

Chapter 1

Introduction

The word epidemiology comes from the Greek words epi meaning “on or upon”, demos meaning “people” and logos meaning “the study of:”. In other words, the word epidemiology has its roots in the study of what befalls a population. Epidemiology is the study of the distribution and determinants of health-related events or conditions in populations. It involves the application of scientific methods to investigate patterns, causes, and effects of diseases, ultimately contributing to the prevention and control of health problems. Epidemiological models allow for the prediction of disease patterns, helping authorities to better plan and distribute resources effectively. This is vital for effectively managing healthcare infrastructure, personnel, and resources during outbreaks of disease.

Diseases defined by aberrant conditions or disturbances in the structure or function of organisms, can be broadly classified into infectious and non-infectious categories. Infectious diseases are caused by pathogens like Bacteria, Fungi, Parasites, and Viruses. They can be spread from person to person or from animals to humans, e.g., Influenza (Flu), Tuberculosis (TB), HIV/AIDS, Malaria, Covid-19 etc. While non-infectious diseases result from variety of factors such as inheritance, surroundings, and how one lives, and cannot be transmitted from person to person, e.g., Heart disease, various cancer (like Lung cancer, Breast cancer, Pancreatic cancer), Diabetes etc. Understanding the nature, causes, and patterns of diseases is essential for effective control, prevention, and treatment. This investigation sheds light on the patterns of occurrence of both infectious and non-infectious diseases and offering real-world examples for a thorough grasp of the diverse landscape of human health challenges.

Mathematical modelling has emerged as a valuable tool in understanding the epidemiology and transmission dynamics of infectious diseases [2, 19, 22, 54, 90, 102, 134]. Mathematical analysis is a key aspect of epidemiological modelling, as it provides an analytical framework to understand the dynamics of disease transmission in populations. It helps in estimating parameters such as the transmission rate, recovery rate, and other key variables, which are essential for making accurate predictions. It also helps identify which parameters have the most significant impact on the model’s outcomes. This information is crucial for prioritizing interventions and resources. Mathematical models allow for the simulation of

different scenarios, helping policymakers assess the potential outcomes of various approaches and make informed decisions. Through mathematical analysis, one can validate the accuracy of models by comparing their predictions with observed data. This ensures the reliability of the models for decision-making.

Fractional calculus, an emerging area of mathematics, addresses limitations in classical derivatives by employing non-integer or fractional order operators and these operators possess memory and hereditary properties making them valuable for modelling natural phenomena with non-local dynamics and anomalous behaviour [106]. In the branch of fractional calculus, fractional derivatives and fractional integrals are important aspects. Many classical models have proven to be less effective to predict the future behaviour of systems due to their local nature which hinders to collect information from its past. The study of epidemiological dynamical processes with memory effects is particularly relevant as it involves fractional derivative operators.

Originating from a correspondence between Leibniz and L'Hospital in 1695, fractional calculus has evolved into a thriving field of research, extending beyond mathematics into physics, biology, and engineering. Leibniz's prediction of "useful consequences" has indeed materialized in various disciplines. Over the past decades, several fractional operators, such as Riemann–Liouville, Caputo, Marchaud, Weyl, Grünwald–Letnikov, Jumarie, Erdélyi–Kober, Katugampola, Hadamard, Riesz, Conformable derivative, Caputo–Fabrizio, Atangana–Baleanu, and others, have been proposed.

To gain better insights into model dynamics, various types of fractional operators have been employed to redesign classical models. Several analytic, semi-analytic, and numerical methods are available for solving systems of fractional differential equations, accommodating different fractional derivative operators. Using a variety of mathematical techniques, the connection between mathematical models and natural phenomena has been studied, most notably integer-order differential equations [21, 30, 32, 96, 151]. Fractional calculus not only overcomes the limitations of classical derivatives but also provides a versatile toolkit for understanding and modelling complex systems with memory effects.

