Mathematical Analysis and its Contemporary Applications
Volume 4, Issue 3, 2022, 9–16
doi: 10.30495/maca.2022.1953296.1051
ISSN 2716-9898

Stability analysis of transmitter receptors model

D. Dhamodharan*, B. Mohamed Harif, and Bonyah Ebenezer

Abstract. The Jumarie fractional-order transmitter receptors model is discussed in this paper. Transmitter receptors can be found in a variety of states, including accumulated, freed, combined with receptors, and recycled for storage. For such a system, a collection of equations is proposed and analyzed. We considered the solution's asymptotically stability and discussed the physiological effect of transmitter receptor transport in a synaptic chasm in the presence of receptors and transporters with different kinetic properties under these limited conditions.

1. Introduction

Synaptic transmission has been thoroughly studied for many years [**2**, **3**, **4**, **6**], and the roles of various transmitters, as well as some of the pre and post synaptic events, are well established. Various publications describe the introduction of transmitter receptors kinetics with a mathematical foundation ([**9**, **13**]). In biochemical systems, ordinary differential equations are used to describe the dynamics of transmitter receptor reactions. The use of fractional -order differential equations to model biological systems has more advantages than classical order mathematical modelling. The fractional order differential equations (FODEs) model is more consistent with biological phenomena than the integer order differential equations model [**12**].

We discussed the physiological effect of the transport of the transmitter receptors ACh (acetylcholine) in synaptic cleft in the presence of a finite number of receptors and transporters with different kinetic properties under certain limited conditions in this article.

2020 *Mathematics Subject Classification.* Primary: 37C75; Secondary: 34A08.
Key words and phrases. Fractional-order model, transmitter receptors, Mittag Leffler function, Jumarie fractional derivative. *Corresponding author

2. Basic functions of fractional calculus

The gamma function and beta function are fundamental mathematical methods in fractional calculus for understanding the origins of its quantitative challenges.

Definition 2.1. [8] The integral $Gamma(z)$ determines the gamma function.

$$\Gamma(z) = \int\limits_0^\infty e^{-t} t^{z-1} dt,\ Re(z) > 0 \tag{1}$$

which is the second-kind Euler's integral and converges in the right half of the complex plane $Re\ z > 0$.

Definition 2.2. [12] The beta function is defined by the integral $b(z, w)$

$$b(z, w) = \int\limits_0^1 t^{z-1}(1-t)^{w-1} dt,\ Re(z) > 0,\ Re(w) > 0 \tag{2}$$

which is the first-kind Euler's integral.

The Mittag-Leffler function is very important in fractional calculus research.

Definition 2.3. [8] The classical Mittag-Leffler function for a single parameter.

$$E_a(z) = \sum_{j=0}^{\infty} \frac{z^j}{\Gamma(aj+1)},\ z \in \mathbb{C},\ Re(a) > 0 \tag{3}$$

The series expansion of the Mittag-Leffler function with two parameters $alpha, beta$ is as follows [12].

$$E_{a,b}(z) = \sum_{j=0}^{\infty} \frac{z^j}{\Gamma(aj+b)},\quad (a > 0,\quad b > 0) \tag{4}$$

3. Fractional Derivative

It is necessary to use an appropriate definition of the fractional derivative when analyzing the dynamical behavior of a fractional system.Indeed, several definitions of the fractional-order derivative, including Grunwald-Letnikov, Riemann-Liouville, Weyl, Riesz, and the Caputo[12] representation, are not unique.
Let $L^1 = L^1[a, b]$ be the class of Lebesgue integrable functions on [a,b], $a < b < \infty$.

