

# Adaptation Reduces Variability of the Neuronal Population Code

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Sequences of events in noise-driven excitable systems with slow variables often show serial correlations among their intervals of events. Here, we employ a master equation for generalized non-renewal processes to calculate the interval and count statistics of superimposed processes governed by a slow adaptation variable. For an ensemble of spike-frequency adapting neurons, this results in the regularization of the population activity and an enhanced post-synaptic signal decoding. We confirm our theoretical results in a population of cortical neurons recorded *in vivo*.

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Statistical models of events assuming the renewal property, that the instantaneous probability for the occurrence of an event depends uniquely on the time since the last event, enjoys a long history of interest and applications in physics. However, many event processes in nature violate the renewal property. For instance, it is known that photon emission in multilevel quantum systems constitutes a non-renewal process [1]. Likewise, the time series of earthquakes typically exhibits a memory of previous shocks [2], as do the times of activated escape from a metastable state, as encountered in various scientific fields such as chemical, biological, and solid state physics [3]. Often, the departure from the renewal property arises when the process under study is modulated by some slow variable, which results in serial correlations among the intervals between successive events. In particular, the majority of spiking neurons in the nervous systems of different species show a serial dependence between inter-event intervals due to the fact that their spiking activity is modulated by an intrinsic slow variable of self-inhibition, a phenomenon known as spike-frequency adaptation [4].

In this letter, we present a non-renewal formalism based on a population density treatment that enables us to quantitatively study ensemble processes augmented with a slow noise variable. We formally derive general expressions for the higher-order interval and count statistics of single and superimposed non-renewal processes for arbitrary observation times. In spiking neurons, intrinsic mechanisms of adaptation reduce output variability and facilitate population coding in neural ensembles. We confirm our analytic results in a set of experimental *in vivo* recordings and analyse their implications for the read-out properties of a postsynaptic neural decoder.

*Non-renewal Master Equation.* We define the limiting probability density for an event given the state variable  $x$  by the so-called hazard function  $h(x)$  [5]. Here, we assume  $x$  has a shot-noise-like dynamics, which is widely used as a phenomenological model of spike induced neu-

ronal adaptation [6]

$$\dot{x} := -x(t)/\tau + q \sum_k \delta(t - t_k), \quad (1)$$

where  $\delta$  is the Dirac delta function,  $t_k$  is the time of the  $k^{\text{th}}$  event, and  $q$  is the quantile change in  $x$  at each event. The dynamics of  $x$  deviates from standard treatments of shot-noise (such as in [7]) in that the rate of events has a dependence on  $x$  as expressed by the hazard function  $h(x)$ . It is straightforward to show that the distribution of  $x$  in an ensemble, denoted by  $Pr(x, t)$ , is governed by

$$\begin{aligned} \partial_t Pr(x, t) = & \partial_x \left[ \frac{x}{\tau} Pr(x, t) \right] + h(x - q, t) Pr(x - q, t) \\ & - h(x, t) Pr(x, t). \end{aligned} \quad (2)$$

Much insight can be gained by applying the method of characteristics [8] to establish a link between the state variable  $x$  and its time-like variable  $t_x$ . For Eq. (1) we define  $t_x = \eta(x) := -\tau \ln(x/q)$ , whereby  $\frac{d}{dt} t_x = 1$ . When an event occurs,  $t_x \mapsto \psi(t_x)$ , where  $\psi(t_x) = \eta(\eta^{-1}(t_x) + q) = -\tau \ln(e^{-t_x/\tau} + 1)$  with its inverse given by  $\psi(t_x)^{-1} = -\tau \ln(e^{-t_x/\tau} - 1)$ . This transformation of variables to  $t_x$  elucidates the connection of the model to renewal theory. Here, the reset condition after each event is not  $t_x \mapsto 0$  (renewal) but  $t_x \mapsto \eta(x+q)$  [5]. Therefore, the variable  $t_x$  that we may call a 'pseudo age' is a general state variable that no longer represents the time since the last event (age). Transforming variables in Eq. (2) from  $x$  to  $t_x$  yields in the steady state

$$\begin{aligned} \partial_{t_x} Pr(t_x) = & -h(t_x) Pr(t_x) \\ & + (1 - \Theta_0(t_x)) [h(\psi^{-1}(t_x)) Pr(\psi^{-1}(t_x))], \end{aligned} \quad (3)$$