Recent research studies have demonstrated that fractional-order operators exhibit superior modelling capabilities, as compared to classical ordinary operators, in capturing the non-local and complex characteristics of various diseases including Breast cancer [132, 133, 136], Chickenpox [111], Diabetes [72, 77], Dengue [108], Diarrhea [109], Human Liver [18], Lung cancer [92, 97, 103], Measles [7], Monkeypox [94], Tuberculosis(TB) [145] Cancer treatment model [37, 39, 42, 154], HIV/AIDS [81, 82], Covid-19 [40, 43, 129, 137, 140] and the sources cited within.

In several other scientific and technological disciplines like biology [153, 156], chemistry [152], physics [52, 53], engineering [17, 36, 69, 71, 91, 155, 158], and most of the references cited therein. The various techniques such as the analytical methods [28, 139, 159], semi-analytic methods [27, 74, 76, 78, 114, 128] and numerical method [6, 12, 15, 83, 107, 127] are found in the literature for solving fractional differential equations. In [112] Qureshi et al. studied the transmission dynamics of varicella zoster virus modeled by classical and novel fractional operators using real statistical data. Qureshi et al. [113] developed fractional modelling of blood ethanol concentration system with real data application. The authors in [120] provided mathematical analysis of fractional Hepatitis C virus model. In [148] the author proposed fractional-order Chlamydia disease transmission in United States between 1989 to 2019. Addai et al. [3] focused on epidemic fractional age-specific smoking disease system. In [70], the authors carried out numerical study of fractional-order waterborne disease model. A numerical stimulation based on Haar wavelet collocation methods of fractional order antidotal computer virus model is provided in [162]. The study on fractional Nipah virus system with the transmission of dynamics using Caputo derivative is given in [41].

Moreover, in [75], solution of fractional Sawada–Kotera–Ito equation using Caputo and AB derivatives have been derived. In [73], a robust computational analysis of residual power series involving general transform to solve fractional differential equations has been proposed. Abdeljawad et al. in [1] derived a higher-order extension of AB fractional operators with respect to another function and a Gronwall-type inequality. In [160], the authors provide studies on coupled snap system with integral boundary conditions in the G- Caputo sense.

The authors in [138], studied the nonlocal multiorder implicit differential equation involving Hilfer fractional derivative on unbounded domains. In [110], an efficient variable step-size rational method for stiff, singular and singularly perturbed problems have been given. The development of the reproducing kernel Hilbert space algorithm for numerical pointwise solution of the time-fractional nonlocal reaction-diffusion equation is provided in [11]. Solution of fractional Sharma–Tasso–Olver differential equation with novel technique [27, 28], Fractional-order mathematical model of magnetic drug targeting during Casson blood flow in a micro-vessel [157], Numerical studies of the neural network-based fractional mathematical model of immunotherapy and chemotherapy for Breast cancer [119], Mathematical modelling of integer and fractional order and its simulations for Q-fever [13], An examination of the glucose-insulin alliance scheme in the fractional-order diabetes model [72, 77], Evaluation of a fractional vector-host disease system mathematically using the CF operator [29], ABC derivative based numerical and geometric interpretation of a fractional-order model of the cancer-immune mode [89], Rezapour et al. [117] described a fractional-order anthrax disease model for animals, Jena et al. [61] presented an epidemic model of childhood diseases.

The remaining of the thesis is structured as follows: Chapter 2 explores a Cauchy-Schwarz-type inequality for a fractional Sturm-Liouville boundary value problem that involves a Caputo derivative of order α , where $1 < \alpha \leq 2$. In Chapter 3, we present three fractional mathematical models for Breast cancer dynamics using Caputo, CF and ABC fractional derivative operators by utilizing real data from Breast cancer incidences in Saudi Arabia from 2004 to 2016. Chapter 4 focuses on mathematical modelling of chikungunya virus dynamics employing Caputo fractional derivatives. Chapter 5 introduce a fractional mathematical model for assessing the cancer risk due to smoking habit. Chapter 6 assess the effectiveness of Caputo fractional order hard water treatment model to reduce water borne disease incidence. Chapter 7 introduces fractional models for Pancreatic cancer, utilizing both Caputo and Atangana-Baleanu fractional derivative operators. Chapter 8 investigates arbitrary-order tumor growth model using Caputo fractional derivative operator.

