Abstract  The theoretical basis of neuronal coding, associated with the short term degradation in synaptic transmission, is matter of debate in the literature. In fact, electrophysiological signals are characterized as inversely proportional to stimulus intensity. Among theoretical descriptions for this phenomenon, models based on $1/f$-dependency are employed to investigate the biophysical properties of the short term synaptic depression. Thus, considering $1/f$-model, as starting point for describing synaptic depletion, we adopt a paradigmatic $q$-differential equation to obtain a generalized formalism for investigation of nonextensivity in this specific type of synaptic plasticity. Our analysis reveal nonextensivity in data from electrophysiological recordings, also uncovering a statistical crossover in neurotransmission, which gives additional support to the hypothesis of heterogenous release probability of neurotransmitters. On the other hand, the $1/f$-model achieved a satisfactory agreement with data only at lower frequency stimulations. Thus, the present work presents a method to demonstrate that short term depression is ruled by a nonextensive behavior. Our findings also better conciliate morphological and electrophysiological investigations in a coherent biophysical scenario.

Keywords  Nonextensivity, Crossover Statistics, Synaptic Depression, Neural Plasticity

1 Introduction

Neural communication is an intricate molecular process still not well understood. Information processing in the central nervous system (CNS) is mainly achieved by specialized structures called chemical synapses.
Synaptic transmission is mediated by one or more neurotransmitter substances and it is accomplished in the following steps [35, 23, 20]: (1) action potential triggers opening of voltage gated calcium channels in the nerve ending; (2) opening of these channels allows influx of calcium into the neuron terminus; (3) on the active zone (AZ) of the cell membrane, calcium triggers vesicle fusion and neurotransmitter release into the synaptic cleft; (4) secreted neurotransmitters diffuse into the synaptic cleft, reaching receptors located in the postsynaptic neuron. Postsynaptic excitatory or inhibitory current ($I_{PSC}$) or potential ($V_{PSP}$) are prompted by neurotransmitters bound in the postsynaptic receptors. These electrical events are readily assessed by electrophysiological measurements. However, sustained presynaptic activity does not necessarily release the same amount of neurotransmitter into the synaptic cleft. Within the synaptic terminal, vesicles share a crowded environment forming the readily releasable, recycling and reserve pools. These pools are successively recruited under sustained presynaptic stimulation, which initially promotes fusion of readily releasable or docked vesicles on the AZ. Higher frequencies promote an enhancement of fusion and release probability of recycling and reserve pools, respectively. In other words, there is recruitment of vesicles from both pools toward synaptic fusion. The ability of neurons to change their vesicular dynamics, affecting synaptic strength, defines the neuronal plasticity. For instance, a particular form of neuroplasticity, known as short term depression (STD), exhibited by different synapses in the brain, is characterized by $I_{PSC}$ or $V_{PSP}$ amplitude decrement or degradation of temporal fidelity of synaptic transmission, influencing the statistical properties of neurotransmission [37]. To explain this mechanism, models for STD characterization based on $1/f$-dependency were developed to be tested over different experimental paradigms [33]. Nevertheless, such models show limitations in accurately explaining experimental data. In addition, studies have shown that neurotransmitter release does not behave like a haphazard process. Therefore, it is evident the need to develop more robust theoretical strategies. In this context, a possible nonextensivity role on STD certainly contributes to clarify the complex mechanisms involved in synaptic transmission [17, 3, 34]. Bernard Katz and colleagues introduced a statistical pillar for neurotransmission, quantifying the vesicular fusion as a Gaussian phenomenon [2]. Additional reports expanded this statistical description after considering other distribution functions. Relative to STD, in spite of its limitations, binomial statistics is the conceptual basis to characterize the degradation of plasticity. However, the exploration of statistical heterogeneity in neuroplasticity has not been contemplated. We hypothesize that a possible existence of statistical transitions and nonextensivity can overcome restrictions of previous models by providing a more general scenario.

Nonextensive Statistical Mechanics (NSM) describes systems in which the entropy is not proportional to the system size, a property commonly observed in complex systems that display long-range interactions or that are out of equilibrium [27]. In this framework, Tsallis Statistics is successfully employed to investigate a variety of phenomena due to its ability to model power law phenomena [28]. Although its application is widespread, NSM remains scarcely applied to the physiology of neurotransmission, despite the confirmation of nonextensivity associated to spontaneous release at the mammalian neuromuscular junction [21, 22]. However, our previous reports did not include neither brain synapses nor the possible role of electrical stimulus on nonextensivity. To overcome these limitations, which results from using electrophysiological results collected at different synapses, we investigate whether there is nonextensivity and statistical transitions governing the neuronal communication involved in STD mechanism.

