Progress in Fractional Differentiation and Applications
An International Journal

http://dx.doi.org/10.18576/pfda/110402

Dynamics of DNA Methylation: Fractional Model Approach

Praveen Agarwal[1,2,3,*], *Hossein Nasrolahpour*[4], *Nezha Maamri*[5], *Jean-Claude Trigeassou*[6], *Rashid Nasrolahpour*[7] *and Shaher Momani* [3,8]

[1] Peoples' Friendship University of Russia (RUDN University), 6 Miklukho-Maklaya St, 117198 Moscow, Russian Federation
[2] Applied Nonlinear Science Lab, Anand International College of Engineering, Jaipur 303012, India
[3] Nonlinear Dynamics Research Centre (NDRC),Ajman University, Ajman, UAE
[4] School of Computational Science and Engineering, University of Tehran, Tehran, Iran
[5] LIAS Laboratory, ENSIP, University of Poitiers, France
[6] IMS-LAPS, University of Bordeaux, Talence, France
[7] Department of Physics, University of Mazandaran, P. O. Box 47416-95447, Babolsar, Iran
[8] Department of Mathematics, Faculty of Science,the University of Jordan,Amman 11942, Jordan

Received: 11 Nov. 2024, Revised: 23 Dec. 2024, Accepted: 5 Jan. 2025
Published online: 1 Oct. 2025

Abstract: In this paper, we present a fractional calculus-based model to explore the dynamics of deoxyribonucleic acid (DNA) methylation. The advantage of using fractional calculus in the modeling of biological phenomena is that we can consider both space nonlocality and memory effect simultaneously which play an essential role in describing the complex dynamics of all biological systems and in particular dynamics of DNA.

Keywords: DNA Methylation, Fractional Dynamics, Memory Effect, Infinite state approach.

1 Introduction

DNA methylation is an epigenetic process by which methyl (CH3) groups are added to the DNA molecule and is a key epigenetic mechanism that cells use to control gene expression.Recent researches shows that there is a close connection between DNA methylation status and a variety of diseases including cancer, Alzheimer and Parkinson's disease, cardiovascular disease, and so on [1,2,3,4,5,6,7,8]. Over the years mathematical models have been a key to exploring the complexities of DNA methylation dynamics and its connection with health and in particular in the ageing process [9, 10,11]. Very recently a new model for the dynamics of the key intracellular interactions which characterize DNA methylation has been presented in [9] however, their model is based on the integer-order classical differential systems. As we have mentioned in previous works [12,13,14,15] the classical integer-order derivatives have some limitations as they are local in nature and do not possess the memory effects which are appear in most of biological systems. To overcome such limitations of traditional derivatives, in particular in the study of biological systems we have to use the powerful tool of fractional calculus [16,17,18,19,20,21,22,23,24,25]. For this purpose, in the next section, we describe the fractional calculus approach in biology, in the Sec. 3 and 4 we present our new model for DNA Methylation and in Sec.5 we show the corresponding numerical simulations.

2 Fractional calculus approach in biology

The study of complex systems and investigation of their structural and dynamical properties have attracted considerable interests among scientists in general and physicists, biologists and medical scientists in particular. Complex systems can be found almost everywhere however the highest level of complexities can be observed in the dynamics of living and

* Corresponding author e-mail: goyal.praveen2011@gmail.com

biological organisms and systems. Due to the lack of a reliable and effective tool to investigate such systems, we have not reached to the complete understanding and comprehensive pictures of the phenomena and processes which occur in these systems. Fortunately, in recent years the powerful tool of fractional calculus has been proposed for study of complex and nonlinear phenomena. It is in fact a very useful tool for describing the behavior of nonlinear systems which are characterized by: special kind of non-locality, long-term memory and fractal properties [26,27,28,29,30,31]. There exist many biological objects and systems with memory, nonlocal effects and nonlinear behaviors and such these non-localities and memory effects in biological objects and systems mean that the next state of the organism or system relies not only on its present state but also upon all of its previous states. As a result, the concept of fractional dynamics and in fact adopting fractional calculus can play an important role in the study of dynamical biological systems. As a physicist or biologist, we always are able to model natural phenomena for instance modeling of protein folding dynamics using systems of differential equations and nowadays it is well known that the fractional-order ones are more comprehensive and also incorporate memory effect and the concept of non-locality in the model.Mathematically the idea is in fact, to rewrite the ordinary governing differential equations in the fractional form by replacing the standard derivative with a fractional derivative of arbitrary order .

