On the spike train variability characterized by variance-to-mean power relationship

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\textbf{Abstract}

We propose a statistical framework for modeling the non-Poisson variability of spike trains observed in a wide range of brain regions. Central to our approach is the assumption that the variance and mean of interspike interval are related in the form of a power function, the exponent of which can be arbitrary value. It is shown that this single assumption allows the spike trains to have various dependencies of the variability on the firing rate in the spike count statistics as well as in the interval statistics, depending on the exponent of the power function. We also propose a statistical model of spike trains that exhibits the variance-to-mean power relationship, based on which a maximum likelihood method is developed for inferring the exponent from rate-modulated spike trains. The ability of the proposed method is demonstrated with simulated and experimental spike trains.
1 Introduction

Variability of neural firing is of central importance in the study of signal processing carried out by the nervous system. Reliable transmission of sensory signal, integration of neural information and precise control of neural-motor system depend significantly on the variability of the neural responses to identical sensory or behavioral variables, as well as on the average responses (Mainen and Sejnowski, 1995; de Ruyter van Steveninck et al., 1997; Harris and Wolpert, 1998; Shadlen and Newsome, 1998; Ma et al., 2006; Lu et al., 2013).

Two types of measurement, inter-spike interval (ISI) and spike count, are commonly used for quantifying the variability of spike trains. The variability of ISI, expressed in the variance, quantifies how irregular firing time is on a short time scale characterized by the typical ISI. Since the variance of ISI is computed within single spike trains, it signifies intra-trial variability. The variance of the spike count across repeated observations, by contrast, quantifies the trial-to-trial variability in relatively long time intervals. These two quantities are by no means independent variables, but are closely related (Nawrot et al., 2008). In general, the variances of both ISI and spike count are scaled by the mean, the degree of which may vary across the brain regions (Kara et al., 2000; Maimon and Assad, 2009).

In this article, we formulate a statistical framework for modeling the variability of spike trains in terms of both the ISI and counting statistics. Our approach is motivated by observation made by Troy and Robson (1992). They reported that for steady discharges of X retinal ganglion cells of cat in response to stationary visual patterns, the standard deviation of ISI approximately increases as the 3/2 power of the mean ISI. Motivated by their observation, we make a single assumption on the ISI statistics as

\[ \text{Var(ISI)} \propto E(\text{ISI})^\alpha, \quad (1) \]

where \( \alpha \) is the exponent controlling how the variance is scaled by the mean. Here, it should be emphasized that this statistical law is a generalization of the finding of Troy and Robson (1992), in a way that the exponent \( \alpha \) can be arbitrary value in theory. On the basis of the power law (1), we show that this allows the spike trains to have various dependencies of the variability on the firing rate in the counting statistics as well as in the ISI statistics widely observed across the brain areas, depending on the value of
α. By combining Eq. (1) with the time-rescaling transformation (Barbieri et al., 2001; Berman, 1981; Koyama and Kass, 2008; Koyama and Kostal, 2014; Nawrot et al., 2008; Pillow, 2008; Reich et al., 1998), we propose “generalized” rate-modulated renewal process for a statistical model of spike trains. This enables us to develop a maximum likelihood method to infer the exponent α from rate-modulated spike trains, the ability of which is demonstrated with simulated and experimental spike trains. Finally, we discuss possible implications for the exponent of the power law in terms of characterizing the intrinsic variability of neuronal discharges.

2 Theory

2.1 Statistical law

Consider spike trains whose ISIs are independent and identically distributed with mean μ and variance σ². The central assumption in our approach is that the variance of ISI has a power function of the mean as

\[ \sigma^2 = \phi \mu^\alpha, \]

where α is the exponent and φ > 0 is the scale factor. The scale factor φ, on one hand, controls the overall amplitude of the power law. The exponent α, on the other hand, controls how the variance is scaled by changing the mean or the signal. For a Poisson process, whose ISIs obey an exponential distribution, α = 2. By contrast, α > 2(< 2) implies the tendency for the timing of event occurrence to be over (under) dispersed for large means, and under (over) dispersed for small means.

