Chapter 7

Qualitative Analysis of Fractional modelling of Pancreatic Cancer Dynamics

7.1 Introduction

Pancreatic cancer is a complicated and challenging disease that affects millions of people globally. It is the world's sixth greatest cause of cancer-related fatalities. It is, however, prevalent in more advanced countries. The causes of such huge variations in Pancreatic cancer mortality rates are unknown, however they might be due to a lack of adequate disease detection, treatment, and recording. Although symptoms aren't noticed until the illness has progressed, Pancreatic cancer represents among most harmful malignant tumors [115]. It is a kind of cancer that begins in the pancreas, an abdominal gland that produces digestive enzymes as well as hormones that control blood sugar levels. It is known for its extreme aggressiveness and for rapidly spreading to other parts of the body. It might be difficult to identify cancer in its early stages since symptoms may not appear until the malignancy has advanced.

Pancreatic cancer is divided into numerous types, the most common being Pancreatic ductal adenocarcinoma (PDAC). Cells that lining the ducts that transport digestive enzymes from the pancreas to the small intestine create PDAC. Neuroendocrine tumors (NETs) and acinar cell carcinoma are two types of Pancreatic cancer that are less common. Pancreatic cancer warning signs include age, a family history of the illness, smoking, obesity, chronic pancreatitis, and particular genetic abnormalities. Treatment options for Pancreatic cancer differ according to the phase and location of the illness and may include surgery, radiation therapy, chemotherapy, and targeted therapy. Despite therapeutic advances, Pancreatic cancer remains a tough illness to treat. It has a high mortality rate, with a less than 10% five-year chance of survival. As a consequence, research into better understanding Pancreatic cancer biology and developing more effective treatment options is ongoing [57, 84, 88].

Pancreatic cancer mathematical models attempt to represent cancer cell dynamics and response to different medications. These models are often made up of a sequence of differential equations that describe the rate of change of distinct cell populations over time, such as normal cells, immune cells and cancerous cells. The physical significance of these mathematical models is that they enable us to predict the creation and spread of Pancreatic cancer, as well as the effect of different treatments on cancer cells and healthy tissue around them. For example, the models may be used to determine the optimal dosage and timing of chemotherapy or radiation therapy, as well as to predict the probability of treatment resistance. In addition to predicting treatment response, these models may provide insights into the underlying biology of Pancreatic cancer.

Yoram et al., in their study [88], created a mathematical framework for Pancreatic cancer and utilized it to elucidate various biological and clinical facts in a qualitative manner. The basic mathematical model for Pancreatic cancer involves T tissue, macrophages, PSCs, and PCCs. These cells interact in complex ways, with malignant cells and PSCs influencing macrophage behavior (M1 to M2 shift), while T cells rely on M1 macrophages for their proliferation. To better understand this biology, an extended "full model" was developed, encompassing cytokine interactions among these cell categories, as indicated in [88]. Through a quasi-steady-state approach, a more concise "reduced model" was derived, featuring four ODEs that encapsulate PCCs, PSCs, T cells, and the M1 to M2 macrophage ratio. which demonstrated that the occurance of cancer-inhibiting medications hinges upon the immune-induced cell death occurring within a specific limit. This highlights the immune system's limited time frame for effectively suppressing cancer during therapy. The classical model from Equations (25-28) of [88] consists of a system of four first order nonlinear ordinary differential equations that takes the following form:

$$
\begin{aligned}
\frac{dC}{dt} &= (k_c + \mu_c P)\, C^{3/4} \left(1 - (C/C_0)^{1/4}\right) - \frac{\lambda_c C T}{\mathrm{K}_c + (1 - R)}, \\
\frac{dP}{dt} &= \left(k_p + \frac{\mu_p C}{\mathrm{K}_p + C}\right) P \left(1 - \frac{P}{P_0}\right) - \lambda_p P, \\
\frac{dR}{dt} &= k_r - (\lambda_r + \gamma_p P + \gamma_c C)\, R, \\
\frac{dT}{dt} &= \frac{k_t R}{\mathrm{K}_t + (1 - R)} - \lambda_t T.
\end{aligned}
\tag{7.1}
$$

The following description is associated to the above classical model:

Table 7.1: Description of variables/constants and its notations.

Variable/Constant	Description
C	Density of cancer cells
P	Density of Pancreatic stellate cells (PSC)
$R(=\frac{M_1}{M})$	Fraction of pro-inflammatory macrophages
$M(=M_1+M_2)$	Total number of macrophages
M_1	Density of pro-inflammatory cells
M_2	Density of anti-inflammatory cells
T	Density of cytotoxic CD8+ T cells (CTL)
T_β	Concentration of cytokine TGFβ
I_6	Concentration of cytokine IL6
I_{10}	Concentration of cytokine IL10
I_{12}	Concentration of cytokine IL12
S	Concentration of cytokine MCSF
G	Concentration of cytokine GMCSF

This chapter includes Caputo and Atangana -Baleanu-Caputo fractional derivative operator to model dynamics of Pancreatic cancer. Moreover, we explore aspects such as existence, uniqueness, and global stability for the system of both the models. The first part of the chapter has the following framework: Section 7.2.1 defines the Caputo and Reimann - Liouville fractional derivative and integral operations. Section 7.2.2 presents a fractional mathematical model of Pancreatic cancer via the caputo derivative operator. Section 7.2.3 discusses the model's well-posedness. In section 7.2.4, we addressed various stability theorems. The outline of the second part of the chapter is as follows: we Firstly present some basic concepts in Section 7.3.1 to understand the rest of the analysis. Section 7.3.2 is devoted to formulate the fractional mathematical model of Pancreatic cancer incorporating Pancreatic ductal adenocarcinoma. Section 7.3.3 then discusses the existence and uniqueness of the system, while Section 7.3.4 analyzes the stability of the system. Finally, Section 7.4 concludes all the major findings of the present research study.

7.2 Mathematical analysis of a Pancreatic cancer with Caputo derivative

7.2.1 Preliminaries

We will review some fundamental ideas about the Caputo fractional derivative and the Caputo fractional differential equation in this section.

Definition 7.2.1. *For order* $\mathfrak{r} > 0$ *and* $e : \mathbb{R}^+ \to \mathbb{R}$*, Riemann-Liouvillie [106] established a fractional integral operator as:*

$$ {}_0I^{\mathfrak{r}}(e(\varkappa)) = \frac{1}{\Gamma(\mathfrak{r})} \int_0^{\varkappa} (\varkappa - \Upsilon)^{\mathfrak{r}-1} e(\Upsilon) d\Upsilon, \qquad \varkappa > 0. $$

Definition 7.2.2. *The Riemann-Liouville fractional differential operator for the function* $e(\varkappa)$ *with order* $\mathfrak{r} > 0$ *is defined to be [106]:*

$$ {}_0D^{\mathfrak{r}}(e(\varkappa)) = \frac{1}{\Gamma(\mathfrak{j} - \mathfrak{r})} \left(\frac{d}{d\varkappa} \right)^{\mathfrak{j}} \int_0^{\varkappa} (\varkappa - \Upsilon)^{\mathfrak{j}-\mathfrak{r}-1} e(\Upsilon) d\Upsilon, \qquad \varkappa > 0, $$

where, $\mathfrak{j} - 1 < \mathfrak{r} \leq \mathfrak{j}, \mathfrak{j} \in \mathbb{N}$.

Definition 7.2.3. *Caputo [106] contributed in the field of fractional calculus by defining the derivative of fractional order* $\mathfrak{r} > 0$ *for the function* $e(\varkappa) \in \mathbb{C}^{\mathfrak{j}}$ *as*

$$ {}_{0}^{C}D^{\mathfrak{r}}(e(\varkappa)) = \frac{1}{\Gamma(\mathfrak{j}-\mathfrak{r})} \int_{0}^{\varkappa} (\varkappa - \Upsilon)^{\mathfrak{j}-\mathfrak{r}-1} e^{\mathfrak{j}}(\Upsilon) d\Upsilon, \qquad \varkappa > 0, $$

and is defined for absolute continuous functions where, $\mathfrak{j} - 1 < \mathfrak{r} \leq \mathfrak{j}, \mathfrak{j} \in \mathbb{N}$.