where  $\Theta_0(t_x)$  is the Heaviside step function, and for convenience we defined  $\psi^{-1}(t_x \geq 0) \equiv 0$ . An efficient algorithm for solving Eq. (3) is given in [6]. We denote this solution by  $Pr_{eq}(t_x)$ . The distribution of  $t_x$  just prior to an event is a quantity of interest and it is derived as  $Pr^*(t_x) = h(t_x) Pr_{eq}(t_x) / r_{eq}$ , where  $r_{eq} = \int h(t_x) Pr_{eq}(t_x) dt_x$  is a normalizing constant and also the process intensity or rate of the ensemble. Similarly, one

can derive the distribution of  $t_x$  just after the event,  $\Pr^\dagger(t_x)$ , as it is related to  $\Pr^*(t_x)$  by  $\psi$  [6]. Then the relationship between  $t_x$  and the ordinary inter-event interval distribution can be written as

$$\rho(\Delta) = \int h(t_x + \Delta) \Omega(t_x + \Delta) \Pr^\dagger(t_x) dt_x, \quad (4)$$

where  $\Omega(t_x + \Delta) = e^{-\int_{t_x}^{t_x + \Delta} h(t_x + u) du}$ . Now the  $n^{\text{th}}$  moment  $\mu_n$  of the distribution and its coefficient of variation  $C_v$  can be easily determined.

*Counting Statistics.* In order to derive the count distribution of a continuous time state-dependent process, we generalize the elegant approach for deriving the moment generating function as introduced in [9]. We define the joint probability density  $\rho_n(t_n, t_x^n | t_x^0)$  that an  $n^{\text{th}}$  event occurs at time  $t_n$  where the state variable is  $t_x^n$ . Thereafter, we recursively derive the Laplace transform of this joint density and apply the Bra-ket notation

$$\tilde{\rho}_{n+1}(s, t_x^{n+1} | t_x^0) = \tilde{\rho}_n(s, t_x^n | t_x^0) |\tilde{\rho}(s, t_x^{n+1} | t_x^n)\rangle, \quad (5)$$

where  $\rho_1(t_1, t_x^1 | t_x^0) = \rho(t_1, t_x^1 | t_x^0)$ . Next, defining the operator  $\mathbf{P}_n(s)$  as suggested in [9] we obtain

$$\tilde{\rho}_n(s) = \langle 1 | \mathbf{P}_n(s) | \text{Pr}_{eq} \rangle = \langle 1 | [\mathbf{P}(s)]^n | \text{Pr}_{eq} \rangle, \quad (6)$$

where the operator  $\mathbf{P}$  relates to  $\tilde{\rho}(s)$ , which interestingly corresponds to the moment generating function of the sum of  $n$  non-independent intervals  $\tilde{f}_n(s)$  as defined in [10]. Now, following Eqs. (2.15) and (2.16) in [10] we can derive the Laplace transform of the probability density of observing  $n$  events in a given time window, denoted as  $\tilde{P}(n, s)$ .

The Fano factor provides an index for the quantification of the count variability. It is defined as  $J_T = \sigma_T^2 / \mu_T$ , where  $\sigma_T^2$  and  $\mu_T$  are the variance and the mean of the number of events in a certain time window  $T$ . It follows from the additive property of the expectation that  $\mu_T = \int_0^T r(u) du$  and since we assumed a homogeneous process, the firing rate is constant, hence  $\mu_T = r_{eq} T = T / \mu_1$ . To calculate the second moment of  $\tilde{P}(n, s)$  we derive the autocorrelation function

$$\tilde{\mathcal{A}}_s = r_{eq} \sum_k \tilde{\rho}_k(s) = r_{eq} \langle 1 | \mathbf{P}(s) / (\mathbf{I} - \mathbf{P}(s)) | \text{Pr}_{eq} \rangle, \quad (7)$$

where  $\mathbf{I}$  is the identity operator. Note, when assuming a renewal interval distribution in Eq. (4) one obtains  $\tilde{\mathcal{A}}_s^r = \tilde{\rho}(s) / (1 - \tilde{\rho}(s))$ . Now, by using Eq. (7) and the Eq. (3.3) in [10], the second moment of the count statistics can be derived. Thus, we obtain the Fano factor

$$J_T = 1 + (2/T) \int_0^T (T - u) \mathcal{A}(u) du - r_{eq} T, \quad (8)$$

where  $\mathcal{A}(t) = \mathcal{L}^{-1}[\tilde{\mathcal{A}}_s]$ . The asymptotic property of  $F = \lim_{T \rightarrow \infty} J_T$  can be derived from the result stated in Eq. (7.8) in [10] as

$$\lim_{s \rightarrow 0} [\tilde{\mathcal{A}}_s - 1/\mu_1 s] = C_v^2 [1/2 + \sum_{k=1}^{\infty} \xi_k] - 1/2, \quad (9)$$

where  $\xi_k$  is the linear correlation coefficient between two  $k$  lagged intervals. Provided the limit exists, we find  $F = C_v^2 [1 + 2 \sum_{k=1}^{\infty} \xi_k]$  in [11].