2 Methods

2.1 Experimental data

We now justify the use of the selected experimental data, before introducing the theoretical analysis (see references for detailed experimental procedures). Electrophysiology, represented by a family of empirical tools, is largely employed to investigate neuronal activity, used in clinical examinations and in high-
throughput screenings. Electrophysiological recordings are commonly applied for in vitro studies, where patch-clamp and extracellular field potential techniques are employed to understand the substrate of neuronal plasticity. Among preparations used for STD studies, one can highlight the auditory and limbic systems. Located within the auditory brainstem, the synapse formed by the calyx of Held and the main neuron medial nucleus of the mammalian trapezoid body (MNTB) is an important preparation to study STD due to their large cellular size that facilitate empirical manipulations. Additionally, due to the same morphological argument, avian bulb of Held and the nucleus laminaris make these models suitable for electrophysiological recordings, including STD assessment. Moreover, the avian end bulb of Held and the nucleus laminaris are relevant to address important questions in evolutionary neuroscience and comparative physiology of synaptic plasticity. Thus, these preparations must expand our findings beyond those computed in mammalian species. The hippocampus, part of the limbic system, is a crucial brain area responsible for spatial memory, learning and navigation. Hippocampus extraction is a straightforward process that allow cytoarchitecture preservation and accurate visualization of its different areas, being a highly used preparation for neuronal electrophysiology. Summarizing, data used here were collected from intracellular IPSC and extracellular V_PSP studies carried out in auditory synapses and hippocampal slices. Importantly, in spite of the methodological differences between extracellular and intracellular measurements, there is evidence that intracellular electrophysiological properties can be predicted by extracellular recordings. This argument supports applications of nonextensive analysis to intra or extracellular electrophysiological recordings.

2.2 Theoretical modeling

Boltzmann-Gibbs statistics (BG) states that the entropy additivity law, only valid for extensive systems, is governed by \( S = -k \int P(x) \ln P(x) \). In this case, the exponential probability density \( P(x) \propto \exp(-x) \), represents the entropy distribution of noninteracting systems. Because it considers long range correlations, NSM brings a plausible generalization of the classical description, since in their foundations a nonextensive or nonadditive entropy rule is assumed for \( S_q \) written as:

\[
S_q(A + B) = S_q(A) + S_q(B) + (1 - q)S_q(A)S_q(B)
\]  

In this case \( A \) and \( B \) are two independent systems with

\[
P(x, x')_{A+B} = P(x)_AP(x')_B
\]

In this sense, \( P(x) \) represents the probability density distribution of the macroscopic variable \( x \). Therefore, the so-called entropic index \( q \) express a nonextensivity magnitude playing a role in the system. In more concrete terms, maximization of the \( q \)-entropy leads to:

\[
S_q = \frac{k}{(q-1)} \left( 1 - \int[P(x)]^q dx \right), \quad q \in \mathbb{R}
\]

Its optimization produces a \( q \)-exponential distribution:

\[
P_q(x) \propto e_x^q \equiv [1 + (1 - q)x]^{1/(1-q)}
\]

if \( 1 + (1 - q)x \geq 0 \) and \( e_x^q = 0 \) otherwise. In the limit \( q \to 1 \) the usual BG entropy is recovered, \( S_1 \equiv S_{BG} \), and Eq.(4) converges to the usual exponential distribution.

Injection of a repetitive stimulation in the pre-synaptic terminal promotes postsynaptic efficacy decrement in \( I_{PSC} \) or \( V_{PSP} \) responses yielding STD. In order to simplify the notation lets consider a variable \( R \)
representing $I_{PSC}$ or $V_{PSP}$ responses. Assuming this simplification and considering a stimulation frequency $(f)$ injected into the presynaptic terminal one can write a nonextensive differential equation:

$$\frac{dR}{df} = -\lambda q R^q,$$

(5)

The solution of Eq.(5) is written as:

$$R = \left(\frac{1}{1 + \lambda q (q - 1)f}\right)^\frac{1}{q - 1}$$

(6)

