The we have

$$\sum_{s=0}^{j_0-1} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} \lambda(s) + \frac{(j_0-(j_0-1))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} \lambda(j_0) \geq$$
$$\sum_{s=0}^{j_0-1} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} v(s) + \frac{(j_0-(j_0-1))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} v(j_0),$$

which can be written in the form

$$\frac{(j_0-(j_0-1))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)}\lambda(j_0)-\frac{(j_0-(j_0-1))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)}v(j_0)\geq$$
$$\sum_{s=0}^{j_0-1}\frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)}(v(s)-\lambda(s)),$$
$$0>\lambda(j_0)-v(j_0)\geq\sum_{s=0}^{j_0-1}\frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)}(v(s)-\lambda(s))\geq 0.$$

Finally, we attain the contradiction that $0>\lambda(j_0)-v(j_0)\geq 0$.

Similarly, we can prove $\lambda(t)\leq w(t)$.

Suppose $\lambda(t)\nleq w(t)$. For the initial value problem, we obtain $v(t_0)\leq\lambda(t)\leq w(t_0)$. Let i_0= min$\{i\in[t_0,t_n]$: $\lambda(i_0)>w(i_0)\}$. Then we have $\lambda(i_0-1)\leq w(i_0-1)$, and consequencelly, we obtain

$$\nabla^\alpha\lambda(i_0)=f(i_0,p(i_0,\lambda(i_0)))=f(i_0,w(i_0))\geq\nabla^\alpha w(i_0),$$

where $p(i_0,\lambda(i_0))=max\{v(i_0),min\{\lambda(i_0),w(i_0)\}\}=w(i_0)$.

From the modified problem, we have

$$\nabla^\alpha\lambda(i_0)\leq\nabla^\alpha w(i_0)$$

$$\nabla^\alpha\lambda(t)\mid_{t=i_0}\leq\nabla^\alpha w(t)\mid_{t=i_0}.$$

First, by Definition of the nabla operator, we have

$$\nabla\nabla^{-(1-\alpha)}\lambda(t)\mid_{t=i_0}\leq\nabla\nabla^{-(1-\alpha)}w(t)\mid_{t=i_0}.$$

Then by Definition 1.2.1, we obtain

$$\nabla\sum_{s=0}^{t}\frac{(t-\rho(s))^{\overline{-\alpha}}}{\Gamma(1-\alpha)}\lambda(s)\mid_{t=i_0}\leq\nabla\sum_{s=0}^{t}\frac{(t-\rho(s))^{\overline{-\alpha}}}{\Gamma(1-\alpha)}v(s)\mid_{t=i_0}.$$

By using the Lemma 1.2.3 (iv) we have

$$\sum_{s=0}^{t} \nabla \frac{(t-\rho(s))^{\overline{-\alpha}}}{\Gamma(1-\alpha)} \lambda(s) \mid_{t=i_0} \le \sum_{s=0}^{t} \nabla \frac{(t-\rho(s))^{\overline{-\alpha}}}{\Gamma(1-\alpha)} w(s) \mid_{t=i_0} .$$

Doing some algebra, we get the following inequality

$$\sum_{s=0}^{t} \frac{(-\alpha)(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(1-\alpha)} \lambda(s) \mid_{t=i_0} \le \sum_{s=0}^{t} \frac{(-\alpha)(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(1-\alpha)} w(s) \mid_{t=i_0}$$

$$\sum_{s=0}^{t} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} \lambda(s) \mid_{t=i_0} \le \sum_{s=0}^{t} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} w(s) \mid_{t=i_0}$$

$$\sum_{s=0}^{j_0} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} \lambda(s) \le \sum_{s=0}^{j_0} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} w(s).$$

The we have

$$\sum_{s=0}^{i_0-1} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} \lambda(s) + \frac{(i_0-(i_0-1))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} \lambda(i_0) \le$$
$$\sum_{s=0}^{i_0-1} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} w(s) + \frac{(i_0-(i_0-1))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} w(i_0),$$

which can be written in the form

$$\frac{(i_0-(i_0-1))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} \lambda(i_0) - \frac{(i_0-(i_0-1))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} w(i_0) \le$$
$$\sum_{s=0}^{i_0-1} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} (w(s)-\lambda(s)),$$
$$0 < \lambda(i_0) - w(i_0) \le \sum_{s=0}^{i_0-1} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} (w(s)-\lambda(s)) \le 0.$$

We obtain the contradiction that $0 < \lambda(i_0) - w(i_0) \le 0$. Thus, we have $\lambda(t) \le w(t)$.

Therefore, we conclude that $\lambda \in [v, w]$.

□

In consequence, this method allows us to ensure the existence of a solution of the considered problem lying between the lower and upper solution, which are well ordered. The first example below is given to show the existence of solution of the initial value problem between the lower and upper solution, which are well ordered. For the second example, we show that if lower solutions and upper solutions are not ordered we cannot assert there exists a solution lying between them.

EXAMPLE: The sequences v ={1, -1, -1}, and w ={1, 1, 2} are, respectively, a lower and an upper solution of the initial value problem

$$\nabla_0^\alpha x(t) = \frac{2}{x^2(t)+1} - \alpha, \qquad t = \{1,2\}, \qquad x(0) = 1.$$

$$x(t) = \nabla_1^{-\alpha} f(t, x(t)) + \frac{(t-t_0+1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} x_0$$

$$x(t) = \nabla_1^{-\alpha}\left(\frac{2}{x^2(t)+1} - \alpha\right) + \frac{(t-t_0+1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} x_0$$

$$= \sum_{s=1}^{t} \frac{(t-\rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)}\left(\frac{2}{x^2(s)+1} - \alpha\right) + \frac{(t-t_0+1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)}.$$

When $t = 1$, $x(1) = \{1\}$.

When $t = 2$, $x^3(2) - (\frac{\alpha}{2} - \frac{\alpha^2}{2})x^2(2) + x(2) + \frac{\alpha^2}{2} - \frac{\alpha}{2} - 2 = 0$.

It is difficult to find $x(2)$, so we pick up $\alpha = \frac{1}{2}$. Then the above function can be written

$$x^3 - \frac{1}{8}x^2 + x - \frac{17}{8} = 0.$$

Finally, we find $x(2) \approx 1.0635$.

Therefore, the solution $\{1,\ 1,\ 1.0635\}$between v and w.

EXAMPLE: The sequences v ={1, 1, 0}, and w ={1, 0, 0} are a lower and an upper solution respectively, of the initial value problem

$$\nabla_0^\alpha x(t) = x^2(t) - \alpha, \qquad t = \{1,2\}, \qquad x(0) = 1.$$

$$x(t) = \nabla_1^{-\alpha} f(t, x(t)) + \frac{(t - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} x_0$$

$$x(t) = \nabla_1^{-\alpha} (\frac{x^2(t)}{2} - \alpha) + \frac{(t - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} x_0$$

$$= \sum_{s=1}^{t} \frac{(t - \rho(s))^{\overline{(\alpha-1)}}}{\Gamma(\alpha)} (\frac{x^2(t)}{2} - \alpha) + \frac{(t - t_0 + 1)^{\overline{(\alpha-1)}}}{\Gamma(\alpha)}$$

When $t = 1$, we obtain $x(1) = \{0, 1\}$.

When $t = 2$, we obtain $x(2) = \{\frac{1 \pm \sqrt{2\alpha^2 + 2\alpha + 1}}{2}, \frac{1 \pm \sqrt{2\alpha^2 - 2\alpha + 1}}{2}\}$.

Clearly, $x(2)$ doesn't lie between v and w.