Definition 3.1. The fractional integral (or the Riemann-Liouville integral) of order $p \in \mathbb{R}^+$ of the function $f(t), t > 0$ ($f : \mathbb{R}^+ \to \mathbb{R}$) is defined by [13]

$$I_a^p x(t) = \frac{1}{\Gamma(p)} \int_a^t (t-s)^{p-1} x(s) ds, t > a \tag{5}$$

The fractional derivative of f(t) of order $\pi(n-1,n)$ can be defined in two (non-equivalent) cases:
(i)The fractional derivative of Riemann-Liouville: Take the fractional integral of order $(n-p)$, then the nth derivative as follows:

$$\Delta_\star^p f(t) = \Delta_\star^n I_a^{n-p} f(t), \quad \Delta_\star^n = \frac{d^n}{dt^n},\ n = 1, 2... \tag{6}$$

(ii) Caputo's fractional derivative is as follows: take the nth derivative, and then a fractional integral of order $(n-p)$.

$$\Delta^p f(t) = I_a^{n-p} \Delta_\star^n f(t), \quad n = 1, 2, 3... \tag{7}$$

4. System of linear fractional differential equations

Consider the system of fractional-order differential equations.

$$\begin{cases} {}^J\Delta^p[x] & = ax + by \\ {}^J\Delta^p[y] & = cx + dy \end{cases} \tag{8}$$

Here, $a, b, c,$ and $d$are constants, and the operator ${}^J D^a$ is the Jumarie fractional derivative operator, which we will refer to as such for convenience. ${}^J\Delta^p \equiv \dfrac{\Delta^p}{dt^p}$, where x and y are functions of t. The above equation system can be modified as

$$\begin{cases} {}^J\Delta^p[x] - ax - by = 0 \\ {}^J\Delta^p[y] - cx - dy = 0 \end{cases} \tag{9}$$

It has the solution of the form

$$x = A_1 E_p(\mu_1 t^p) + B_1 E_p(\mu_2 t^p) \tag{10}$$
$$y = A_2 E_p(\mu_1 t^p) + B_2 E_p(\mu_2 t^p) \tag{11}$$

where A_1, B_1 are arbitrary constants and

$$A_2 = \frac{A_1(\mu_1 - d)}{c},\ B_2 = \frac{B_1(\mu_2 - d)}{c}$$

5. Equilibrium points and their asymptotic stability

We describe the equilibrium points and asymptotic stability of a fractional order linear system from [1]. Consider the system and $\pi(0,1)$.

$$\begin{cases} \Delta_\star^p x(t) = f_1(x, y) \\ \Delta_\star^p y(t) = f_2(x, y) \end{cases} \tag{12}$$

with initial values $x_1(0) = x_0,\ y_1(0) = y_0$.
To assess equilibrium points, let

$$\Delta_\star^p x(t) = 0 \Rightarrow f_1(x^{eq}, y^{eq}) = 0$$
$$\Delta_\star^p y(t) = 0 \Rightarrow f_2(x^{eq}, y^{eq}) = 0$$

To assess asymptotic stability, let

$$x(t) = x^{eq} + \epsilon_1(t)$$
$$y(t) = y^{eq} + \epsilon_2(t)$$

then

$$\Delta_\star^p(x^{eq} + \epsilon_1) = f_1(x^{eq} + \epsilon_1, y^{eq} + \epsilon_2)$$
$$\Delta_\star^p(y^{eq} + \epsilon_2) = f_2(x^{eq} + \epsilon_1, y^{eq} + \epsilon_2)$$

which implies that

$$\Delta_\star^p \epsilon_i(t) = f_i(x^{eq} + \epsilon_1, y^{eq} + \epsilon_2),\ i = 1, 2$$

but

$$\begin{aligned} f_i(x^{eq} + \epsilon_1, y^{eq} + \epsilon_2) &\simeq f_i(x^{eq}, y^{eq}) + \frac{\partial f_i}{\partial x}\Big|_{eq}\epsilon_1 + \frac{\partial f_i}{\partial y}\Big|_{eq}\epsilon_2 + ... \\ \Rightarrow f_i(x^{eq} + \epsilon_1, y^{eq} + \epsilon_2) &\simeq \frac{\partial f_i}{\partial x}\Big|_{eq}\epsilon_1 + \frac{\partial f_i}{\partial y}\Big|_{eq}\epsilon_2 \end{aligned}$$

