ISSN (Online): 2350-0530
ISSN (Print): 2394-3629
International Journal of Research -GRANTHAALAYAH
January 2021, Vol 9(1), 7 – 15
DOI: https://doi.org/10.29121/granthaalayah.v9.i1.2021.2918

APPLICATION OF MULTIDIMENSIONAL TIME MODEL TO DYNAMICAL RELATION OF POISSON SPIKE TRAINS IN NEURAL ION CURRENT MODELS AND FORMATION OF NON-CANONICAL BASES, ISLANDS, AND G-QUADRUPLEXES IN DNA, MRNA, AND RNA AT OR NEAR THE TRANSCRIPTION

Michael Fundator [*1]

[*1] Division of Behavioral and Social Sciences and Education and Board on Physics and Astronomy of the National Academy of Sciences, Engineering, and Medicine, USA

DOI: https://doi.org/10.29121/granthaalayah.v9.i1.2021.2918

Article Type: Research Article

Article Citation: Michael Fundator. (2021). APPLICATION OF MULTIDIMENSIONAL TIME MODEL TO DYNAMICAL RELATION OF POISSON SPIKE TRAINS IN NEURAL ION CURRENT MODELS AND FORMATION OF NON-CANONICAL BASES, ISLANDS, AND G-QUADRUPLEXES IN DNA, MRNA, AND RNA AT OR NEAR THE TRANSCRIPTION. International Journal of Research - GRANTHAALAYAH, 9(1), 7-15. https://doi.org/10.29121/granthaalayah.v9.i1.2021.2918

Received Date: 27 November 2020

Accepted Date: 21 December 2021

Keywords:
Kolmogorov-Chentsov Continuity Theorem
Fokker-Plank Stochastic Differential Equation
Translation and Transcription
Neural Networks

ABSTRACT

Ground breaking application of mathematics and biochemistry to explain formation of non-canonical bases, islands, G-quadruplex structures, and analog bases in DNA and mRNA at or near the transcription with connection to neural networks is implemented using statistical and stochastic methods apparatus with the addition of quantum principles. As a result the usual transience of Poisson spike trains (PST) becomes very instrumental tool for finding periodical type of solutions to Fokker-Plank (FP) stochastic differential equation (SDE). The present study develops new multidimensional methods of finding solutions to SDE. This is based on more rigorous approach to mathematical apparatus through Kolmogorov-Chentsov continuity theorem (KCCT) that allows the stochastic processes with jumps under certain conditions to have γ-Holder continuous modification, which is used as basis for finding analogous parallels in dynamics of formation of CpG and non-CpG islands (CpGI or non CpGI), repeats of G-quadruplexes, and non canonical bases during DNA (de)- methylation and neural networks.

1. INTRODUCTION

"Thousands of diseases are produced by genetic defects in channels, including many diseases of profound importance, like cystic fibrosis, epilepsy, atrial and ventricular fibrillation, and so on, as documented in many papers …. among thousands of others. Many of these diseases are caused by problems in the construction of channels, or the insertion of channels in the wrong places in the wrong cells, or in the regulation and control of channels". (Bob Eisenberg

"Crowded Charges in Ion Channels".)

Recent numerous applications of FP SDE for flux rate to the to describe the mathematics of neural networks were introduced more than 60 years ago [21]. FitzHugh's consideration of stochasticity in neural networks was based on earlier works including Hodkin's article after Kramers introduced FP SDE to the theory of rate of chemical reactions. He used notions of equilibrium, energy barrier, and memory friction. Focus on development of kinetic and dynamical theory for integrate and fire (I&F) neurons with application to simple (with inhibitory usually linear responses) and complex (characterized by strong cortical nonlinear and significant second harmonic responses excitation) cells (determined by balance between cortico-cortical input and lateral geniculate nucleus (LGN)) in visual cortex provided qualitative intuition for dynamic phenomena related to transitions to bistability and hysteresis, where system jumps back and forth between the two branches of stable states for different, critical values of some control parameter that can result in optical binding.