3.3. Monotone Iterative Method : A Quasilinearization Method

In this section, a monotone iterative method is employed for studying the existence of solutions of up to the first order nabla fractional difference equation with an initial condition. The initial approximations are the upper solution $w(t)$ and lower solution $v(t)$ which are ordered. The method of upper and lower solutions is a well-known tool that has been used to prove results for the existence of solutions for many classes of equations with initial condition. Recently there have been a lot of activity as far as upper and lower solution method is considered [**15, 16, 17**]. In addition, under certain conditions, we can apply this theory to give constructive proofs of existence of solution by defining monotone sequences for the considered problem in a sector defined by a lower and an upper solution. We refer readers to the paper [**18**].

THEOREM 3.3.1. *Assume that there exists a constant $m > 0$ such that*

$$f(t,y) + my \le f(t,x) + mx, \qquad \textit{for} \quad v(t) \le y \le x \le w(t),\ t \in [t_0, t_n].$$

Then there exist two monotone and convergent sequences in $\mathbb{R}^{N+1}$, v_n and w_n such that $v = v_0 \le v_n \le w_n \le w_0 = w$, where $v_0(t)$ is a lower solution and $w_0(t)$ is an upper solution for the initial value problem (2.1).

PROOF. Consider the following modified problem

$$\nabla_{t_0}^{\alpha} \lambda(t) = f(t, v_0(t)) + m(v_0(t) - \lambda(t)). \tag{3.8}$$

Since v_0 is a lower solution of $\nabla_{t_0}^{\alpha} y(t) = f(t, y(t))$, then we have

$$\nabla_{t_0}^{\alpha} v_0(t) \le f(t, v_0(t)),$$

$$\nabla_{t_0}^{\alpha} v_0(t) \le f(t, v_0(t)) + m(v_0(t) - v_0(t)).$$

In consequence, $v_0(t)$ is a lower solution of $\nabla_{t_0}^{\alpha} \lambda(t) = f(t, v_0(t)) + m(v_0(t) - \lambda(t))$.

We also have $v_0(t) \le w_0(t)$, then

$$f(t, v_0(t)) + m(v_0(t)) \le f(t, w_0(t)) + m(w_0(t)),$$

$$f(t, v_0(t)) + m(v_0(t)) - m(w_0(t)) \le f(t, w_0(t)).$$

Since $f(t, w_0(t)) \le \nabla_{t_0}^{\alpha} w_0(t)$, then

$$f(t, v_0(t)) + m(v_0(t)) - m(w_0(t)) \le \nabla_{t_0}^{\alpha} w_0(t).$$

Therefore, $w_0(t)$ is an upper solution of $\nabla_{t_0}^{\alpha}\lambda(t) = f(t, v_0(t)) + m(v_0(t) - \lambda(t))$.

By using Theorem 3.2.1, there exists a solution v_1 for the modified problem $\nabla_{t_0}^{\alpha}\lambda(t) = f(t, v_0(t)) + m(v_0(t) - \lambda(t))$ such that $v_0 < v_1 < w_0$.

Next, we want to show v_0 and w_0 are a lower solution and an upper solution for another modified problem

$$\nabla_{t_0}^{\alpha}\gamma(t) = f(t, w_0(t)) + m(w_0(t) - \gamma(t)). \tag{3.9}$$

Since w_0 is an upper solution of $\nabla_{t_0}^{\alpha}y(t) = f(t, y(t))$. Then

$$\nabla_{t_0}^{\alpha}w_0(t) \geq f(t, w_0(t)),$$

$$\nabla_{t_0}^{\alpha}w_0(t) \geq f(t, w_0(t)) + m(w_0(t) - w_0(t)).$$

In consequence, $w_0(t)$ is an upper solution of $f(t, w_0(t)) + m(w_0(t) - w_0(t))$.

We also have $v_0(t) \leq w_0(t)$, then

$$f(t, v_0(t)) + m(v_0(t)) \leq f(t, w_0(t)) + m(w_0(t)),$$

$$f(t, v_0(t)) \leq f(t, w_0(t)) + m(w_0(t)) - m(v_0(t)).$$

Since $v_0(t)$ is a lower solution of $\nabla_{t_0}^{\alpha}y(t) = f(t, y(t))$, we obtain

$$\nabla_{t_0}^{\alpha}v_0(t) \leq f(t, v_0(t)),$$

$$\nabla_{t_0}^{\alpha}v_0(t) \leq f(t, v_0(t)) + m(w_0(t)) - m(v_0(t)).$$

Therefore, $v_0(t)$ is a lower solution of $\nabla_{t_0}^{\alpha}\gamma(t) = f(t, w_0(t)) + m(w_0(t) - \gamma(t))$.

Similarly, by using Theorem 3.2.1, there exists a solution w_1 for the modified problem $\nabla_{t_0}^{\alpha}\gamma(t) = f(t, w_0(t)) + m(w_0(t) - \gamma(t))$ such that $v_0 < w_1 < w_0$.

Now we need to show that $v_1(t) \le w_1(t)$. Assume there exists a smallest k such that $v_1(k) > w_1(k)$. Obviously, $v_1(k-1) \le w_1(k-1)$.

Define

$$\beta(k) = w_1(k) - v_1(k) < 0,$$

$$\nabla_{t_0}^{\alpha}\beta(k) = \nabla_{t_0}^{\alpha}w_1(k) - \nabla_{t_0}^{\alpha}v_1(k),$$

$$\nabla_{t_0}^{\alpha}\beta(k) = f(k, w_0(k)) + m(w_0(k) - w_1(k)) - f(k, v_0(k)) - m(v_0(k) - v_1(k)),$$

$$\nabla_{t_0}^{\alpha}\beta(k) = f(k, w_0(k)) + mw_0(k) - f(k, v_0(k)) - mv_0(k) + m(v_1(k) - w_1(k)) > 0.$$

Therefore,

$$\nabla_{t_0}^{\alpha}\beta(k) > 0,$$

$$\nabla_{t_0}^{\alpha}\beta(k) = \nabla_{t_0}^{\alpha}w_1(k) - \nabla_{t_0}^{\alpha}v_1(k) > 0.$$

Then we obtain the inequality as follow.

$$\nabla_{t_0}^{\alpha}w_1(k) > \nabla_{t_0}^{\alpha}v_1(k)$$

$$\nabla_{t_0}^{\alpha}w_1(t)\mid_{t=k} > \nabla_{t_0}^{\alpha}v_1(t)\mid_{t=k}$$

$$\nabla\nabla_{t_0}^{-(1-\alpha)}w(t)\mid_{t=k} > \nabla\nabla_{t_0}^{-(1-\alpha)}v_1(t)\mid_{t=k}$$

$$\nabla\sum_{s=t_0}^{t}\frac{(t-\rho(s))^{\overline{-\alpha}}}{\Gamma(1-\alpha)}w_1(t)\mid_{t=k} > \nabla\sum_{s=t_0}^{t}\frac{(t-\rho(s))^{\overline{-\alpha}}}{\Gamma(1-\alpha)}v_1(t)\mid_{t=k}$$

$$\sum_{s=t_0}^{t} \nabla \frac{(t-\rho(s))^{\overline{-\alpha}}}{\Gamma(1-\alpha)} w_1(t) \mid_{t=k} > \sum_{s=t_0}^{t} \nabla \frac{(t-\rho(s))^{\overline{-\alpha}}}{\Gamma(1-\alpha)} v_1(t) \mid_{t=k}$$

$$\sum_{s=t_0}^{t} \frac{(-\alpha)(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(1-\alpha)} w_1(t) \mid_{t=k} > \sum_{s=0}^{t} \frac{(-\alpha)(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(1-\alpha)} v_1(t) \mid_{t=k}$$

$$\sum_{s=t_0}^{t} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} w_1(t) \mid_{t=k} > \sum_{s=t_0}^{t} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} v_1(t) \mid_{t=k}$$

$$0 > w_1(k) - v_1(k) > \sum_{s=t_0}^{k-1} \frac{(t-\rho(s))^{\overline{-\alpha-1}}}{\Gamma(-\alpha)} (v_1(s) - w_1(s)) \geq 0.$$

We obtain a contradiction. Therefore, $v_1(k) \leq w_1(k)$. By doing the same process, we obtain

$$v_0 \leq v_1 \leq \cdots \leq v_n \leq w_n \leq \cdots \leq w_1 \leq w_0.$$

Now we need to show that v_n and w_n are convergent to the solution of the initial value problem.