where $\quad f_i(x^{eq}, y^{eq}) = 0$, then

$$\Delta_\star^p \epsilon_i(t) \simeq \frac{\partial f_i}{\partial x}\Big|_{eq}\epsilon_1 + \frac{\partial f_i}{\partial y}\Big|_{eq}\epsilon_2$$

and we get the system

$$\Delta_\star^p \epsilon = A\epsilon \tag{13}$$

with the initial values $\epsilon_1(0) = x(0) - x^{eq}$ and $\epsilon_2(0) = y(0) - y^{eq}$,
where

$$A\epsilon = \begin{bmatrix} \epsilon_1 \\ \epsilon_2 \end{bmatrix}, \quad A = \begin{bmatrix} \frac{\partial f_1}{\partial x}\Big|_{eq} & \frac{\partial f_1}{\partial y}\Big|_{eq} \\ \\ \frac{\partial f_2}{\partial x}\Big|_{eq} & \frac{\partial f_2}{\partial y}\Big|_{eq} \end{bmatrix}$$

We have $B^{-1}AB = C$, where C is a diagonal matrix of A given by

$$C = \begin{bmatrix} \mu_1 & 0 \\ 0 & \mu_2 \end{bmatrix}$$

where $\mu_1$and μ_2 are the eigen values of A and B is the eigenvalue vectors of A, then $AB = BC, \quad A = BCB^{-1}$,
which implies that

$$\Delta_\star^p \epsilon = (BCB^{-1})\epsilon,\ \Delta_\star^p(B^{-1}\epsilon) = C(B^{-1}\epsilon),$$

then

$$\Delta_\star^p \eta = C\eta,\ \eta = B^{-1}\epsilon, \tag{14}$$

$$\eta = \begin{bmatrix} \eta_1 \\ \eta_2 \end{bmatrix},$$

i.e.

$$\Delta_\star^p \eta_1 = \mu_1 \eta_1, \tag{15}$$

$$\Delta_\star^p \eta_2 = \mu_2 \eta_2 \tag{16}$$

Mittag-Leffler functions[5] provide the solution to Equations15 - 16.

$$\eta_1(t) = \sum_{n=0}^{\infty} \frac{(\mu_1)^n t^{np}}{\Gamma(np+1)} \eta_1(0) = E_p(\mu_1 t^p)\eta_1(0), \tag{17}$$

$$\eta_2(t) = \sum_{n=0}^{\infty} \frac{(\mu_2)^n t^{np}}{\Gamma(np+1)} \eta_2(0) = E_p(\mu_2 t^p)\eta_2(0) \tag{18}$$

Using the result of Matignon [11] then, if $|arg(\tau_1)| > p\pi/2$ and $|arg(\tau_2)| > p\pi/2$ then $\eta_1(t),\quad \eta_2(t)$ are decreasing and then $\epsilon_1(t),\ \epsilon_2(t)$ are decreasing.

If both eigenvalues of the matrix A are negative ($|arg(\tau_1)| > p\pi/2,\ |arg(\tau_2)| > p\pi/2$), the equilibrium point (x_1^{eq}, x_2^{eq}) is locally asymptotically stable.

