Fractional Field Theory Approach to Protein Folding Dynamics

Hosein Nasrolahpour*
Department of Physics, School of Sciences, Tarbiat Modares University, P.O. Box 14155-4838, Tehran, Iran

Abstract
Understanding biological complexity is one of the most important scientific challenges nowadays. Protein folding is a complex process involving many interactions between the molecules. Fractional calculus is an effective modeling tool for complex systems and processes. In this work we have proposed a new fractional field theoretical approach to protein folding.

Keywords: protein folding, protein misfolding, complex process, fractional field theory

1. Introduction
Protein folding is a complex process involving many different interactions between the molecules that has attracted many attentions from physicist, chemists and biologists in recent years. Protein folding is the process by which proteins achieve rapidly and spontaneously their highly structured conformation with a certain biological function in a self-assemble manner, while misfolding process of protein can be seen as the failure to attain this fully functional conformation that may causes many different diseases such as: bone fragility, Alzheimer's disease, Parkinson disease and so on [1, 2]. There are many different approaches to address this issue such as: statistical mechanics and polymer dynamics etc. [3-7]. In the last decades, fractional calculus have found extensive applications in various fields of science from physics to biology, chemistry, engineering, economy and even in modeling of some human autoimmune diseases such as psoriasis[8-26]. Today fractional calculus is well known as an important effective modeling tool for complex systems and processes and can be used for describing various complex phenomena such as viscoelasticity, dielectric relaxations, fluid transport in fractal networks and so on [27-29].
The fractional variational principle can be considered as an important part of fractional calculus. Recently Agrawal has written a review article on this subject that can be found in [30] and discussed about various features of fractional variational calculus. Applications of fractional variational calculus have gained considerable popularity in science and engineering and many important results were obtained [31-39]. In our recent work we have propose the fractional sine-Gordon Lagrangian density, then using the fractional Euler-Lagrange equations, we have obtained fractional sine-Gordon equation [40]. Generalizing our previous results and using the approach present in [41, 42], we will propose a new fractional field theoretical approach to protein folding.
In the following, we will briefly review our mathematical tools. Then in Sec. 3 we present a new fractional protein Lagrangian density. Then using the fractional Euler-Lagrange equations we obtain its related equation of motion. Finally, in Sec. 4, we will present some conclusions.

2. Mathematical Tools
The fractional derivative has different definitions such as: Grünwald–Letnikov, Riemann-Liouville, Weyl, Riesz, Hadamard and Caputo fractional derivative [43], however in the papers cited above, the problems have been formulated mostly in terms of two types of fractional derivatives, namely Riemann-Liouville (RL) and Caputo. Among mathematicians, RL fractional derivatives have been popular largely because they are amenable to many mathematical manipulations. However, the RL derivative of a constant is not zero, and in many applications it requires fractional initial conditions

*Correspondence: Hosein Nasrolahpour, Tarbiat Modares University, Tehran, Iran.
E-Mail: hnasrolahpour@gmail.com

which are generally not specified. Many believe that fractional initial conditions are not physical. In contrast, Caputo derivative of a constant is zero, and a fractional differential equation defined in terms of Caputo derivatives require standard boundary conditions. For these reasons, Caputo fractional derivatives have been popular among engineers and scientists. In this section we briefly present some fundamental definitions. The left and the right partial Riemann–Liouville and Caputo fractional derivatives of order α_k , $0<\alpha_k<1$ of a function f depending on n variables, $x_1,...,x_n$ defined over the domain $\Omega=\prod_{i=1}^{n}[a_i,b_i]$ with respect to x_k are as follow [35]:

The Left (Forward) RL fractional derivative

$$\left({}_{+}\partial_k^{\alpha} f\right)(x)=\frac{1}{\Gamma(1-\alpha_k)}\partial x_k\int_{a_k}^{x_k}\frac{f(x_1,...,x_{k-1},u,x_{k+1},...,x_n)}{(x_k-u)^{\alpha_k}}du \tag{1}$$