Then consider $\lambda(t)$ is a solution of the initial value problem

$$\begin{cases} \nabla_{t_0}^{\alpha} \lambda(t) = f(t, \lambda(t)), \\ \nabla_{t_0}^{-(1-\alpha)} \lambda(t) \mid_{t=t_0} = \lambda(t_0) = v(t_0). \end{cases} \tag{3.10}$$

Consider the modified problem (3.8)

$$\nabla_{t_0}^{\alpha} \lambda(t) = f(t, v_n(t)) + m(v_n(t) - \lambda(t)),$$

$$\lambda(t) = \nabla_{t_0+1}^{-\alpha} (f(t, v_n(t) + m(v_n(t) - \lambda(t))) + \frac{(t-t_0+1)^{\overline{\alpha-1}}}{\Gamma(\alpha)} \nabla_{t_0}^{-(1-\alpha)} \lambda(t) \mid_{t=t_0}.$$

Substitute $v_{n+1}(t)$ into $\lambda(t)$

$$v_{n+1}(t) = \nabla_{t_0+1}^{-\alpha} (f(t, v_n(t) + m(v_n(t) - v_{n+1}(t))) + \frac{(t-t_0+1)^{\overline{\alpha-1}}}{\Gamma(\alpha)} \nabla_{t_0}^{-(1-\alpha)} \lambda(t) \mid_{t=t_0},$$

$$\lim_{n\to\infty} v_{n+1}(t) = \nabla_{t_0+1}^{-\alpha}(f(t, \lim_{n\to\infty} v_n(t) + m(\lim_{n\to\infty} v_n(t) - \lim_{n\to\infty} v_{n+1}(t)))$$
$$+\frac{(t-t_0+1)^{\overline{\alpha-1}}}{\Gamma(\alpha)}\nabla_{t_0}^{-(1-\alpha)}\lambda(t)\mid_{t=t_0}.$$

Since $v_n(t)$ is a monotone and convergent sequence, then

$$\lim_{n\to\infty} v_n(t) = \lim_{n\to\infty} v_{n+1}(t),$$

$$\lim_{n\to\infty} v_n(t) = \nabla_{t_0+1,}^{-\alpha}(f(t, \lim_{n\to\infty} v_n(t) + \frac{(t-t_0+1)^{\overline{\alpha-1}}}{\Gamma(\alpha)}\nabla_{t_0}^{-(1-\alpha)}\lambda(t)\mid_{t=t_0}.$$

So $\lim_{n\to\infty} v_n(t)$ is also a solution of the initial value problem (3.10).

Therefore, $\lim_{n\to\infty} v_n(t) = \lambda(t)$.

Similarly, we consider $\gamma(t)$ is a solution of the initial value problem

$$\begin{cases} \nabla_{t_0}^{\alpha}\gamma(t) = f(t,\gamma(t)), \\ \nabla_{t_0}^{-(1-\alpha)}\gamma(t)\mid_{t=t_0} = \gamma(t_0) = w(t_0). \end{cases} \tag{3.11}$$

Consider the modified problem (3.9)

$$\nabla_{t_0}^{\alpha}\gamma(t) = f(t, w_n(t)) + m(w_n(t) - \gamma(t)),$$

$$\gamma(t) = \nabla_{t_0+1,}^{-\alpha}(f(t, w_n(t) + m(w_n(t) - \gamma(t))) + \frac{(t-t_0+1)^{\overline{\alpha-1}}}{\Gamma(\alpha)}\nabla_{t_0}^{-(1-\alpha)}\gamma(t)\mid_{t=t_0}.$$

Substitute $w_{n+1}(t)$ into $\gamma(t)$

$$w_{n+1}(t) = \nabla_{t_0+1,}^{-\alpha}(f(t, w_n(t) + m(w_n(t) - w_{n+1}(t))) + \frac{(t-t_0+1)^{\overline{\alpha-1}}}{\Gamma(\alpha)}\nabla_{t_0}^{-(1-\alpha)}\gamma(t)\mid_{t=t_0},$$

$$\lim_{n\to\infty} w_{n+1}(t) = \nabla_{t_0+1,}^{-\alpha}(f(t, \lim_{n\to\infty} w_n(t) + m(\lim_{n\to\infty} w_n(t) - \lim_{n\to\infty} w_{n+1}(t)))$$
$$+\frac{(t-t_0+1)^{\overline{\alpha-1}}}{\Gamma(\alpha)}\nabla_{t_0}^{-(1-\alpha)}\gamma(t)\mid_{t=t_0}.$$

Since $w_n(t)$ is a monotone and convergent sequence, then

$$\lim_{n\to\infty} w_n(t) = \lim_{n\to\infty} w_{n+1}(t),$$

$$\lim_{n\to\infty} w_n(t) = \nabla_{t_0+1,}^{-\alpha}(f(t, \lim_{n\to\infty} w_n(t)) + \frac{(t-t_0+1)^{\overline{\alpha-1}}}{\Gamma(\alpha)} \nabla_{t_0}^{-(1-\alpha)} \gamma(t) \mid_{t=t_0}.$$

So $\lim_{n\to\infty} w_n(t)$ is also a solution of the initial value problem (3.11).

Therefore, we obtain $\lim_{n\to\infty} w_n(t) = \gamma(t)$.

Note that $\lambda(t)$ is always less than $\gamma(t)$. In fact, $\lim_{n\to\infty} v_n(t) = \lambda(t)$, $\lim_{n\to\infty} w_n(t) = \gamma(t)$, and $v_n \leq w_n$, so $\lambda(t) \leq \gamma(t)$.

Let $\varepsilon > 0$ be given. Since $\lim_{n\to\infty} v_n(t) = \lambda(t)$, there exists $n_1 \in \mathbb{N}$, such that

$$|v_n(t) - \lambda(t)| < \frac{\varepsilon}{2}, \text{ whenever } n \geq n_1.$$

Then we have

$$\lambda(t) - \frac{\varepsilon}{2} < v_n(t) < \lambda(t) + \frac{\varepsilon}{2}.$$

Since $\lim_{n\to\infty} w_n(t) = \gamma(t)$, there exists $n_2 \in \mathbb{N}$, such that

$$|w_n(t) - \gamma(t)| < \frac{\varepsilon}{2}, \text{ whenever } n \geq n_2.$$

Then we have

$$\gamma(t) - \frac{\varepsilon}{2} < w_n(t) < \gamma(t) + \frac{\varepsilon}{2}.$$

Therefore, we obtain $\lambda(t) - \frac{\varepsilon}{2} < v_n(t) \leq w_n(t) < \gamma(t) + \frac{\varepsilon}{2}$, whenever $n \geq n_1, n_2$.