Chapter 2

Eigenvalue Estimates for Fractional Sturm-Liouville Boundary Value Problem

2.1 Introduction

The Lyapunov inequality [85] has proved to be very useful in the study of spectral properties and oscillation theory of ordinary differential equations. This inequality can be stated as follows [23]:

The nontrivial solution to the boundary value problem

$u''(t) + q(t)u(t) = 0, a < t < b, u(a) = u(b) = 0$, exists, where $q : [a, b] \rightarrow \mathbb{R}$ is a continuous function, then

$$\int_a^b |q(s)| ds > \frac{4}{b-a}.$$

The research on Lyapunov-Type Inequalities (LTIs) for Fractional Boundary Value Problems (FBVPs) has begun since 2013. In [45, 46, 47, 48, 63, 64, 99, 100, 101, 118], the authors have established LTIs for FBVPs of order α with different boundary conditions. In [100], Pathak obtained LTI for fractional boundary value problem with Hilfer derivative of order $\alpha, 1 < \alpha \leq 2$. Furthermore, the author applied LTI to obtain the lower bound for the smallest eigenvalue of corresponding eigenvalue problem. In addition, the Cauchy-Schwarz type inequality (CSI) is established to improve the lower bound estimation of the smallest eigenvalue and applied it to obtain intervals where certain Mittag-Leffler (M-L) function has no real zeros. The CSI provides better results than that of LTI. Motivated by the above work, we consider the following problem with Sturm-Liouville boundary conditions [64]:

$${}^C D_t^\alpha u(t) + q(t)u(t) = 0, \quad a < t < b, \quad 1 < \alpha < 2 \quad (2.1)$$

$$pu(a) - ru'(a) = u(b) = 0, \quad (2.2)$$

where $p > 0, r \geq 0$ and $q : [a, b] \rightarrow \mathbb{R}$ is a continuous function. In [64], Jleli and Samet established a Lyapunov-type inequality for FBVP (2.1)-(2.2) as follows:

For $\frac{r}{p} > \frac{b-a}{\alpha-1}$

$$\int_a^b |q(s)| ds \geq \left(1 + \frac{p}{r}(b-a)\right) \frac{\Gamma\alpha}{(b-a)^{\alpha-1}} \quad (2.3)$$

and for $0 \leq \frac{r}{p} \leq \frac{b-a}{\alpha-1}$

$$\int_a^b |q(s)| ds \geq \frac{\Gamma\alpha}{\max\{A(\alpha, \frac{r}{p}), B(\alpha, \frac{r}{p})\}}. \quad (2.4)$$

We establish CSI for FBVP (2.1)-(2.2). The outline of the chapter is as follows: first, we provide some preliminaries in section 2.2 which we will use in this paper. In section 2.3, we establish CSI for fractional Sturm-Liouville boundary value problem containing Caputo derivative of order α , $1 < \alpha \leq 2$. We also give a comparison between the lower bound estimates of the smallest eigenvalue obtained from the LTI and CSI. In section 2.4, we use these inequalities to obtain an interval where a linear combination of certain Mittag-Leffler functions have no real zeros. Finally, a conclusion is given in section 2.5.

2.2 Preliminaries

In this section, we recall some basic definitions which are further used in this paper.

Definition 2.2.1. *The Caputo derivative of fractional order $\alpha > 0$ is defined by*

$${}_a^C D_t^\alpha (f(t)) = \frac{1}{\Gamma(m-\alpha)} \int_a^t (t-s)^{m-\alpha-1} f^{(m)}(s) ds, t \in [a, b],$$

where m is the smallest integer greater or equal to α .

Definition 2.2.2. *The two-parameter M-L function is defined by*

$$E_{\alpha, \beta}(z) = \sum_{k=0}^{\infty} \frac{z^k}{\Gamma(\alpha k + \beta)}, \quad (\alpha, \beta, z \in \mathbb{R}; \alpha, \beta > 0).$$

Definition 2.2.3. *The Pfaff Transformation is defined as*

$${}_2F_1(a, b; c; t) = (1 - t)^{-a} {}_2F_1\left(a, c - b; c; \frac{t}{t - 1}\right); |t| < \frac{1}{2},$$

where, ${}_2F_1(a, b; c; t)$ is a hypergeometric function.