Consider next the spike count. Let \( N_\Delta \) be the number of spikes falling in the counting window of duration \( \Delta \). The variability of spike count is often measured by the Fano factor, defined by the ratio of the variance to the mean,

\[ F_\Delta := \frac{\text{Var}(N_\Delta)}{\text{E}(N_\Delta)}, \]

where the expectation is computed over repeated observations. For large counting window \( \Delta \gg 1 \), the mean and variance of \( N_\Delta \) are asymptotically evaluated as \( \text{E}(N_\Delta) \sim \Delta/\mu \) and \( \text{Var}(N_\Delta) \sim \sigma^2 \Delta/\mu^3 \), respectively (Cox, 1962). Suppose that the variance of
ISIs obeys Eq. (2). Then, the Fano factor asymptotically exhibits the power law,

\[ F_{\Delta} \sim \phi \lambda^\gamma, \]  

(4)

where

\[ \lambda := \frac{\text{E}(N_{\Delta})}{\Delta} \]  

(5)

is the mean firing rate, and the exponent \( \gamma \) is related to that of the ISI statistics via the scaling relation as

\[ \gamma = 2 - \alpha. \]  

(6)

Eq. (4) describes the dependency of the Fano factor on the mean firing rate. For \( \gamma = 0 \) (i.e., \( \alpha = 2 \)), the Fano factor does not depend on the firing rate; in other words, the variance of the spike count is proportional to the mean. On the other hand, if \( \gamma > 0 \) (\( \alpha < 2 \)), the Fano factor increases as the mean firing rate is increased, while the Fano factor is inversely related to the mean firing rate if \( \gamma < 0 \) (\( \alpha > 2 \)).

Note that the Fano factor depends on the length of the counting window. In the limit of short counting window \( \Delta \ll 1 \), since the probability of occurring two and more events is negligible, the event count can be approximated to be a Bernoulli random variable with a value of 1 or 0, the probabilities of which are given by \( P(N_{\Delta} = 1) = \lambda \Delta \) and \( P(N_{\Delta} = 0) = 1 - \lambda \Delta \), respectively. The variance of the Bernoulli distribution is \( \lambda \Delta (1 - \lambda \Delta) \), so that for any value of \( \alpha \) and \( \phi \) the Fano factor approaches unity (Teich et al., 1997):

\[ \lim_{\Delta \to 0} F_{\Delta} = \lim_{\Delta \to 0} \frac{\lambda \Delta (1 - \lambda \Delta)}{\lambda \Delta} = 1. \]  

(7)

For a short but finite duration \( \Delta \), numerical results suggests that in order for the Fano factor to effectively exhibit the power law with the exponent \( \xi \), it is necessary to use a counting window that shows at least a few spikes on average (Appendix A).

### 2.2 Statistical model

#### 2.1 Generalized rate-modulated renewal process

We construct a statistical model of spike trains whose variability is characterized by the variance-to-mean power law. Consider first stationary renewal process, a class of point process in which intervals between successive spikes are independent and identically
distributed with a fixed ISI distribution. It follows from Eq. (2) that by rescaling ISI as $X \to \lambda X$, $\lambda = 1/\mu$ being mean firing rate, the parameters are rescaled as $\mu \to 1$ and $\phi \to \lambda^{2-\alpha} \phi$. Thus, a parametric ISI density function $f(x; \mu, \phi)$ with mean $\mu$ and variance $\phi \mu^\alpha$ that is invariant under the rescaling satisfies

$$f(x; \mu, \phi) = \lambda f(\lambda x; \lambda^{2-\alpha} \phi), \quad (8)$$

where $f(x; \phi) := f(x; 1, \phi)$. Eq. (8) suggests that one can always reparametrize arbitrary probability density function with unit mean and variance $\phi$ so that the variance has the power function of the mean (2).

We extend the stationary renewal process defined by Eq. (8) to rate-modulated process. For this purpose, we utilize the idea of construction of inhomogeneous Poisson processes, given as follows. Consider a stationary Poisson process with unit rate defined on dimensionless time $s$. Then, the probability of occurring a spike in a short interval $(s, s + ds]$ is given by $ds$. Let $\lambda(t)$ be a time-varying firing rate on the real time $t$, and define

$$\Lambda(t) := \int_0^t \lambda(u) \, du. \quad (9)$$

By transforming the time $s$ into $t$ satisfying $s = \Lambda(t)$, one obtain an inhomogeneous Poisson process with time-varying firing rate $\lambda(t)$, for which the probability of occurring a spike in a short interval $(t, t + dt]$ is $\lambda(t)dt$. In the same manner, any renewal process with unit rate can be transformed by $s = \Lambda(t)$ into a rate-modulated renewal process with the time-varying firing rate $\lambda(t)$ (Barbieri et al., 2001; Berman, 1981; Koyama and Kass, 2008; Koyama and Kostal, 2014; Nawrot et al., 2008; Pillow, 2008; Reich et al., 1998). However, this transformation does not allow the Fano factor to have the power law with the exponent (6).