In addition, $v_n \leq w_n$, so $w_n - v_n \geq 0$.

$$0 \leq w_n(t) - v_n(t) \leq \gamma(t) + \frac{\varepsilon}{2} - \lambda(t) + \frac{\varepsilon}{2}$$

Thus, $\gamma(t) - \lambda(t) + \varepsilon \geq 0$, and we obtain $\gamma(t) \geq \lambda(t)$.

$\square$

Chapter 4

INTRODUCTION OF SIGMOIDAL CURVES IN FRACTIONAL CALCULUS

We introduced nabla difference equation of fractional order along with suitable initial conditions and proved the existence and uniqueness of the solution in the previous chapters. The structure of the solutions with ordered lower and upper solution was discussed. Very recently there has been progress in developing the theory of the discrete fractional calculus. In several recent papers by Atici and Eloe some basic results for discrete fractional equation have been obtained. In this chapter, we find solutions for up to the first order homogeneous nabla continuous and discrete fractional difference equations. Obtaining the solutions of the initial value problem will help us to define sigmoidal curves in fractional calculus.

4.1. First Order Differential Equation and Nabla Difference Equation

In this section, we consider the first order differential equation that approximates to the first order difference equation. First recall the definition of derivative of a function in calculus

Definition 4.1.1. *The derivative of y at t is given by*

$$y'(t) = \lim_{h\to 0}\frac{y(t+h)-y(t)}{h}$$

provided the limit exists. For all t for which this limit exists, y' is a function of t.

Let us omit the limit in this definition. We obtain

$$y'(t) \approx \frac{y(t+h) - y(t)}{h}.$$

Letting $h = 1$, we have

$$y'(t) \approx y(t+1) - y(t) = \Delta y(t).$$

Then we obtain

$$y'(t) \approx y(t+1) - y(t) = \nabla y(t+1).$$

Next, we solve for the first order differential equation and the first order difference equation.

Consider the first order homogenous initial value problem

$$\begin{cases} \dfrac{dy(t)}{dt} = -ay(t), \quad t \geq 0 \\ y(0) = 1 \end{cases} \tag{4.1}$$

First, (4.1) can be formed as

$$\frac{dy(t)}{y(t)} = -adt.$$

Then integrating on both sides, we have

$$\int \frac{dy(t)}{y(t)} = \int -adt.$$

After some algebra steps, we get

$$\ln y(t) = -at + c.$$

Thus,

$$y(t) = e^{-at+c}.$$

Our initial condition is $y(0) = 1$. Therefore, $c = 0$.

Therefore, the solution of (4.1) is

$$y(t) = e^{-at}.$$

Next, we consider a first order nabla difference equation

$$\nabla y(t+1) = -ay(t), \quad t = 1, 2, \cdots$$

Then we shift t by one unit of time, we obtain

$$\nabla y(t) = -ay(t-1), \quad t = 1, 2, \cdots$$

Then we solve for the first order nabla difference equation with initial condition.

$$\begin{cases} \nabla y(t) = -ay(t-1), \quad t = 1, 2, \cdots \\ y(t) \mid_{t=0} = y(0) = 1. \end{cases} \tag{4.2}$$

By the Definition of the ∇ operator, we have

$$y(t) - y(t-1) = -ay(t-1).$$

Then we get

$$y(t) = (1-a)y(t-1).$$

After iterating steps we obtain

$$y(t) = (1-a)^t.$$

In the following chapter, we will use the approximation

$$e^{-at} \approx (1-a)^t.$$

For example, we know the continuous type of Richards curve with four parameters is

$$Y(t) = \frac{a}{(1+e^b(e^{-c})^t)^{\frac{1}{d}}}.$$

Then we define the discrete type of Richards curve with four parameters to be

$$Y(t) = \frac{a}{(1+e^b(1-c)^t)^{\frac{1}{d}}}.$$

4.2. Exponential Functions of Continuous and Discrete Fractional Calculus

The Mittag-Leffler function naturally occurs as a part of the solution of fractional order differential equations or fractional order integral equations. In this section, we find continuous and discrete fractional forms for the exponential function.

As we stated in Chapter 1, we have

$$E_{\alpha,\beta}(x) = \sum_{k=0}^{\infty} \frac{x^k}{\Gamma(\alpha k+\beta)},$$

$$E_{\alpha,\alpha}(x) = \sum_{k=0}^{\infty} \frac{x^k}{\Gamma(\alpha k + \alpha)},$$
$$E_{\alpha,\alpha}(at^{\alpha}) = \sum_{k=0}^{\infty} \frac{(at^{\alpha})^k}{\Gamma(\alpha k + \alpha)}.$$

Based on the Mittlag-Leffler function, the generalized form of the exponential function can be written as

$$e_{\alpha,\alpha}(a,t) = t^{\alpha-1} E_{\alpha,\alpha}(at^{\alpha}).$$

Therefore, the continuous nabla fractional exponential function is

$$e_{\alpha,\alpha}(a,t) = t^{\alpha-1} \sum_{k=0}^{\infty} \frac{(at^{\alpha})^k}{\Gamma(\alpha k + \alpha)} = \sum_{k=0}^{\infty} a^k \frac{t^{\alpha k+\alpha-1}}{\Gamma(\alpha k + \alpha)}.$$

Note that when $\alpha = 1$, we have $e_{1,1} = e^{at}$.

For any real number v, the discrete Mittag-Leffler function has been defined by Atici and Eloe [**32**] as

$$F_{\alpha,\beta}(at^{\overline{v}}) = \sum_{k=0}^{\infty} \frac{a^k t^{\overline{kv}}}{\Gamma(\alpha k + \beta)},$$

where α and β are positive real numbers and $|a| < 1$.

When $\alpha = \beta$, we have

$$F_{\alpha,\alpha}(at^{\overline{v}}) = \sum_{k=0}^{\infty} \frac{a^k t^{\overline{kv}}}{\Gamma(\alpha k + \alpha)}.$$

Therefore, the discrete nabla fractional exponential function is

$$\hat{e}_{\alpha,\alpha}(a, t^{\overline{\alpha}}) = \sum_{k=0}^{\infty} a^k \frac{(t-k+1)^{\overline{(k+1)\alpha-1}}}{\Gamma(\alpha k + \alpha)}.$$

Note that when $\alpha = 1$, we have $\hat{e}_{1,1}(a, t^{\overline{1}}) = (1+a)^t$.

4.3. Successive Approximations Method

Successive approximations method appears throughout numerical optimization, where a solution to an optimization problem is sought as the limit of solutions to a succession of simpler approximation problems. For more examples, we refer reader to the paper [**29**]. In this section, we use the method of successive approximations to solve for up to the first order nabla difference equation with initial value condition.

Consider the $\alpha - th$ order homogenous initial value problem

$$\begin{cases} \nabla_0^{\alpha} y(t) = -ay(t-1), \quad t = 1, 2, \cdots \\ \nabla_0^{-(1-\alpha)} y(t) \mid_{t=0} = y(0) = c, \end{cases}$$

where $0 < \alpha < 1$ and $\mid a \mid < 1$.