This power law, with analogous format to the $q$-exponential function in Eq.(4), was applied to biological systems to discriminate superdiffusive patterns in dissociated cells from Hydra and to describe internucleotide interval distributions [32,5]. Still adopting $R$ notation one may write the electrical response for the vesicle depletion model as follows [33]:

$$R = \frac{1}{1 + f p r \tau}$$

(7)

where $f$, $\tau$ e $p_r$ are frequency, time constant and release probability, respectively; the Eq.(7) agree with Eq.(6) when $q = 2$, so the case approach in [33] can be seen as a special case. Briefly speaking, this model neglects vesicle interactions into the terminal, being consistent with a binomial statistical description as well. Aiming at a more generalized framework one can write:

$$\frac{dR}{df} = -\mu_r R - (\lambda q - \mu_r) R^q$$

(8)

Equation (8) predicts that frequency increasing leads to a statistical crossover from nonextensive $(q \neq 1)$ to extensive $(r = 1)$ behavior. Its solution is:

$$R = \left(\frac{1}{1 - \frac{\lambda q}{\mu_r} + \frac{\lambda q}{\mu_r} \exp\left[\frac{1}{(q - 1)\mu_r f}\right]}\right)^\frac{1}{q - 1}$$

(9)

When $\mu_r \ll \lambda q$, Eq.(9) reduces to Eq.(6) whereas for larger frequency values it undergoes a crossover to an exponential behavior. Interestingly, under assumptions Eq.(9) can also be seen as a generalization of Planck statistics [1]. However, to better understand the electrophysiological response as a function of frequency, in general terms, one can consider the following expression:

$$\frac{dR}{df} = -\mu R - (\lambda q - \mu) R^q.$$  

(10)

According to our simulations, $\lambda$ adjusts the function concavity whereas $\mu$ defines the knee position of the curve. This equation admits an analytical but approximate solution in terms of hypergeometric functions [30]. For this reason, we choose to numerically integrate Eq.(10) to investigate if nonextensivity plays a role on STD. The general format of Eq.(10) was successfully employed to detect nonextensivity and to determine the statistical crossover in studies of the flux of cosmic rays [29] and protein folding [30]. Crossover frequencies are given by the following equations. The first crossover $(f_{q}^*)$ and the second crossover $(f_1^*)$ are both obtained from Eq.(10), if $r = 1$ and $\mu_1 \ll \lambda q$:

$$f_{q}^* = \frac{1}{(\lambda q(q - 1))}.$$  

(11)
\[
f_1^* = \frac{1}{(\mu_1(q-1))}.
\]

From Eq. (10) the second crossover \((f_r^{**})\), for \(1 < r < q\) and \(\mu_r \ll \lambda_q\) is given by:

\[
f_r^{**} = \frac{[(q-1)\lambda_q]^{\frac{r}{q-1}}}{[\mu_r(r-1)]^{\frac{q-r}{q-1}}}
\]

2.3 Data analysis and optimization

We use Web Plot Digitizer to extract data from articles [15]. Parameters from Eq. (10) are estimated using genetic algorithms (GA), a class of optimization or parameter search algorithms incorporating biological evolution mechanisms [13]. We use GA to find a vector in parameter space that minimizes the root mean squared difference between experimental data and simulated points from equation (10). Computer simulations are performed in R-cran and MATLAB.

3 Results

We first apply Eq. (10) to determine either \(q\) and \(r\) indexes and crossover frequencies [9] from the calyx of Held data (Figure 1, Top). In experimental protocols of STD, this synapse is characterized by a rapid \(I_{PSC}\) decay followed by a pronounced steady-state region at higher frequency. Our simulations show a statistical transition from nonextensive \((q = 1.22)\) to extensive regime \((r = 1.00)\) at the first frequency crossover only \((f_q^* = 3.39\) Hz). We also hypothesize whether nonextensivity could be verified in non-mammalian synapses by investigating \(V_{PSP}\) data from the avian auditory system (Figure 1, Bottom) [7]. Transitions from nonextensivity \((q = 4.32)\) to extensivity \((r = 1.00)\) are observed with first and second crossover frequencies given by \(f_q^* = 15.61\) Hz and \(f_1^* = 67.48\) Hz, respectively. Next, we investigate data from the hippocampus [12] (Figure 2), which gives as estimated parameters \(q = 7.93\) and \(r = 1.01\) with \(f_q^* = 0.18\) Hz and \(f_1^* = 16.09\) Hz. Adjustments with the \(1/f\)-based equation are only partially achieved in all cases. Our results are summarized in table 1. We conclude: (a) there are statistical transition playing role in STD phenomena; (b) nonextensivity is present in auditory system synapses of mammalia and non-mammalian species; (c) nonextensivity are observed in data from intracellular and extracellular enviroments; (d) nonextensivity in dentate gyrus plasticity suggests a relation between nonextensivity and neuronal substrate involved in learning and memory of other hippocampal areas; (e) diversified statistical transitions point out that although neurotransmitter secretion has similar machinery, fine structural and functional aspects of each synapse may dictate significantly the type of statistical transition [36].