For more details, refer [79] and [106].

2.3 Main result

The main result is given in Theorem 2.3.1.

Lemma 2.3.1. *The FBVP (2.1)-(2.2) can be written in its equivalent integral form as [64]*

$$u(t) = \int_a^b G(t, s)q(s)u(s)ds, \quad t \in [a, b], \quad (2.5)$$

where G is the Green's function given by

$$G(t, s) = \frac{1}{\Gamma(\alpha)} \begin{cases} \frac{\left(\frac{r}{p} + t - a\right)(b - s)^{\alpha-1}}{\left(\frac{r}{p} + b - a\right)} - (t - s)^{\alpha-1}, & a \leq s \leq t \leq b, \\ \frac{\left(\frac{r}{p} + t - a\right)(b - s)^{\alpha-1}}{\left(\frac{r}{p} + b - a\right)}, & a \leq t \leq s \leq b. \end{cases} \quad (2.6)$$

Lemma 2.3.2. [100] *Let $u \in L^2[a, b]$, then the Cauchy-Schwarz-type inequality of FBVP (2.1)-(2.2) is given by*

$$1 \leq \left\{ \int_a^b \int_a^b |G(t, s)q(s)|^2 ds dt \right\}. \quad (2.7)$$

Proof. Taking the Cauchy-Scharz inequality in (2.5) we get,

$$|u(t)| \leq \left[\int_a^b |G(t, s)q(s)|^2 ds \right]^{\frac{1}{2}} \left[\int_a^b |u(s)|^2 ds \right]^{\frac{1}{2}}.$$

Squaring and integrating from a to b w.r.to. t gives

$$\int_a^b |u(t)|^2 dt \leq \int_a^b \left\{ \left[\int_a^b |G(t, s)q(s)|^2 ds \right] \left[\int_a^b |u(s)|^2 ds \right] \right\} dt$$

$$\|u\|_2 \leq \int_a^b \int_a^b |G(t, s)q(s)|^2 ds dt \|u\|_2,$$

which proves the Lemma. □

Now, we consider Fractional Sturm-Liouville eigen value problem (FEP):

$$\begin{cases} {}^C D_t^\alpha (u(t)) + \lambda u(t) = 0, & a < t < b, 1 < \alpha < 2 \\ pu(a) - ru'(a) = u(b) = 0. \end{cases} \quad (2.8)$$

We are ready to state and prove our main results.

Theorem 2.3.1. *If a nontrivial continuous solution of the problem (2.8) exists, then for FEP (2.8) the CSI is*

$$\lambda \geq \frac{1}{\Gamma(\alpha)} \left\{ \frac{1}{(2\alpha - 1)\left(\frac{r}{p} + b - a\right)^2} \left[\left(\frac{r}{p} - a\right)^2 (b - a) + \left(\frac{r}{p} - a\right)(b^2 - a^2) + \frac{(b^3 - a^3)}{3} \right] \right. \\ \left. + \frac{(b - a)^{2\alpha}}{2\alpha(2\alpha - 1)} - \frac{2\beta(1, \alpha)(b - a)^\alpha}{\left(\frac{r}{p} + b - a\right)} \int_a^b \left(\frac{r}{p} - a + t\right)(t - a)^\alpha \frac{{}_2F_1\left(1, 2\alpha, 1 + \alpha, \frac{a-t}{b-t}\right)}{(b - t)} dt \right\}^{-\frac{1}{2}}, \quad (2.9)$$

where $\beta(m, n)$ is a Beta function.

Proof. Taking $q(t) = \lambda$ in (2.7) gives the inequality

$$\lambda \geq \left[\int_a^b \int_a^b |G(t, s)|^2 ds dt \right]^{-\frac{1}{2}}. \quad (2.10)$$

By substituting equation (2.6) in (2.10), after some simplifications we obtain (2.9), which concludes the proof. \square

We consider following two cases.