Apply the operator $\nabla_1^{-\alpha}$ to each side of the equation to obtain

$$\nabla_1^{-\alpha} \nabla_0^{\alpha} y(t) = \nabla_1^{-\alpha}(-ay(t-1)),$$

which can be written in the form

$$\nabla_1^{-\alpha} \nabla \nabla_0^{-(1-\alpha)} y(t) = \nabla_1^{-\alpha}(-ay(t-1)).$$

Then we have

$$\nabla \nabla_0^{-\alpha} \nabla_0^{-(1-\alpha)} y(t) = \nabla_1^{-\alpha}(-ay(t-1)).$$

Hence

$$y(t) = \frac{(t+1)^{\overline{\alpha-1}}}{\Gamma(\alpha)} c + \nabla_1^{-\alpha}(-ay(t-1)).$$

We employ the method of successive approximations. Set

$$y_0(t) = \frac{(t+1)^{\overline{\alpha-1}}}{\Gamma(\alpha)} c,$$

$$y_n(t) = y_0(t) + \nabla_1^{-\alpha}(-a y_{n-1}(t-1)), \quad n = 1, 2, \ldots.$$

Apply the power rule to show that

$$y_1(t) = y_0(t) + \nabla_1^{-\alpha}(-a y_0(t-1)) = \frac{(t+1)^{\overline{\alpha-1}}}{\Gamma(\alpha)} c - ac \frac{t^{\overline{2\alpha-1}}}{\Gamma(2\alpha-1)}.$$

With repeated applications of the power rule it follows inductively that

$$y_n(t) = c \sum_{i=0}^{n} (-a)^i \frac{(t-i+1)^{\overline{(i+1)\alpha-1}}}{\Gamma((i+1)\alpha)}, \quad n = 0, 1, 2, \ldots.$$

Formally, take the limit $n \to \infty$ to obtain

$$y(t) = c \sum_{i=0}^{\infty} (-a)^i \frac{(t-i+1)^{\overline{(i+1)\alpha-1}}}{\Gamma((i+1)\alpha)}.$$

Next, we use mathematical induction to prove

$$y_n(t) = c \sum_{i=0}^{n} (-a)^i \frac{(t-i+1)^{\overline{(i+1)\alpha-1}}}{\Gamma((i+1)\alpha)}, \quad n = 0, 1, 2, \ldots.$$

Proof. Initial Step. When $n = 0$, $y_0 = \frac{(t+1)^{\overline{\alpha-1}}}{\Gamma(\alpha)} c$, which is true.

Inductive Step. Assume when $n = k$,

$$y_k(t) = c \sum_{i=0}^{k} (-a)^i \frac{(t-i+1)^{\overline{(i+1)\alpha-1}}}{\Gamma((i+1)\alpha)}, \quad k = 0, 1, 2, \ldots.$$

We must prove $n = k+1$,

$$y_{k+1}(t) = c\sum_{i=0}^{k+1}(-a)^i \frac{(t-i+1)^{\overline{(i+1)\alpha-1}}}{\Gamma((i+1)\alpha)}, \quad k = 0,1,2,\ldots.$$

When $n = k+1$, $y_{k+1}(t) = y_0(t) + \nabla_1^{-\alpha}(-ay_k(t-1))$

$$= \frac{(t+1)^{\overline{\alpha-1}}}{\Gamma(\alpha)}c + \nabla_1^{-\alpha}(-a)c\sum_{i=0}^{k}(-a)^i \frac{(t-i)^{\overline{(i+1)\alpha-1}}}{\Gamma((i+1)\alpha)}$$

$$= \frac{(t+1)^{\overline{\alpha-1}}}{\Gamma(\alpha)}c + c\sum_{i=0}^{k}(-a)^{i+1}\nabla_1^{-\alpha} \frac{(t-i)^{\overline{(i+1)\alpha-1}}}{\Gamma((i+1)\alpha)}.$$

By using Lemma 1.2.3(iv), we have

$$\nabla_1^{-\alpha}\frac{(t-i)^{\overline{(i+1)\alpha-1}}}{\Gamma((i+1)\alpha)} = \frac{(t-i)^{\overline{(i+1)\alpha+\alpha-1}}}{\Gamma((i+1)\alpha+\alpha)} = \frac{(t-i)^{\overline{i\alpha+2\alpha-1}}}{\Gamma(i\alpha+2\alpha)}.$$

Then

$$y_{k+1}(t) = \frac{(t+1)^{\overline{\alpha-1}}}{\Gamma(\alpha)}c + c\sum_{i=0}^{k}(-a)^{i+1}\frac{(t-i)^{\overline{i\alpha+2\alpha-1}}}{\Gamma(i\alpha+2\alpha)}$$

$$= c\sum_{i=0}^{k+1}(-a)^i \frac{(t-i+1)^{\overline{(i+1)\alpha-1}}}{\Gamma((i+1)\alpha)}, \quad k = 0,1,2,\ldots.$$

$\square$

Chapter 5

PARAMETER ESTIMATIONS OF SIGMOIDAL MODELS OF CANCER

Today, we are faced with a host of health problems that cannot be completely cured. Cancer is one of leading cause of death worldwide. It can be overwhelmingly complicated to treat more than almost any other disease. Although there are many recent encouraging successes in cancer research, there is still a lot to be known about its causes and treatments. Cancer treatment can involve one or several different treatments. Surgery, radiotherapy, chemotherapy, biologic therapy and clinical trials are standard methods of treatment in many types of cancer. But in many cases they do not result a complete cure, because it takes a long period of time to observe the outcomes of the above mentioned treatments. For a treatment with better outcome, mathematical models which simulate rate of given tumor growth data, needs to be developed. Based on these mathematical models, researchers can predict the behavior of growth more accurately. A better understanding of the growth of tumors is of paramount importance for the development of more successful treatment strategies.

Growth curve analysis plays an important role in cancer research. An early contribution to the theory of growth curves was made by Gompertz in 1825 [**19**]. There are other mathematical models used to study tumor growth as well [**20, 21, 22, 23**]. The Gompertz, Logistic and Richards models are just only three of many models that we study in this chapter. We show that fractional equations can be used to define models for tumor growth by way of fractional, discrete Gompetz and Logistic equations. Nihan Acar [**1**] has already worked on Gompertz and Logistic models with three parameters. For the range of tumor, there are minor difference between Gompertz and Logistic growth given probable parameters. We present the Richards model, which has four parameters. Modeling can provide valuable information to plan effective biological experiments for testing cancer study. We have the data of growth rates of tumors from twenty eight mice. Dr. William Hruskesky gave us permission to use his published data obtained at the Medical Chronobiology Laboratory, University of South Caroline [**24**]. In addition, we use statistical computation techniques such as residual sum of squares and cross-validation to compare fitting and predictive performance of these models. The objective of this chapter is to develop discrete fractional models in order to find the best data fitting for a given tumor growth data.

5.1. Parameter Estimations with the Fractional Richards Curve

In this section, we consider Richards models which contain four parameters. For each model, we consider continuous, discrete, continuous fractional and discrete fractional forms. In these forms, a, b, c and d are parameters and $\alpha \in (0,1)$ is the order of the fractional difference equation.

We consider the continuous, discrete, continuous fractional and discrete fractional types of Richards curve as in the following:

$$Y(t) = \frac{a}{(1+e^{b}(e^{-c})^{t})^{\frac{1}{d}}} \qquad (continuous)$$

$$Y(t) = \frac{a}{(1+e^b(1-c)^t)^{\frac{1}{d}}} \qquad (discrete)$$

$$Y(t) = \frac{a}{(1+e^b \sum_{n=0}^{\infty} (-c)^n \frac{t^{(n+1)\alpha-1}}{\Gamma((n+1)\alpha)})^{\frac{1}{d}}} \qquad (continuous\ fractional)$$

$$Y(t) = \frac{a}{(1+e^b \sum_{n=0}^{\infty} (-c)^n \frac{(t-n+1)^{\overline{(n+1)\alpha-1}}}{\Gamma((n+1)\alpha)})^{\frac{1}{d}}} \qquad (discrete\ fractional)$$

where $0 < \alpha < 1$.