6. The fractional order model

The kinetics of those reactive systems can be accurately represented by using fractional calculus, which are similar to those obtained by the law of mass action [7].
Because the relationship between instantaneous end-plate current and voltage is linear, the end-plate current is proportional to the end-plate conductance for a fixed voltage. As a result, rather than studying the end plate current, the end plate conductance is sufficient. But since end plate conductance is proportional to ACh concentration, we focus on ACh kinetics in the synaptic cleft. We assume that ACh reacts enzymatically with its receptor, R, as shown below.

$$ACh + R \rightleftharpoons^{j_1}_{[j_2]} ACh.R \rightleftharpoons^{\mu}_{[\tau]} ACh.R^\star$$

and that the ACh receptor complex only conducts current when it is in the open state $ACh.R^\star$. The concentrations of the reactants and products are denoted by lower case letters $c = [ACh], y = [ACh.R],\ x = [ACh.R^\star]$, where [ ] denotes the concentration of reactants, and it follows from the law of mass action that

$$\frac{dx}{dt} = -\tau x + \mu y \tag{19}$$

$$\frac{dy}{dt} = \tau x + j_1 c(N - x - y) - (\mu + j_2)y \tag{20}$$

$$\frac{dc}{dt} = f(t) - j_e c - j_1 c(N - x - y) + j_2 y \tag{21}$$

where N (the total concentration of ACh receptor) is assumed to be conserved and ACh decays at the rate $-j_e$ by a simple first order process. The rate of ACh formation is assumed to be some given function of f, and the post synaptic conductance is assumed to be proportional to $f(t)$.
Model equations in dimensional form can be converted to non-dimensional equations by substituting $X = \frac{x}{N},\ Y = \frac{y}{N},\ C = \frac{j_1 c}{j_2}\ \ and\ \tau = \tau t$, then we get,

$$\frac{dX}{d\tau} = -X + \frac{\mu}{\tau}Y \tag{22}$$

$$\epsilon\frac{dY}{d\tau} = \epsilon X + C(1 - X - Y) - (\epsilon\frac{\mu}{\tau} + 1)Y \tag{23}$$

$$\epsilon\frac{dC}{d\tau} = \epsilon F(\tau) - \frac{j_e}{j_2}C - \frac{N}{J}C(1 - X - Y) + \frac{N}{J}Y \tag{24}$$

$where\ \epsilon = \dfrac{\tau}{j_2} << 1\ \ , J = \dfrac{j_2}{j_1},\ \ F(\tau) = \dfrac{f(t)}{\tau J}$ and the rate $-j_e$by a simple first order process

Now we look at the fractional order in the Magleby [10] model. The new system is described by the fractional differential equations listed below

$$\frac{d^\gamma X}{d\tau^\gamma} = -X + \frac{\mu}{\tau}Y \tag{25}$$

$$\epsilon\frac{d^\gamma Y}{d\tau^\gamma} = \epsilon X + C(1 - X - Y) - (\epsilon\frac{\mu}{\tau} + 1)Y \tag{26}$$

$$\epsilon\frac{d^\gamma C}{d\tau^\gamma} = \epsilon F(\tau) - \frac{j_e}{j_2}C - \frac{N}{J}C(1 - X - Y) + \frac{N}{J}Y \tag{27}$$

γ is a parameter describing the order of the fractional time derivative in Caputo sense and $0 < \gamma < 1$.

7. Stability analysis of the Model

The equations (26) and(27) are non autonomous simultaneous differential equations. When $f(t)$ (the rate of ACh formation) equals zero and N(the total concentration of ACh) equals $x + y$, the original Magleby modelled equations are reduced to fractional order linear autonomous simultaneous equations as follows:

$$\frac{d^\gamma x}{dt^\gamma} = -\tau x + \mu y \tag{28}$$

$$\frac{d^\gamma y}{dt^\gamma} = \tau x - (b + j_2)y \tag{29}$$

$$\frac{d^\gamma c}{dt^\gamma} = -j_e + j_2 y \tag{30}$$

Equations (28 - 30) are linear autonomous system of equations, so we can use phase plane analysing them. Equation (28) and (29) are coupled and independent of c. Here $x = 0,\ y = 0,\ c = 0$ is the critical point of the system.
Consider the equations (28) and (29).
Then its characteristic equation is as follows:

$$\tau^2 + (\tau + b + j_2)\tau + \tau j_2 = 0... \tag{31}$$

and its eigenvalues values are

$$\tau_1 = \frac{-(\tau + \mu + j_2) + \sqrt{(\tau + \mu + j_2)^2 - 4\tau j_2}}{2}$$

and

$$\tau_2 = \frac{-(\tau + \mu + j_2) - \sqrt{(\tau + \mu + j_2)^2 - 4\tau j_2}}{2}$$