2. FOKKER-PLANK STOCHASTIC DIFFERENTIAL EQUATIONS FOR FLUX RATE

Large part of neural networks analysis consists of a study of reduction of infinite models to finite models that include different types of bifurcations. Bifurcations occurring in neural networks include double period bifurcations, Hopf bifurcations, saddle-node bifurcations, torus bifurcations, and homoclinic bifurcations. Thus, the analysis is related to numerous quantum theoretical assumptions.

For example in the visual cortex the kinetic equations for evolution of the probability density:

$$p = p(v, g; x, t) \tag{1}$$

to find a neuron at time t within the x^{th} the coarse-grained (CG) patch that the cortex is tiled with and are sufficiently small for the cortical architecture not to change systematically across it, but are sufficiently large to contain many (hundreds) of neurons) with voltage (v, v+ dv) and conductance (g, g + dg) that in quantum theory could be considered probability current, involves writing of the FP SDE for the probability evolution process and flux rate equation:

$$\partial_t p = -\partial_v J(v,g;t) + \frac{1}{\sigma}\partial_g(gp) + v_0\left\{p\left(v, g - \frac{f}{\sigma}; t\right) - p(v,g;t)\right\} + Nm(t)\left\{p\left(v, g - \frac{S}{N\sigma}; t\right) - p(v,g;t)\right\} \tag{2}$$

Where τ is the "leakage" time constant, σ is the time constant of the AMPA synapse (mediating transmission of electrical or chemical signal in Nervous System) , f is the synaptic strength from LGN connections, N is number of neurons, and S is the cortico-cortical coupling strength.

$$J(v,g;t) = \frac{1}{\tau}\{(v - V_R) + g(v - V_E)\}p(v,g;t) \tag{3}$$

is the flux along v, $v_0(t)$ is the (temporally modulated) rate for the Poisson spike train from the LGN

$$m(t) = \int_0^\infty J(v,g;t)|_{v=V_T}\,\partial g \tag{4}$$

Is the population-averaged firing rate per neuron in the CG patch, determined by the J-flux at the threshold to firing with normalized, dimensionless potentials related to original Hodkin-Huxley model $V_T = 1$, $V_R = 0$, and V_E = constant.

The evolution processes are certainly the stochastic processes with jumps[28], e.g. transitions between metastates and to bistability and hysteresis, Poisson spike train etc…, and only application of Kolmogorov-Chentsov continuity theorem [20, 21, 23, 24] assures the existence of $\tilde{X}$ sample continuous modification of stochastic processes with the same probability law:

$$P\ (X_t\ =\ \widetilde{X_t}) = 1; \tag{5}$$

under the conditions of existence of the constants α, ε, C for some metrics d;

$$\mathbb{E}\ \{d(X_t, X_s)^\alpha\}\ \leq \text{C}\ |\text{t-s}|^{1+\varepsilon} \text{ for all } 0\ \leq\ s, t\ \leq \text{T}; \tag{6}$$

and the modified process $\widetilde{X_t}$ would be γ- Holder continuous for every $0 < \gamma < \frac{\varepsilon}{\alpha}$. The importance of Kolmogorov's continuity criterion for the whole theory of Brownian Motion Stochastic Calculus including stochastic differentiation and integration and Stochastic Differential Equations is emphasized in [20], where the authors used this criterion for the constriction of Brownian motion.

The presence of equilibrium and voltage threshold of spike activation justifies the existence of smooth modification $\widetilde{X_t}$ for the solution of Equation (2) in the presence of Poisson spike train from the LGN for the majority of experimental conditions.