7.2.2 Model formulation in Caputo sense

We create our fractional derivative model by replacing the classical-order model (7.1) with the Caputo fractional derivative. As we are aware, the fundamental notion of fractional-order modification is that fractional-order derivatives are simply used in place of integer-order derivatives is unlikely to be appropriate since such generalization might result in an unphysical model. In such instance, a correct generalization requires absolute equal dimensionality. This is accomplished by applying the fractional order $\mathfrak{r}$ on every time-dimensional parameter, leading to a corresponding time-dimension $time^{-\mathfrak{r}}$ on both sides of the model. As a consequence, the Caputo fractional model for Pancreatic cancer resembles this into initial value problem(IVP):

$$
\begin{aligned}
{}_{0}^{C}D_{\varkappa}^{\mathfrak{r}}\left(C\left(\varkappa\right)\right) &= \left(k_c{}^{\mathfrak{r}} + \mu_c{}^{\mathfrak{r}}P\right)C^{3/4}\left(1 - \left(C/C_{max}\right)^{1/4}\right) - \frac{\lambda_c{}^{\mathfrak{r}}CT}{\mathrm{K}_c{}^{\mathfrak{r}} + (1-R)}, \\
{}_{0}^{C}D_{\varkappa}^{\mathfrak{r}}\left(P\left(\varkappa\right)\right) &= \left(k_p{}^{\mathfrak{r}} + \frac{\mu_p{}^{\mathfrak{r}}C}{K_p{}^{\mathfrak{r}} + C}\right)P\left(1 - \frac{P}{P_{max}}\right) - \lambda_p{}^{\mathfrak{r}}P, \\
{}_{0}^{C}D_{\varkappa}^{\mathfrak{r}}\left(R\left(\varkappa\right)\right) &= k_r{}^{\mathfrak{r}} - \left(\lambda_r{}^{\mathfrak{r}} + \gamma_p{}^{\mathfrak{r}}P + \gamma_c{}^{\mathfrak{r}}C\right)R, \\
{}_{0}^{C}D_{\varkappa}^{\mathfrak{r}}\left(T\left(\varkappa\right)\right) &= \frac{k_t{}^{\mathfrak{r}}R}{\mathrm{K}_t{}^{\mathfrak{r}} + (1-R)} - \lambda_t{}^{\mathfrak{r}}T.
\end{aligned}
\tag{7.2}
$$

The initial conditions for the proposed model are $C\left(0\right) = C_0, P\left(0\right) = P_0, R\left(0\right) = R_0$ and $T\left(0\right) = T_0$ with C_0, P_0, R_0 and $T_0 > 0$.

7.2.3 Qualitative analysis

Using Sadovskii's fixpoint theorem, we discuss the existence and uniqueness of Caputo's FDE solution by considering banach space $\mathfrak{S}$ with $\varkappa \in [0, \mathfrak{T}]$, $C, P, R, T \in \mathbb{C}(\mathfrak{R}, \mathfrak{S}) \cap L^1{}_{loc}(\mathfrak{R}, \mathfrak{S})$ and $\mathfrak{R} = \{(\varkappa, K) : \varkappa \in [0, \mathfrak{T}]\}$, $K \in B(0, \bar{\mathfrak{r}})$ for some $\mathfrak{T}, \bar{\mathfrak{r}} > 0$.

Theorem 7.2.1. *Consider $\mathbb{B} \subset \mathfrak{S}$ and let $\Phi : \mathbb{B} \to \mathbb{B}$ be a mapping with condensation property. Then, there exists a definite point of the mapping Φ within the set $\mathbb{B}$.*

Examine IVP on $\mathfrak{R} = \{(\varkappa, K) \in \mathbb{R} \times \mathfrak{S} : \varkappa \in [0, \mathfrak{T}], K \in B(0, \bar{\mathfrak{r}})\}$ for some fixed $\mathfrak{T}, \bar{\mathfrak{r}} > 0$. Assume that $\exists\, \mathfrak{p} \in (0, \bar{\mathfrak{r}})$, $\mathfrak{M}_1, \mathfrak{M}_2, L, L_1 \in L_{1/\mathfrak{p}}([0, \mathfrak{T}], \mathbb{R}^+)$ & $\mathfrak{C}_1, \mathfrak{P}_1, \mathfrak{R}_1, \mathfrak{T}_1$, $\mathfrak{C}_2, \mathfrak{P}_2, \mathfrak{R}_2, \mathfrak{T}_2 \in \mathbb{C}(\mathbb{R}, \mathfrak{S}) \cap L^1{}_{loc}(\mathbb{R}, \mathfrak{S})$ such that $C = \mathfrak{C}_1 + \mathfrak{C}_2, P = \mathfrak{P}_1 + \mathfrak{P}_2, R = \mathfrak{R}_1 + \mathfrak{R}_2, T = \mathfrak{T}_1 + \mathfrak{T}_2$ and the subsequent premises are legitimate

Assumption 1– *$\mathfrak{C}_1, \mathfrak{P}_1, \mathfrak{R}_1$, and $\mathfrak{T}_1$ are bounded and Lipschitz.*

Assumption 2– *$\mathfrak{C}_2, \mathfrak{P}_2, \mathfrak{R}_2$, and $\mathfrak{T}_2$ are compact and bounded.*

Assumption 3– $|\mathbb{R}(\varkappa, K) - \mathbb{R}(\varkappa, J)| \leq L_1(\varkappa)\, \|K - J\|$, $\forall\, (\varkappa, K), (\varkappa, J) \in \mathbb{R}$.

Applying (4.3.1) on (7.2), the Lemma (7.2.1) can be formulated as follows:

Lemma 7.2.1. *As the current model was derived with only one requirement for each equation, the provided array of IVP is identical to the subsequent set of integral equations:*

$$
\begin{aligned}
C(\varkappa) &= C(0) + \frac{1}{\Gamma(\mathfrak{r})} \int_0^{\varkappa} (\varkappa - \Upsilon)^{\mathfrak{r}-1} \mathfrak{C}_1(\Upsilon, C(\Upsilon))\, d\Upsilon \\
&\quad + \frac{1}{\Gamma(\mathfrak{r})} \int_0^{\varkappa} (\varkappa - \Upsilon)^{\mathfrak{r}-1} \mathfrak{C}_2(\Upsilon, C(\Upsilon))\, d\Upsilon, \\
P(\varkappa) &= P(0) + \frac{1}{\Gamma(\mathfrak{r})} \int_0^{\varkappa} (\varkappa - \Upsilon)^{\mathfrak{r}-1} \mathfrak{P}_1(\Upsilon, P(\Upsilon))\, d\Upsilon \\
&\quad + \frac{1}{\Gamma(\mathfrak{r})} \int_0^{\varkappa} (\varkappa - \Upsilon)^{\mathfrak{r}-1} \mathfrak{P}_2(\Upsilon, P(\Upsilon))\, d\Upsilon, \qquad (7.3) \\
R(\varkappa) &= R(0) + \frac{1}{\Gamma(\mathfrak{r})} \int_0^{\varkappa} (\varkappa - \Upsilon)^{\mathfrak{r}-1} \mathfrak{R}_1(\Upsilon, R(\Upsilon))\, d\Upsilon
\end{aligned}
$$

$$+\frac{1}{\Gamma(\mathfrak{r})}\int_0^{\varkappa}(\varkappa-\Upsilon)^{\mathfrak{r}-1}\mathfrak{R}_2(\Upsilon, R(\Upsilon))\,d\Upsilon,$$

$$T(\varkappa) = T(0) + \frac{1}{\Gamma(\mathfrak{r})}\int_0^{\varkappa}(\varkappa-\Upsilon)^{\mathfrak{r}-1}\mathfrak{T}_1(\Upsilon, T(\Upsilon))\,d\Upsilon$$

$$+\frac{1}{\Gamma(\mathfrak{r})}\int_0^{\varkappa}(\varkappa-\Upsilon)^{\mathfrak{r}-1}\mathfrak{T}_2(\Upsilon, T(\Upsilon))\,d\Upsilon.$$

As demonstrated by the next two theorems, it is now relatively straightforward to establish the existence and uniqueness of solution (7.2)

Theorem 7.2.2. *In accordance with* ***Assumption 1,2*** *the IVP has a minimum of one solution in* $[0, \mathfrak{T}]$*, given*

$$\Theta = \frac{c\|L\|_{1/\mathfrak{p}}(\mathfrak{T})^{\beta}}{\Gamma(\mathfrak{r})} < 1, \qquad where\ \ \beta = (\mathfrak{r}-\mathfrak{p}), c = \left(\frac{1-\mathfrak{p}}{\mathfrak{r}-\mathfrak{p}}\right)^{1-\mathfrak{p}}$$

Proof. Select $\bar{\mathfrak{r}} \ni |C_0| + \Gamma(\mathfrak{r})^{-1}c\left(\|\mathfrak{M}_1\|_{1/\mathfrak{p}} + \|\mathfrak{M}_2\|_{1/\mathfrak{p}}\right)(\mathfrak{T})^{\beta} \leq \bar{\mathfrak{r}}$ & let $B_{\bar{\mathfrak{r}}} = \{K : \|K\| \leq \bar{\mathfrak{r}}\}$ be the closed $\bar{\mathfrak{r}}$-ball in $\mathbb{BC}([0, \mathfrak{T}], \mathfrak{S})$ with sup norm $\|.\|$. Using Lemma (7.2.1) one can obtain that point of $C : B_{\bar{\mathfrak{r}}} \to \mathbb{BC}([0, \mathfrak{T}], \mathfrak{S}), K \mapsto \mathfrak{C}_1 K + \mathfrak{C}_2 K$ with the following:

$$\mathfrak{C}_1 K(\varkappa) = C(0) + \frac{1}{\Gamma(\mathfrak{r})}\int_0^{\varkappa}(\varkappa-\Upsilon)^{\mathfrak{r}-1}\mathfrak{C}_1(\Upsilon, K(\Upsilon))\,d\Upsilon,$$

$$\mathfrak{C}_2 K(\varkappa) = \frac{1}{\Gamma(\mathfrak{r})}\int_0^{\varkappa}(\varkappa-\Upsilon)^{\mathfrak{r}-1}\mathfrak{C}_2(\Upsilon, K(\Upsilon))\,d\Upsilon.$$

as a solution of the model (7.2). In three phases, we demonstrate that $C(\varkappa)$ is condensing, and hence the presence of a fixpoint for $C(\varkappa)$ emerges from Theorem (7.2.1).