Hence, we propose a generalization of the transformation so that the Fano factor has a power function of the firing rate. To do so, we start with a general definition of point processes. Let $N(t)$ be the number of spikes that have already occurred at time $t$. A point process is generally defined by a conditional intensity function (Daley and Vere-Jones, 2003; Kass and Ventura, 2001),

$$r(t; H(t)) = \lim_{\Delta t \to 0} \frac{P\{N(t + \Delta t) - N(t) = 1; H(t)\}}{\Delta t}, \quad (10)$$

1 In fact, this transformation results in the Fano factor being constant (i.e., the variance of the spike count is proportional to the mean).
where $H(t)$ denotes the history of spikes up to time $t$. For a renewal process whose ISI density function is given by $f(x; \phi)$, the conditional intensity function, also called the hazard function, is given by

$$r(s; s_s, \phi) = \frac{f(s - s_s; \phi)}{1 - \int_{s_s}^s f(u - s_s; \phi)du},$$

(11)

where $s_s(< s)$ is the last spike time preceding $s$. Analogously to Eq. (8), by rescaling the parameter $\phi \rightarrow \lambda(t)^{2-\alpha} \phi$ as well as the time with $s = \Lambda(t)$, the conditional intensity function of a “generalized” rate-modulated renewal process is obtained as

$$r(t; t_s, \{\lambda(t)\}, \phi, \alpha) = \frac{\lambda(t) f(\Lambda(t) - \Lambda(t_s); \lambda(t)^{2-\alpha} \phi)}{1 - \int_{t_s}^{t} \lambda(v) f(\Lambda(v) - \Lambda(t_s); \lambda(v)^{2-\alpha} \phi)dv}.$$

(12)

Note that Eq. (12) is reduced to the conditional intensity function associated with Eq. (8) if $\lambda(t) = \lambda$, and corresponds to that of the “conventional” rate-modulated renewal process if $\alpha = 2$.

### 2.2 Likelihood function

By using the conditional intensity function (12), the likelihood function of $(\phi, \alpha)$, given a sequence of spikes $\{t_i\} := \{t_1, t_2, \ldots, t_n\}$ and the firing rate $\{\lambda(t)\}$, is expressed as

$$l(\phi, \alpha; \{t_i\}, \{\lambda(t)\}) = \left[ \prod_{i=2}^{n} r(t_i; t_{i-1}, \{\lambda(t)\}, \phi, \alpha) \right] \times \exp \left[ -\int_{t_1}^{t_n} r(u; t_N(u), \{\lambda(t)\}, \phi, \alpha)du \right],$$

(13)

where the exponential factor represents the probability of no event in each interspike interval (Daley and Vere-Jones, 2003; Kass and Ventura, 2001). Substituting Eq. (12) into Eq. (13), it can be expressed in more tractable form (see Appendix B for the derivation),

$$l(\phi, \alpha; \{t_i\}, \{\lambda(t)\}) = \prod_{i=2}^{n} \lambda(t_i) f(\Lambda(t_i) - \Lambda(t_{i-1}); \lambda(t_i)^{2-\alpha} \phi).$$

(14)

For spike trains consisting of $M$ repeated trials, $\{t_{ij}\}^M_{j=1} := \{t_{i1}, \ldots, t_{in_j}\}^M_{j=1}$, the likelihood function is the product of the likelihood function for single trials, the logarithm of which is given by

$$L(\phi, \alpha; \{t_{ij}\}^M_{j=1}, \{\lambda(t)\}) = \sum_{j=1}^{M} \sum_{i=2}^{n_j} \{ \log \lambda(t_{ij}) + \log f(\Lambda(t_{ij}) - \Lambda(t_{i-1}); \lambda(t_{ij})^{2-\alpha} \phi) \}.$$

(15)
If the firing rate $\lambda(t)$ is not known, an estimated firing rate $\hat{\lambda}(t)$ may be used, and then the maximum likelihood estimator (MLE) is obtained by maximizing Eq. (15) with respect to $(\phi, \alpha)$.