A sufficient condition for the local asymptotic stability of the equilibrium point $(x_1^{eq}, x_2^{eq}) = (0, 0)$ is $|arg(\tau_1)| > \gamma\pi/2$ and $|arg(\tau_2)| > \gamma\pi/2$.
In the special case $a = 1.5$, $b = 1.5$ and $j_2 = 4.5$ we get the system is asymptotically stable.

8. Conclusion

In this paper, we demonstrated that the critical point of a fractional order system is the same as its integer order counterpart. For $a = 1.5$, $b = 1.5$, and $j2 = 4.5$ in this transmitter receptors kinetic model, the system is asymptotically stable, and we can conclude that fractional-order differential equations are at least as stable as their integer order counterpart.

Acknowledgment

The authors are appreciative of the anonymous referees for their insightful comments, which significantly improved the paper's presentation.

References

[1] E. Ahmed, A. M. A. El-Sayed and H. A. A. El-Saka, *Equilibrium points, stability and numerical solutions of fractional-order predator-prey and rabies models*, J. Math. Anal. Appl., **325**(2007), 542-553.

[2] M. V. L. Bennett, *Synaptic transmission and neuronal interaction*, Raven Press, New York, 1974.

[3] A. V. Chalyi and E. V. Zaitseva, *Strange Attractor in kinetic model of Synaptic Transmission*, J. Phys. Stud., **11**(3)(2007).

[4] J. C. Eccles, *The physiology of synapses*, Springer-Verlag, Berlin, 1964.

[5] A. M. A. El-Sayed, *Fractional differential-difference equations*, J. Fract. Calc., **10**(1996), 101-106 .

[6] B. Katz, *Nerve, muscle, and synapse*, New York: McGraw-Hill, 1966.

[7] J. Keenar and J. Snyed, *Mathematical physiology*, Springer, New York, Chapter 7, 2008.

[8] A. A. Kilbas, H. M. Srivastava and J. J. Trujillo, *Theory and applications of fractional differential equations*, Elsevier, 2006.

[9] K. N. Leibovic and F. Andrietti, *Analysis of a model for transmitter kinetics*, Bio. Cyber., **27**(1977), 165-173.

[10] K. L. Magleby and C. F. Stevens, *A quantitative description of end-plate currents*, J. Physio., **223**(1972), 173-197.

[11] D. Matignon, *Stability results for fractional differential equations with applications to control processing*, Comput. Engin. Syst. Appl., **2**(1)(1996).

[12] I. Podlubny, *Fractional differential equations*, Academic Press, San Diego, CA, 1999.

[13] F. A. Rihan, A. Hashish, F. Al-Maskari, M. S. Hussein, E. Ahmed, M. B. Riaz and R. Yafia, *Dynamics of tumor-immune system with fractional-order*, J. Tumor Res., **2**(1)(2016), 109-115.

Department of Mathematics, Jamal Mohamed College (Autonomous)(Affiliated to Bharathidasan University), Tiruchirapplli-620020, India

Email address: dharan_raj28@yahoo.co.in

Department of Mathematics, Serfoji Govt. College (Autonomous) (Affiliated to Bharathidasan University), Tanjavour, Tamilnadu, India

Email address: harif1984@gmail.com

Department of Mathematics Education, Akenten Appiah Menka University of Skills Training and Entrepreneurial Development, Kumasi, Ghana, South Africa

Email address: ebbonya@yahoo.com,

Received : February 2022

Accepted : April 2022