| Reference       | \(q\) | \(\lambda\) | \(\mu\) | \(r\) | \(\tau\) | \(p_r\) |
|-----------------|-------|-------------|---------|------|--------|--------|
| Figure 1, top   | 1.22  | 1.33        | -4.998  | 1.00 | 4.20   | 0.07   |
| Figure 1, bottom| 4.32  | 0.19        | 0.004   | 1.00 | 1.10   | 0.57   |
| Figure 2        | 7.93  | 0.79        | 0.009   | 1.01 | 8.00   | 0.68   |
Fig. 1 Auditory system data recorded with patch clamp technique (log-log and linear-linear scales) and respective adjustments for both models. Full lines represent fitting with Eq. (10), while traced lines correspond to adjustments with Eq. (7). Top: Data points adapted from excitatory $I_{PSC}$ recordings measured by von Gersdorff et al. ([9], fig. 2A), also analysed in Weis et al. ([33], fig. 2B) and Trommershauser et al. ([25], fig. 4A). Bottom: Fits using excitatory $V_{PSP}$ data ([7], fig. 1D).

4 Discussion

Nonextensive statistical crossovers are still not documented in brain synapses, although they have been reported in physical systems. Therefore, motivated by the nonextensive theory and limitation of the $1/f$ model in describing STD, we propose a new approach to reveal nonextensive behavior in this type of plasticity. We use a nonextensive differential equation to investigate the excitatory $I_{PSC}$ and $V_{PSP}$ responses, collected from distinct synapses. A remarkable advantage of our proposal is the simplicity to evaluate the $q$-index and the statistical crossover embedded in the experimental data. In this sense, our results are in agreement with empirical findings, while $1/f$-dependency are not adequate to describe higher frequency stimulation range.
Synaptic ending is a propitious biological system to observe the existence of nonextensivity due to its peculiar ultrastructural features [18]. For instance, at the calyx of Held, AZ area is 0.1 $\mu m^2$, with 2 docked vesicles per AZ in a terminal volume of 480$\mu m^3$, while at the hippocampal bouton, AZ area is 0.039$\mu m^2$ with 10 docked vesicles per AZ in a terminal volume of 0.08$\mu m^3$ [19]. From such morphology, one may presume that smaller volume and higher number of docked vesicles in hippocampal synapses constitute a physiological substrate consistent with a higher $q$-index, as compared to giant auditory synapses. Indeed, in restricted spatial dimensions, vesicle fusion on AZs can influence the remaining vesicles to get a probability to be dragged in a multiquantal release or even inhibiting the nearest vesicle to fuse with the terminal [4]. During the early stimulation phase the readily releasable pool is mobilized. However, further exocytosis in response to sustained stimulus, leads to depletion of the readily available pool and recruitment of the other pools of vesicles. This non-uniform or heterogenous neurotransmission is also supported by evidences of physical interactions among vesicles on the same AZ STD [10]. A heterogenous framework for STD was achieved by Trommershauser et al. assuming two $p_r$ classes. They associated a high $p_r$ to the readily releasable vesicles, released during early stimulus, and low $p_r$, for those fusing at higher stimulation levels [25]. These assumptions led the authors to study previous experiments from Gersdoff et al., whose theoretical modelling are in agreement with empirical results. However, they do not consider physical interactions between vesicles as source for a heterogenous STD mechanism.

In the present work we suggest nonextensivity and statistical crossover as important factors to explain STD heterogeneity. Heterogenous synapses, represented by statistical transitions, guarantee fidelity on the transmission of a broad range of stimulations without abolishing the postsynaptic response. Since $q > 1$ reflects fractality, our results show that STD presents a fractal behavior not previously computed in other reports. A correspondent physiological environment for $r = 1$ in auditory giant synapses and hippocampus can be interpreted still using the morphological argument discussed above. As it is well known, higher frequencies promotes a decrement of $p_r$ by exhaustion of the readily releasable pool, accelerating the recruitment of vesicles from other storages. If we consider that electrical stimulations promote neural swelling vesicle traffic facilitation is expected from these storages due to enhancement of intracellular milieu size [24]. High frequency stimulus can also accelerate the metabolism, decreasing the physical interaction likelihood on each AZ. Combined, both aspects constitute an argument for a transition from
nonextensive to extensive behavior. Altogether, we advocate that, despite similarities in exocytosis mechanisms shared by different synapses, structural and functional elements inherent to each terminal reflects STD statistical properties and nonextensivity degree.