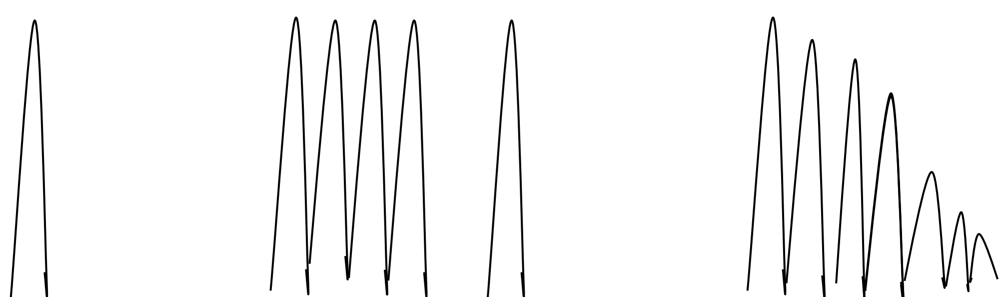
For n-dimensional process $\dot{\boldsymbol{x}}$ based on multidimensional BM $(\mathbf{W}_{\text{t}})_{t\geq 0} = (W_t^1, \ldots W_t^n)_{t\geq 0}$ linear multidimensional FP SDE is derived below (12-17) and has a form [4-17]:

$$\frac{\partial \text{p}(\dot{\text{x}},\text{t})}{\partial \text{t}} = [\ -\sum_{\text{i}=1}^{\text{d}} \frac{\partial}{\partial \text{x}_\text{i}} \text{D}_\text{i}^1(\dot{\boldsymbol{x}}\ ) + \sum_{\text{i}=1}^{\text{d}} \sum_{\text{j}=1}^{\text{d}} \frac{\partial^2}{\partial \text{x}_\text{i}\, \partial \text{x}_\text{j}} \text{D}_{\text{ij}}^2\ (\dot{\mathbf{x}}\ )\ ]\ \text{p}(\dot{\boldsymbol{x}},\text{t}) \tag{7}$$

$$\text{Operators } \sum_{\text{i}=1}^{\text{d}} \frac{\partial}{\partial \text{x}_\text{i}} \text{D}_\text{i}^1(\dot{\boldsymbol{x}}\ ) \text{ and } \sum_{\text{i}=1}^{\text{d}} \sum_{\text{j}=1}^{\text{d}} \frac{\partial^2}{\partial \text{x}_\text{i}\, \partial \text{x}_\text{j}} \text{D}_{\text{ij}}^2\ (\dot{\mathbf{x}}\ ) \tag{8}$$

are called drift vector and diffusion (correlation or dispersion) matrix respectively and include memory friction or viscosity coefficient that is involved in derivation of FP SDE.

The Poisson spike train that was mentioned in the relation to initial conditions in Equations (3) and (4) is transient in most applications of the Hodgkin-Huxley model that makes it highly instrumental tool for finding solutions to different SDE, as in the (Figure1(a and b))



a. b.

Figure1 (a and b): Possible appearances of transient Poisson spike train.

This could be explained by the argument of [22]. Simulation of the Hodgkin-Huxley model depending on the different steps increase in current produces outcomes such as:

1) Damped oscillation,
2) A single spike that is followed by a transient spike, and
3) Sustained firing.

Consideration of the case (2) can be applied to find solutions to many other examples of SDE with or without jumps. Because the spike is transient the following theorem for the multidimensional Brownian motion (BM) can be applied [20, 24]

3. TRANSIENCE

Theorem1. BM is
Point recurrent in dimension d=1. For reference and discussion look [19].
Neighborhood recurrent, but not point recurrent in d=2.
Transient in d ≥ 3.
Proposition2. The continuous modification of the solution of FP SDE is a function of BM.
Proposition3. The continuous modification of the solution of FP SDE is transient if BM is the multidimensional BM.
Definition4. Multidimensional stochastic process $(\mathbf{W}_t)_{t\geq 0} = (W_t^1, \dots W_t^n)_{t\geq 0}$ is called multidimensional BM if the processes $(W_t^1)_{t\geq 0}, \dots (W_t^n)_{t\geq 0}$ are independent BMs.