*Superposition.* We now generalize our results on the counting statistics to the superposition of independent point processes. This is of practical interest in all cases where we observe superimposed events that stem from multiple independent process, e.g. in photon detection devices, or in the case of a postsynaptic neuron that receives converging inputs from multiple lines. We study the superposition of  $k$  stationary, orderly, and independent processes. The ensemble process will have a rate  $\tilde{r} = \sum_{i=1}^k r_i$ . The autocorrelation function of the ensemble process is given by Eq. (4.18) in [12] where  $\tilde{\mathcal{A}}(u) = \tilde{r} + \tilde{r}^{-1} \sum_{i=1}^k r_i [\mathcal{A}_i(u) - r_i]$ . Therefore, the ensemble autocorrelation function is the linear sum of individuals. Clearly, if the individual  $\mathcal{A}_i(u)$  are non-renewal, then the resulting process will also be non-renewal. Here, for the sake of simplicity, we derive the desired relationship between  $C_v^2$  and  $\tilde{F}$  for  $k$  identical processes. Thus, the autocorrelation of  $k$  similar processes is  $\tilde{\mathcal{A}}(u) = k \mathcal{A}_i(u)$ , and therefore Eq. (9) becomes  $\lim_{s \rightarrow 0} [\tilde{\mathcal{A}}_s - 1/\mu_1 s] = \text{CV}^2 [1/2 + \Xi] - 1/2$ , where  $\text{CV}$  and  $\Xi = \sum_{i=1}^{\infty} \Xi_i$  are the coefficient of variation and the interval correlations of the superimposed process. Substituting into Eq. (9), we find

$$\text{CV}^2 [1 + 2\Xi] = C_v^2 [1 + 2 \sum_{i=1}^{\infty} \xi_i]. \quad (10)$$

The left hand side of Eq. (10) is indeed the Fano factor  $\tilde{F}$  of the ensemble process as desired. Now, [12] suggests as  $k \rightarrow \infty$ ,  $\text{CV}^2 \rightarrow 1$ . Interestingly, if all individual processes fulfill the renewal condition, it follows from Eq. (10) that  $\tilde{F} = C_v^2 = [1 + 2\Xi]$ , and therefore if  $C_v^2 \neq 1$  the population activity is non-renewal with  $\Xi < 0$  ( $\Xi > 0$ ) for processes with  $C_v^2 > 1$  ( $C_v^2 < 1$ ). This important finding explains the numerical observation in [13]. Generally, Eq. (10) expresses that the relationship between  $C_v^2$  and  $F$  of the individual processes transfers to the superimposed process.

*Adaptation in a Neuronal Ensemble.* In [6] it has been shown by an adiabatic elimination of fast variables that the master equation description of a detailed neuron model including voltage dynamics, conductance-based synapses, and spike-induced adaptation reduces to a stochastic process of the form  $x(t)$  in Eq. (1). The corresponding hazard function can be approximated as

$$\hat{h}(x) = a_t \exp(-b_t x), \quad (11)$$

where  $a_t$  and  $b_t$  are determined by the statistics of inputs [5] and the equilibrium rate consistency equation  $r_{eq} \approx \hat{h}(r_{eq} \tau)$  [6] with the solution

$$r_{eq} = \mathcal{W}(abq\tau) / (bq\tau), \quad (12)$$

where  $\mathcal{W}$  is the Lambert function. In the case of vanishing adaptation ( $bq \rightarrow 0$ ) the process approaches the Poisson process with  $r_{eq} \rightarrow a$ .