We use Mathematica to estimate parameters for the continuous and discrete forms of the Richards curves. We fix parameter c and compare graphs of the continuous and discrete forms of Richards curves in order to get better parameters a, b, d and α. Then we substitute the same parameters into continuous fractional and discrete fractional curves to find estimated data value $Y(t)$ for each iteration. We also use statistical computation techniques such as square residual sum and cross validation to compare fitting and predictive performance of these models. Residual sum of squares is the sum of squares of residual. It is a measure of the variance between the data and an estimation model. In our study, residual sum of squares is considering y_i as original value and estimated data $Y(t)$ as predicted value, therefore,

$$\sum_{i=1}^{17} (y_i - Y(t))^2, \qquad \text{for } 1 \le i \le 17.$$

We do this process 17 times for each mouse. A small residual sum squares indicates a better fit of the model to the data.

5.2. Cross Validation Method

Cross validation is a technique of model evaluation for an independent data set. The goal of cross validation is to estimate the expected level of fit of a model to a data set that is independent of the data which we used to train the model. The idea for cross validation originated in the 1930 [**33**]. In the paper [**33**], one fold is used for validation and a second for prediction. Mosteller and Turkey [**34**], and various other people further developed the idea. A clear statement of cross validation, which is similar to current version of k-fold cross validation, first appeared in [**35**].

A common type of cross validation is k-fold cross validation. In k-fold cross validation the data is first partitioned into k folds. One is retained as the validation data for testing the model which is called testing set. The remaining $k-1$ sets are used as training set. The advantage of this method over repeated random sets is that all observations are used for both training and validation, and each observation is used for validation exactly once. Cross validation is widely used to compare the performances of different predictive modeling procedures and variable selection. For more, we refer reader to the papers [**25, 26**].

In our study, we work on tumor growth data of 28 control mice for 17 days. For experimental values, we divide growth value by 10000, because it is more convenient to obtain our parameters. We have $k = 17$ independent observation as a training set. We call this statistical method 17-fold cross validation, then we repeat this program 17 times. We leave out one experimental value each time, so our training set $G_i = 16$ where $1 \le i \le 17$ and we call testing set T. The Table 5.2.1 shows the training set G and testing set T where $1 \le i, j \le 17$.

For example, we calculate cross validation for id number 21. The data from day 1 are used as testing data, and the rest of 16 days' data are used as training data. We use Findfit in Mathematica to search for parameters of 16 days' data except day 1, and substitute parameters into the continuous, discrete, continuous fractional and discrete fractional forms. We get a new predictive value $Y'(t)$ for id number 21 of day 1. We repeat this process 17 times and calculate the residual sum of squares.

Training Set	*Selected Observations*	*Test Set*	*Selected Observations*
G_i	$(Y_j)_{j \neq i}^{17}$	T_i	Y_i

TABLE 5.2.1. 17-fold cross-validation

5.3. Comparisons and Conclusions

In this section, as we mentioned before, we use Findfit in Mathematica to estimate parameters for continuous and discrete forms of Richards curves. We sometime fix parameter c in order to get better parameters a, b, d and α. Then we substitute the same parameters into continuous fractional and discrete fractional curves to find estimated data values $Y(t)$ for each iteration. Then we calculate the square residual sum and cross validation to compare fitting and predictive performance of these models. We demonstrate this with some tables and graphs.

Table 5.3.1 is the data analysis for the Richards curves. We compare residual sum of squares in continuous, discrete, continuous fractional and discrete fractional forms. The bold one in each row indicates the minimum residual sum of squares. It is clearly seen that only one mouse has minimum residual sum of squares in continuous form, twenty of the mice have minimum residual sum of squares in discrete form, seven have minimum residual sum of squares in continuous fractional form and none are in discrete fractional form. In addition, the total number of minimum residual sum of squares is twenty in discrete and discrete fractional, compare to the continuous and continuous fractional forms, where the total number of minimum residual sum of squares is eight. Therefore, we can conclude that discrete case has better data fitting of tumor growth for twenty-eight mice than the continuous case for Richards curve. In addition, we have the range of α for continuous fractional and discrete fractional forms, respectively. In continuous fractional case, we have $0.99993 \leq \alpha \leq 0.999998$. In the discrete fractional case, we have $0.99995 \leq \alpha \leq 0.999999$. We calculate the difference between the residual sum of squares from continuous form and the minimum residual sum of squares from discrete, continuous fractional or discrete fractional forms, then use the difference divide the residual sum of squares from continuous form in order to get the percentage of improvement. We observe that the discrete form has 12.164% better data fitting than the continuous form of Richards curve in some cases. Compare to continuous form, the range of percentage of improvement is from 0.001% to 12.164% in discrete, continuous fractional and discrete fractional forms.

Table 5.3.2 is the data analysis of cross validation for the Richards model. We use the cross validation method to calculate residual sum of squares for each mouse in continuous, discrete, continuous fractional and discrete fractional forms. We compare the performances of predictive modeling procedures It is shown that fifteen minimum residual sum of squares are in discrete forms and thirteen of them are in continuous forms.

In Table 5.3.3, we list minimum residual sum of squares from the Gompertz, Logistic and Richards curves for each mouse. We get the data of Gompertz and Logistic curves from the paper [**1**]. The minimum residual sum of squares could be from continuous (C), discrete (D), continuous fractional (C F), discrete fractional (D F) or some of them at the same time. Then we calculate how many percentage of improvement between the largest residual sum of squares and the smallest residual sum of squares. Note that Richards model is 40.593% working better than Gompertz model in some cases, and 21.633% working better than Logistic model in some cases. Therefore, we conclude that the Richards model has better data fitting of tumor growth for these twenty-eight mice.

The last comparison is the mean value of residual sum of squares for the Gompertz, Logistic and Richards curves as shown in Table 5.3.4. We calculate the mean value of data for each day and use Findfit in Mathematica to estimate parameters a, b, c and d. By following the same steps, we obtain the residual sum of squares in continuous, discrete, continuous fractional and discrete fractional forms. The minimum residual sum of squares is in continuous form. In FIGURE 5.3.1, the line indicates the mean value of the data.