3 Fractional differential system (FDS) and the infinite state approach

It is well known that the integration operator plays a fundamental role in modeling and simulation of differential systems since it allows to take into account past history, initial conditions, energyand permits to predict the future of the system thanks to its distributed state [48,49]. In this paper, we will describe the fractional integrator, also called Riemann-Liouville integration operator, thanks to its infinite state representation [50,51].

3.1 . Riemann-Liouville integration

The α^{th} fractional order Riemann-Liouville integral (α real positive) of a causal function is defined by the relation [52, 53]:

$$I^{\alpha}(f(t)) = \frac{1}{\Gamma(\alpha)} \int_0^{\infty} (t-\tau)^{\alpha-1} f(\tau) d\tau, \tag{1}$$

where $\Gamma(\alpha)$ is the Gamma function. $I^{\alpha}(f(t))$ is the convolution of the function $f(t)$ with the impulse response of the fractional integration operator

$$h_{\alpha}(t) = \frac{t^{\alpha-1}}{\Gamma(\alpha)}. \tag{2}$$

whose Laplace transform is

$$I^{\alpha}(s) = L\{h_{\alpha}(t)\} = \frac{1}{s^{\alpha}} \tag{3}$$

3.2 Fractional integrator state-space representation

Practically, the Riemann-Liouville integral is carried out by a fractional integrator.It has been already demonstrated in [51,53], that $\frac{1}{s^{\alpha}}$ is a linear frequency distributed system (also known as diffusive representation [54,55]). Its frequency distributed state $z(\omega,t)$ verifies the differential equation:

$$\begin{cases} \frac{\partial z(\omega,t)}{\partial t} = -\omega z(\omega,t) + v(t) & \omega \in [0;+\infty) \\ x(t) = \int_0^{\infty} \mu_{\alpha}(\omega) z(\omega,t) d\omega \\ \mu_{\alpha}(\omega) = \frac{\sin n\pi}{\pi} \omega^{-\alpha} \quad 0 < \alpha < 1 \end{cases} \tag{4}$$

where $v(t)$ and $x(t)$ are respectively the input and the output of the fractional integrator.Because of its definition in (4), $x(t)$ is only the weighted sum of the variables $z(\omega,t)$ (with weight $\mu_{\alpha}(\omega)$ and ω ranging from 0 to $+\infty$), thus it is only a pseudo state variable whereas is the true distributed state variable [51,53]. The infinite state approach is so called by reference to the infinite dimension of $z(\omega,t)$ [52].

*Remark.*If $v(t) = \delta(t)$, the output $x(t)$ of (4) provides the fractional integrator impulse response

$$h_{\alpha}(t) = \int_0^{\infty} \mu_{\alpha}(\omega) e^{-\omega t} d\omega \tag{5}$$

Unlike (2), definition (5) stresses that $h_{\alpha}(t)$ is composed of an infinity of modes, ranging from 0 to $+\infty$. Notice that the lower modes ($\omega \to \infty$) explain the long memory behavior of the fractional integrator and fractional order systems [56].

3.3 Initial conditions

The output $x(t)$ can be obtained by the convolution of the input $v(t)$ with the fractional integrator impulse response $h_\alpha(t)$:

$$x(t) = h_\alpha(t) * v(t) = \int_{-\infty}^{t} h_\alpha(t-\tau)v(\tau)d\tau \tag{6}$$

So,

$$x(t) = \int_0^\infty \mu_\alpha(\omega)z(\omega,t_0)e^{-\omega(t-t_0)}d\omega + \int_0^t h_\alpha(t-\tau)v(\tau)d\tau \tag{7}$$

The first term represents the free response of $\frac{1}{s^\alpha}$ initialized by the initial state $z(\omega,t_0)$, whereas the second term is the forced response. This equation stresses that past history (i.e. $t < t_0$) is completely summarized by the initial condition $z(\omega,t_0)$ which is an infinite dimensional distributed variable (see [51,57,58] and references therein).

3.4 Application to Fractional differential systems (FDS)

Let us consider, the general SISO FDS governed by the following equation

$$\begin{cases} D^\alpha(\underline{X}(t)) = A\underline{X}(t) + \underline{B}e(t) & 0 < \alpha < 1 \\ y(t) = \underline{C}\underline{X}(t) \end{cases} \tag{8}$$

where D^α denotes the derivative operator of order α , $\underline{X}(t) \in R^{N\times 1}$ the pseudo-state, $y(t)$ the output, $e(t)$ the input. A, $\underline{B}$, $\underline{C}$ are known matrices and of appropriate dimension.