The Right (Backward) RL fractional derivative

$$\left({}_{-}\partial_k^{\alpha} f\right)(x)=\frac{-1}{\Gamma(1-\alpha_k)}\partial x_k\int_{x_k}^{b_k}\frac{f(x_1,...,x_{k-1},u,x_{k+1},...,x_n)}{(u-x_k)^{\alpha_k}}du \tag{2}$$

The Left (Forward) Caputo fractional derivative

$$\left({}_{+}^{C}\partial_k^{\alpha} f\right)(x)=\frac{1}{\Gamma(1-\alpha_k)}\int_{a_k}^{x_k}\frac{\partial_u f(x_1,...,x_{k-1},u,x_{k+1},...,x_n)}{(x_k-u)^{\alpha_k}}du \tag{3}$$

The Right (Backward) Caputo fractional derivative

$$\left({}_{-}^{C}\partial_k^{\alpha} f\right)(x)=\frac{-1}{\Gamma(1-\alpha_k)}\int_{x_k}^{b_k}\frac{\partial_u f(x_1,...,x_{k-1},u,x_{k+1},...,x_n)}{(u-x_k)^{\alpha_k}}du \tag{4}$$

The fractional variational principle represents an important part of fractional calculus and has found many applications in physics. As it is mentioned in [30] there are several versions of fractional variational principles and fractional Euler-Lagrange equations due to the fact that we have several definitions for the fractional derivatives**.** In this work we use new approach presented in [35, 40] where authors developed the action principle for field systems described in terms of fractional derivatives, by use of a functional $S(\phi)$ as:

$$S(\phi)=\int L\left(\phi(x_k),\left({}_{+}^{C}\partial_k^{\alpha}\right)\phi(x_k),\left({}_{-}^{C}\partial_k^{\alpha}\right)\phi(x_k),x_k\right)(dx_k) \tag{5}$$

where $L\left(\phi(x_k),\left({}_{+}^{C}\partial_k^{\alpha}\right)\phi(x_k),\left({}_{-}^{C}\partial_k^{\alpha}\right)\phi(x_k),x_k\right)$ is a Lagrangian density function. Accordingly, x_k represents n variables x_1 to x_n, $\phi(x_k)\equiv\phi(x_1,...,x_n)$, $L\left(*,{}_{+}^{C}\partial_k^{\alpha},*,*\right)\equiv L\left(*,{}_{+}^{C}\partial_1^{\alpha},...,{}_{+}^{C}\partial_n^{\alpha},*,*\right)$, $(dx_k)\equiv dx_1...dx_n$ and the integration is taken over the entire domain Ω. From these definitions, we can obtain the fractional Euler-Lagrange equation as:

$$\frac{\partial L}{\partial\phi}+\sum_{k=1}^{n}{}_{-}\partial_k^{\alpha}\frac{\partial L}{\partial\left({}_{+}^{C}\partial_k^{\alpha}\phi\right)}+\sum_{k=1}^{n}{}_{+}\partial_k^{\beta}\frac{\partial L}{\partial\left({}_{-}^{C}\partial_k^{\beta}\phi\right)}=0 \tag{6}$$

Above equation is the Euler–Lagrange equation for the fractional field system and for $\alpha,\beta\to 1$, gives the usual Euler–Lagrange equations for classical fields.