5 Conclusion

In this report we present a new theoretical approach to understand the neuronal code. To the best of our knowledge, this is the first work which provides evidence for nonextensivity at a particular type of plasticity depression. We show that STD is well described by a \( q \)-differential equation solution, from which it is possible to evaluate both nonextensivity and statistical crossovers. The presence of crossovers provides a novel evidence in favour of statistical heterogeneity in synaptic transmission. In addition, the strategy to use extracellular and intracellular recordings from mammalian and non-mammalian synapses extrapolate nonextensivity validation to different species and brain areas. Further theoretical work will take into account a detailed investigation about the relation between the \( \rho_r \) and nonextensivity.

Acknowledgements

The authors would like to thank Constantino Tsallis for his valuable suggestions and discussions.

References

1. Beck, C., Benedek, G., Rapisarda, A., Tsallis, C.: Complexity, Metastability and Nonextensivity. World Scientific, Singapore (2005)
2. Bennett, M.R.: The origin of gaussian distributions of synaptic potentials. Prog. in Neurobiol. 46(04), 331–350 (1995). DOI 10.1016/0301-0082(94)00061-L
3. Bennett, M.R., Kears, J.L.: Statistics of transmitter release at nerve terminals. Prog. in Neurobiol. 60(06), 454–606 (2000). DOI 10.1016/S0301-0082(99)00040-4
4. Bennett, M.R., Robinson, J.: Probabilistic secretion of quanta from nerve terminals at synaptic sites on muscle cells: non-uniformity, autoinhibition and the binomial hypothesis. Proc. R. Soc. Lond. B Biol. Sci. 239(1296), 329–358 (1990)
5. Bogachev, M.I., Kayumov, A.R., Bunde, A.: Universal internucleotide statistics in full genomes: A footprint of the dna structure and packaging? PLoS ONE 9(12), e112534 (2014). DOI 10.1371/journal.pone.0112534
6. Brenowitz, S., Trussell, L.O.: Minimizing synaptic depression by control of release probability. J. Neurosci. 21(06), 1857–1867 (2001)
7. Cook, D.L., Schwindt, P.C., Grande, L.A., Spain, W.J.: Synaptic depression in the localization of sound. Nature 421(6936), 66–70 (2003). DOI 10.1038/nature01248
8. von Gersdorff, H., Borst, J.G.G.: Short-term plasticity at the calyx of held. Nat. Rev. Neurosci. 03(01), 53–64 (2002). DOI 10.1038/nn705
9. von Gersdorff, H., Schneggenburger, R., Weis, S., Neher, E.: Presynaptic depression at a calyx synapse: The small contribution of metabotropic glutamate receptors. J. Neurosci. 17(21), 8137–8146 (1997)
10. Harlow, M.L., Ress, D., Stoschek, A., Marshall, R.M., McMahan, U.J.: The architecture of active zone material at the frog’s neuromuscular junction. Nature 409(6819), 417–428 (2001). DOI 10.1038/35054000
11. Henze, D.A., Borhegyi, Z., Csicsvari, J., Mamiya, A., Harris, K.D., Buzsaki, G.: Intracellular features predicted by extracellular recordings in the hippocampus in vivo. J. Neurophysiol. 84(01), 390–400 (2000)
12. Kilbride, J., Rush, A.M., Rowan, M.J., Anwyl, R.: Presynaptic group ii mglur inhibition of short-term depression in the medial perforant path of the dentate gyrus in vitro. J. Neurophysiol. 85(06), 2509–2515 (2001)
13. Mitchell, M.: An Introduction to Genetic Algorithms. MIT Press, Cambridge (1996)
14. Oleskevich, S., Youssoufian, Walmsley, B.: Presynaptic plasticity at two giant auditory synapses in normal and deaf mice. J. Physiol. (London) 560(03), 709–719 (2004). DOI 10.1113/jphysiol.2004.066662