Similarly, to the integer order case (ODE) for which the integer integrator is the key element(see Ref. [49]). In Refs. [50,59] it has been shown that the previous FDS behaves like a fractional integrator inserted in a closed-loop (see bloc diagram depicted on figure (1)). The diagonal block $[I^\alpha]$ represents the fractional integrator operators and $\underline{z}(\omega,0)$ their corresponding initial conditions. The infinite state approach consists to associate a distributed frequency state variable

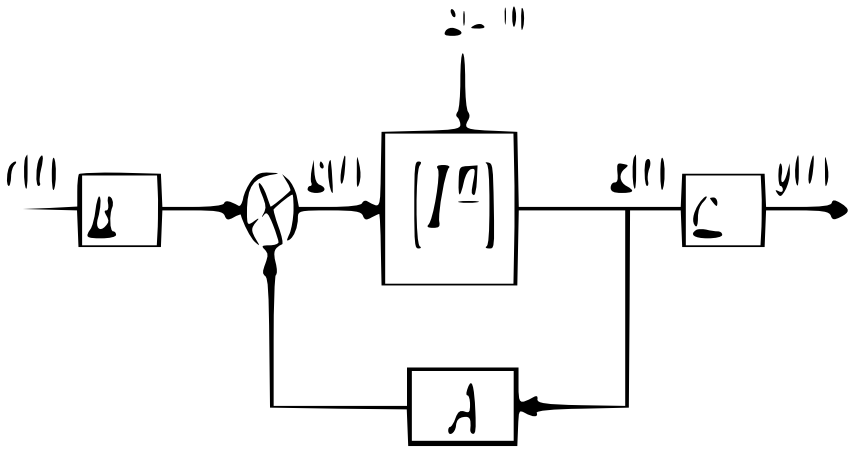

Fig. 1: FDS bloc diagram

$z_i(\omega,t)$ to the i^{th} fractional integrator $(i = 1,2\ldots,N)$.
The true state vector of FDS is then

$$\underline{Z}(\omega,t)^T = [z_1(\omega,t)\ldots z_i(\omega,t)\ldots z_N(\omega,t)] \tag{9}$$

Whereas $\underline{X}(t) = [x_1(t)\ldots x_i(t)\ldots x_N(t)]$ is the pseudo state one.
Thus,from Eqs.(4) and (8), one can derive the FDS state-space representation:

$$\begin{cases} \frac{\partial \underline{z}(\omega,t)}{\partial t} = -\omega\underline{z}(\omega,t) + A\underline{X}(t) + Be(t) \\ \underline{X}(t) = \int_0^\infty \mu_\alpha(\omega)\underline{z}(\omega,t)d\omega \\ \mu_\alpha(\omega) = \frac{\sin\alpha\pi}{\pi}\omega^{-\alpha} \quad 0 < \alpha < 1 \end{cases} \tag{10}$$

which is useful to simulate and analyze the FDS thanks to its initial conditions $\underline{z}(\omega,0)$ (see, [50] for more details).

4 Fractional dynamics of DNA methylation

In [9] authors presented a mathematical model for the dynamics of DNA methylation based on the biological assumptions (see [9] and references therein]. In their work they considered two cases of linear and nonlinear system of differential equations. In the linear case they translated DNA methylation processes as a set of ordinary differential equations as follows:

$$\begin{cases} \frac{dx_1(t)}{dt} = -k_1x_1(t) + (k_3 + \frac{1}{2}d)x_2(t) \\ \frac{dx_2(t)}{dt} = -k_1x_1(t) - (k_2 + k_3 + \frac{1}{2}d)x_2(t) + (k_4 + d)x_3(t) \\ \frac{dx_3(t)}{dt} = k_2x_2(t) - (k_4 + d)x_3(t) \end{cases} \tag{11}$$