Case 1: Taking $a = 0, b = 1, p = 1$ and $r = 2$ in (2.8), we get the following FEP:

$${}_0^C D_t^\alpha (u(t)) + \lambda u(t) = 0, 0 < t < 1, 1 < \alpha < 2 \quad (2.11)$$

$$u(0) - 2u'(0) = u(1) = 0. \quad (2.12)$$

Case 2: Taking $a = 0, b = 1, p = 2$ and $r = 1$ in (2.8), gives the eigenvalue problem:

$${}_0^C D_t^\alpha (u(t)) + \lambda u(t) = 0, 0 < t < 1, 1 < \alpha < 2 \quad (2.13)$$

$$2u(0) - u'(0) = u(1) = 0. \quad (2.14)$$

Next, we give three methods to estimate the lower bound for the smallest eigenvalue of problems (2.11)-(2.12) and (2.13)-(2.14) by using the following definitions given in [100].

Definition 2.3.1. A *Lyapunov-Type Inequality Lower Bound (LTILB)* is defined as a lower bound estimate for the smallest eigenvalue obtained from Lyapunov-type inequalities given by (2.3) and (2.4).

We obtain a lower bound for the smallest eigenvalue of problem (2.11) with boundary conditions (2.12) is:

$$\lambda \geq \frac{3}{2} \Gamma(\alpha), \quad (2.15)$$

and for the problem (2.13)-(2.14) it is:

$$\lambda \geq \frac{\Gamma\alpha}{\max\{A(\alpha, \frac{1}{2}), B(\alpha, \frac{1}{2})\}}. \quad (2.16)$$

Definition 2.3.2. A Cauchy-Schwarz Inequality Lower Bound (CSILB) is defined as an estimate of the lower bound for the smallest eigenvalue obtained from the Cauchy-Schwarz inequality of type given in equation (2.9).

We obtain the CSIs of problems (2.11)-(2.12) and (2.13) -(2.14), after some simplifications and using Pfaff transformation in (2.9) respectively as follows :

$$\lambda \geq \frac{1}{\Gamma(\alpha)} \left\{ \frac{1}{(2\alpha - 1)} \left[\frac{19}{27} + \frac{1}{2\alpha} \right] - \frac{2}{3} \int_0^1 (2+t)t^\alpha \beta(1, \alpha) {}_2F_1(1 - \alpha, 1; \alpha + 1, t) dt \right\}^{-\frac{1}{2}}, \quad (2.17)$$

$$\lambda \geq \frac{1}{\Gamma(\alpha)} \left\{ \frac{1}{(2\alpha - 1)} \left[\frac{13}{27} + \frac{1}{2\alpha} \right] - \frac{4}{3} \int_0^1 \left(\frac{1}{2} + t\right) t^\alpha \beta(1, \alpha) {}_2F_1(1 - \alpha, 1; \alpha + 1, t) dt \right\}^{-\frac{1}{2}}, \quad (2.18)$$

provided $\alpha > \frac{1}{2}$.

In [38], eigenvalues $\lambda \in \mathbb{R}$ of problems (2.11)-(2.12) and (2.13)-(2.14) are the solutions of the linear combination of certain M-L functions are respectively as follows:

$$2E_{\alpha,1}(-\lambda) + E_{\alpha,2}(-\lambda) = 0, \quad (2.19)$$

$$E_{\alpha,1}(-\lambda) + 2E_{\alpha,2}(-\lambda) = 0. \quad (2.20)$$

Now, comparing the non-zero solutions of equations (2.19)-(2.20) for $1.5 < \alpha \leq 2$ with CSILB given by equations (2.17)-(2.18) and LTILB given by the equations (2.15)-(2.16) respectively, we get the following comparison figures.

