

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 neurons with spike-frequency adaptation, this results in the regularization of the population activity and an enhanced postsynaptic 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 various species show a serial dependence between interevent intervals (ISI) 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 Rapid Communication, 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 theoretical results in a set of experimental *in vivo* recordings and analyze their implications for the readout 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 $h_x(x, t)$ where t denotes explicit dependence on time due to external input following [5,6]. Here, we assume x has a shot-noise-like dynamics, which is widely used as a model of spike-induced neuronal adaptation [6]:

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

where δ is the Dirac delta function, t_k is the time of the k 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 $h_x(x, t)$. It is straightforward to show that the distribution of x in an ensemble, denoted by $\Pr(x, t)$, is governed by the master equation

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

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 $\psi(t_x)^{-1} = -\tau \ln(e^{-t_x/\tau} - 1)$. Thus, we define $h(t_x, t) := h_x(\eta^{-1}(t_x), t)$. 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 $\Pr_{\text{eq}}(t_x)$. Further, the time-like transformation in Eq. (3) allows computation of the ISI by analogy to the renewal theory [6] and also permits the comparison to the master equation for a renewal process as given in Eq. (6.43) in [9]. The distribution of t_x just prior to an event is a quantity of interest and is derived as $\Pr^*(t_x) = h(t_x) \Pr_{\text{eq}}(t_x) / r_{\text{eq}}$, where $r_{\text{eq}} = \int h(t_x) \Pr_{\text{eq}}(t_x) dt_x$ 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, $\Pr^\dagger(t_x) = \Pr^*(\psi^{-1}(t_x)) \frac{d}{dt_x} \psi^{-1}(t_x)$ [6]. Then the relationship between t_x and the ordinary ISI distribution can be written as

$$\rho(\Delta) = \int_{-\infty}^{+\infty} h(t_x + \Delta) \Omega(t_x + \Delta) \Pr^\dagger(t_x) dt_x, \quad (4)$$

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where $\Omega(t_x + \Delta) = e^{-\int_{t_x}^{t_x+\Delta} h(t_x+u)du}$ and Δ is the ISI length. Now the n th moment μ_n of the distribution and its coefficient of variation C_v can be numerically determined.

Counting statistics. In order to derive the count distribution, we generalize the elegant approach for deriving the moment-generating function as introduced in [10]: Let $\rho_n(t_n, t_x^n | t_x^0)$ be the joint probability density given its initial state t_x^0 , where t_n stands for time to the n th event and t_x^n is the corresponding adaptive state of the process. Thereafter, one can recursively derive

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

where $\tilde{\rho}_{n+1}(s, t_x^{n+1} | t_x^0) = \mathcal{L}[\rho_{n+1}(t_{n+1}, t_x^{n+1} | t_x^0)]$ and \mathcal{L} is the Laplace transform with respect to time, assuming $\tilde{\rho}_1(s, t_x^1 | t_x^0) = \tilde{\rho}(s, t_x^1 | t_x^0)$ [10]. Next, defining the operator $\mathbf{P}_n(s)$ and applying bra-ket notation as suggested in [10] leads to the Laplace transform of the n th event's ordinary density:

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

where the operator \mathbf{P} is associated with $\tilde{\rho}(s)$, which interestingly corresponds to the moment-generating function of the sum of n non-independent intervals $\tilde{f}_n(s)$ as defined in [11]. Now, following Eqs. (2.15) in [11], the Laplace transform of the count distribution is 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 σ_T^2 and μ_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 assuming constant firing rate $\mu_T = r_{\text{eq}}T$. To calculate the second moment of $\tilde{P}(n, s)$, we require $\tilde{A}_s = \sum_k \tilde{\rho}_k(s)$; thus

$$\tilde{A}_s = \langle 1 | \mathbf{P}(s) [\mathbf{I} - \mathbf{P}(s)]^{-1} | \text{Pr}^\dagger \rangle, \quad (7)$$