4. RULES FOR FINDING CONTINUOUS SOLUTIONS TO FOKKER-PLANK SDE [36-40].

Rule1. If there is a transient condition the solution should be sought in form of function of multidimensional BM.
Rule2. Jump processes are associated with Poisson processes [25]. If Poisson spike train is supposed to be terminated, then Rule1 should be applied. Otherwise, time interval could be divided into smaller intervals that would lead to m-dimensional time parameter $t = (t_1 \dots t_m)$ and modification of Kolmogorov's continuity criterion [23 p3]:

$$\mathbb{E}\,\{d(X_t, X_s)^{\alpha}\} \leq C_k\, |t-s|^{m+\varepsilon} \text{ for all } 0 \leq s, t \leq T; \quad (9)$$

such that $s_i, t_i \leq k$, i = 1,…,m.
Rule3. Many solutions of Hodkin- Huxley model look like periodical with period T. Then the solution is sought in form of product of sums of trigonometric functions with period T and Brownian bridge (BB) over time interval [0, T] from x to y. BB is a Gaussian process that can be described as [23]:

$$B^{x,T,y} \sim \{x + (y-x)\tfrac{t}{T} + W_t - \tfrac{t}{T} W_t\,;\ 0 \leq t \leq T\}. \quad (10); \quad \text{Or}$$

$$dB_t = \frac{y-B_t}{T-t}dt + dW_t\,;\ 0 \leq t \leq T, \text{ and } B_0 = x \quad (11).$$

It can be observed that this process is a solution to the above SDE and another remarkable property of BB is that it can be well approximated by simple combinations of multidimensional BMs.
Rule4. For special problems n-dimensional Bessel process could be used [23]:

$$R_t^{(n)} = \left((W_t^{(1)})^2 + (W_t^{(2)})^2 + \cdots + (W_t^{(n)})^2\right)^{1/2} \quad (12)$$

Or some functions of this process [23].
Rule5. For different techniques of finding appropriate number of dimensions and subsequent reduction see [6, 7, and 9].
In the above example (1)-(4) the application of FP SDE to neural networks implements reduction of dimensions to (1+1)D from originally used 3D or (2+1)D in neural networks [17] due to involvement of Poisson spike trains.

5. MAIN PROPOSITIONS 1, 2, AND 3

Main Proposition 1 According to Theorem1, existence of additional dimensions in the continuous modification of solution of FP SDE which according to Proposition2 is a function of BM.

Main Proposition 2 The same mathematical reasoning in construction of Fokker-Plank equation for the rate of transcription and translation in different fragments of DNA, messenger RNA (mRNA), and RNA and multiplicity of other experimental and theoretical factors suggest existence of the same additional dimensions of Main Proposition 1 of the continuous modification of solution of Fokker-Plank equation in neural network model.

Main Proposition 3 These additional dimensions that are mentioned in Main Proposition 1 and Main Proposition 2 are the factors in the formation of islands (CpGI and non-CpGI) of different analog bases, e.g. CpG and non-CpG (CpA, CpC, and CpT) sites that are found in bigger proportions at or near the transcription ends defying statistically supposed distributional assumptions, and non-canonical base pairs contributing to disruption of double helix in DNA.

Most, perhaps all CpGIs are usually related to the sites of transcription initiation, including thousands that are remote from currently annotated promoters [30].

6. DNA TRANSLATION AND TRANSCRIPTION AND HYPOTHESES 1 AND 2 [26, 36-40].

The addition of methyl groups to DNA is called DNA methylation, whereas deletion is called demethylation. Both processes are studied in cancer research and other genetic related diseases.

To understand the necessity of application of quantum type principles to proteins and further facilitate the discussion of what kind of principles should be applied, it would be appropriate to mention the following questions and problems in investigation of proteins, DNA, and RNA structures [26].

In contrast to RNA, DNA has a double helix structure under Watson-Crick base pairs model that identifies standard base pairs (e.g. A-T, G-C). Non-canonical base pairs contribute to disruption of double helix in DNA.