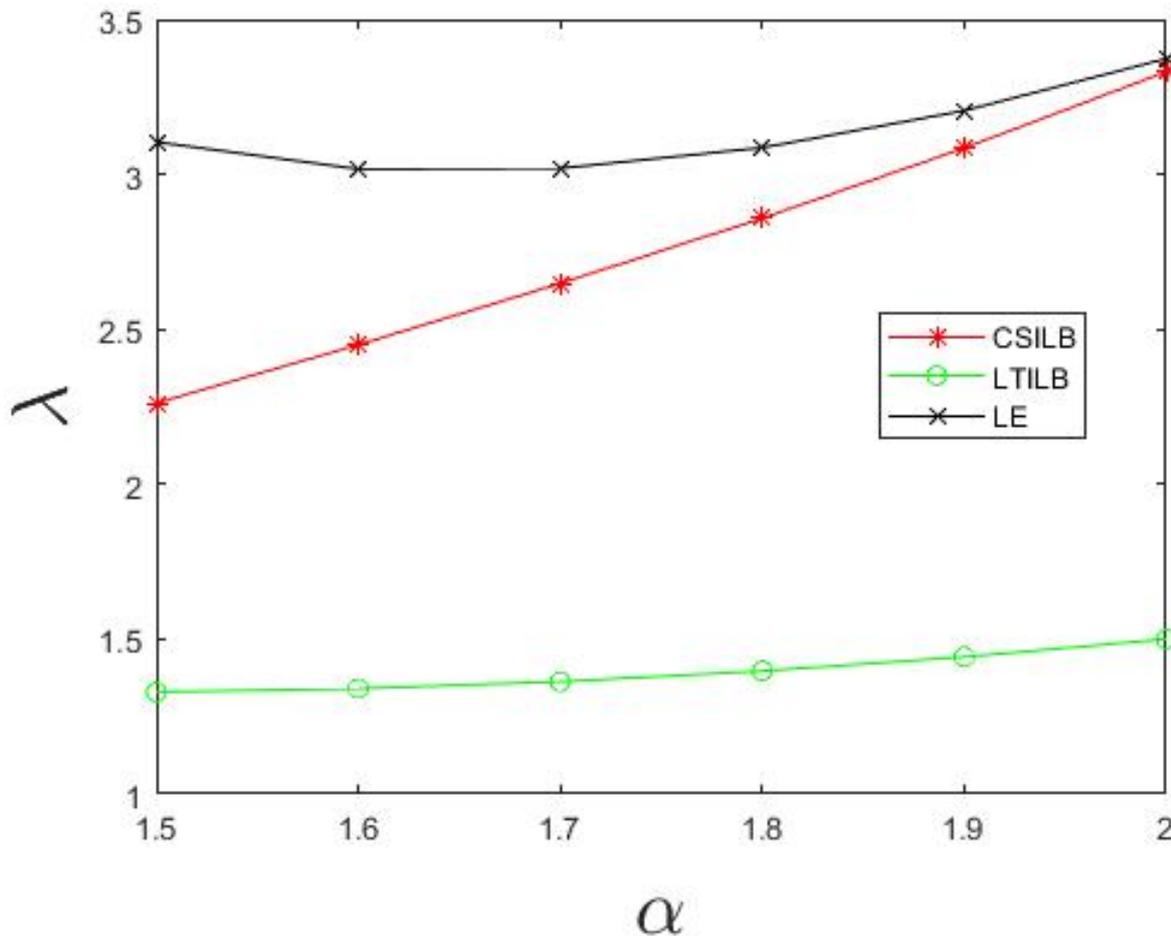


Figure 2.1: Comparison of the lower bounds for λ obtained from Lyapunov-type and Cauchy-Schwarz inequalities with the lowest eigenvalue for (2.11)-(2.12). ($- \circ -$: LTILB; $- * -$: CSILB; $- \times -$:LE - the Lowest Eigenvalue λ)

These figures clearly demonstrates that between the two estimates considered here, the LTILB provides the worse estimate and the CSILB provide better estimate for the smallest eigenvalues of (2.11)-(2.12) as in figure 2.1 and (2.13)-(2.14) as in figure 2.2.