where \mathbf{I} is the identity operator. Note, assuming a renewal interval distribution in Eq. (4) one obtains $\tilde{A}_s = \tilde{\rho}(s) / [1 - \tilde{\rho}(s)]$ and $\mathcal{L}^{-1}[r_{\text{eq}} \tilde{A}_s] = r_{\text{eq}} \mathcal{A}(u)$ is the joint density of an event at time t and another event at time $t + u$. Thus, the autocorrelation of events is $A(u) = r_{\text{eq}}[\delta(u) + \mathcal{A}(u)]$. Now, by using Eq. (7), and Eq. (3.3) in [11], the second moment of the count statistics can be derived. Thus, we obtain the Fano factor

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

The asymptotic property of $F = \lim_{T \rightarrow \infty} J_T$ can be derived from the result stated in Eq. (7.8) in [11] as

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

where ξ_k is the linear correlation coefficient between two k lagged intervals. Provided the limit exists, we find $F = C_v^2 [1/2 + 2 \sum_{k=1}^{\infty} \xi_k]$ in [12].

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 $\check{r} = \sum_{i=1}^k r_i$ and following Eq. (4.18) in [13] $\check{A}(u) = \check{r} + \check{r}^{-1} \sum_{i=1}^k r_i [\mathcal{A}_i(u) - r_i]$. Here, for the sake of simplicity, we derive the desired relationship between C_v^2 and the ensemble \check{F} for k identical processes. To this end, we plug \check{r} and $\mathcal{L}[\check{A}(u)]$ into the Eq. (9) and therefore it becomes $\lim_{s \rightarrow 0} [\check{A}_s - 1/(\mu_1 s)] = \check{C}_v^2 [1/2 + \Xi] - 1/2$, where \check{C}_v and $\Xi = \sum_{i=1}^{\infty} \Xi_i$ are the coefficient of variation and the interval correlations of the superimposed process. Note that the left-hand side of this equation and Eq. (9) are similar. Thus, we obtain

$$\check{C}_v^2 [1 + 2 \Xi] = C_v^2 \left[1 + 2 \sum_{i=1}^{\infty} \xi_i \right]. \quad (10)$$

The left-hand side of Eq. (10) is indeed the Fano factor \check{F} of the ensemble process as desired. Now, Palm-Khintchine theorem [13] suggests as $k \rightarrow \infty$, $\check{C}_v^2 \rightarrow 1$. Interestingly, if all individual processes fulfill the renewal condition, it follows from Eq. (10) that $\check{F} = C_v^2 = [1 + 2\Xi]$, 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 [14] regarding emergence of non-renewal processes as the result of the superposition operation.

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 point process similar to Eq. (3). The corresponding hazard function can be approximated as

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

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

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

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

We show in [5] that the adaptation dynamics in Eq. (1) produces negative serial correlations $\xi_k < 0$. The strength of serial correlation decays with increasing lag k and depends on the mean adaptation, $E[x] = r_{\text{eq}} q \tau$.

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 in Eq. (8) for the single process as well as for the population model of superimposed processes.

We validate our theoretical 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 [15] where the empirical sum over correlation coefficients amounts to an average $\sum_{i=1}^{10} \xi_i = -0.28$. We construct the population

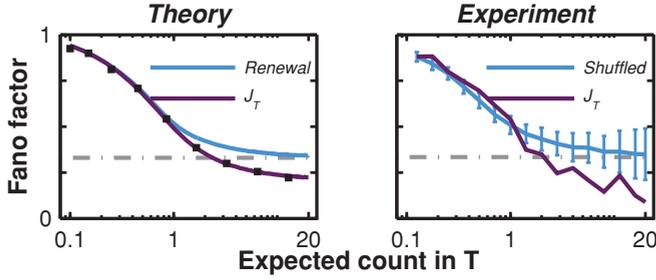


FIG. 1. (Color) Adaptation reduces the Fano factor of the ensemble process. Left panel: Magenta: J_T for arbitrary observation time T according to Eqs. (8) and (11) with $bq = 1.4$, $a = 5.0$, and $\tau = 400$ ms. Blue: Fano factor for equivalent renewal ensemble process with interval distribution of Eq. (4). Square dots: Numerically 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 panel: 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.