3. Fractional Protein Lagrangian Density

In this section we present our new fractional Lagrangian model on protein folding that is in fact a fractional generalized version of the model presented recently in [41]. Using fractional Lagrangian

model we will be able to consider complex nature of protein folding. Following the model presented in [41, 42] we propose the protein Lagrangian including three terms:

I- Nonlinear unfolding ϕ^4 –protein at the initial state:

$$L_I = \frac{1}{2}\eta(x_\mu)^{2(\alpha-1)}\left(\left({}^{C}_{+}\partial^{\alpha}_{\mu}\right)\phi(x_\mu)\right)^{\dagger}\left(\left({}^{C}_{+}\partial^{\mu}_{\alpha}\right)\phi(x_\mu)\right)+\frac{m_\phi^{4\alpha}}{\lambda_\phi^{\alpha}}\left[1-\cos\left(\frac{\sqrt{\lambda_\phi}}{m_\phi}|\phi|\right)\right] \tag{7}$$

II- Nonlinear sources injected into the backbone, modeled by ψ^4 self-interaction:

$$L_{II} = \frac{1}{2}\eta(x_\mu)^{2(\alpha-1)}\left(\left({}^{C}_{+}\partial^{\alpha}_{\mu}\right)\psi(x_\mu)\right)^{\dagger}\left(\left({}^{C}_{+}\partial^{\mu}_{\alpha}\right)\psi(x_\mu)\right)+\frac{\lambda_\psi^{\alpha}}{4!}\left(\psi^{\dagger}\psi\right)^2 \tag{8}$$

III- The interaction term (with the coupling constant Λ):

$$L_{III} = -\Lambda_\alpha\left(\phi^{\dagger}\phi\right)\left(\psi^{\dagger}\psi\right) \tag{9}$$

where $\eta(x_\mu)$ is an arbitrary quantities with dimension of [second for $\mu=0$] and dimension of [meter for $\mu=1,2,3$]to ensure that all quantities have correct dimensions. The total potential (from all three terms) reads:

$$V_{tot}(\phi,\psi) = \frac{m_\phi^{4\alpha}}{\lambda_\phi^{\alpha}}\left[1-\cos\left(\frac{\sqrt{\lambda_\phi}}{m_\phi}|\phi|\right)\right]+\frac{\lambda_\psi^{\alpha}}{4!}\left(\psi^{\dagger}\psi\right)^2-\Lambda_\alpha\left(\phi^{\dagger}\phi\right)\left(\psi^{\dagger}\psi\right) \tag{10}$$

Assuming that λ_ϕ is small enough to be approximately at the same order with λ_ψ , the first term can be expanded in term of $\sqrt{\lambda_\phi}$, giving (up to the second order accuracy):

$$V_{tot}(\phi,\psi) \approx \frac{m_\phi^{2\alpha}}{2}\phi^{\dagger}\phi-\frac{\lambda_\phi^{\alpha}}{4!}(\phi^{\dagger}\phi)^2+\frac{\lambda_\psi^{\alpha}}{4!}(\psi^{\dagger}\psi)^2-\Lambda_\alpha(\phi^{\dagger}\phi)(\psi^{\dagger}\psi) \tag{11}$$

from which the total fractional Lagrangian: $L_{tot} = L_I + L_{II} + L_{III}$ can be (up to the second order accuracy) approximated by:

$$\begin{aligned} L_{tot}\left(\phi,\psi\right) = {} & \frac{1}{2}\eta(x_\mu)^{2(\alpha-1)}\left[\left(\left({}^{C}_{+}\partial^{\alpha}_{\mu}\right)\phi(x_\mu)\right)^{\dagger}\left(\left({}^{C}_{+}\partial^{\mu}_{\alpha}\right)\phi(x_\mu)\right)+\left(\left({}^{C}_{+}\partial^{\alpha}_{\mu}\right)\psi(x_\mu)\right)^{\dagger}\left(\left({}^{C}_{+}\partial^{\mu}_{\alpha}\right)\psi(x_\mu)\right)\right] \\ & +\frac{m_\phi^{2\alpha}}{2}\phi^{\dagger}\phi-\frac{\lambda_\phi^{\alpha}}{4!}(\phi^{\dagger}\phi)^2+\frac{\lambda_\psi^{\alpha}}{4!}(\psi^{\dagger}\psi)^2-\Lambda_\alpha(\phi^{\dagger}\phi)(\psi^{\dagger}\psi) \end{aligned} \tag{12}$$