We consider the integer order case, i.e. $\alpha = 2$. For this case, the LTILB and CSILB for the smallest λ of (2.11)-(2.12) are given as 1.5 and 3.3310 and for (2.13)-(2.14), 2.6667 and 5.1117 respectively. (See equations (2.15), (2.16), (2.17) and (2.18)). For $\alpha = 2$, the problems (2.11)-(2.12) and (2.13)-(2.14) can be solved in closed form using the tools from integer order

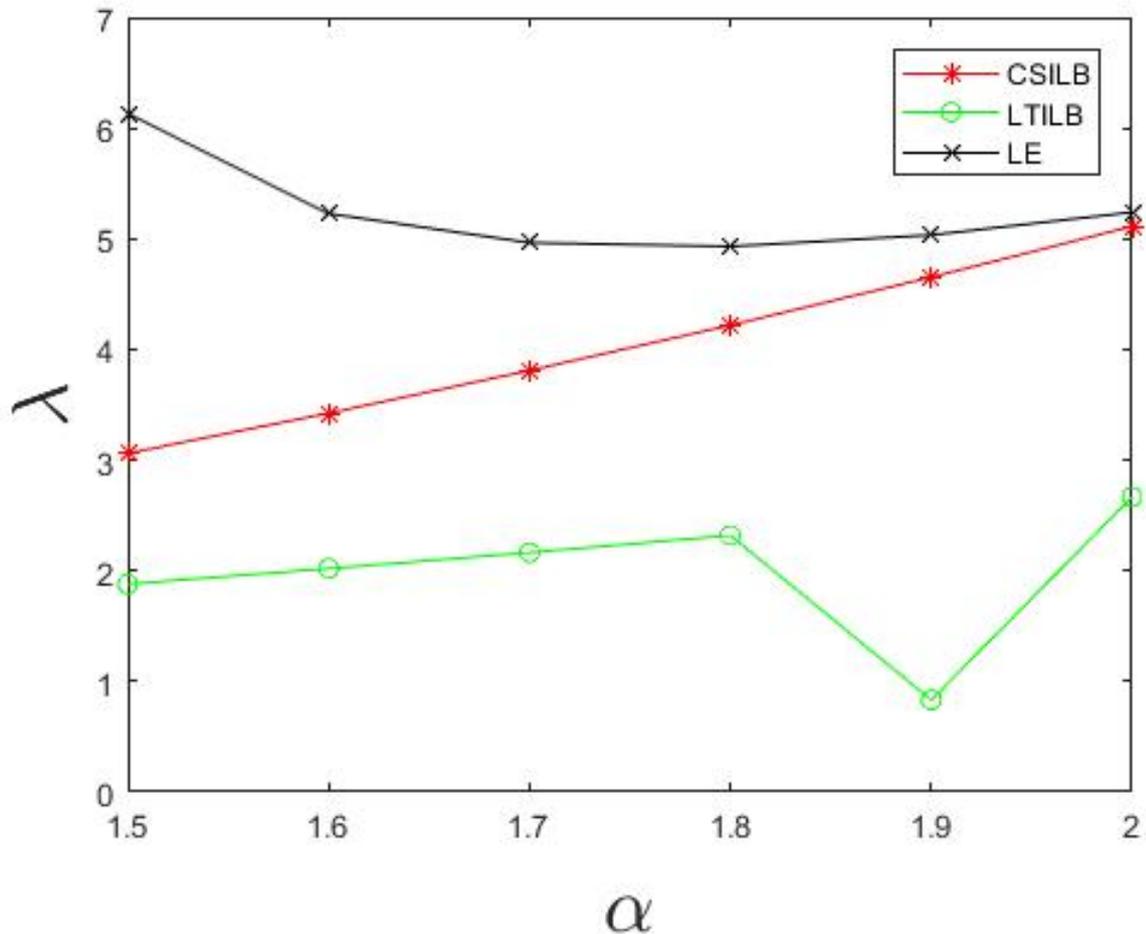


Figure 2.2: Comparison of the lower bounds for λ obtained from Lyapunov-type and Cauchy-Schwarz inequalities with the lowest eigenvalue for (2.13)-(2.14). ($- \circ -$: LTILB; $- * -$: CSILB; $- \times -$:LE - the Lowest Eigenvalue λ)

calculus. Results show, the smallest eigenvalues of (2.11)-(2.12) and (2.13)-(2.14) are the roots of equations (2.19) and (2.20) respectively, which give the smallest eigenvalues as 3.3731 and 5.2392. Comparing these λ with its estimate above, it is clear that between LTILB and CSILB for the integer α the CSILB provides the best estimate for the smallest eigenvalue.