In the beginning of investigation it was supposed that the approach to structure or sequence of bases or other properties should be probabilistic or statistical because all the alternatives seemed to be equally possible. This led to some distribution assumptions about 70 years ago which were followed by careful experimental investigations until different authors became convinced that the sequences of the bases do not follow any known probability distribution function, even in the fragments of DNA. This resulted in additional investigation and served as guide to researchers until there were found two additional analog bases: 5 methylC (the fifth base analog) and 5 hydroxymethylC (the sixth base). However, the belief that the structure would be described by some Probabilistic or Statistical Mechanics Principals was still very disorienting. This situation caused some additional questions that were finally resolved with finding two more analog bases: 5-formylcytosine and 5 carboxylcytosine which are actually versions of cytosine that have been modified by Tet proteins, molecular entities that are thought to play a role in the DNA demethylation and stem cell reprogramming.

Much in contrast the dynamical approach makes the situation quite different, and certain quantum principles that were applied by Kramers during introduction of FP SDE to the theory of rate of chemical reactions suggest similar application of FP SDE to the rate of translation and transcription of different fragments of DNA and RNA. This in its turn would suggest that the formation of islands and informal pairs of bases, analog bases, or G-quadruplexes is a result of some multidimensional stochastic process involving a continuous modification of solutions of FP SDE to the rate of translation and transcription. Similarity in application of FP SDE to the rate of translation and transcription in DNA and to neural ions model with many other different facts from these theories implies that formation of islands and informal pairs of bases in DNA depends on spike trains and the like phenomena:

1) The process of transcription involves translation from certain parts of DNA that is double stranded to mRNA, where the fragments are modified and are bind to a small RNA. As a result, mRNAs bind metabolites with untranslated regions (UTR) of RNA, and then the modified parts are copied back to DNA. These parts and stages of translation and transcription and translation naturally serve as memory friction or viscosity in the formation of Fokker-Plank equation. There are also additional steps that make the process sufficiently complicated to consider application of stochastic analysis. However, as mentioned previously such considerations are insufficient, but
2) There are certain constraints in the transcription process that make it highly similar to the corresponding subject of the velocity of chemical reactions in the sense that the translation has to go through some kind of a barrier, as in the case of the particle that has to go over potential barrier. To make a partial list:

- The steps accounting for primary transcription involve consist from multiple molecular interactions followed by the transcription of DNA.
- Depending on cellular activity transcripts from DNA contribute to different RNA translations into functional proteins.
- Sequences of DNA in their turn control initiation of RNA primary transcription.

The a. and b. constraints correspond to probability of escape barrier for the particle for reaction activation in the theory of the rate of chemical reactions, c. corresponds to the notion of equilibrium, besides that these constrains also contribute to the corresponding notion of memory friction that is included in operators

$$\sum_{i=1}^{d} \frac{\partial}{\partial x_i} D_i^1(\dot{\boldsymbol{x}}) \text{ and } \sum_{i=1}^{d}\sum_{j=1}^{d} \frac{\partial^2}{\partial x_i \partial x_j} D_{ij}^2(\dot{\mathbf{x}}) \tag{13}$$

For n-dimensional process $\dot{\boldsymbol{x}}$ based on multidimensional BM linear FP SDE as in above (7) [4-17]

$$\frac{\partial p(\dot{x},t)}{\partial t} = \left[-\sum_{i=1}^{d} \frac{\partial}{\partial x_i} D_i^1(\dot{\boldsymbol{x}}) + \sum_{i=1}^{d}\sum_{j=1}^{d} \frac{\partial^2}{\partial x_i \partial x_j} D_{ij}^2(\dot{\mathbf{x}}) \right] p(\dot{\boldsymbol{x}},t) \tag{14}$$

For example, in 1D velocity of Brownian particle $\dot{x}$ = (x,v) moving in U(x) potential is given by Langevin equation:

$$\frac{dv}{dt} = -\frac{\gamma}{m} v - \frac{U'(x)}{m} + \frac{1}{m}\xi(t) \tag{15}$$

Where x, v, and m are the position, velocity, and a mass of the particle and $\xi(t)$ is noise, and γ is a coefficient of viscosity or memory friction. The Langevin equation after substitution into probability conservation equation would be written in form of FP SDE:

$$\frac{\partial p(x,v,t)}{\partial t} = -\frac{\partial(\dot{x}p(x,v,t))}{\partial x} - \frac{\partial \dot{v}p(x,v,t)}{\partial v} \tag{16}$$