2.3 Choice of $f(x; \phi)$

The ISI density function $f(x; \phi)$ is one of the building blocks of the proposed statistical model. Any ISI density function identifies a generalized rate-modulated renewal process (12). Here, we particularly employ a Tweedie exponential dispersion model for $f(x; \phi)$ (Jorgensen, 1987, 1997). Exponential dispersion models are two-parameter family of distributions consisting of a linear exponential family with an additional dispersion parameter, and play an important role in statistics because they are the response distributions for generalized linear models (McCullagh and Nelder, 1989). A Tweedie model is an exponential dispersion model that has the scale invariance (8), including probability distributions commonly used for describing the ISI variability such as gamma (for $\alpha = 2$) and inverse Gaussian (for $\alpha = 3$) as special cases; these properties make a Tweedie model an obvious choice for $f(x; \phi)$.

Exponential dispersion models have probability density function of the form,

$$f(x; \mu, \phi) = c(x, \phi) \exp \left[ \frac{1}{\phi} \{ x\theta - \kappa(\theta) \} \right], \quad (16)$$

for suitable functions $c(x, \phi)$ and $\kappa(\theta)$. $\theta$ is the canonical parameter, and $\kappa(\theta)$ is called the cumulant function, the derivatives of which give the cumulants of the distribution. In particular, the mean and variance of the distribution are given by $\mu = \kappa'(\theta)$ and $\sigma^2 = \phi \kappa''(\theta)$, respectively. The mapping from $\theta$ to $\mu$ is invertible, so it is written $\kappa(\theta) = V(\mu)$ for a suitable function $V(\mu)$, called the variance function. A Tweedie model is identified by a particular choice of the variance function as $V(\mu) = \mu^\alpha$. By equating $\kappa(\theta) = d\mu/d\theta = \mu^\alpha$ and solving for $\mu$ and $\kappa$, $\theta$ and $\kappa$ for a Tweedie model are obtained as

$$\theta = \begin{cases} \frac{\mu^{1-\alpha}-1}{1-\alpha} & \alpha \neq 1 \\ \log \mu & \alpha = 1 \end{cases}, \quad (17)$$

and

$$\kappa(\theta) = \begin{cases} \frac{\mu^{2-\alpha}-1}{2-\alpha} & \alpha \neq 2 \\ \log \mu & \alpha = 2 \end{cases}. \quad (18)$$
The factor $c(x, \phi)$ in Eq. (16), which is determined by the normalization condition, does not have closed form expression except for the special cases. We employ numerical methods for computing $c(x, \phi)$, implemented by series expansion and Fourier inversion formula (Dunn and Smyth, 2005, 2008).

3 Results

3.1 Simulation study

We first performed numerical simulations to generate spike trains. The probability of occurring a spike in a short interval $(t, t + dt]$ is given by the conditional intensity function (12) as,

$$P(N_{t+dt} - N_t = 1; t_*, \{\lambda(t)\}, \phi, \alpha) = r(t; t_*, \{\lambda(t)\}, \phi, \alpha)dt + o(dt).$$

(19)

Spike trains were numerically simulated by discretizing the time into sufficiently small bins and evaluating the probability of occurring a spike in each bin. In the simulations, we used the firing rate function as

$$\lambda(t) = 0.04 + 0.02 \sin \frac{2\pi}{500} t,$$

(20)

and generated $M = 10^4$ spike trains in the time interval $t \in (0, 1000]$ for each $\alpha = 2$ and 3. For illustration, Figure 1 top shows raster plots of 20 of the simulated spike trains. To compute the firing rate and the Fano factor, we used a sliding window of duration $\Delta = 125$ in which 5 spikes were expected to fall on average. Let $N^j_\Delta(t)$ denote the number of spikes of the $j$th spike train in the counting window centered at $t$. The firing rate $\hat{\lambda}(t)$ and the Fano factor $\hat{F}_\Delta(t)$ in this window were computed by averaging across trials as

$$\hat{\lambda}(t) = \frac{1}{M} \sum_{j=1}^{M} \frac{N^j_\Delta(t)}{\Delta},$$

(21)

and

$$\hat{F}_\Delta(t) = \frac{1}{M-1} \sum_{j=1}^{M-1} \left( \frac{N^j_\Delta(t) - \hat{\lambda}(t)\Delta}{\hat{\lambda}(t)\Delta} \right)^2.$$  