2.4 Applications

We now consider an application of the lower bounds for the smallest eigenvalues of FEPs (2.11)-(2.12) and (2.13)-(2.14) found in equations (2.15)-(2.20).

Theorem 2.4.1. *Let $1.5 < \alpha \leq 2$. The linear combination of certain Mittag-Leffler functions $2E_{\alpha,1}(-z) + E_{\alpha,2}(-z)$ have no real zeros in the following domains:*

LTILB:

$$z \in \left(-\frac{3}{2}\Gamma(\alpha), 0 \right] \quad (2.21)$$

CSILB:

$$z \in \left(-\frac{1}{\Gamma(\alpha)} \left\{ \frac{1}{(2\alpha-1)} \left[\frac{19}{27} + \frac{1}{2\alpha} \right] - \frac{2}{3}C_1(\alpha) \right\}^{-\frac{1}{2}}, 0 \right], \quad (2.22)$$

where, $C_1(\alpha) = \int_0^1 (2+t)t^\alpha \beta(1, \alpha) {}_2F_1(1-\alpha, 1; \alpha+1, t) dt$.

Proof. Let λ be the smallest eigenvalue of the equation (2.12), then $z = \lambda$ is the smallest value for which $2E_{\alpha,1}(-z) + E_{\alpha,2}(-z) = 0$. If there is another z smaller than λ for which $2E_{\alpha,1}(-z) + E_{\alpha,2}(-z) = 0$, then it will contradict that λ is the smallest eigenvalue. Therefore, $2E_{\alpha,1}(-z) + E_{\alpha,2}(-z)$ have no real zeros for $z \in (-\lambda, 0]$. Thus, $2E_{\alpha,1}(-z) + E_{\alpha,2}(-z)$ have no real zeros for

$$z \in \left(-\frac{1}{\Gamma(\alpha)} \left\{ \frac{1}{(2\alpha-1)} \left[\frac{19}{27} + \frac{1}{2\alpha} \right] - \frac{2}{3}C_1(\alpha) \right\}^{-\frac{1}{2}}, 0 \right].$$

This proves (2.22). Proof of (2.21) is given in [64]. □

Theorem 2.4.2. *Let $1.5 < \alpha \leq 2$. The linear combination of certain Mittag-Leffler functions $E_{\alpha,1}(-z) + 2E_{\alpha,2}(-z)$ have no real zeros in the following domains:*

LTILB:

$$z \in \left(-\frac{\Gamma\alpha}{\max\{A(\alpha, \frac{1}{2}), B(\alpha, \frac{1}{2})\}}, 0 \right]. \quad (2.23)$$

CSILB:

$$z \in \left(-\frac{1}{\Gamma(\alpha)} \left\{ \frac{1}{(2\alpha-1)} \left[\frac{13}{27} + \frac{1}{2\alpha} \right] - \frac{4}{3} C_2(\alpha) \right\}^{-\frac{1}{2}}, 0 \right], \quad (2.24)$$

where, $C_2(\alpha) = \int_0^1 \left(\frac{1}{2} + t \right) t^\alpha \beta(1, \alpha) {}_2F_1(1 - \alpha, 1; \alpha + 1, t) dt$.

Proof. The proof is similar to the proof of Theorem 2.4.1 . □

2.5 Conclusion

We established Cauchy-Schwarz-type inequality for fractional Sturm-Liouville boundary value problem containing Caputo derivative of order α , $1 < \alpha \leq 2$ to determine a lower bound for the smallest eigenvalues. We give a comparison between the smallest eigenvalues and its lower bounds obtained from the Lyapunov-type and Cauchy-Schwarz-type inequalities. The results indicate that the Cauchy-Schwarz-type inequality gives better lower bound estimates for the smallest eigenvalues than the Lyapunov-type inequality. We then used these inequalities to obtain an interval where a linear combination of certain Mittag- Leffler functions have no real zeros.