where $x_i(t), i = 1,2,3$ denote the number of unmethylated, hemimethylated and methylatedCpG, respectively. Also, the rates of the transitions between the possible states of the CpG dyads were in turn represented by the rate constants $k_i, i = 1,..,4$ namely: methylation rate of un methylated CpG dyads, the methylation rate of hemimethylated CpG dyads, the demethylation rate of hemimethylatedCpG dyads, and the rate of DNA demethylation of methylated CpG dyads, respectively and finally the cell division rate is represented by d. However, as we mentioned in Sec. (1) the above model is based on the integer-order classical differential systems and so is not able to consider nonlocal time effects (which in particular in time domain is called memory effect) which seem to play essential role in biological systems. So, it is reasonable that we look for a comprehensive model such that it can be able to consider space-time nonlocalities. The best way for this is using the approach of fractional calculus and the framework of fractional dynamics. The commonest way to obtain a fractional differential equation for describing the evolution of a typical system is to generalize the ordinary derivative in the standard differential equation into the fractional derivative:

$$\frac{d}{dt} \to \frac{d^\alpha}{dt^\alpha} = D^\alpha \tag{12}$$

Therefore, we can easily arrive at the system of fractional differential equations for the fractional dynamics of DNA methylation by changing the first order derivative in the Eqs. (11) to a derivative of order α $(0 < \alpha < 1)$:

$$\begin{cases} D^\alpha(x_1(t)) = -k_1x_1(t) + (k_3 + \frac{1}{2}d)x_2(t) \\ D^\alpha(x_2(t)) = -k_1x_1(t) - (k_2 + k_3 + \frac{1}{2}d)x_2(t) + (k_4 + d)x_3(t) \\ D^\alpha(x_3(t)) = k_2x_2(t) - (k_4 + d)x_3(t) \end{cases} \tag{13}$$

So, the above differential equations describe the rate of change of abundance of the 3 CpG dyads in the framework of fractional dynamics. For the case of evolution of a population of CpG sites in a specific region of the genome with fixed length, the total number of CpG dyads has to be constant. Thus, we will have, $x_1(t) + x_2(t) + x_3(t) = c$ with $c > 0$ substituting the conditions in the Eqs. (13), we will derive:

$$\begin{cases} D^\alpha(x_1(t)) = (-(k_1 + k_2 + \frac{1}{2}d)x_1(t) - (k_3 + \frac{1}{2}d)x_3(t) + c(k_3 + \frac{1}{2}d) \\ D^\alpha(x_3(t)) = (-k_2x_1(t) - (k_2 + k_4 + d)x_3(t) + ck_2) \end{cases} \tag{14}$$

$$x_2(t) = c - x_1(t) - x_3(t) \tag{15}$$

As it is mentioned in [9,10] we can set the rates of the transitions i.e. k_i parameters as $k_1 = 0.012d$, $k_2 = 99d$, $k_3 = 0.11d$, $k_4 = 0.08d$ for the case of calculation of methylation levels in gene promoters, and $k_1 = 0.205d$, $k_2 = 99d$, $k_3 = 0.04d$, $k_4 = 0.08d$ for the case of calculation global genome methylation levels, also we can chose $c = 100$ for a CpG cluster of a hundred CpG dyads size.
Let us consider biological model (14) in the FDS form:

$$D^\alpha(\underline{X}(t)) = F(t, X(t)), \quad 0 < \alpha < 1 \tag{16}$$

where $\underline{X}(t) = [x_1(t), x_3(t)]^T$ and F is a continuous real-valued vector function represented by:

$$F = \begin{bmatrix} (-(k_1 + k_2 + \frac{1}{2}d)x_1(t) - (k_3 + \frac{1}{2}d)x_3(t) + c(k_3 + \frac{1}{2}d) \\ (-k_2x_1(t) - (k_2 + k_4 + d)x_3(t) + ck_2) \end{bmatrix} \tag{17}$$

Or equivalently

$$D^{\alpha}(\underline{X}(t)) = A\underline{X}(t) + \underline{B}e(t) \quad 0 < \alpha < 1 \tag{18}$$

with

$$A = \begin{bmatrix} -(k_1 + k_2 + \frac{1}{2}d) & -(k_3 + \frac{1}{2}d) \\ -k_2 & -(k_2 + k_4 + d) \end{bmatrix} \underline{B} = \begin{bmatrix} (k_3 + \frac{1}{2}d) \\ k_2 \end{bmatrix} e(t) = c \tag{19}$$