From the fractional Euler–Lagrangian equations for the total Lagrangian Eq. (6) we have:

$$\frac{\partial L_{tot}}{\partial\phi}-{}^{C}_{-}\partial^{\alpha}_{\mu}\frac{\partial L_{tot}}{\partial\left({}^{C}_{+}\partial^{\alpha}_{\mu}\phi\right)}=0 \quad , \quad \frac{\partial L_{tot}}{\partial\psi}-{}^{C}_{-}\partial^{\alpha}_{\mu}\frac{\partial L_{tot}}{\partial\left({}^{C}_{+}\partial^{\alpha}_{\mu}\psi\right)}=0 \tag{13}$$

the following coupled and perturbed fractional Sine–Gordon equation and (nonlinear) fractional Klein–Gordon equation with cubic forcing in (1+1) dimension are derived:

$$\eta(\mathrm{t})^{2(\alpha-1)}\,{}_{-}\partial^{\alpha}_{t}\left({}^{C}_{+}\partial^{\alpha}_{t}\phi\right)=\eta(x)^{2(\alpha-1)}\,{}_{-}\partial^{\alpha}_{x}\left({}^{C}_{+}\partial^{\alpha}_{x}\phi\right)-\frac{m_\phi^{3\alpha}}{\sqrt{\lambda_\phi}}\sin\left(\frac{\sqrt{\lambda_\phi}}{m_\phi}|\phi|\right)+2\Lambda_\alpha|\phi||\psi|^2 \tag{14}$$

$$\eta(\mathrm{t})^{2(\alpha-1)}\,{}_{-}\partial^{\alpha}_{t}\left({}^{C}_{+}\partial^{\alpha}_{t}\psi\right)=\eta(x)^{2(\alpha-1)}\,{}_{-}\partial^{\alpha}_{x}\left({}^{C}_{+}\partial^{\alpha}_{x}\psi\right)-\frac{\lambda_\psi^{\alpha}}{6}|\psi|^3+2\Lambda_\alpha|\psi||\phi|^2 \tag{15}$$

where λ_ϕ – and λ_ψ –terms determine nonlinearities of backbone and source, respectively.

Solving these two coupled partial differential equations with specific boundary conditions would describe the contour of conformational changes for protein folding.

4. Conclusion

There are many different approaches addressing complex phenomena such as protein folding/misfolding however we believe that such these phenomena can be comprehensively understood by using fractional calculus. In this work we have proposed a new fractional field theoretical approach to protein folding. We have derived two coupled partial differential equations (i.e. fractional Sine–Gordon equation and fractional Klein–Gordon equation) that their solutions with specific boundary conditions would describe the contour of conformational changes for protein folding. We hope to present our other result in future showing important role of fractional calculus in describing complex phenomena in bio structures such as protein, DNA and RNA dynamics.