Hypothesis 1 that can be viewed as explanation of Main Propositions 1, 2, and 3. The information transmitted by transient spike train is stored in the inside or surrounding human body systems and contributes to the memory friction coefficient in the process of transcription and translation, and the rate of transcription and translation can be described by multidimensional Fokker-Plank equation, based on multidimensional BM $(W_t)_{t\geq 0}$. This in its turn implies

Hypothesis 2 The number of dimensions that are involved in formation of Fokker-Plank equations in ion channels model and in the processes of transcription and translation of DNA and RNA can be considered equal.

7. FACTS AND EXAMPLES SUPPORTING MAIN PROPOSITIONS1, 2, 3 AND HYPOTHESES 3 AND 4.

Most, perhaps all CGIs are usually related to the sites of transcription initiation, including thousands that are remote from currently annotated promoters [29]. This fact in combination with Main Propositions 1, 2, and 3, Notion 1 and Hypothesis 1 imply Hypothesis 3 The intensity of distribution of CpGIs around transcription initiation can be distributed according to some probability distribution, and, if found to follow some stochastic law, could help in further investigations.

DNA methylation in many instances is transient [29,32,33].

Recent studies suggest high impact of DNA methylation on memory [35].

DNA methylation depends on stress [29].

Contrary to the expected that the connectivity of organs would require biochemical similarity (see adipose tissue [32] in #4 in Applications of Main Propositions 1, 2, and 3), only some of the total possibility of genes are expressed in any given tissue. For example, a protein that is active in a nerve cell is not expressed in the liver. [33]

The most profound examples to support the theory of CpG and GpC islands and non regular bases formation due to additional dimensions involvement in transcription and translation processes is the discrepancy of DNA methylation levels in twin children or astronauts under changing environmental conditions in questions if the changes are transient or long-lived.

Multidimensional approach to skeletal muscles and biological motion that contains information about actions, intentions, and emotions [34], and their effect through exercise on methylation process.

- Patients with amyotrophic lateral sclerosis or frontotemporal dementia develop from 500 to few thousands G_4C_2 repeats in contrast to a normal person that usually has below 8 G_4C_2s. As in the 1.
- G_4s tend to occur near end 3'.
- Hypothesis 4. Ions that are found inside G_4 structure imply ion currents which are hardly detectable, but depend as in Hypothesis 1 on different factors including the memory and the information transmitted by

transient spike trains and was stored in the inside or surrounding human body systems and later contribute to the process of transcription and translation.

8. APPLICATIONS OF MAIN PROPOSITIONS 1, 2, AND 3 HYPOTHESES 1, 2, 3 AND 4

Theoretical approach based on multidimensionality of Brownian motion in formation of Fokker-Plank equations for ion channels model and rate of transcription and translation of DNA and RNA allows multiple applications:

1) During first stages of genetic diseases.
2) In palliative care and opens a new approach of computational study during palliative care.
3) DNA methylation can carry effective predictive functions, as in the different types of diabetes due to complex correlation of DNA methylation and insulin gene expression.
4) Provides access to multiple discoveries in the direction of tissue analysis.
5) Analysis of the above 3 applications suggests that the information from the transient spikes is stored in electro-magnetical or bioossilations contributing to atrial fibrillation and similar diseases and acts only after long period of time depending on different factors. For example adipose tissue is essential in regulating whole body energy metabolism and besides adipocytes, adipose tissue contains connective tissue matrix, nerve tissue, stromovascular cells, and immune cells, and under some conditions it contributes to suppression of genes transcription[31].

9. CONCLUSION

Translation and transcription of DNA and RNA through transience, hidden dimensional consideration, memory friction, and other factors can be highly connected to neural networks and this connection can be mathematically modeled.

SOURCES OF FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST

The author have declared that no competing interests exist.

ACKNOWLEDGMENT

The author is grateful to Yehuda Goldgur from Sloan Kettering Cancer Center for the initial review and very valuable suggestions about this article.