First of all, notice that, independently of the derivative order, matrix A has 2 eigenvalues λ_1, λ_2 which depend only on parameter d, k_1, k_2, k_3, k_4 and values. For example, with $d = 1, k_1 = 0.012d, k_2 = 99d, k_3 = 0.11d$ and $k_4 = 0.08d$, we have $\lambda_1 = -100.68$ and $\lambda_2 = -0.0185$, which corresponds to pseudo-time constants $\tau_1 = 54.05$ seconds and $\tau_2 = 9.93 \times 10^{-3}$ seconds. So, the ratio $\frac{\tau_1}{\tau_2} = 5.443 \times 10^3$ is very large, which means that both of x_1 and x_3 exhibit very fast and very slow transients. Since system (18) is linear, we can use the Laplace representation, which leads to

$$\begin{cases} X_1(s) = (\frac{b_{11}}{s^{\alpha} - \lambda_1} - \frac{b_{12}}{s^{\alpha} - \lambda_2})E(s) \equiv X_{11}(s) + X_{12}(s) \\ X_2(s) = (\frac{b_{31}}{s^{\alpha} - \lambda_3} - \frac{b_{32}}{s^{\alpha} - \lambda_2})E(s) \equiv X_{31}(s) + X_{32}(s) \end{cases} \tag{20}$$

with

$$\begin{cases} b_{11} = 0.6036 \quad b_{12} = 0.0064 \\ b_{21} = 99.01 \quad b_{32} = -0.0064 \end{cases} \tag{21}$$

where s, $E(s)$, $X_1(s)$ and $X_3(s)$ represent respectively, the Laplace variable and the Laplace Transform of $e(t)$, $x_1(t)$ and $x_3(t)$.

5 Numerical simulation

Simulations have been performed thanks to the infinite-state approach presented in section 3 (see [43] for more details) and Matlab [61] with $e(t) = c = 100$; $d = 1$; $k_1 = 0.012d$; k_2=99d ; $k_3 = 0.11d$; $k_4 = 0.08d$ and for different derivative orders α .In order to take into account the ratio $\frac{\tau_1}{\tau_2}$, we present $x_1(t)$, $x_3(t)$ and $x_2(t)$ with two time scales: on figure (2) for fast transients, and on figure 3 for slow transients.The integer order case $\alpha = 1$ is the reference to compare the different graphs. As explained by model (20), the mode λ_1 is dominant for fast transients (seefigure (2)), whereas the mode λ_2 characterizes the slow transients (see figure (3)).Notice, that the fast mode λ_1 is equivalent to a constant as t tends to the $+\infty$, i.e. $x_1(t) \approx \frac{-100b_{11}}{\lambda_1}$ and $x_3(t) \approx \frac{-100b_{31}}{\lambda_1}$ for slow transients (see figure (3)).Also, in (21)that $b_{32} < 0$, which explains the decrease of $x_3(t)$ on figure (3). When $\alpha < 1$, we can notice that the fast transients of pseudo-mode λ_1 is more quick than in the integer order case (see figure (2)), and reciprocally, that the transients of pseudo-mode λ_2 is more slow than with $\alpha = 1$ (see figure(3)).Notice also, that this phenomenon, which is the main feature of fractional systems, is exacerbated as α decreases.

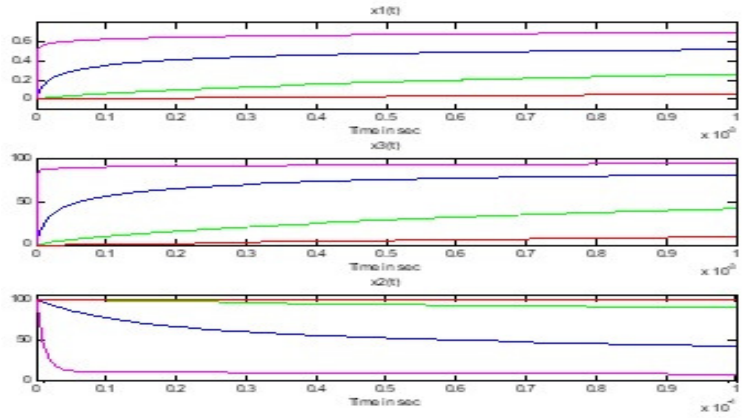

Fig. 2: $x_1(t)$, $x_3(t)$ and $x_2(t)$: $\alpha = 0.75$(green);$\alpha = 0.5$(blue);$\alpha = 0.25$(magenta)and $\alpha = 1$(red)