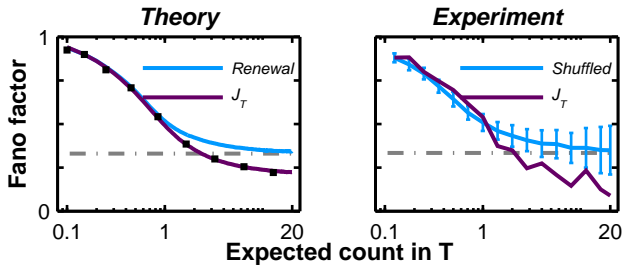


FIG. 1. Adaptation reduces the Fano factor of the ensemble process. **Left** Magenta:  $J_T$  for arbitrary observation time  $T$  according to Eqs. (8) and (11) with  $bq = 1.4$ ,  $a = 5.0$  and  $\tau = 400ms$ . Blue: Fano factor for equivalent renewal ensemble process with interval distribution of Eq. (4). Square Dots: Numerical estimated Fano factor for superposition of the 5 realization runs of the full-detailed adaptive neuron model as in [6]. Dash-dotted line:  $C_v^2$ . **Right** Magenta: Empirical  $\hat{J}_T$  estimated from the pooled spike trains of 5 cortical neurons. Blue: Fano factor for the pool of shuffled spike trains. Dash-dotted: Average  $C_v^2$  of the 5 individual spike trains.

We show in [5] that the adaptation dynamics in Eq. (1) produces negative serial correlations  $\xi_k < 0$  among arbitrary inter-event intervals of lag  $k$ . The strength of serial correlation decays with increasing lag  $k$  and depends on the mean adaptation,  $E[x] = r_{eq}q\tau$ . Such a vanishing of negative serial interval correlations with increasing lag is well supported by a large body of experimental evidence [4]. The departure from the renewal property induced by adaptation reduces the Fano factor Eq. (8) for the single process as well as for the population model of superimposed processes.

We validate our analytic result of the reduced Fano factor in a set of experimental spike trains of  $N = 5$  *in vivo* intracellular recorded neurons in the somatosensory cortex of the rat. The spontaneous activity of each of these neurons shows negative serial interval correlations [14] where the empirical sum over correlation coefficients amounts to an average  $\sum_{i=1}^{10} \xi_i = -0.28$ . We construct the population activity by superimposing all 5 spike trains. Thereafter, we estimate the Fano factor as a function of the observation time and compare it to the case where, prior to superposition, renewal statistics is enforced for each individual neuron through interval shuffling. Our experimental observation in Fig. 1 (Right) confirms the theoretical prediction of a reduced Fano factor due to the non-renewal statistics of the individual neurons.

**Benefits for Neural Coding.** We provide three arguments that demonstrate how the mechanism of spike-frequency adaptation benefits neural processing and population coding. First, our result of a reduced Fano factor  $\tilde{F} < C_v^2$  for the population activity of stationary adaptive processes ( $bq > 0$ ) directly implies a reduction of the noise in the neuronal population rate code. Our analysis of a set of cortical data suggests a reduction of  $> 50\%$

for long observation times. The reduction of  $J_T$  in Fig. 1 becomes significant even for small observation times of  $\approx 2$  average intervals, which is a relevant time scale for the transmission of a population rate signal. This result is reminiscent of an effect that has previously been acknowledged as noise shaping expressed in the reduction of the low frequency power in a spectral analysis of spike trains with negative serial interval correlations [15]. Our result confirms their findings at the population level.

Our second argument is concerned with the transmission of a population rate signal. We may define a functional neural ensemble by the common postsynaptic target neuron that receives the converging input of all ensemble members. To elucidate the postsynaptic effect of adaptation we simplify the ensemble autocorrelation function  $\mathcal{A}(u)$  following [16] with an exponential approximation

$$\hat{\mathcal{A}}(u) = r_{eq}\delta(u) + [(F - 1)/2\tau_c] \exp(-u/\tau_c). \quad (13)$$

For given observation time window  $u$ , the reduction of  $F$  implies that  $\hat{\mathcal{A}}_u^r < \hat{\mathcal{A}}_u$ . Therefore, the postsynaptic neuron receives inputs from an adaptive ensemble that expresses an extended autocorrelation structure as compared to the inputs from a non-adaptive ensemble. Following the theory on the effect of input autocorrelation on signal transmission in spiking neurons as developed in [16], this facilitates a faster and more reliable transmission of the modulated input rate signal by the postsynaptic target neuron.