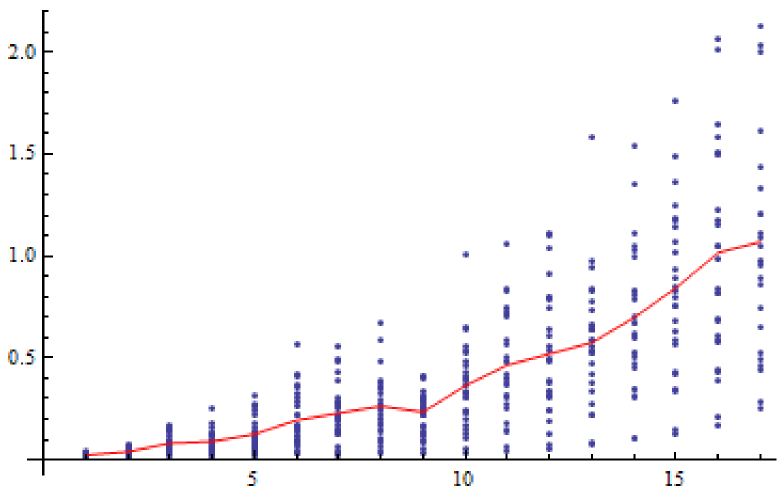

FIGURE 5.3.1. Mean Value of the Data

id#	*Continuous* ($\alpha = 1$)	*Discrete* ($\alpha = 1$)	*Continuous Fractional*	*Discrete Fractional*
21	.07055390406	**.06293114988**	.07056336766 $\alpha = 0.99998$	.06301147442 $\alpha = 0.99998$
22	.3202907564	**.3150651669**	.3203234818 $\alpha = 0.99998$	.3161597197 $\alpha = 0.99998$
23	.09469001895	**.09468867515**	.09471757867 $\alpha = 0.99998$	.09554155663 $\alpha = 0.99998$
26	.01209893079	**.01155143364**	.01210037247 $\alpha = 0.99998$	.01156999186 $\alpha = 0.99998$
27	.05359395890	.05411107944	**.05359189805** $\alpha = \mathbf{0.99997}$	.05419484160 $\alpha = 0.99998$
28	.09265912772	**.0926578624**	.09267296839 $\alpha = 0.99998$	.09405281205 $\alpha = 0.99998$
29	.006019372197	**.006019138354**	.006026833337 $\alpha = 0.99998$	.006202556461 $\alpha = 0.99998$
30	**.07972749954**	.07976148148	.07972769672 $\alpha = 0.99998$	.07976041358 $\alpha = 0.99992$
31	.07623475353	**.0735450628**	.07623929625 $\alpha = 0.99998$	.07358019622 $\alpha = 0.99998$
32	.008837186353	**.008837102086**	.008846053178 $\alpha = 0.99998$	.009064834404 $\alpha = 0.99998$
33	.04919938086	**.04900239451**	.04920355913 $\alpha = 0.99998$	.04942261774 $\alpha = 0.99998$
34	.3032336354	**.2951961514**	.3032506720 $\alpha = 0.99998$	.2955719851 $\alpha = 0.99998$
35	.02810434607	**.02468561651**	.02810983488 $\alpha = 0.99998$	.02474659675 $\alpha = 0.99998$
136	.02136638617	.02162574067	**.02136563279** $\alpha = \mathbf{0.99998}$	.02167654152 $\alpha = 0.99998$
137	.2542107669	**.2517539004**	.2542131842 $\alpha = 0.99998$	.2517774575 $\alpha = 0.99998$
138	.1510070102	**.1510039993**	.1511861288 $\alpha = 0.99998$	.1557005256 $\alpha = 0.99998$
139	.1334861748	**.1293800537**	.1334960618 $\alpha = 0.99998$	.1296131875 $\alpha = 0.99998$
140	.05152899720	**.05152836781**	.05154251740 $\alpha = 0.99998$	.05206399482 $\alpha = 0.99998$
141	.02963481694	.02998502565	**.02963366498** $\alpha = \mathbf{0.99997}$	.02998351286 $\alpha = 0.99997$
142	.003023750895	**.003023604093**	.0030277895360 $\alpha = 0.99998$	.003027245575 $\alpha = 0.999999$
143	.1333747739	.1354905621	**.1333610592** $\alpha = 0.9999$	.135474485 $\alpha = 0.999984$
144	.1850708062	**.1788737819**	.1850832654 $\alpha = 0.99998$	.1788799357 $\alpha = 0.999999$
145	.2920427998	.2957495615	**.2920227196** $\alpha = \mathbf{0.99993}$	.2957366131 $\alpha = 0.99995$
146	.2319182403	**.2300531995**	.2319506111 $\alpha = 0.99998$	.2300800150 $\alpha = 0.999999$
147	.04239796707	.04524070618	**.04236747212** $\alpha = \mathbf{0.9999}$	.04519901286 $\alpha = 0.999983$
148	.1049185309	**.1041125459**	.1049223579 $\alpha = 0.99998$	.1041132890 $\alpha = 0.99999$
149	.1223959432	**.1140944052**	.1224008080 $\alpha = 0.99998$	.1140957980 $\alpha = 0.999999$
150	.3031961400	.3089462610	**.3031836220** $\alpha = \mathbf{0.99994}$	.3089011267 $\alpha = 0.999989$

TABLE 5.3.1. Data Analysis for Richards Curves

id#	*Continuous* ($\alpha = 1$)	*Discrete* ($\alpha = 1$)	*Continuous Fractional*	*Discrete Fractional*
21	.1405917696	.1218063122	.1293271074 $\alpha = 0.99369$	**.1125818035** $\alpha = \mathbf{0.99922}$
22	.5832983454	.5737454049	.5344919987 $\alpha = 0.99958$	**.5140349471** $\alpha = \mathbf{0.99987}$
23	.1553465299	.1584424949	**.1539153181** $\alpha = \mathbf{0.99958}$	.1569667765 $\alpha = 0.99997$
26	.01907594064	**.01903043297**	.01907306413 $\alpha = 0.9999$	.01903584769 $\alpha = 0.99998$
27	**.08227777737**	.08351258726	.08230450460 $\alpha = 0.99998$	.08397187477 $\alpha = 0.99998$
28	.1255406226	.1267120107	**.1254689200** $\alpha = \mathbf{0.99994}$	.1274534278 $\alpha = 0.99998$
29	**.01435046770**	.0143517433	.01436817016 $\alpha = 0.99998$	.01467021702 $\alpha = 0.99998$
30	.1318085013	.1353622957	**.1265760520** $\alpha = \mathbf{0.97708}$	.1294509256 $\alpha = 0.99418$
31	**.1275216366**	0.1310244537	.127522443 $\alpha = 0.99998$	.1310292422 $\alpha = 0.99998$
32	.01204896226	**.01204793761**	.01207279151 $\alpha = 0.99998$	.01247371960 $\alpha = 0.99998$
33	**.07565989157**	.07902384173	.07572089670 $\alpha = 0.99998$	.08049313863 $\alpha = 0.99998$
34	.9964810358	.9881602600	.6185429849 $\alpha = 0.99279$	**.5834927878** $\alpha = \mathbf{0.99929}$
35	.06158704618	.05097936849	.05835387197 $\alpha = 0.99805$	**.04851260724** $\alpha = \mathbf{0.99979}$
136	**.03226623637**	.03447290807	.03228766069 $\alpha = 0.99998$	.03475807249 $\alpha = 0.99998$
137	.3872726009	.3979061012	**.3817079627** $\alpha = \mathbf{0.98463}$	.3926527359 $\alpha = 0.99709$
138	.2530693257	**.2530387709**	.2535977126 $\alpha = 0.99998$	.2624174712 $\alpha = 0.99998$
139	.3360922189	.3370544192	.2571769786 $\alpha = 0.99647$	**.2466325799** $\alpha = \mathbf{0.99966}$
140	.06257182852	**.06254893216**	.06259634046 $\alpha = 0.99998$	.06323933624 $\alpha = 0.99998$
141	**.04351283812**	.04383337665	.04351995634 $\alpha = 0.99975$	.04397370742 $\alpha = 0.99998$
142	.004056322000	**.004055986860**	.004241599240 $\alpha = 0.9999$	.004241599240 $\alpha = 0.99998$
143	.2161237449	.2302311946	.2110330971 $\alpha = 0.99925$	**.2090766940** $\alpha = \mathbf{0.99975}$
144	.2858417083	.2886065636	.2882367079 $\alpha = 0.99949$	**.2857918010** $\alpha = \mathbf{0.99998}$
145	.5786459411	.6023383487	.5409487262 $\alpha = 0.99925$	**.5222692563** $\alpha = \mathbf{0.99975}$
146	.4345501758	.4384384658	.4103854055 $\alpha = 0.999$	**.4083285884** $\alpha = \mathbf{0.99991}$
147	.1016978584	.1118139375	**.1011928925** $\alpha = \mathbf{0.99975}$	.1089126292 $\alpha = 0.9998$
148	**.1582913765**	.1623966760	2.368012031 $\alpha = 0.99998$	.1627646250 $\alpha = 0.99998$
149	.6757906497	.6687533260	0.4536768853 $\alpha = 0.99335$	**.2591408123** $\alpha = \mathbf{0.99412}$
150	**.4074120406**	.4216746870	.5184745904 $\alpha = 0.99395$	.5232677097 $\alpha = 0.999928$