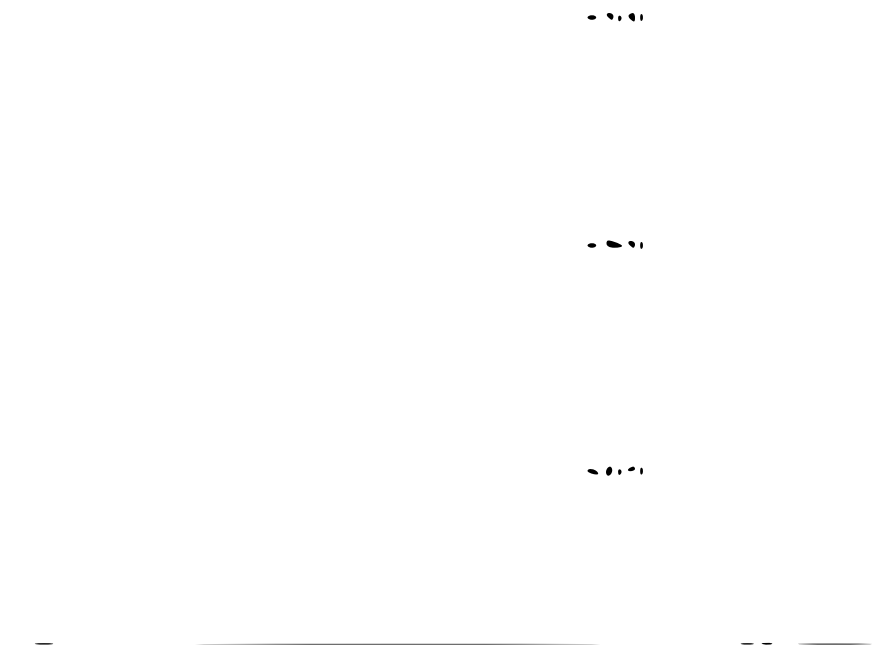

Fig. 3: $x_1(t)$, $x_3(t)$ and $x_2(t)$: $\alpha = 0.75$(green);$\alpha = 0.5$(blue);$\alpha = 0.25$(magenta)and $\alpha = 1$(red)

6 Conclusion

A number of physical and mathematical models have been presented in last few years, for the investigation of the dynamics of DNA methylation. But, almost all of these models are based on traditional integer order derivative. In order to better explore the complex dynamics of DNA methylation, in this paper, a fractional order differential model has been simulated. The analysis and the numerical simulation of this fractional model provide a first investigation on the introduction of fractional derivatives in the DNA model. Future works will investigate the relevance of this fractional model based on the ad equation between experimental data and theoretical simulations.

Acknowledgments: The article and its translation were prepared within the framework of the agreement between the Ministry of Science and High Education of the Russian Federation and the Peoples Friendship University of Russia No. 075-15-2021-603: Development of the new methodology and intellectual base for the new-generation research of Indian philosophy in correlation with the main World Philosophical Traditions. This article has beensupported also by the RUDN University Strategic Academic Leadership Program. The authors are also thankful to NBHM (DAE) Grant Number: 02011/12/2020 NBHM (R.P)/RD II/7867and Ministry of Science and High Education of the Russian Federation and the Peoples' Friend-ship University of Russia, Grant No. 104701-2-000 "Cognitive strategies of the main philosophical traditions of Eurasia" of the RUDN Strategic Academic Leadership Program "Priority-2030"

References

[1] K. D. Robertson, DNA methylation and human disease, *Nat. Rev. Genet.*, **6(8)**, 597-610,(2005).
[2] M. Kulis and M. B. Esteller, DNA Methylation and Cancer, *Adv. Genet.*, **70**, 27-56,(2010).
[3] B. P. Berman et al., Regions of focal DNA hypermethylation and long-range hypomethylation in colorectal cancer coincidewithnuclear lamina–associateddomains, *Nat. Genet.*, **44(1)**, 40–46,(2010).
[4] M. Barrachina and I. Ferrer, DNA methylation of Alzheimer disease and tauopathy-related genes in postmortem brain, *J. Neuropathol. Exp. Neurol.*, **68**, 880–891,(2009).
[5] K. G. Coupland et al., DNA methylation of the MAPT gene in Parkinson'sdiseasecohorts and modulation by vitamin E in vitro, *Mov. Disord.*, **29**, 1606–1614,(2014).
[6] L. De Mena et al., No differential DNA methylation of PARK2 in brain of Parkinson'sdisease patients and healthycontrols,*Mov. Disord.*, **28**, 2032–2033, (2013).
[7] Z. Huo et al., DNA methylation variability in Alzheimer's disease, *Neurobiol Aging.*, **76**, 35-44,(2019).