REFERENCES

[1] M. Fundator Applications of Multidimensional Time Model for Probability Cumulative Function for Parameter and Risk Reduction. In JSM Proceedings HPS 433-441.

[2] M. Fundator. Multidimensional Time Model for PDF. In JSM Proceedings . 4029-4039.

[3] M. Fundator. Testing Statistical Hypothesis in Light of Mathematical of Probability Pre.

[4] M. Fundator. Various Extensions of Original Born-Kramers-Slater Model for Reactions Kinetics Based on Brownian Motion and Fokker-Plank Equation Including 1D, 2D, 3D, and Multi-dimensional …J. Chem 11, 90-94

[5] M. Fundator. Application of mass spectrometry to analysis of applications of Fokker-Plank equation to the velocity of chemical reactions Abstracts of papers of the ACS 256

[6] M. Fundator. Multidimensional Time Model for Probability Cumulative Function Applied to Geometrical Predictions Applied and Computational Mathematics 7 (3), 89-93
[7] M. Fundator. Geometrical, Algebraic, Functional and Correlation Inequalities Applied in Support of James-Stein Estimator for Multidimensional Projections ACM
[8] M. Fundator. Applications of multidimensional time model for PDF applied to Fokker-Planck equation and multi-scale time analysis to the rate of transcription ACS 255
[9] M. Fundator. Applications of multidimensional time model for PDF applied to Brownian motion on fractals to solution of different questions of equilibrium, depolarizati ACS 255
[10] M. Fundator. Applications of Multidimensional Time Model for PDF to Model Permeability of Plasma Membrane and Transcription of DNA for vaccination trails.
[11] M. Fundator. Applications of multidimensional time model for probability cumulative function to Brownian motion on fractals to kinetics of chemical reactions and ACS 254
[12] M. Fundator Application Of Multidimensional Time Model For Probability Cumulative Function To Brownian motion on fractals in chemical reactions Academia Journal of Scientific Research (ISSN 2315-7712) DOI: 10.15413/ajsr.2016.0167
[13] Michael Fundator Developments in Application of Multidimensional Time Model For Probability Cumulative Function to Brownian motion on fractals in chemical reactions Academia Journal of Scientific Research . In preparation for publication.
[14] Michael Fundator Multidimensional Time Model for Probability Cumulative Function and Connections Between Deterministic Computations and Probabilities Journal of Mathematics and System Science 7 (2017) 101-109 doi: 10.17265/2159-5291/2017.04.001
[15] Michael Fundator Applications of Multiple-scale Time Analysis and Different Pseudospectral Methods Along with MTM for CDF to Modeling, Estimation, Control, and Optimization of Large Scale Systems with Big Data SIAM Conferen on Control and Its Appl, Pittsburgh, Pennsylvania, July 10-12/17 in publication in Journal of Applied and Computational Mathematics.
[16] Michael Fundator Novel application of Fokker- Planck equation to the rate of transcription or translation controlled by riboswitches following Kramers Model for the Rate of Chemical Reactions and recent applications to Hodgkin-Huxley ion channel model. 7th Cambridge Symposium on Nucleic Acids Chemistry and Biology, Cambridge, UK, September 3-6/17.
[17] Michael Fundator Applications of Multidimensional Time Model for PDF to Model Permeability of Plasma Membrane and Transcription of Cytoplasmic DNA. 26th International Genetic Epidemiology Society (IGES) Annual Meeting September 09 – 11/ 17 at Queens College, Cambridge, UK.
[18] Michael Shelley et al “An effective kinetic representation of fluctuation-driven neuronal networks with application to simple and complex cells in visual cortex” PNAS May 18, 2004 101 (20) 7757-7762
[19] Michel Loeve Probability Theory. Springer
[20] Revuz, Yor Continious Martingales and Brownian Motion. Springer
[21] Guiseppe Da Prato et al Stochastic Equations in infinite Dimensions. Cambridge University Press
[22] Richard Naud, et al Neuronal Dynamics: From Single Neurons to Networks and Models of Cognition. Cambridge University Press
[23] A. N. Borodin, P. Salminen Handbook of Brownian Motion. Birkhuaser
[24] Peter Morters et al Brownian Motion Cambridge University Press
[25] E Platen et al Numerical Solutions Of Stochastic Differential Equations With Jumps in Finance Springer
[26] Michael Fundator. Various types of quantum coherence in biological systems implies scale dependence of spatio-temporal coherance. American Chemical Society Northwest Regional Meeting Portland, Oregon June 16-19/2019
[27] Hugh P. C. Robinson Stages of spike time variability during neuronal responses to transient inputs Phys. Rev. E 66, 061902 – Published 10 December 2002
[28] A. V. Rangan, G. Kovačič, and David Cai Kinetic theory for neuronal networks with fast and slow excitatory conductances driven by the same spike train. March 2008 Physical Review E 77(4 Pt 1)
[29] J. Whelan et al, Stress induced gene expression drives transient DNA methylation changes at adjacent repetitive elements.
[30] Bird A.et al CpG islands and the regulation of transcription. Genes Dev. 2011;25(10):1010-1022. doi:10.1101/gad.2037511