15. Kohatgi, A.: Webplotdigitizer: Html5 based online tool to extract numerical data from plot images. http://arohatgi.info/WebPlotDigitizer Version 3.9 (2015)
16. Rouach, N., Nicoll, R.: Endocannabinoids contribute to short-term but not long-term mglur-induced depression in the hippocampus. Eur. J. Neurosci. 19(04), 1017–1020 (2003). DOI 10.1046/j.1460-9586.2003.02823.x
17. Sakaba, T., Schneggenburger, R., Neher, E.: Estimation of quantal parameters at the calyx of held synapse. Neurosci. Res. 44(04), 343–356 (2002). DOI 10.1016/S0168-0102(02)00174-8
18. Satzler, K., Sohl, L.F., Bollmann, J.H., Borst, J.G.G., Frotscher, M., Sakmann, B., Lubke, J.H.R.: Three-dimensional reconstruction of a calyx of Held and its postsynaptic principal neuron in the medial nucleus of the trapezoid body. J. Neurosci. 22(24), 10,567–10,579 (2002)
19. Schikorski, T., Stevens, C.F.: Quantitative ultrastructural analysis of hippocampal excitatory synapses. J. Neurosci. 25(15), 5857–5867 (1997)
20. Schneggenburger, R., Forsythe, I.D.: The calyx of Held. Cell Tissue Res. 326(02), 311–337 (2006). DOI 10.1007/s00441-006-0272-7
21. Silva, A.J., Lima, R.F., Moret, M.A.: Nonextensivity and self-affinity in the mammalian neuromuscular junction. Physical Review E 84(01), 041,925–1–041,925–6 (2011). DOI 10.1142/S0218127412300303
22. Silva, A.J., Trindade, M.A.S., Santos, D.O.C., Lima, R.F.: Maximum-likelihood q-estimator uncovers the role of potassium at neuromuscular junctions. Biol. Cybern. 110(01), 31–40 (2016). DOI 10.1007/s00422-015-0673-3
23. Sudhof, T.C.: The synaptic vesicle cycle. Annu. Rev. Neurosci. 27, 509–547 (2004). DOI 10.1146/annurev.neuro.26.041002.131412
24. Tasaki, I., Byrne, P.M.: Volume expansion of nonmyelinated nerve fibers during impulse conduction. Biophys. J. 57(03), 633–635 (1990). DOI 10.1016/S0006-3495(90)82580-7
25. Trommershauser, J., Schneggenburger, R., Zippelius, A., Neher, E.: Heterogeneous presynaptic release probabilities: functional relevance for short-term plasticity. Biophys. J. 84(6819), 1563–1579 (2003). DOI 10.1016/S0006-3495(03)74967-4
26. Trussell, L.O., Popper, A.N., Fay, R.R.: Synaptic Mechanisms in the Auditory System. Springer, New York (2012)
27. Tsallis, C.: Some open points in nonextensive statistical mechanics. International Journal of Bifurcation and Chaos 22(09), 1230,030 (2012). DOI 10.1142/S0218127412300303
28. Tsallis, C., Anjos, J.C., Borges, E.P.: Fluxes of cosmic rays: a delicately balanced stationary state. Phys. Letters 310(05-06), 372–376 (2003). DOI http://dx.doi.org/10.1016/S0375-9601(03)00377-3
29. Tsallis, C., Bemski, G., Mendes, R.S.: Is re-association in folded proteins a case of nonextensivity? Phys. Letters 27(01-02), 93–98 (1999). DOI http://dx.doi.org/10.1016/S0375-9601(99)00270-4
30. Wei, S., Schneggenburger, R., Neher, E.: Properties of a model of calcium-dependent vesicle pool dynamics and short term synaptic depression. Biophys. J. 77(05), 2418–2429 (1999). DOI 10.1016/S0006-3495(99)77079-7
31. Wernig, A.: Estimates of statistical release parameters from crayfish and frog neuromuscular junctions. J. Physiol. (London) 244(01), 207–221 (1975). DOI 10.1113/jphysiol.1975.sp010792
32. Xu-Friedman, M.A., Regehr, W.G.: Structural contributions to short-term synaptic plasticity. Physiol. Rev. 84(01), 69–85 (2004). DOI 10.1152/physrev.00016.2003
33. Zucker, R., Regehr, W.G.: Structural contributions to short-term synaptic plasticity. Annu. Rev. Physiol. 64(01), 355–455 (2002). DOI 10.1146/annurev.physiol.64.092501.114547