[8] M. E. Pepin et al., DNA methylation reprograms cardiac metabolic gene expression in end-stage human heart failure, *Am. J. Physiol. Heart Circ. Physiol.*, **317(4)**, H674-H684, (2019).
[9] L. Zagkos et al., *Journal of Theoretical Biology*, **462**, 184-193,(2019).
[10] A. P. McGovern et al., A dynamic multi-compartmental model of DNA methylation, *Journal of Theoretical Biology*, **310**, 14–20,(2012).
[11] M. T. Mc Auley et al., Computational modelling folate metabolism and DNA methylation, *Brief Bioinform.*, **19(2)**, 303–317, (2016).
[12] H. Nasrolahpour, Fractional Field Theory Approach to Protein Folding Dynamics , *bioRxivdoi*: 10.1101/153999,(2017)
[13] H. Nasrolahpour, Fractional Dynamics in Bioscience and Biomedicine and the Physics of Cancer, *bioRxivdoi*: 10.1101/214197,(2017).
[14] H. Nasrolahpour, Fractional Dynamics of Cancer Cells and the Future of Research in Biomedicine, *Cancer Research Journal*, **6(1)**, 16-19,(2018) .
[15] H. Nasrolahpour, Promising Role of Fractional Calculus in Biomedicine and Biophysics, *Open Access Journal of Oncology and Medicine*, **1 (1)**, 1-2,(2018).
[16] J. A. Tenreiro Machado, Fractional-Order Fourier Analysis of Human DNA, *IFAC Proceedings Volumes*, **45(2)**, 560-564,(2012).
[17] J. A. Tenreiro Machado, Fractional order description of DNA, *Applied Mathematical Modelling*, **39(14)**, 4095-4102,(2015).
[18] C. Ionescu et al., The role of fractionalcalculus in modeling biologicalphenomena: A review, *Commun.Nonlinear Sci. Numer. Simulat.*, **51**, 141-159,(2017).
[19] M. A. Khan, The dynamics of Zika virus with Caputo fractional derivative, *AIMS Math.*, **4**, 134–146,(2019).
[20] A.Mvogo et al., Fractional nonlinear dynamics of DNA breathing, *Commun Nonlinear SciNumerSimulat.*, **48**, 258-269, (2017).
[21] B. Bodo et al., Chaos, Fractional dynamical behavior of electrical activity in a model of pancreatic β-cells, *Solitons and Fractals*, **102**, 426–432,(2017).
[22] C. M.A.Pintoa, A. R.M.Carvalho, Diabetes mellitus and TB co-existence: Clinical implications from a fractional order modelling, *Appl. Math. Mod.*, **68**, 219-243,(2019).
[23] J. A. T. Machado et al., Fractional dynamics in DNA, *Commun. Nonlinear Sci. Numer. Simulat.*, **16 (8)**, 2963-2969, (2011).
[24] A. R. M. Carvalho, C. M. A. Pintoa, A delay fractional order model for the co-infection of malaria and HIV/AIDS, *Int. J.Dyn. Cont.*,**5**, 168–186,(2017).
[25] C. M. A. Pintoa, A. R. M. Carvalho, Fractional dynamics of an infection model with time-varying drug exposure, *J. Comput. Nonlinear Dynam.*, **13(9)**, 090904, (2018).
[26] V. E. Tarasov, Fractional Dynamics, *Springer*, (2011).
[27] R. Herrmann, Fractional Calculus, *World Scientific Press*, (2011).
[28] J. Klafteret al. (Eds.), Fractional Dynamics: Recent Advances, *World Scientific*, (2011).
[29] H. Nasrolahpour, N-theory: Do Quarks Have Memory?, *Prespacetime J.*,**10 (7)**, 860-865, (2019).
[30] H. Nasrolahpour, On the Memory of Nature, *Prespacetime J.*, **10 (1)**,27-33, (2019).
[31] H. Nasrolahpour, Fractional electromagnetic metamaterials, *Optik*, **203**, 163969,(2020).
[32] V. E. Tarasov, General non-local electrodynamics: Equations and non-local effects, *Annals of Physics*, **445**, 169082, (2022).
[33] V. E. Tarasov, Fractional dynamics with non-local scaling, *Commun Nonlinear Sci NumerSimulat.*, **102**, 105947,(2021).
[34] M. D.Ortigueira, J. T. Machado, The 21st century systems: An updated vision of continuous-time fractional models, *IEEE Circuits and Systems Magazine*, **22(2)**, 36-56, (2022).
[35] M. D. Ortigueira,Two-sided and regularisedRiesz-Feller derivatives, *Mathematical Methods in the Applied Sciences*, **44 (10)**, 8057-8069,(2021).
[36] H. Nasrolahpour, Algebraic long-time decay in fractional classical mechanics, *Prespacetime J.*, **3**, 1194-1196,(2012).
[37] H. Nasrolahpour, N-Theory: From LHC to Webb, *Prespacetime J.*, **13(3)**, 406-408,(2022).
[38] H. Nasrolahpour, Fotonics: Fractional dynamics of optical and photonic phenomena in complex media, *Prespacetime J.*, **13(1)**, 25-31,(2022).
[39] H. Nasrolahpour, Physics of Virus: The Special Case of Novel Coronavirus, *Prespacetime J.*, **13(1)**, 84-86,(2022).
[40] O. P. Agrawal, D.Baleanu, A Hamiltonian formulation and a direct numerical scheme for fractional optimal control problems, *Journal of Vibration and Control*, **13**, 1269-1281,(2007).
[41] D. Baleanu, O. P. Agrawal, Fractional Hamilton formalism within Caputo's derivative, *Czechoslovak Journal of Physics*, **56**, 1087-1092, (2006).
[42] D. Baleanu et al., Time-Optimal Control of Systems with Fractional Dynamics, *Journal of Vibration and Control*, **15**, 583-597,(2009).
[43] D. Baleanu, T.Avkar, Lagrangians with linear velocities within Riemann-Liouville fractional derivatives, arXiv preprint math-ph/0405012.
[44] D. Baleanuet al., On fractional Euler–Lagrange and Hamilton equations and the fractional generalization of total time derivative, *Nonlinear Dynamics*, **53**, 67-74,(2008).
[45] S. I.Muslih, D.Baleanu, Formulation of Hamiltonian equations for fractional variational problems, *Czechoslovak Journal of Physics*, **55**, 633-642,(2005).
[46] B. J. West, The Fractal Tapestry of Life: III Multifractals Entail the Fractional Calculus, *Fractal and Fractional*, **6 (4)**, 225, (2022).
[47] B. J. West, The Fractal Tapestry of Life: II Entailment of Fractional Oncology by Physiology Networks, *Frontiers in Network Physiology*, **2**, 845495,(2022).