Finally we argue that a postsynaptic neuron can better decode a small change in its input if the presynaptic neurons are adaptive. To this end, we compute the information gain of the postsynaptic activity of an adaptive presynaptic ensemble when  $\hat{h}(x)$  is adiabatically transferred to  $\hat{h}(x - \epsilon)$  with a small change  $\epsilon$  in the input ensemble. We apply the Kullback-Leibler divergence to the counting statistics in Eq. (6) before and after the adiabatic change in the input

$$D_{KL}(\tilde{\rho}_n^\epsilon || \tilde{\rho}_n) = \sum_i \tilde{\rho}_i^\epsilon(s) \ln(\tilde{\rho}_i^\epsilon(s)/\tilde{\rho}_i(s)), \quad (14)$$

where  $i$  is the number of events in a given time window. Using Eq. (7) we obtain  $D_{KL}(\tilde{\rho}_s^\epsilon || \tilde{\rho}_s) = \mathcal{A}_s^\epsilon [\ln(\mathcal{A}_s^\epsilon/\mathcal{A}_s)]$ . From Eqs. (1) and (12) we know that the mean adaptation after the change is  $E[x^\epsilon] = \tau q r_{eq}^\epsilon$ . If  $\epsilon > 0$  it follows that  $r_{eq}^\epsilon \geq r_{eq}$ . Therefore the mean adaptation level increases and the adapted process exhibits stronger negative serial correlations and  $\mathcal{A}_s^\epsilon > \mathcal{A}_s$ . Thus, by Eq. (13), it is straight forward to deduce that  $D_{KL} > D_{KL}^r$ , for non-adaptive and adaptive processes with identical identical interval distributions.

We now compute the information gain of the adaptive ensemble process relative to a matched Poisson rate model. For different initial rate values  $r_{eq}$  we assume a small but fixed increase  $\epsilon$  in the input that we express in parameter changes  $a^\epsilon$  and  $b^\epsilon$  in Eq. (11) as outlined in

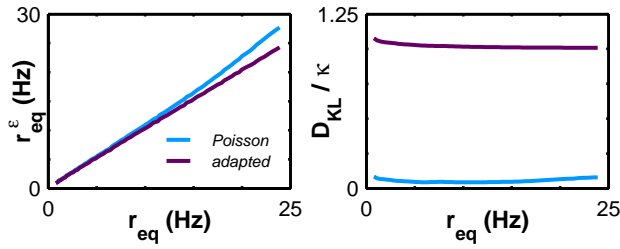


FIG. 2. Information gain due to adaptation. **Left:** Transfer of equilibrium rate for fixed  $\epsilon$  in adaptive and Poisson rate model. **Right:** Kullback-Leibler Divergence per spike for counting statistics is higher in the adaptive process.

[5]. This leads to an increase  $\kappa = r_{eq}^\epsilon - r_{eq}$  in rate that is effectively constant over a wide range of initial values  $r_{eq}$  (Fig. 2, Left). In the rate model, assuming the same initial value of  $r_{eq}$ , the same input step leads to a higher equilibrium rate increase  $\kappa^{Poisson} > \kappa$ , which depends on the initial rate (Fig. 2, Left) because the rate model lacks a mechanism of self-inhibition, which in the adaptive model counteracts the rate increase. Thereafter, we compute the Kullback-Leibler divergence for both models and normalize it by the change in the output rate  $\kappa$ . The result in Fig. 2 (Right) shows that  $D_{KL}/\kappa$  is larger for the adaptive model than for the rate model across the range of tested input rates. Thus, the information per extra spike is larger in the adaptive ensemble than in the renewal ensemble, and a postsynaptic neuron can discriminate small changes  $\epsilon$  more efficiently, even though the absolute change in firing rate is lower.

*Discussion.* Our results point out a new aspect of spike frequency adaptation that benefits the reliable transmission and postsynaptic decoding of the neural population code. This aspect adds to the known properties of compression and temporal filtering of sensory input signals [17] in spike frequency adapting neurons. The specific result of Eq. (10) is also of practical consequence for the empirical analysis of the so-called multi-unit activity. By estimating Fano factor and serial correlations we readily obtain an estimate of the average  $C_v$  and serial correlation of the individual processes.

We developed a new formalism to treat event emitting systems that are influenced by a slow state variable, and we provide a number of useful general results on the higher order event statistics of superimposed renewal and non-renewal event processes, which are applicable to a wide range of event-based systems in nature [5]. The derivation of the state dependent hazard and master equation [6] assumes incoherent input fluctuation as

in the mean-field theory, where common input is negligible. Treating a network with coherent fluctuations as encountered in finite size networks requires an alternative derivation of the hazard function [5].

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