(22)

Figure 1 depicts $\hat{\lambda}(t)$ and $\hat{F}_\Delta(t)$ as a function of $t$, showing that $\hat{F}_\Delta(t)$ remains nearly constant for $\alpha = 2$, while it is inversely related to $\hat{\lambda}(t)$ for $\alpha = 3$, as expected from Eqs. (4) and (6).
Next, the ability of the MLE to infer the exponent $\alpha$ was examined with the simulated spike trains. Figure 2 plots the estimated exponent $\hat{\alpha}$ against the number of spike trains used for the inference, in which we see that the MLE can infer the exponent reasonably well from repeated trials.

### 3.2 Real data analysis

We applied the method of data analysis to two experimental datasets. One dataset, labeled by “nsa2004.1”, is publicly available from Neural Signal Archive (Britten et al., 2004). The spike data was recorded from 216 neurons in the visual cortical area MT of adult rhesus macaques. The recordings were obtained while a visual stimulus consisting of dynamic random dot pattern was presented. Further experimental details are found in (Britten et al., 1992). The other dataset, labeled by “ia-1”, is available from CRCNS data sharing website (Rokem et al., 2009). Spike trains were recorded from 43 auditory receptor cells of grasshoppers while an auditory stimulus consisting of random amplitude modulations of wave was presented. See Rokem et al. (2006) for the details of the experiments.

Both datasets were divided into sub-datasets that consist of multiple spike trains recorded from one cell under identical stimulus conditions. We selected sub-datasets containing $\geq 50$ trials and with the mean firing rate $\geq 10$ spikes/s, due to sufficiency of spikes for the analysis. Consequently, 193 sub-datasets for nsa2004.1 and 138 sub-datasets for ia-1 were selected. Representative sub-datasets for nsa2004.1 and ia-1 are shown in Figure 3 together with the firing rate $\hat{\lambda}(t)$ and the Fano factor $\hat{F}_\Delta(t)$ computed with the sliding window whose length $\Delta$ was taken so that five spikes on average fall.

For each sub-dataset, we obtained the MLE $\hat{\alpha}$ of the exponent. Figure 4a depicts the distributions of $\hat{\alpha}$ for 193 sub-datasets of nsa2004.1 (solid line) and for 138 sub-datasets of ia-1 (dashed line). The mean and standard deviations are $\hat{\alpha} = 2.43 \pm 0.38$ for nsa2004.1 and $\hat{\alpha} = 2.96 \pm 0.58$ for ia-1. It is observed that a large portion of $\hat{\alpha}$ are greater than two, and $\hat{\alpha}$ of ia-1 is greater than that of nsa2004.1 on average. This indicates that the firing variability tends to be reduced as the firing rate increases, and this tendency is greater in ia-1 than in nsa2004.1. To confirm this result, we empirically estimated the exponent $\gamma$ of the Fano factor for each sub-dataset by performing linear
regression of \( \{ \log \hat{F}_\Delta(t) \} \) on \( \{ \log \hat{\lambda}(t) \} \) (see Figure 3a2,b2). The estimated exponents \( \hat{\gamma} \) are distributed with \( \hat{\gamma} = -0.17 \pm 0.51 \) for nsa2004.1 and \( \hat{\gamma} = -0.94 \pm 0.33 \) for ia-1 (Figure 4b), suggesting that the count variability also decreases as the firing rate increases (for \( \hat{\gamma} < 0 \) on average), the tendency of which is greater in ia-1 than in nsa2004.1, same as the result on \( \hat{\alpha} \). It is seen that the estimated exponents \( \hat{\alpha} \) and \( \hat{\beta} \) approximately satisfies the scaling relation (6) on average.

4 Discussion

This article concerned the variability of spike trains that is described by the power mean-variance relationship (2). It was shown that this single assumption allows the spike trains to have various dependency of the variability on the firing rate, depending on the value of the exponent of the power function. By combining the power law with the time-rescaling transformation, we proposed the generalized rate-modulated renewal processes, based on which a statistical method was developed for inferring the exponent from rate-modulated spike trains.

It is often assumed in the analysis of the variability of spike trains that the variance of spike count is proportional to the mean (Averbeck, 2009), where the coefficient of proportionality (which corresponds to the Fano factor) may differ from unity due to deviation from a Poisson statistic. In our formulation, this assumption is further relaxed so that the ratio of the count variance to the mean can change with the firing rate (Eq. (4)), that is observed in a wide range of the brain regions (Kara et al., 2000).