[48] B. J. West, Fractional Calculus and the Future of Science, *Entropy*, **23 (12)**, 1566, (2021).
[49] T. Kailath, Linear system, Prentice-Hall Inc, *Englewood Cliffs, NJ,*, (1980).
[50] J.C. Trigeassou and N. Maamri, Analysis, Modeling and Stability of Fractional Order Differential Systems: The Infinite State Approach, volumes I and II, *John Wiley*, (2019).
[51] J. C. Trigeassouet al., The pseudo state space model of linear fractional differential systems, *FDA Conference*, October, Badajoz, Spain,(2010).
[52] J. C. Trigeassou et al., Improved initialization of fractional order systems, *Computers and MathematicswithApplications*, **6 (5)**, 892–907,(2013).
[53] J. C. Trigeassouand N. Maamri, State space modeling of fractional differential equations and the initial condition problem, *IEEE 6th International Conference on Systems*, Signals and Devices, SSD'09. Tunisia,(2009).
[54] D. Heleschewitz, D. Matignon, Stability properties for generalized fractional differential systems, *IFAC Conference on System, Structure and Control*, 243–248,(1998).
[55] G. Montseny, Diffusive representation of pseudo-differential time-operators, *Proceedings of ESSAIM*, **5**, 159–175,(1998).
[56] M. D. Ortigueira et al., Integer/fractional decomposition of the impulse response of fractional linearsystems, *Signal Processing*,**114** 85-88, (2015).
[57] J.C. Trigeassou, N. Maamri, Initial conditions and initialization of linear fractional differential equations,*Signal Processing*,**91(3)**, 427–436,(2011).
[58] N. Maamri et al., Physical interpretation and initialization of the fractional integrator,*International Conference on Fractional Differentiation and Its Applications*, ICFDA'14, Catania, Italy,(2014).
[59] J. C.Trigeassou, et al., *European Control Conference (ECC)*, 2453-245,(1999).
[60] N. Maamri, J. C. Trigeassou, A comparative analysis of two algorithms for the simulation of fractional differential equations, *Int. J. Dynam. Control*,**8**, 302–311,(2020).
[61] MATLAB 2014a, *TheMathWorks*, Natick, (2014).