[31] Romain Barres, Jie Yan, Brendan Egan, Jonas Thue Treebak, Morten Rasmussen, Tomas Fritz, Kenneth Caidahl, Anna Krook, Donal J. O'Gorman, and Juleen R. Zierath Acute Exercise Remodels Promoter Methylation in Human Skeletal Muscle.

[32] J. S. Flier, et al, Adipose Tissue as an Endocrine Organ, The Journal of Clinical Endocrinology & Metabolism, Volume 89, Issue 6, 1 June 2004, Pages 2548–2556,

[33] Kangaspeska, S., Stride, B., Metivier, R., Polycarpou-Schwarz, M., Ibberson, D., Carmouche, R. P., ... Reid, G. (2008). Transient cyclical methylation of promoter DNA.

[34] N. F. Troje; Decomposing biological motion: A framework for analysis and synthesis of human gait patterns. Journal of Vision 2002;2(5):2

[35] Fisher A., Halder R, et al. DNA methylation changes in plasticity genes accompany the formation and maintenance of memory. Nature Neuroscience. 2016 Jan;19(1):102-110.

[36] Rutherford, Nicola J et al. "Length of normal alleles of C9ORF72 GGGGCC repeat do not influence disease phenotype." Neurobiology of aging vol. 33,12 (2012).

[37] Fay, Marta M et al. "RNA G-Quadruplexes in Biology: Principles and Molecular Mechanisms." Journal of molecular biology vol. 429,14 (2017): 2127-2147.

[38] Henderson, A. et al. "Detection of G-quadruplex DNA in mammalian cells." Nucleic acids research vol. 42,2 (2014): 860-9.

[39] Bochman, M. L et al. "DNA secondary structures: stability and function of G-quadruplex structures." Nature reviews. Genetics vol. 13,11 (2012): 770-80.

[40] Fundator M. Application of continuous modification of solutions of Fokker-Plank stochastic differential equations for flux rate to the Mathematics of Neural networks. #78 Biological Physics/Physics of Living Systems: A Decadal Survey

[41] Fundator M. Various types of quantum coherence in biological systems implies scale dependence of spatio-temporal coherance. #79 Biological Physics/Physics of Living Systems: A Decadal Survey

[42] Fundator M. Applications of Multidimensional Time Model for Probability Cumulative Function to model Biology, Chemical Dynamics, and Electrophysiology of Plasma Cell Membrane and for Topographic and Retinotopic Mapping. # 88White Paper for Biological Physics/Physics of Living Systems: A Decadal Survey

[43] Fundator M. Applications of Multidimensional Time Model for PDF to Model Permeability of Plasma Membrane and Transcription of Cytoplasmic DNA. # 89 White Paper for Biophysics Decadal Survey

[44] Fundator M. Applications of Multidimensional Time Model for Probability Cumulative Function to model simulations of single fiber vs. a bundle. #90 White Paper for Biophysics Decadal Survey