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 similar to individual neurons [16] in the population level.

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 $\check{F} < C_v^2$ 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 ≈ 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 and weak stimuli detection expressed in the reduction of the low-frequency power in a spectral analysis of spike trains with negative serial interval correlations [17]. 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 $A(u)$ following [18] with an exponential approximation

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

where the second term is the approximation of $r_{\text{eq}}A(u)$. For a given observation time window u and τ_c the reduction of F implies that $\hat{A}_u^r < \hat{A}_u$. 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 [18], a longer τ_c reduces the input current fluctuations and 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 between two counting distributions of an adaptive presynaptic ensemble when $\hat{h}_x(x)$ is adiabatically transferred to $\hat{h}_x(x - \epsilon)$ with a small change ϵ in the input ensemble. It is convenient to use $\tilde{\rho}_n(s)$ which is associated with the counting distribution $\tilde{P}(n, s)$. Thus, we apply the Kullback-Leibler divergence to Eq. (6) before and after the adiabatic change in the input:

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

Using Eq. (7) we obtain $D_{\text{KL}}(\tilde{\rho}_n^\epsilon || \tilde{\rho}_n) = \mathcal{A}_s^\epsilon [\ln(\mathcal{A}_s^\epsilon/\mathcal{A}_s)]$. Due to Eqs. (1) and (12), the mean adaptation after the change is $E[x^\epsilon] = \tau q r_{\text{eq}}^\epsilon$. If $\epsilon > 0$ it follows that $r_{\text{eq}}^\epsilon \geq r_{\text{eq}}$. 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 straightforward to deduce that $D_{\text{KL}} > D_{\text{KL}}^r$, for renewal and adaptive processes with 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 ϵ in the input that we express in parameter changes a^ϵ and b^ϵ in Eq. (11) as outlined in the Supplementary material at [5]. This leads to an increase $\kappa = r_{\text{eq}}^\epsilon - r_{\text{eq}}$ 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 $\kappa^{\text{Poisson}} > \kappa$, 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. Therefore, we compute the Kullback-Leibler divergence for both models and normalize it by the change in the output rate κ . The result in Fig. 2 (right) shows that D_{KL}/κ is larger for the adaptive model than for the rate model across

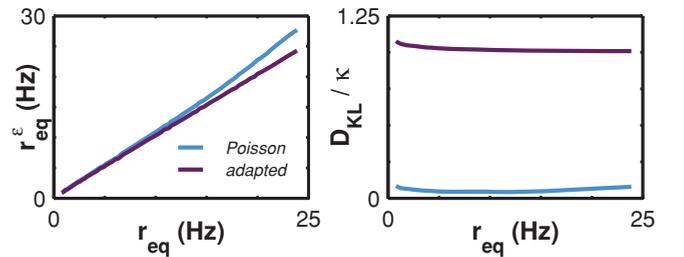


FIG. 2. (Color) Information gain per spike due to adaptation. Left panel: Transfer of equilibrium rate for fixed ϵ change of the input in adaptive and Poisson model. Right panel: Kullback-Leibler divergence per extra spike as the measure of information gain for n th event density of adaptive and Poisson processes while $u = 200$ ms and $\epsilon = 0.01$ nS with the same initial r_{eq} and $\kappa = r_{\text{eq}}^\epsilon - r_{\text{eq}}$.

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 ϵ more efficiently, even though the absolute change in firing rate is lower.

Discussion. Our results point out an important 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 [19] 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 the Fano factor or serial correlations and \check{C}_v at the population level, we readily obtain an estimate of the average C_v by assuming renewal processes for individual spike trains.

We developed a formalism to treat event-emitting systems that are influenced by a slow state variable, and we provided

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 (Supplementary material at [5]). The derivation of the state-dependent hazard function 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 (Supplementary material at [5]).

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