Step 1: We must demonstrate $C(B_{\bar{\mathfrak{r}}}) \subset B_{\bar{\mathfrak{r}}}$. For $K \in B_{\bar{\mathfrak{r}}}$, we have

$$|C(\varkappa)| \leq |C_0| + \frac{1}{\Gamma(\mathfrak{r})}\int_0^{\varkappa}(\varkappa-\Upsilon)^{\mathfrak{r}-1}|C(\Upsilon, K(\Upsilon))|\,d\Upsilon$$

$$
\begin{aligned}
&\leq |C_0| + \frac{1}{\Gamma(\mathfrak{r})}\int_0^{\varkappa} (\varkappa-\Upsilon)^{\mathfrak{r}-1}\left|\mathfrak{C}_1(\Upsilon, K(\Upsilon))\right| d\Upsilon \\
&+ \frac{1}{\Gamma(\mathfrak{r})}\int_0^{\varkappa} (\varkappa-\Upsilon)^{\mathfrak{r}-1}\left|\mathfrak{C}_2(\Upsilon, K(\Upsilon))\right| d\Upsilon \\
&\leq |C_0| + \frac{1}{\Gamma(\mathfrak{r})}\int_0^{\varkappa} (\varkappa-\Upsilon)^{\mathfrak{r}-1}\mathfrak{M}_1(\Upsilon)\, d\Upsilon + \frac{1}{\Gamma(\mathfrak{r})}\int_0^{\varkappa} (\varkappa-\Upsilon)^{\mathfrak{r}-1}\mathfrak{M}_2(\Upsilon)\, d\Upsilon \\
&\leq |C_0| + \frac{1}{\Gamma(\mathfrak{r})}\left(\int_0^{\varkappa} (\varkappa-\Upsilon)^{\frac{\mathfrak{r}-1}{1-\mathfrak{p}}} d\Upsilon\right)^{1-\mathfrak{p}}\left(\int_0^{\varkappa} (\mathfrak{M}_1(\Upsilon))^{\frac{1}{\mathfrak{p}}} d\Upsilon\right)^{\mathfrak{p}} \\
&+ \frac{1}{\Gamma(\mathfrak{r})}\left(\int_0^{\varkappa} (\varkappa-\Upsilon)^{\frac{\mathfrak{r}-1}{1-\mathfrak{p}}} d\Upsilon\right)^{1-\mathfrak{p}}\left(\int_0^{\varkappa} (\mathfrak{M}_2(\Upsilon))^{\frac{1}{\mathfrak{p}}} d\Upsilon\right)^{\mathfrak{p}} \\
&\leq |H_0| + \frac{c\left(\|\mathfrak{M}_1\|_{\frac{1}{\mathfrak{p}}} + \|\mathfrak{M}_2\|_{\frac{1}{\mathfrak{p}}}\right)}{\Gamma(\mathfrak{r})}(\mathfrak{T})^{\beta} \leq r,
\end{aligned}
$$

and thus $C(B_{\bar{\mathfrak{r}}}) \subset B_{\bar{\mathfrak{r}}}$.

Step 2: We illustrate that $\mathfrak{C}_1$ is a contraction. If $K, J \in B_{\bar{\mathfrak{r}}}$ we lead to

$$
\begin{aligned}
\left|\mathfrak{C}_1(K(\varkappa)) - \mathfrak{C}_1(J(\varkappa))\right| &\leq \frac{1}{\Gamma(\mathfrak{r})}\int_0^{\varkappa} (\varkappa-\Upsilon)^{\mathfrak{r}-1} L(\Upsilon)\left|K(\Upsilon) - J(\Upsilon)\right| d\Upsilon \\
&\leq \frac{1}{\Gamma(\mathfrak{r})}\left(\int_0^{\varkappa} (\varkappa-\Upsilon)^{\frac{\mathfrak{r}-1}{1-\mathfrak{p}}} d\Upsilon\right)^{1-\mathfrak{p}}\left(\int_0^{\varkappa} L^{\frac{1}{\mathfrak{p}}}(\Upsilon)\, d\Upsilon\right)^{\mathfrak{p}} \|K-J\| \\
&\leq \frac{c\|L\|_{\frac{1}{\mathfrak{p}}}(\mathfrak{T})^{\beta}}{\Gamma(\mathfrak{r})}\|K-J\|
\end{aligned}
$$

and hence $\mathfrak{C}_1(\varkappa)$ is a contraction with, $\|\mathfrak{C}_1(K) - \mathfrak{C}_1(J)\| \leq \Theta\|K-J\|$.

Step 3: $\mathfrak{C}_2$ is compact. For $0 \leq \wp_1 \leq \wp_2 \leq \mathfrak{T}$, we have

$$
\left|\mathfrak{C}_2(K(\wp_2)) - \mathfrak{C}_2(K(\wp_1))\right| \leq \frac{1}{\Gamma(\mathfrak{r})}\left|\int_0^{\wp_2} (\wp_2-\Upsilon)^{\mathfrak{r}-1}\mathfrak{C}_2(\Upsilon, K(\Upsilon))\, d\Upsilon\right|
$$

$$
\begin{aligned}
&-\frac{1}{\Gamma(\mathfrak{r})}\left|\int_0^{\wp_1}(\wp_1-\Upsilon)^{\mathfrak{r}-1}\mathfrak{C}_2(\Upsilon,K(\Upsilon))\,d\Upsilon\right| \\
&\leq \frac{1}{\Gamma(\mathfrak{r})}\left|\int_0^{\wp_1}(\wp_2-\Upsilon)^{\mathfrak{r}-1}\mathfrak{C}_2(\Upsilon,K(\Upsilon))\,d\Upsilon\right| \\
&+\frac{1}{\Gamma(\mathfrak{r})}\left|\int_{\wp_1}^{\wp_2}(\wp_2-\Upsilon)^{\mathfrak{r}-1}\mathfrak{C}_2(\Upsilon,K(\Upsilon))\,d\Upsilon\right| \\
&-\frac{1}{\Gamma(\mathfrak{r})}\left|\int_0^{\wp_1}(\wp_1-\Upsilon)^{\mathfrak{r}-1}\mathfrak{C}_2(\Upsilon,K(\Upsilon))\,d\Upsilon\right|
\end{aligned}
$$

$$
\begin{aligned}
|\mathfrak{C}_2K(\wp_2)-\mathfrak{C}_2K(\wp_1)| &\leq \frac{1}{\Gamma(\mathfrak{r})}\int_0^{\wp_1}\left((\wp_1-\Upsilon)^{\mathfrak{r}-1}-(\wp_2-\Upsilon)^{\mathfrak{r}-1}\right)|\mathfrak{C}_2(\Upsilon,K(\Upsilon))|\,d\Upsilon \\
&+\frac{1}{\Gamma(\mathfrak{r})}\int_{\wp_1}^{\wp_2}(\wp_2-\Upsilon)^{\mathfrak{r}-1}|\mathfrak{C}_2(\Upsilon,K(\Upsilon))|d\Upsilon \\
&\leq \frac{1}{\Gamma(\mathfrak{r})}\int_0^{\wp_1}((\wp_1-\Upsilon)^{\mathfrak{r}-1}-(\wp_2-\Upsilon)^{\mathfrak{r}-1})\mathfrak{M}_2(\Upsilon)d\Upsilon \\
&+\frac{1}{\Gamma(\mathfrak{r})}\int_{\wp_1}^{\wp_2}(\wp_2-\Upsilon)^{\mathfrak{r}-1}\mathfrak{M}_2(\Upsilon)d\Upsilon \\
&\leq \frac{1}{\Gamma(\mathfrak{r})}\left(\left(\int_0^{\wp_1}\left((\wp_1-\Upsilon)^{\frac{\mathfrak{r}-1}{1-\mathfrak{p}}}-(\wp_2-\Upsilon)^{\frac{\mathfrak{r}-1}{1-\mathfrak{p}}}\right)d\Upsilon\right)^{1-\mathfrak{p}}\right) \\
&\times\left(\int_0^{\wp_1}(\mathfrak{M}_2(\Upsilon))^{\frac{1}{\mathfrak{p}}}d\Upsilon\right)^{\mathfrak{p}} \\
&+\frac{1}{\Gamma(\mathfrak{r})}\left(\int_{\wp_1}^{\wp_2}(\wp_2-\Upsilon)^{\frac{\mathfrak{r}-1}{1-\mathfrak{p}}}d\Upsilon\right)^{1-\mathfrak{p}}\left(\int_0^{\wp_1}(\mathfrak{M}_2(\Upsilon))^{\frac{1}{\mathfrak{p}}}d\Upsilon\right)^{\mathfrak{p}} \\
&\leq \frac{c}{\Gamma(\mathfrak{r})}\|\mathfrak{M}_2\|_{\frac{1}{\mathfrak{p}}}\left[\left((\wp_2-\wp_1)^{\frac{\mathfrak{r}-1}{1-\mathfrak{p}}}\right)^{1-\mathfrak{p}}+(\wp_2-\wp_1)^{\mathfrak{r}-\mathfrak{p}}\right]
\end{aligned}
$$

$$\leq \frac{2c\|\mathfrak{M}_2\|_{\frac{1}{\mathfrak{p}}}}{\Gamma\left(\mathfrak{r}\right)}\left(\wp_2-\wp_1\right)^{\mathfrak{r}-\mathfrak{p}}.$$