TABLE 5.3.2. Cross Validation for Richards Curves

id#	*Gompertz Curve*	*Logistic Curve*	*Richards Curve*	*Percentage of Improvement*
21	.09320807348 *C and D*	.07720652925 *D*	**.06293114988** *D*	32.48315566%
22	.3334575178 *C F*	.3258675032 *D*	**.3150651669** *D*	5.515650396%
23	.099979266879 *D F*	.09474826414 *D*	**.09468867515** *D*	5.291688861%
26	.01504232032 *D*	.01325261841 *C and D*	**.01155143364** *D*	23.2071024%
27	**.05129960785** *C F*	.05247699452 *C F*	.05359189805 *D*	4.277307361%
28	.09877841550 *D F*	.09269992014 *D*	**.09265786241** *D*	6.196245464%
29	.006858511228 *D F*	.006022041787 *D*	**.006019138354** *D*	12.23841219%
30	.08160721610 *D*	.07976180993 *C*	**.0797249954** *D*	2.30643905%
31	.08094056469 *D*	.07471837868 *D*	**.07354750628** *D*	9.133934806%
32	.00979888886 *D F*	.008848677223 *D*	**.008837102086** *D*	9.815261233%
33	.04977301896 *D F*	.04950751166 *C*	**.04900239451** *D*	1.548277493%
34	.3197937942 *C*	.3125897049 *D*	**.2951961514** *D*	7.691719866%
35	.04155372344 *C*	.03150005505 *C*	**.02468561651** *D*	40.59349087%
136	**.02069668479** *c*	.02091409925 *C F*	.02136563279 *C F*	3.130953371%
137	.2605491124 *C*	.2552786642 *C and D*	**.2517539004** *D*	3.375644583%
138	.1689272298 *D F*	.1511871712 *D*	**.1510039993** *D*	10.61003044%
139	.1444468940 *C*	.1389586529 *C*	**.1293800537** *D*	10.43071255%
140	.05338370310 *D F*	.05156530341 *D F*	**.0512836781** *D*	3.933831634%
141	**.02861367403** *C F*	.02903453028 *C F*	.02963366498 *C F*	3.44200068%
142	.003657090481 *D*	.003026069415 *D*	**.003023604093** *D*	17.3221415%
143	**.1279762340** *D F*	.1301131682 *D F*	.1333610592 *C F*	4.037779268%
144	.2024468349 *C and D*	.1942945348 *C*	**.1788737819** *D*	2.3573053%
145	**.2808836341** *C F*	.2850144884 *C F*	.2920227196 *C F*	3.814458617%
146	.2419516991 *D F*	.2325981230 *D*	**.2300531995** *D*	4.917716901%
147	**.03264789880** *D F*	.03702966456 *D F*	.04236747212 *C F*	22.94112165%
148	.1113379834 *D*	.1077952924 *C*	**.1041125459** *D*	6.489642869%
149	.1394980990 *D*	.1242478059 *C and D*	**.1140944052** *D*	18.21078135%
150	.3029542604 *C F*	**.3004077982** *C F and D F*	.3031836220 *C F*	0.9155586247%

TABLE 5.3.3. Data Analysis For Gompertz, Logistic and Richards Curves

	Gompertz Curve	*Logistic Curve*	*Richards Curve*
Continuous (α=1)	0.01467378953	0.01511114565	**0.01540620032**
Discrete (α=1)	0.01467353864	0.01511114569	0.01540642082
Continuous Fractional	**0.01467346239** α = 0.99996	**0.01511043545** α = 0.99989	0.0154063081 α = 0.99998
Discrete Fractional	0.01467360877 α = 0.99997	0.01511068031 α = 0.99993	0.01552613559 α = 0.99998

TABLE 5.3.4. Gompertz, Logistic and Richards Curves Mean Table

Chapter 6

CONCLUSION AND FUTURE WORK

We have studied fractional calculus which considered the derivative of a function to non-integer order, and discrete fractional calculus which dealt with any positive real order of sum or difference. In the first chapter, we introduced some special functions, basic concepts and notations in nabla fractional calculus. Then we presented fractional difference equations involving Riemann-Liouville operator of real number order between zero and one. In chapter two, we focused on proving that there exits a solution for up to the first order nabla fractional difference equation with an initial condition. In order to show the existence of solution for up to the first order nabla fractional difference equation with an initial condition, we applied the Brouwer fixed point theorem and the Contraction Mapping Theorem. Then we defined a lower and an upper solution for up to the first order nabla fractional difference equation with an initial condition in chapter three. The method of defining a lower and upper solution is a useful tool to prove results for the existence of a solution. Under certain assumptions, we showed that there exists a solution between lower and upper solution which are well ordered. Then we gave constructive proofs of existence of a solution by defining monotone sequences. In chapter four, we introduced the sigmoidal curves in fractional calculus. We considered the first order differential equation that approximates to the first order difference equation. In addition, we showed the fractional continuous Mittag-Leffler function.

Then we used the successive approximations method to calculate the discrete form of Mittag-Leffler function.

Nabla fractional calculus is widely used in the modeling process of real world problems. We developed nabla fractional calculus and applied it in analyzing tumor growth of cancer in chapter five. We considered the Richards sigmoidal curves with four parameters and an alpha parameter. We used Findfit in Mathematica to estimate the parameters of continuous and discrete forms of Richards curves. Then we used the same parameters for continuous fractional and discrete fractional forms. In addition, we used statistical methods such as residual sum of squares and k-fold cross validation to predict the performance of tumor growth. Considering tables of this data, we compared continuous, discrete, continuous fractional and discrete fractional forms of residual sum of squares, we concluded that discrete version of Richards model fit the data best for the twenty-eight mice studied. We also compared the minimum residual sum of squares in the Gompertz, Logistic and Richards curves. Since Richards curves had the largest number of minimum residual sum of squares among these three, we concluded that Richards curve was working better than the Gompertz and Logistic curves for the data fitting of twenty-eight mice.

There are still many open questions to be considered in future work in fractional calculus. We have applied a quasilinearization method to give constructive proofs of existence of a solution by defining monotone sequences for the initial value problem (2.1) in a sector defined by a lower and an upper solution. Now we can study that how fast the monotone sequences approach and converge to the solution. The Weibull model should also be considered, it has four parameters a, b, c, d and $\alpha \in (0,1)$ which is the order of the fractional difference equation. We can use Findfit in Mathematica to estimate parameters a, b, c and d in continuous and discrete form similar to the work done on Richards model. These parameters can be substituted into continuous fractional and discrete fractional curves to find $Y(t)$ for each iteration. Then residual sum of squares and cross validation can be used to compare fitting and predictive performance of Weibull models:

$$Y(t) = a - b(e^{-c})^{t^d} \qquad (continuous)$$

$$Y(t) = a - b(1-c)^{t^d} \qquad (discrete)$$

$$Y(t) = a - b\Big(\sum_{n=0}^{\infty}(-c)^n \frac{t^{(n+1)\alpha-1}}{\Gamma((n+1)\alpha)}\Big)^{t^{d-1}} \qquad (continuous\ fractional)$$

$$Y(t) = a - b\Big(\sum_{n=0}^{\infty}(-c)^n \frac{(t-n+1)^{\overline{(n+1)\alpha-1}}}{\Gamma((n+1)\alpha)}\Big)^{t^{d-1}} \qquad (discrete\ fractional)$$

A comparison can then be made between Gompertz, Logistic, Richards and Weibull curves to conclude which model will have the best data fitting of tumor growth for twenty-eight mice.

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