The degree of irregularity of neural firing, which is measured by the ISI statistics such as the local variation \( L_V \) (Shinomoto et al., 2003), is generally maintained in vivo cortical areas while the firing rate varies in time (Maimon and Assad, 2009; Shinomoto et al., 2009). This implies that the exponent of the power law (2) in the ISI statistics is \( \alpha \approx 2 \), from which a linear relationship between the mean and variance of spike counts (\( \gamma \approx 0 \)) is expected. On the other hand, steady discharges of X retinal ganglion cells in response to stationary visual patterns approximately obey the power law with \( \alpha \approx 3 \) (Troy and Robson, 1992), implying that a fixed ratio of variance to the mean spike count is no longer hold but the spike counts are less variable at the higher rates (Berry and Meister, 1998; Reich et al., 1998).
In the nervous system, neurons produce an action potential by integrating presynaptic inputs within tens milliseconds, in which typically a few spikes come from each presynaptic neuron. This implies that the variance of spike count in the integration time exhibits the power law (Appendix A), so that the presynaptic inputs have signal-dependent noise that may be relevant to the computation carried out by the nervous system. Ma et al. (2006) suggested a hypothesis that the Poisson-like statistics in the responses of populations of cortical neurons may represent probability distributions over the stimulus and implement Bayesian inferences by linear combinations of the responses. A necessary condition making the Bayesian inferences possible in their hypothesis is that the variance of spike count is proportional to the mean spike count ($\gamma = 0$). Lu et al. (2013) showed that in controlling dynamical systems with noisy signals, precise control is achievable if the control signal has sub-Poisson noise ($\gamma < 0$), while it is not achievable if the control signal has Poisson or supra-Poisson noise ($\gamma \geq 0$).

By analyzing a stochastic leaky integrate-and-fire model, we gave a possible mechanistic explanation for the origin of the power law (2) with various exponents (Koyama, 2014): $\alpha = 3$ may imply a supra-threshold firing regime in which firing is driven by excitatory input; while $\alpha = 2$ may be interpreted as a sub-threshold firing regime in which the membrane potential fluctuates below the threshold; $\alpha = 1$ may emerge when firing is strongly caused by large fluctuation of the membrane potential. It is thus speculated that the “intrinsic” exponent may reflect electrophysiological properties of individual cells or dynamical states of networks and may vary across the brain areas. The proposed statistical framework offers a systematic way to explore the diversity of the variability of neural responses.

2 With a temporal resolution of this integration time, spike trains may be described as

$$\frac{dN(t)}{dt} \approx \lambda(t) + \xi(t),$$

(23)

where $\xi(t)$ is a white noise with $E[\xi(t)] = 0$ and $E[\xi(t)\xi(s)] = \phi \lambda(t)^{\gamma+1}\delta(t-s)$. 

11
A  Finite \( \Delta \)

We examine behavior of the Fano factor computed with a counting window of finite duration \( \Delta \). For equilibrium renewal processes whose ISI variance obeys the power law \((2)\), by using the asymptotic expansion formula of the count variance \((\text{Cox, 1962})\) the Fano factor is evaluated for \( E(N_\Delta) \gg 1 \) as

\[
F_\Delta = \phi \lambda^\gamma + \frac{1}{E(N_\Delta)} \left( \frac{1}{6} + \frac{\phi^2 \lambda^{4-2\alpha}}{2} - \frac{\mu_3 \lambda^3}{3} \right) + o(E(N_\Delta)^{-1}),
\]

where \( \mu_3 = E[(X - \mu)^3] \) is the third central moment of ISI. Figure 5 depicts the Fano factor as a function of the mean spike count on a log-log scale. Here, the Tweedie model (introduced in the section 2.3) with \( \alpha = 3 \) was used for the ISI distribution, and the length of the counting window was taken to be \( \Delta = 1 \). In addition to the analytical curves (solid lines; based on Eq. (24)), we performed numerical simulations, calculating the Fano factor with \( 10^4 \) independent trials (symbols). The Fano factor effectively obeys the power law with the exponent \( \gamma = -1 \) (= \( 2 - \alpha \) by Eq. (6)) even if a few spikes on average are observed in the counting window. The asymptotic expansion formula \((24)\) is also in good agreement with the numerical results in this range.