The right side of this inequality is unaffected by K. We establish the compactness of $\mathfrak{C}_2$ by its relative compactness in $\mathfrak{C}_2(B_{\bar{\mathfrak{r}}})$ using the Arzela-Ascoli theorem. Due to the fact that $\mathfrak{C}_1$ and $\mathfrak{C}_2$ have distinct features (contraction and compactness respectively), their composite, represented as C, forms a condensing map on B_r. This, along with Theorem (7.2.1), ensures a fixpoint for C, which is relevant to remaining variables such as $P(\varkappa), R(\varkappa), T(\varkappa)$. □

Theorem 7.2.3. *Under consideration of* ***Assumption 3*** *and* $\Theta = \frac{c\|L_1\|_{1/\mathfrak{p}}(\mathfrak{T})^{\beta}}{\Gamma(\mathfrak{r})} < 1$, *the IVP has unique solution on* $[0, \mathfrak{T}]$.

Proof. Define the mapping F by

$$FC\left(\varkappa\right) = C\left(0\right) + \frac{1}{\Gamma\left(\mathfrak{r}\right)}\int\limits_0^{\varkappa}\left(\varkappa-\Upsilon\right)^{\mathfrak{r}-1}C\left(\Upsilon, C\left(\Upsilon\right)\right)d\Upsilon.$$

For $C(\varkappa), \mathfrak{C}_1(\varkappa) \in B_r$, we have

$$\begin{aligned}\left|FC\left(\varkappa\right)-F\mathfrak{C}_1\left(\varkappa\right)\right| &\leq \frac{1}{\Gamma\left(\mathfrak{r}\right)}\int\limits_0^{\varkappa}\left(\varkappa-\Upsilon\right)^{\mathfrak{r}-1}L_1\left(\Upsilon\right)\left|C\left(\Upsilon\right)-\mathfrak{C}_1\left(\Upsilon\right)\right|d\Upsilon \\ &\leq \frac{1}{\Gamma\left(\mathfrak{r}\right)}\left(\int\limits_0^{\varkappa}\left(\varkappa-\Upsilon\right)^{\frac{\mathfrak{r}-1}{1-\mathfrak{p}}}d\Upsilon\right)^{1-\mathfrak{p}}\left(\int\limits_0^{\varkappa}{L_1}^{\frac{1}{\mathfrak{p}}}\left(\Upsilon\right)d\Upsilon\right)^{\mathfrak{p}}\|C-\mathfrak{C}_1\| \\ &\leq \frac{c\|L_1\|_{1/\mathfrak{p}}(\mathfrak{T})^{\beta}}{\Gamma\left(\mathfrak{r}\right)}\|C-\mathfrak{C}_1\|.\end{aligned}$$

Thus the condition $\Theta = \dfrac{c\|L_1\|_{1/\mathfrak{p}}(\mathfrak{T})^{\beta}}{\Gamma\left(\mathfrak{r}\right)} < 1$ ensure the existence of a unique solution. Similarly unique solution exists for other model equations. □

7.2.4 Stability analysis

Let

$$ {}_{0}^{C}D_{\varkappa}^{\mathfrak{r}}\mathfrak{u}_1(\varkappa) = \mathfrak{g}(\varkappa, \mathfrak{u}_1(\varkappa)), \qquad where, 0 < \mathfrak{r} < 1. \tag{7.4} $$

with initial condition $\mathfrak{u}_1(0) = \mathfrak{u}_{10}$, where, $\mathfrak{u}_1 \in \mathbb{R}, \varkappa \in (0, +\infty)$.

We are currently examining the global stability of (7.4). Given $\varepsilon > 0$, and considering a continuous function φ defined over the interval $[0, +\infty)$ with values in the positive real numbers. Consider following relations:

$$ \left| {}_{0}^{C}D_{\varkappa}^{\mathfrak{r}}\mathfrak{u}_1(\varkappa) - \mathfrak{g}(\varkappa, \mathfrak{u}_1(\varkappa)) \right| \leq \varepsilon, \tag{7.5} $$

$$ \left| {}_{0}^{C}D_{\varkappa}^{\mathfrak{r}}\mathfrak{u}_1(\varkappa) - \mathfrak{g}(\varkappa, \mathfrak{u}_1(\varkappa)) \right| \leq \varphi(\varkappa), \tag{7.6} $$

$$ \left| {}_{0}^{C}D_{\varkappa}^{\mathfrak{r}}\mathfrak{u}_1(\varkappa) - \mathfrak{g}(\varkappa, \mathfrak{u}_1(\varkappa)) \right| \leq \varepsilon\varphi(\varkappa). \tag{7.7} $$

Definition 7.2.4. *The IVP* (7.4) *exhibits Ulam-Hyers(U-H) stability if* $\exists\, c_{\mathfrak{g}} > 0$ *such that* $\forall\, \varepsilon > 0$ *and each* $\mathfrak{u}_1 \in C[0, +\infty)$ *satisfying* (7.5)*, a solution* $\mathfrak{u}_2 \in C[0, +\infty)$ *of* (7.4) *is present, satisfying*

$$ |\mathfrak{u}_1(\varkappa) - \mathfrak{u}_2(\varkappa)| \leq \varepsilon c_{\mathfrak{g}}. $$

Definition 7.2.5. *The IVP* (7.4) *demonstrates Generalized Ulam-Hyers(G-U-H) stability if* $\exists\, c_{\mathfrak{g}} \in \mathbb{R}^+$ *such that* $c_{\mathfrak{g}}(0) = 0$*,* $\forall\, \varepsilon > 0$ *and* $\mathfrak{u}_1 \in C$ *of* (7.6)*, there exists a solution* $\mathfrak{u}_2 \in C$ *of* (7.4) *fullfilling*

$$ |\mathfrak{u}_1(\varkappa) - \mathfrak{u}_2(\varkappa)| \leq c_{\mathfrak{g}}(\varepsilon). $$

Definition 7.2.6. *The IVP* (7.4) *is Ulam-Hyers-Rassias(U-H-R) stable if* $\exists\, c_{\mathfrak{g},\varphi} \in \mathbb{R}$*,* $\forall\, \varepsilon > 0$ *and every* $\mathfrak{u}_1 \in C$ *of* (7.7)*, there exists a solution* $\mathfrak{u}_2 \in C$ *of* (7.4) *addressing*

$$ |\mathfrak{u}_1(\varkappa) - \mathfrak{u}_2(\varkappa)| \leq \varepsilon c_{\mathfrak{g},\varphi}\varphi(\varkappa). $$

Definition 7.2.7. *The IVP* (7.4) *reveals Generalized Ulam-Hyers-Rassias(G-U-H-R) stability if* $c_{\mathfrak{g},\varphi} \in \mathbb{R}$*, for every* $\mathfrak{u}_1 \in C$ *of* (7.6)*, there exists a solution* $\mathfrak{u}_2 \in C$ *of* (7.4) *with*

$$|\mathfrak{u}_1(\varkappa) - \mathfrak{u}_2(\varkappa)| \leq c_{\mathfrak{g},\varphi}\varphi(\varkappa).$$

Hypothesis 3. *Let* $\varphi \in C[0, +\infty)$ *is an accumulating function, then* $\exists\ \chi_\varphi > 0$*, implying that*

$$\frac{1}{\Gamma(\mathfrak{r})} \int_0^{\varkappa} (\varkappa - \Upsilon)^{\mathfrak{r}-1} \varphi(\Upsilon)\, d\Upsilon \leq \chi_\varphi \varphi(\varkappa), \qquad \varkappa > 0.$$