References

[1] T. R. Jahn, S. E. Radford, *Arch. Biochem. Biophys.* **469** (2008) 100–117.
[2] C. Soto, *FEBS Letters* **498** (2001) 204-207.
[3] M. Thommen et al., *Current Opinion in Structural Biology* **42** (2017) 83–89.
[4] R. B. Best and G. Hummer, *Phys. Chem. Chem. Phys.*, **13** (2011) 16902-16911.
[5] C. M. Dobson, *Nature* **426** (2003) 884-890.
E. O. Armah, *Math. Biosci.* **208(1)** (2007)1-25.
C. Z Cai, et al., *Math. Biosci.* **185(2)** (2003) 111-122.
[6] K. A. Dill, et al., *Annu. Rev. Biophys.* **37** (2008) 289–316.
[7] V. S. Pande, *Biophys J.* **73(6)** (1997)3192–3210.
[8] H. Nasrolahpour, *Prespacetime J.* **2 (8)** (2011) 1264-1269.
[9] H. Nasrolahpour, *Prespacetime J.* **2 (13)** (2011) 2053-2059.
[10] H. Nasrolahpour, *Prespacetime J.* **3 (1)** (2012) 99-108.
[11] H. Nasrolahpour, *Prespacetime J.* **3 (12)** (2012) 1194-1196.
[12] H. Nasrolahpour, *Prespacetime J.* **3 (13)** (2012) 1247-1250.
[13] H. Nasrolahpour, *Comm. Nonl. Sci. Num. Simul.* **18(9)** (2013) 2589–2593.
[14] A. Mvogo et al., *Comm. Nonl. Sci. Num. Simul.* **48** (2017) 258–269.
A. Mvogo and T. C. Kofané, *Chaos* **26** (2016) 123120.
J. A. Tenreiro Machado et al., *Comm. Nonl. Sci. Num. Simul.* **16** (2011) 2963–2969.
[15] A. G.O. Goulart et al., *Physica A* **477** (2017) 9–19.
[16] M. C. Rocca et al., *Physica A* **447** (2016) 402–410.
[17] Q. Feng, *Optik* **130** (2017) 310–323.
[18] J. F. Gómez-Aguilar, et al., *Comm. Nonl. Sci. Num. Simul.* **30**(2016)115–127.
[19] Z. Cao et al., *Journal of Molecular Liquids* **222** (2016) 1121–1127.
[20] M.A. Moreles, R. Lainez, *Comm. Nonl. Sci. Num. Simul.* **46** (2017) 81–88.
[21] M. Caputo, C. Cametti, *Physica A* **462** (2016) 705–713.
[22] V. E. Tarasov, *Journal of Mathematical Physics.* **56(10)** (2015) 1035068.
[23] V. E. Tarasov, *Nonlinear Dynamics* **80(4)** (2015) 1665-1672.
[24] V. V. Tarasova, V. E. Tarasov, *Chaos, Soliton and Frcatls* **95** (2017) 84-91.
[25] V. V. Tarasova, V. E. Tarasov, *Prog. Frac. Diff. Appl.* **3 (1)** (2017).
[26] C. Xianbing et al., *J. Syst. Sci. Complex* **29** (2016) 1565–1584.
[27] R. Hilfer, Applications of Fractional Calculus in Physics (World Scientific, 2000).
[28] R. Herrmann, Fractional Calculus (World Scientific Press, 2011).
[29] V. E. Tarasov, Fractional Dynamics (Springer, HEP, 2011).
[30] O. P. Agrawal, *Int. J. Diff. Eq.* **2012**, Article ID 521750.

[31] R. Herrmann, *Phys. Lett. A* **372** (2008) 5515.
[32] E. Goldfain, *Comm. Nonl. Sci. Num. Simul.* **13** (2008) 666–676.
[33] E. Goldfain, *Comm. Nonl. Sci. Num. Simul.* **13** (2008) 1397-1404.
[34] S. I. Muslih et al., *Int. J. Theor. Phys.* **49** (2010) 1746–1752.
[35] S. I. Muslih et al., *J. Phys. A: Math. Theor.* **43** (2010) 055203.
[36] M. J. Lazo, *Phys. Lett. A* **375** (2011) 3541-3546.
[37] R. A. El-Nabulsi, *Int. J. Theor. Phys.* **51** (2012) 3978–3992.
[38] V. E. Tarasov, *Adv. High Energy Phys.*, **2014** (2014), Article 957863.
[39] A. B. Malinowska, *Advances in Dynamical Systems and Applications* 8(1) (2013) 85–94.
[40] H. Nasrolahpour, *Prespacetime J.* **4 (6)** (2013) 604-608.
[41] M. Januar et al., *Int. J. Mod. Phys. Conf. Ser.* **9**(2012)127-132.
[42] V. G. Ivancevic, T. T. Ivancevic, *J Geom Symmetry Phys* **31** (2013) 1-56.
[43] I. Podlubny, Fractional Differential Equations (Academic Press, New York, 1999).