B  Derivation of the likelihood function

In this appendix, we derive Eq. (14) from Eq. (13). Using Eq. (12), the first factor in the rhs of Eq. (13) is rewritten as

\[
\prod_{i=2}^{n} r(t_i; t_{i-1}, \{\lambda(t)\}, \phi, \alpha)
= \prod_{i=2}^{n} \lambda(t_i) f(\Lambda(t_i) - \Lambda(t_{i-1}); \lambda(t_i)^{2-\alpha} \phi)
\times \prod_{i=2}^{n} \left[ 1 - \int_{t_{i-1}}^{t_i} \lambda(v) f(\Lambda(v) - \Lambda(t_{i-1}); \lambda(v)^{2-\alpha} \phi) dv \right]^{-1}.
\]

Taking the derivative of the logarithm of the last factor in the above expression leads to

\[
\frac{d}{dt_i} \log \left[ 1 - \int_{t_{i-1}}^{t_i} \lambda(v) f(\Lambda(v) - \Lambda(t_{i-1}); \lambda(v)^{2-\alpha} \phi) dv \right]
= -\frac{\lambda(t_i) f(\Lambda(t_i) - \Lambda(t_{i-1}); \lambda(t_i)^{2-\alpha} \phi)}{1 - \int_{t_{i-1}}^{t_i} \lambda(v) f(\Lambda(v) - \Lambda(t_{i-1}); \lambda(v)^{2-\alpha} \phi) dv}
\times \left[ 1 - \int_{t_{i-1}}^{t_i} \lambda(v) f(\Lambda(v) - \Lambda(t_{i-1}); \lambda(v)^{2-\alpha} \phi) dv \right]^{-1}.
\]

Using Eq. (12), this expression becomes

\[
\frac{d}{dt_i} \log \left[ 1 - \int_{t_{i-1}}^{t_i} \lambda(t) f(\Lambda(t) - \Lambda(t_{i-1}); \lambda(t)^{2-\alpha} \phi) dv \right]
= -r(t_i; t_{i-1}, \{\lambda(t)\}, \phi, \alpha).
\]
where the last equality comes from Eq. (12). Thus, we obtain
\[
\prod_{i=2}^{n} \left[ 1 - \int_{t_{i-1}}^{t_i} \lambda(v)f(\Lambda(v) - \Lambda(t_{i-1}); \lambda(v)^{2-\alpha} \phi) dv \right] = \exp \left( - \int_{t_1}^{t_n} r(u; t_{N(u)}, \{\lambda(t)\}, \phi, \alpha) du \right).
\] (27)

Substituting Eqs. (25) and (27) into Eq. (13) leads to Eq. (14).

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Figure 1: Raster plots of simulated spike trains (top), estimated firing rate $\hat{\lambda}(t)$ (middle), and estimated Fano factor $\hat{F}_\Delta(t)$ (bottom) for $\alpha = 2$ (a) and $\alpha = 3$ (b). The Fano factor is nearly constant for $\alpha = 2$, while it is inversely related to the firing rate for $\alpha = 3$. 
Figure 2: The estimate of the exponent versus the number of trials used for the inference for $\alpha = 2$ (dashed line) and for $\alpha = 3$ (solid line). The error bars represent the standard deviations computed with 100 repetitions.
Figure 3: Representative sub-datasets for nsa2004.1 (a1) and for ia-1 (b1). (Top) raster plot of 20 spike trains; (middle) estimated firing rate (the horizontal bar indicates the length of counting window); (bottom) the Fano factor. The Fano factor is plotted against the firing rate in a log-log scale (a2 for nsa2004.1 and b2 for ia-1), on which linear regression was performed to obtain the exponent $\hat{\gamma}$. 

$\hat{\gamma} = -0.16$

$\hat{\gamma} = -0.99$
Figure 4: The distributions of estimated exponents $\hat{\alpha}$ (a) and $\hat{\gamma}$ (b). The solid lines represent nsa2004.1, and the dashed lines represents ia-1.

Figure 5: The Fano factor as a function of the mean spike count for $\alpha = 3$. The solid lines represent the analytical results based on Eq. (24) and symbols represent the numerical results. The Fano factor exhibits the power law with the exponent $\gamma = -1$ even if the mean spike count in the window is on the order of a few spikes.