Lemma 7.2.2. *Let us construct two continuous functions namely* $\mathfrak{x}$ *&* $\mathfrak{y}$ *over* $[0, \mathfrak{T}] \times [0, +\infty)$ *where* $\mathfrak{T} \leq \infty$*. If* $\mathfrak{y}$ *is increasing and* $\exists\ \mu, \zeta > 0$*, implying that*

$$\mathfrak{x}(\varkappa) \leq \mathfrak{y}(\varkappa) + \mu \int_0^{\varkappa} (\varkappa - \Upsilon)^{\zeta-1} \mathfrak{x}(\Upsilon)\, d\Upsilon, \qquad \varkappa \geq 0.$$

then

$$\mathfrak{x}(\varkappa) \leq \mathfrak{y}(\varkappa) + \int_0^{\varkappa} \left[\sum_{k=0}^{\infty} \frac{(\mu\Gamma(\zeta))^k}{\Gamma(k\zeta)} (\varkappa - \Upsilon)^{\zeta-1} \mathfrak{y}(\Upsilon) \right] d\Upsilon, \qquad \varkappa \geq 0.$$

If $\mathfrak{y}(\varkappa) = a$ *(constant) on* $\varkappa \in [0, \mathfrak{T})$*, then*

$$\mathfrak{x}(\varkappa) \leq a\mathrm{E}_\zeta\left(\mu\Gamma(\zeta)\, \varkappa^\zeta\right), \qquad \varkappa \geq 0,$$

where $\mathrm{E}_\zeta(\bullet)$ *is the Mittag Leffler function.*

Theorem 7.2.4. *If the criteria of Hypothesis* (3) *is fulfilled, then the IVP* (7.4) *is the G-U-H-R stable.*

Proof. Assuming $\mathfrak{u}_1$ is a solution of (7.6) over the interval $C[0, \mathfrak{T})$, we consider $\mathfrak{u}_2$ as a solution of (7.4). Thus,

$$\left|\mathfrak{u}_1(\varkappa) - \mathfrak{u}_{10}(\varkappa) - \frac{1}{\Gamma(\mathfrak{r})}\int_0^{\varkappa} (\varkappa - \Upsilon)^{\mathfrak{r}-1}\mathfrak{g}(\Upsilon, \mathfrak{u}_1(\Upsilon))d\Upsilon\right|$$
$$\leq \frac{1}{\Gamma(\mathfrak{r})}\int_0^{\varkappa} (\varkappa - \Upsilon)^{\mathfrak{r}-1}\varphi(\Upsilon)\, d\Upsilon$$
$$\leq \chi_{\varphi}\varphi(\varkappa).$$

It follows from these connections:

$$\begin{aligned}|\mathfrak{u}_1(\varkappa) - \mathfrak{u}_2(\varkappa)| &\leq \left|\mathfrak{u}_1(\varkappa) - \mathfrak{u}_{10}(\varkappa) - \frac{1}{\Gamma(\mathfrak{r})}\int_0^{\varkappa} (\varkappa - \Upsilon)^{\mathfrak{r}-1}\mathfrak{g}(\Upsilon, \mathfrak{u}_1(\Upsilon))\, d\Upsilon\right| \\ &\quad + \frac{1}{\Gamma(\mathfrak{r})}\int_0^{\varkappa} (\varkappa - \Upsilon)^{\mathfrak{r}-1}|\mathfrak{g}(\Upsilon, \mathfrak{u}_1(\Upsilon)) - \mathfrak{g}(\Upsilon, \mathfrak{u}_2(\Upsilon))|\, d\Upsilon \\ &\leq \chi_{\varphi}\varphi(\varkappa) + \frac{N}{\Gamma(\mathfrak{r})}\int_0^{\varkappa} (\varkappa - \Upsilon)^{\mathfrak{r}-1}|\mathfrak{u}_1(\Upsilon) - \mathfrak{u}_2(\Upsilon)|\, d\Upsilon.\end{aligned}$$

As per Lemma (7.2.2), $\exists$ constant $N^* > 0$ separated from $\chi_{\varphi}\varphi(\varkappa)$. This constant satisfies $|\mathfrak{u}_1(\varkappa) - \mathfrak{u}_2(\varkappa)| \leq N^*\chi_{\varphi}\varphi(\varkappa) := a_{\mathfrak{g},\varphi}\varphi(\varkappa)$. As a result, the IVP (7.4) can be classified as having G-U-H-R stability. □

Corollary 7.2.1. *Using the same logic as in Theorem* (7.2.4)*, one can demonstrate that IVP* (7.4)*, coupled by* (7.7)*, achieves U-H-R stability.*

Corollary 7.2.2. *By employing the similar methods of Theorem* (7.2.4) *with* (7.5)*, one is able to illustrate IVP* (7.4) *is U-H stable.*

7.3 Mathematical analysis of a Pancreatic cancer with Atangana-Baleanu derivative

7.3.1 Preliminaries

This section consists of some fundamental concepts from fractional calculus that will be helpful in further analysis.

Definition 7.3.1. *Let $g \in \mathbb{H}^1(a,b), a < b, m \in [0,1]$, the Atangana-Baleanu derivative in Caputo sense is given by [14]:*

$$^{ABC}{}_aD_t^m[g(t)] = \frac{L(m)}{1-m}\int_a^t g^{'}(x)\cdot E_m\left(-m\frac{(t-x)^m}{1-m}\right)dx, \tag{7.8}$$

where E_m is the Mittag-Leffler function and $L(m)$ is a normalization function with $L(0) = L(1) = 1$.

Definition 7.3.2. *The fractional integral with the Atangana-Baleanu derivative in Caputo sense is defined by [14]:*

$$^{ABC}{}_aI_t^m[g(t)] = \frac{1-m}{L(m)}g(t) + \frac{m}{L(m)\Gamma(m)}\int_a^t g(\lambda)\cdot(t-\lambda)^{m-1}d\lambda. \tag{7.9}$$

Theorem 7.3.1. *Let g be a continuous function on $[a,b]$. Then the following inequality holds on $[a,b]$ [14]:*

$$\|^{ABC}{}_0D_t^m\left[g\left(t\right)\right]\| \; < \; \frac{L\left(m\right)}{1-m}\|g\left(x\right)\|, \tag{7.10}$$

where, $\|g\left[x\right]\| = \max\limits_{a\leq t\leq b}|g\left(x\right)|$.

Theorem 7.3.2. *The Atangana-Baleanu derivative in Caputo sense satisfies Lipschitz condition for $H > 0$ as follows [14]:*

$$\|^{ABC}{}_0D_t^m\left[g\left(t\right)\right] - {}^{ABC}{}_0D_t^m\left[h\left(t\right)\right]\| \; \leq \; H\|g\left(t\right) - h\left(t\right)\|. \tag{7.11}$$

Theorem 7.3.3. *The fractional differential equation*

$$ {}^{ABC}{}_{0}D_t^m \left[g\left(t\right)\right] = f\left(t, g\left(t\right)\right), \qquad 0 < t \leq T < \infty, \tag{7.12} $$

with $g(0) = g_0$ *has a unique solution*

$$ g\left(t\right) = g_0 + \frac{1-m}{L\left(m\right)} f\left(t, g\left(t\right)\right) + \frac{m}{L\left(m\right)\Gamma\left(m\right)} \int_0^t f\left(\lambda, g\left(\lambda\right)\right) \cdot \left(t-\lambda\right)^{m-1} d\lambda, \tag{7.13} $$

for $0 < m < 1$.

7.3.2 Model formulation in Atangana-Baleanu-Caputo sense

In this section, we modify the system (7.1) in ABC fractional derivative operator sense. The proposed model under consideration for the above discussed operator takes the following form:

$$ \begin{aligned} {}^{ABC}{}_{0}D_t^m \left(C\left(t\right)\right) &= \left(k_c + \mu_c P\right) C^{3/4} \left(1 - \left(C/C_0\right)^{1/4}\right) - \frac{\lambda_c C T}{\mathrm{K}_c + (1-R)}, \\ {}^{ABC}{}_{0}D_t^m \left(P\left(t\right)\right) &= \left(k_p + \frac{\mu_p C}{K_p + C}\right) P \left(1 - \frac{P}{P_0}\right) - \lambda_p P, \\ {}^{ABC}{}_{0}D_t^m \left(R\left(t\right)\right) &= k_r - \left(\lambda_r + \gamma_p P + \gamma_c C\right) R, \\ {}^{ABC}{}_{0}D_t^m \left(T\left(t\right)\right) &= \frac{k_t R}{\mathrm{K}_t + (1-R)} - \lambda_t T. \end{aligned} \tag{7.14} $$

In the next section we discuss the existence and uniqueness of the system (7.14).

7.3.3 Qualitative analysis

In this section, it has been shown that the mathematical model (7.14) describing the dynamics of Pancreatic cancer under the fractional-order derivative operator has unique solution based upon the fixed-point theory of fractional calculus.

Existence of solution for the Atangana - Baleanu model in the Caputo sense

The model discussed in this study is nonlocal and non-linear, maybe there is no method to give exact solutions of (7.14). Even so, in this part using fixed point theory, we will show the existence of the model of solutions and then give uniqueness of the solutions.

Let $\Lambda = V(K) \times V(K) \times V(K) \times V(K)$ and $V(K)$ be a Banach space of continuous $\mathbb{R} \to \mathbb{R}$ valued functions on the interval K with the norm,

$$\|(C, P, R, T)\| = \|C\| + \|P\| + \|R\| + \|T\|,$$

where $\|C\| = \sup\{|C(t)| : t \in K\}, \|P\| = \sup\{|P(t)| : t \in K\}, \|R\| = \sup\{|R(t)| : t \in K\}$ and $\|T\| = \sup\{|T(t)| : t \in K\}$.
For clarity, we rewrite the model (7.14) of the following form:

$$\begin{aligned}
{}^{ABC}{}_{0}D_t^m (C(t)) &= Z_1(t, C), \\
{}^{ABC}{}_{0}D_t^m (P(t)) &= Z_2(t, P), \\
{}^{ABC}{}_{0}D_t^m (R(t)) &= Z_3(t, R), \\
{}^{ABC}{}_{0}D_t^m (T(t)) &= Z_4(t, T),
\end{aligned} \tag{7.15}$$

where,

$$\begin{aligned}
\mathrm{Z}_1(t, C) &= (k_c + \mu_c P) C^{3/4} \left(1 - (C/C_0)^{1/4}\right) - \frac{\lambda_c C T}{\mathrm{K}_c + (1 - R)}, \\
\mathrm{Z}_2(t, P) &= \left(k_p + \frac{\mu_p C}{\mathrm{K}_p + C}\right) P \left(1 - \frac{P}{P_0}\right) - \lambda_p P, \\
\mathrm{Z}_3(t, R) &= k_r - (\lambda_r + \gamma_p P + \gamma_c C) R, \\
\mathrm{Z}_4(t, T) &= \frac{k_t R}{\mathrm{K}_t + (1 - R)} - \lambda_t T.
\end{aligned} \tag{7.16}$$

Using Theorem 7.3.3, the system (7.15) can be written as:

$$\begin{aligned}
C(t) - C(0) &= \frac{1-m}{L(m)}\mathrm{Z}_1(t, C) + \frac{m}{L(m)\Gamma(m)}\int_0^t (t-\lambda)^{m-1}\mathrm{Z}_1(\lambda, C)\,d\lambda, \\
P(t) - P(0) &= \frac{1-m}{L(m)}\mathrm{Z}_2(t, P) + \frac{m}{L(m)\Gamma(m)}\int_0^t (t-\lambda)^{m-1}\mathrm{Z}_2(\lambda, P)\,d\lambda, \\
R(t) - R(0) &= \frac{1-m}{L(m)}\mathrm{Z}_3(t, R) + \frac{m}{L(m)\Gamma(m)}\int_0^t (t-\lambda)^{m-1}\mathrm{Z}_3(\lambda, R)\,d\lambda, \\
T(t) - T(0) &= \frac{1-m}{L(m)}\mathrm{Z}_4(t, T) + \frac{m}{L(m)\Gamma(m)}\int_0^t (t-\lambda)^{m-1}\mathrm{Z}_4(\lambda, T)\,d\lambda.
\end{aligned} \tag{7.17}$$

Theorem 7.3.4. *The kernel Z_1 satisfies Lipschitz condition if the following inequality holds for $\theta_1 > 0$ and Let C, C_1 be two bounded functions, then*

$$\|Z_1(t, C) - Z_1(t, C_1)\| = \theta_1 \|C(t) - C_1(t)\|. \tag{7.18}$$

Consider the system (7.17) in the following recursive formula:

$$\begin{aligned}
C_n(t) &= \frac{1-m}{L(m)}\mathrm{Z}_1(t, C_{n-1}) + \frac{m}{L(m)\Gamma(m)}\int_0^t (t-\lambda)^{m-1}\mathrm{Z}_1(\lambda, C_{n-1})\,d\lambda, \\
P_n(t) &= \frac{1-m}{L(m)}\mathrm{Z}_2(t, P_{n-1}) + \frac{m}{L(m)\Gamma(m)}\int_0^t (t-\lambda)^{m-1}\mathrm{Z}_2(\lambda, P_{n-1})\,d\lambda, \\
R_n(t) &= \frac{1-m}{L(m)}\mathrm{Z}_3(t, R_{n-1}) + \frac{m}{L(m)\Gamma(m)}\int_0^t (t-\lambda)^{m-1}\mathrm{Z}_3(\lambda, R_{n-1})\,d\lambda, \\
T_n(t) &= \frac{1-m}{L(m)}\mathrm{Z}_4(t, T_{n-1}) + \frac{m}{L(m)\Gamma(m)}\int_0^t (t-\lambda)^{m-1}\mathrm{Z}_4(\lambda, T_{n-1})\,d\lambda.
\end{aligned} \tag{7.19}$$

with the initial conditions $C(0) = C_0,\ P(0) = P_0,\ R(0) = R_0,\ T(0) = T_0$.

We find the difference between the successive terms in the expressions:

$$\begin{aligned}
\xi_{1(n)}(t) &= C_n(t) - C_{n-1}(t) \\
&= \frac{1-m}{L(m)}\left[\mathrm{Z}_1(t, C_{n-1}) - \mathrm{Z}_1(t, C_{n-2})\right] \\
&+ \frac{m}{L(m)\Gamma(m)}\int_0^t (t-\lambda)^{m-1}\left[\mathrm{Z}_1(\lambda, C_{n-1}) - \mathrm{Z}_1(\lambda, C_{n-2})\right]d\lambda,
\end{aligned} \tag{7.20}$$

$$\begin{aligned}
\xi_{2(n)}(t) &= P_n(t) - P_{n-1}(t) \\
&= \frac{1-m}{L(m)}\left[\mathrm{Z}_2(t, P_{n-1}) - \mathrm{Z}_2(t, P_{n-2})\right] \\
&+ \frac{m}{L(m)\Gamma(m)}\int_0^t (t-\lambda)^{m-1}\left[\mathrm{Z}_2(\lambda, P_{n-1}) - \mathrm{Z}_2(\lambda, P_{n-2})\right]d\lambda,
\end{aligned}$$

$$\begin{aligned}
\xi_{3(n)}(t) &= R_n(t) - R_{n-1}(t) \\
&= \frac{1-m}{L(m)}\left[\mathrm{Z}_3(t, R_{n-1}) - \mathrm{Z}_3(t, R_{n-2})\right] \\
&+ \frac{m}{L(m)\Gamma(m)}\int_0^t (t-\lambda)^{m-1}\left[\mathrm{Z}_3(\lambda, R_{n-1}) - \mathrm{Z}_3(\lambda, R_{n-2})\right]d\lambda,
\end{aligned}$$

$$\begin{aligned}
\xi_{4(n)}(t) &= T_n(t) - T_{n-1}(t) \\
&= \frac{1-m}{L(m)}\left[\mathrm{Z}_4(t, T_{n-1}) - \mathrm{Z}_4(t, T_{n-2})\right] \\
&+ \frac{m}{L(m)\Gamma(m)}\int_0^t (t-\lambda)^{m-1}\left[\mathrm{Z}_4(\lambda, T_{n-1}) - \mathrm{Z}_4(\lambda, T_{n-2})\right]d\lambda.
\end{aligned}$$

Notice that,

$$\begin{aligned}
C_n(t) &= \sum_{i=1}^{n}\xi_{1(i)}(t), \\
P_n(t) &= \sum_{i=1}^{n}\xi_{2(i)}(t), \\
R_n(t) &= \sum_{i=1}^{n}\xi_{3(i)}(t), \\
T_n(t) &= \sum_{i=1}^{n}\xi_{4(i)}(t).
\end{aligned} \tag{7.21}$$

Taking the norm on both sides of the (7.20) and applying triangular identity, we find

$$\begin{aligned}
\|\xi_{1(n)}(t)\| &= \|C_n(t) - C_{n-1}(t)\| \\
&= \|\frac{1-m}{L(m)}\left[\mathrm{Z}_1(t, C_{n-1}) - \mathrm{Z}_1(t, C_{n-2})\right] \\
&+ \frac{m}{L(m)\Gamma(m)}\int_0^t (t-\lambda)^{m-1}\left[\mathrm{Z}_1(\lambda, C_{n-1}) - \mathrm{Z}_1(\lambda, C_{n-2})\right]d\lambda\|.
\end{aligned} \tag{7.22}$$

Because the kernel Z_1 satisfy Lipschitz condition proved in (7.18), we have

$$\begin{aligned}\|\xi_{1(n)}(t)\| &= \|C_n(t) - C_{n-1}(t)\ \| \\ &\leq \frac{1-m}{L(m)}\theta_1 \|C_{n-1}(t) - C_{n-2}(t)\| \\ &+ \frac{m}{L(m)\,\Gamma(m)}\theta_1 \int_0^t (t-\lambda)^{m-1} \|C_{n-1}(\lambda) - C_{n-2}(\lambda)\, d\lambda\|.\end{aligned} \tag{7.23}$$

$$\begin{aligned}\|\xi_{1(n)}(t)\| &= \|C_n(t) - C_{n-1}(t)\ \| \\ &\leq \frac{1-m}{L(m)}\theta_1 \|\xi_{1(n-1)}(t)\| + \frac{m}{L(m)\,\Gamma(m)}\theta_1 \int_0^t (t-\lambda)^{m-1} \|\xi_{1(n-1)}(\lambda)\, d\lambda\|\end{aligned} \tag{7.24}$$

Analogously, we have the following results:

$$\begin{aligned}\|\xi_{2(n)}(t)\| &= \|P_n(t) - P_{n-1}(t)\ \| \\ &\leq \frac{1-m}{L(m)}\theta_2 \|\xi_{2(n-1)}(t)\| + \frac{m}{L(m)\,\Gamma(m)}\theta_2 \int_0^t (t-\lambda)^{m-1} \|\xi_{2(n-1)}(\lambda)\, d\lambda\|,\end{aligned}$$

$$\begin{aligned}\|\xi_{3(n)}(t)\| &= \|R_n(t) - R_{n-1}(t)\ \| \\ &\leq \frac{1-m}{L(m)}\theta_3 \|\xi_{3(n-1)}(t)\| + \frac{m}{L(m)\,\Gamma(m)}\theta_3 \int_0^t (t-\lambda)^{m-1} \|\xi_{3(n-1)}(\lambda)\, d\lambda\|,\end{aligned} \tag{7.25}$$

$$\begin{aligned}\|\xi_{4(n)}(t)\| &= \|T_n(t) - T_{n-1}(t)\ \| \\ &\leq \frac{1-m}{L(m)}\theta_4 \|\xi_{4(n-1)}(t)\| + \frac{m}{L(m)\,\Gamma(m)}\theta_4 \int_0^t (t-\lambda)^{m-1} \|\xi_{4(n-1)}(\lambda)\, d\lambda\|,\end{aligned}$$

for $\theta_i > 0, i = 1, 2, 3, 4$.

In the light of the results in hand, we give the below theorem.

Theorem 7.3.5. *The fractional model given in* (7.14) *has a solution, if we can find* l_0 *satisfying the relation*

$$\frac{1-m}{L(m)}\theta_i + \frac{{l_0}^m}{L(m)\,\Gamma(m)}\theta_i < 1, \tag{7.26}$$

where $i = 1, 2, 3, 4$.

Proof. We know that $C(t), P(t), R(t)$ and $T(t)$ are bounded functions and satisfy Lipschitz condition. From (7.24) and (7.25), we obtain the succeeding relations:

$$\begin{aligned}
\left\|\xi_{1(n)}\left(t\right)\right\| &\leq \left\|C\left(0\right)\right\| \left[\frac{1-m}{L\left(m\right)}\theta_1 + \frac{t^m}{L\left(m\right)\Gamma\left(m\right)}\theta_1\right]^n \\
\left\|\xi_{2(n)}\left(t\right)\right\| &\leq \left\|P\left(0\right)\right\| \left[\frac{1-m}{L\left(m\right)}\theta_2 + \frac{t^m}{L\left(m\right)\Gamma\left(m\right)}\theta_2\right]^n \\
\left\|\xi_{3(n)}\left(t\right)\right\| &\leq \left\|R\left(0\right)\right\| \left[\frac{1-m}{L\left(m\right)}\theta_3 + \frac{t^m}{L\left(m\right)\Gamma\left(m\right)}\theta_3\right]^n \\
\left\|\xi_{4(n)}\left(t\right)\right\| &\leq \left\|T\left(0\right)\right\| \left[\frac{1-m}{L\left(m\right)}\theta_4 + \frac{t^m}{L\left(m\right)\Gamma\left(m\right)}\theta_4\right]^n
\end{aligned} \tag{7.27}$$

So, (7.21) exists and is smooth. Now we will prove the functions in (7.21) are solutions of system (7.14). Let

$$\begin{aligned}
C\left(t\right) - C\left(0\right) &= C_n\left(t\right) - H_{1(n)}\left(t\right), \\
P\left(t\right) - P\left(0\right) &= P_n\left(t\right) - H_{2(n)}\left(t\right), \\
R\left(t\right) - R\left(0\right) &= R_n\left(t\right) - H_{3(n)}\left(t\right), \\
T\left(t\right) - T\left(0\right) &= T_n\left(t\right) - H_{4(n)}\left(t\right).
\end{aligned} \tag{7.28}$$

Then, we have

$$\begin{aligned}
\|H_{1(n)}\left(t\right)\| = \|&\frac{1-m}{L\left(m\right)}\left[Z_1\left(t,C\right) - Z_1\left(t,C_{n-1}\right)\right] \\
&+ \frac{m}{L\left(m\right)\Gamma\left(m\right)}\int_0^t \left(t-\lambda\right)^{m-1}\left[Z_1\left(\lambda,C\right) - Z_1\left(\lambda,C_{n-1}\right)\right]d\lambda\|.
\end{aligned} \tag{7.29}$$

Using triangular inequality we have,

$$\begin{aligned}
\|H_{1(n)}\left(t\right)\| &\leq \frac{1-m}{L\left(m\right)}\|Z_1\left(t,C\right) - Z_1\left(t,C_{n-1}\right)\| \\
&\quad + \frac{m}{L\left(m\right)\Gamma\left(m\right)}\int_0^t \left(t-\lambda\right)^{m-1}\|Z_1\left(\lambda,C\right) - Z_1\left(\lambda,C_{n-1}\right)\|d\lambda \\
&\leq \frac{1-m}{L\left(m\right)}\theta_1\|C - C_{n-1}\| + \frac{t^m}{L\left(m\right)\Gamma\left(m\right)}\theta_1\|C - C_{n-1}\| \\
&\leq \left[\frac{1-m}{L\left(m\right)} + \frac{t^m}{L\left(m\right)\Gamma\left(m\right)}\right]^{n+1}\left(\theta_1\right)^{n+1}A
\end{aligned}$$

By continuing this method recursively, it gives at l_0

$$\|H_{1(n)}(t)\| \leq \left[\frac{1-m}{L(m)} + \frac{l_0^m}{L(m)\Gamma(m)}\right]^{n+1} (\theta_1)^{n+1}. \tag{7.30}$$

As n approaches to ∞, $\|H_{1(n)}(t)\| \to 0$. In an analogous way, it can be shown

$$\|H_{2(n)}(t)\| \to 0, \|H_{3(n)}(t)\| \to 0, \|H_{4(n)}(t)\| \to 0. \tag{7.31}$$

Finally, proof of existence is verified. □

Uniqueness of solution for the Atangana - Baleanu model in the Caputo sense

Now it is another matter to demonstrate the uniqueness of the solutions of the system (7.14). Let there exists another set of the solutions $C_1(t), P_1(t), R_1(t)$ and $T_1(t)$ we find,

$$\begin{aligned} C(t) - C_1(t) = {} & \frac{1-m}{L(m)}\left[Z_1(t,C) - Z_1(t,C_1)\right] \\ & + \frac{m}{L(m)\Gamma(m)}\int_0^t (t-\lambda)^{m-1}\left[Z_1(\lambda,C) - Z_1(\lambda,C_1)\right] d\lambda. \end{aligned} \tag{7.32}$$

Applying the norm to the above equation and because the kernel satisfies the Lipschitz condition, we find

$$\begin{aligned} \|C(t) - C_1(t)\| \leq {} & \frac{1-m}{L(m)}\|Z_1(t,C) - Z_1(t,C_1)\| \\ & + \frac{m}{L(m)\Gamma(m)}\int_0^t (t-\lambda)^{m-1}\|Z_1(\lambda,C) - Z_1(\lambda,C_1)\| d\lambda. \end{aligned} \tag{7.33}$$

This gives

$$\|C(t) - C_1(t)\| \cdot \left[1 - \left(\frac{1-m}{L(m)}\right)\theta_1 - \left(\frac{t^m}{L(m)\Gamma(m)}\right)\theta_1\right] \leq 0. \tag{7.34}$$

Theorem 7.3.6. *If the below inequality holds*

$$\left[1-\left(\frac{1-m}{L(m)}\right)\theta_1-\left(\frac{t^m}{L(m)\Gamma(m)}\right)\theta_1\right]>0, \tag{7.35}$$

the model (7.14) *has a unique system of solutions.*

Proof. We have $\|C(t)-C_1(t)\|\cdot\left[1-\left(\frac{1-m}{L(m)}\right)\theta_1-\left(\frac{t^m}{L(m)\Gamma(m)}\right)\theta_1\right]\leq 0$ from (7.34) and the condition (7.35) satisfies then,

$$\|C(t)-C_1(t)\|=0$$
$$\therefore C(t)=C_1(t)$$

In the same manner, we obtain $P(t)=P_1(t), R(t)=R_1(t)$ and $T(t)=T_1(t)$. $\square$

7.3.4 Stability analysis

The Atangana-Baleanu derivative in Caputo sense fractional differential equation

$${}^{ABC}{}_0D_t^m[g(t)]=f(t,g(t)) \ , \quad 0<t\leq T<\infty,$$

with $g(0)=g_0=\bar{g}(0)$ has a unique solution as

$$g(t)=g_0+\frac{1-m}{L(m)}f(t,g(t))+\frac{m}{L(m)\Gamma(m)}\int_0^t f(\lambda,g(\lambda))\cdot(t-\lambda)^{m-1}d\lambda,$$

for $0<m<1$.

Let $Y([0,T],\mathbb{R})$ be the Banach space of all continuous functions from $[0,T]$ to $\mathbb{R}$ with the norm $\|g\|=\sup\{|g(t)|:t\in[0,T]\}$. Now, for global stability of the considered fractional model (7.14), we use the Ulam-Hyers(U-H) sense. For this purpose, we define the following inequality for $g\in Y([0,T],\mathbb{R})$,

$$\|{}^{ABC}{}_0D_t^m[g(t)]-f(t,g(t))\|\leq\varepsilon, \qquad \forall t\in[0,T] \tag{7.36}$$

Let $\bar{g}(t) \in Y([0,T], \mathbb{R})$ is solution of (7.36) if and only if there is $n(t) \in Y([0,T], \mathbb{R})$ such that:

(i) $\|n(t)\| < \varepsilon$.

(ii) ${}^{ABC}{}_{0}D_{t}^{m}[\bar{g}(t)] = f(t, \bar{g}(t)) + n(t), \forall t \in [0,T]$ with $g(0) = g_0 = \bar{g}(0)$.

Now, apply the Atangana-Baleanu in Caputo sense fractional integral to both the sides of (ii), we have

$$\begin{aligned}\bar{g}(t) &= \bar{g}(0) + \frac{1-m}{L(m)} f(t, \bar{g}(t)) + \frac{m}{L(m)\Gamma(m)} \int_0^t (t-\lambda)^{m-1} f(\lambda, \bar{g}(\lambda))\, d\lambda \\ &+ \frac{1-m}{L(m)} n(t) + \frac{m}{L(m)\Gamma(m)} \int_0^t (t-\lambda)^{m-1} n(\lambda)\, d\lambda\end{aligned} \tag{7.37}$$

Applying norm on both the sides of (7.37) and then using triangular inequality,

$$\begin{aligned}\|\bar{g}(t) - \bar{g}(0) - \frac{1-m}{L(m)} f(t, \bar{g}(t)) &- \frac{m}{L(m)\Gamma(m)} \int_0^t (t-\lambda)^{m-1} f(\lambda, \bar{g}(\lambda))\, d\lambda\| \\ &\leq \frac{1-m}{L(m)} \|n(t)\| + \frac{m}{L(m)\Gamma(m)} \int_0^t (t-\lambda)^{m-1} \|n(\lambda)\| d\lambda \\ &\leq \varepsilon \left[\frac{1-m}{L(m)} + \frac{m}{L(m)\Gamma(m)} \int_0^t (t-\lambda)^{m-1} d\lambda\right] \\ &\leq \varepsilon \left[\frac{(1-m)\Gamma(m) + T^{*(m)}}{L(m)\Gamma(m)}\right] \\ &\leq \varepsilon\sigma,\end{aligned} \tag{7.38}$$

where, $T^{*(m)} = m \int_0^t (t-\lambda)^{m-1} d\lambda$ and $\sigma = \dfrac{(1-m)\Gamma(m) + T^{*(m)}}{L(m)\Gamma(m)}$.

Definition 7.3.3. *The system* (7.14) *is Ulam-Hyers stable on* $[0,T]$ *if there exists a constant* $B > 0$ *such that for any* $\varepsilon > 0$, *and any* $\bar{g}(t)$ *satisfying* (7.36), *then the system* (7.14) *possesses a solution* $g(t)$ *satisfying*

$$\|\bar{g}(t) - g(t)\| \leq \mathrm{B}\varepsilon, \qquad \forall t \in [0,T]. \tag{7.39}$$

Theorem 7.3.7. *Let* $(i)-(ii)$ *holds. Then the Atangana-Baleanu in Caputo sense fractional model* (7.14) *is Ulam-Hyers stable on* $[0,T]$, *if* $B>0$ *holds.*

Proof. From (7.12) and (7.13), we let $g(t)$ be a unique solution of system (7.14), let $\bar{g}(t)$ satisfy (7.36) with $g(0)=g_0=\bar{g}(0)$. By applying the Atangana-Baleanu in Caputo sense fractional integral on both sides of (7.13), we get

$$g(t)=g_0+\frac{1-m}{L(m)}f(t,g(t))+\frac{m}{L(m)\Gamma(m)}\int_0^t(t-\lambda)^{m-1}f(\lambda,g(\lambda))\,d\lambda \qquad ,\forall\, t\in[0,T].$$

$$\therefore \bar{g}(t)-g(t)=\bar{g}(t)-g_0-\frac{1-m}{L(m)}f(t,g(t))-\frac{m}{L(m)\Gamma(m)}\int_0^t(t-\lambda)^{m-1}f(\lambda,g(\lambda))\,d\lambda$$

Now we compute $\|\bar{g}(t)-g(t)\|$ using above equation as follows:

$$\|\bar{g}(t)-g(t)\|=\|\bar{g}(t)-g_0-\frac{1-m}{L(m)}f(t,g(t))-\frac{m}{L(m)\Gamma(m)}\int_0^t(t-\lambda)^{m-1}f(\lambda,g(\lambda))\,d\lambda\|$$

By adding and subtracting the term, $\left[\frac{1-m}{L(m)}f(t,\bar{g}(t))+\frac{m}{L(m)\Gamma(m)}\int_0^t(t-\lambda)^{m-1}f(\lambda,\bar{g}(\lambda))\,d\lambda\right]$, and using triangular inequality, we have

$$\begin{aligned}\|\bar{g}(t)-g(t)\|\le{}&\|\bar{g}(t)-\bar{g}(0)-\frac{1-m}{L(m)}f(t,\bar{g}(t))-\frac{m}{L(m)\Gamma(m)}\int_0^t(t-\lambda)^{m-1}f(\lambda,\bar{g}(\lambda))\,d\lambda\|\\&+\frac{1-m}{L(m)}f(t,\bar{g}(t))-\frac{1-m}{L(m)}f(t,g(t))+\frac{m}{L(m)\Gamma(m)}\int_0^t(t-\lambda)^{m-1}f(\lambda,\bar{g}(\lambda))\,d\lambda\\&-\frac{m}{L(m)\Gamma(m)}\int_0^t(t-\lambda)^{m-1}f(\lambda,g(\lambda))\,d\lambda\end{aligned}$$

Using (i)-(ii) and the norm properties, we can get

$$\begin{aligned}\|\bar{g}(t)-g(t)\|\le{}&\varepsilon\sigma+\frac{1-m}{L(m)}\|f(t,\bar{g}(t))-f(t,g(t))\|\\&+\frac{m}{L(m)\Gamma(m)}\int_0^t(t-\lambda)^{m-1}\|f(\lambda,\bar{g}(\lambda))-f(\lambda,g(\lambda))\|d\lambda\end{aligned}$$

Using Lipschitz condition we have,

$$\|\bar{g}(t) - g(t)\| \leq \varepsilon\sigma + \frac{1-m}{L(m)}\theta_1 \|\bar{g}(t) - g(t)\| + \frac{t^m}{L(m)\Gamma(m)}\theta_1 \|\bar{g}(t) - g(t)\|$$

$$\therefore \|\bar{g}(t) - g(t)\| \left[1 - \left(\frac{1-m}{L(m)}\right)\theta_1 - \left(\frac{t^m}{L(m)\Gamma(m)}\right)\theta_1\right] \leq \varepsilon\sigma$$

$$\therefore \|\bar{g}(t) - g(t)\| \leq \mathrm{B}\varepsilon.$$

where, $\mathrm{B} = \dfrac{\sigma}{\left[1 - \left(\frac{1-m}{L(m)}\right)\theta_1 - \left(\frac{t^m}{L(m)\Gamma(m)}\right)\theta_1\right]}$, $\sigma = \dfrac{(1-m)\Gamma(m) + T^{*(m)}}{L(m)\Gamma(m)}$,

and $T^{*(m)} = m\displaystyle\int_0^t (t-\lambda)^{m-1} d\lambda.$

As $t \in [0, T]$ $, T > 0$ it gives $\mathrm{B} > 0$. We deduce that the fractional model (7.14) is Ulam-Hyers stable on $[0, T]$. □

7.4 Conclusion

We developed and analysed a fractional mathematical model of Pancreatic cancer that incorporates Pancreatic ductal adenocarcinoma using Caputo and Atangana-Baleanu fractional derivative operators. This study provides insights into the behaviour and progression of this complex disease. Moreover, the establishment of study on the existence and uniqueness of the system, and the model's stability using the Ulam-Hyers criteria adds to the credibility and validity of the fractional mathematical model presented. These findings are crucial for ensuring that the model accurately represents Pancreatic cancer and can be used to make predictions about the diseases' behaviour and progression.