

EFFECT OF SPONTANEOUS ACTIVITY ON STIMULUS DETECTION IN A SIMPLE NEURONAL MODEL

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ABSTRACT. It is studied what level of a continuous-valued signal is optimally estimable on the basis of first-spike latency neuronal data. When a spontaneous neuronal activity is present, the first spike after the stimulus onset may be caused either by the stimulus itself, or it may be a result of the prevailing spontaneous activity. Under certain regularity conditions, Fisher information is the inverse of the variance of the best estimator. It can be considered as a function of the signal intensity and then indicates accuracy of the estimation for each signal level. The Fisher information is normalized with respect to the time needed to obtain an observation. The accuracy of signal level estimation is investigated in basic discharge patterns modelled by a Poisson and a renewal process and the impact of the complex interaction between spontaneous activity and a delay of the response is shown.

1. Introduction. The question how the information from the environment is encoded in the activity of neurons is one of the central problems in neuroscience. Because the time course of the membrane potential during action potentials (spikes) is stereotyped, signals need to be conveyed by the pattern of spikes. Rate coding, based on firing rates of individual cells, is the most commonly studied neural code ([32, 35, 36, 37, 38] and many more). Nevertheless, it is not the only option. The delay from stimulus onset to the first evoked spike, called a first-spike latency, may carry significant information in addition to the spike count, as has been shown e.g. in the auditory [19, 42], visual [20, 52], olfactory [53] and somatosensory systems [47, 50, 51]. When speaking about latency coding, it is inherently supposed that the latency varies as the stimulus level changes and thus the latency can signal what is the actual stimulus level.

A potential objection to the idea of latency coding is that the neuron, which is responsible for decoding the information about the stimulus level, does not have the exact knowledge about timing of the stimulus onset and therefore cannot evaluate the first-spike latency. However, there are several possible ways how nervous system can maintain a temporal reference about stimulus onset, as outlined in [48], and they provide two possible explanations how the latency could be involved in the processing of the information about a stimulus.

Firstly, experimental research done on primate auditory cortex [7] revealed a mechanism based on the existence of two different groups of neurons. Neurons of the first type react to the stimulus rapidly and with a very low variability with

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respect to the quality of the signal, providing the information about stimulus timing but not about its properties. Neurons of the second type respond typically only to some stimuli and with longer and more variable latencies, which are related to the stimulus qualities.

Secondly, the latency may affect the synchronization of the first spikes occurring after the stimulus onset produced by different neurons. Assume that a neuron under consideration receives spikes from a certain group of afferent neurons and can recognize the first evoked spikes from these neurons, but does not know their latencies, because the time of the stimulus onset is unknown. The mean of the latency depends on the stimulus level, so the stronger is the stimulus, the shorter is the latency. We may also expect the variance of the latency to be smaller for stronger stimuli, so the first evoked spikes for weak stimuli are likely to be considerably jittered, whereas the first evoked spikes for stronger stimuli would be elicited approximately at the same time. Thus, latencies relative to one another in the ensemble of neurons might be decoded instead of the absolute latency ([16, 18, 29, 31, 48]). This point is debated in Discussion.

The analysis presented in this paper focuses on the activity of a single neuron. In reality, the information about the stimulus is encoded by a simultaneous activity of a group of neurons. If the population of neurons is homogeneous, i.e. neurons in the ensemble respond independently and stochastically identically ([28, 33, 59]), then their joint activity can be studied using repeated recordings of one particular neuron exposed to a stereotyped stimulus.

Experimental data can be investigated using various statistical methods. Either the nonparametric approach may be applied and then the whole probability density function (pdf) of the time to the first evoked spike is estimated, as was shown e.g. in [46], or the more common strategy is adopted, when a certain stochastic model for the first-spike latency distribution is assumed, and then the problem reduces to the estimation of key parameters of such model. However, the whole distribution of latency is often not studied in detail and only the mean of the latency is investigated.

There are many statistical methods dealing with the estimation of the latency ([4, 17, 40, 46, 55, 56] and many others), a review is provided in [41]. Their precision has been assessed, for example, by means of Monte Carlo simulations. The aim of this paper is to investigate the accuracy of estimation of the key parameters of latency, i.e. parameters related to the stimulation level, using the concept of Fisher information. It shows what is the minimum mean square error attainable by the best unbiased estimator satisfying certain regularity conditions. Application of Fisher information in neural computation has become a common tool, it was used e.g. in [3, 6, 8, 24, 25, 26, 32, 36, 37, 38, 54, 58]. The novel contribution of this paper is to investigate how precisely the signal level of the applied stimulus can be reconstructed from the measurements of the time to the first spike after stimulus onset and how it is affected by the presence of spontaneous neuronal activity and the delay of the response.

2. Spike train model. When a neuronal response is investigated experimentally, occurrence of spikes is recorded in time and it is analysed, how the spiking pattern changes after presentation of a stimulus at a fixed time t_0 . An excitatory response is considered throughout the paper, although an inhibitory response can be also incorporated in some of the models introduced here. In an excitatory case, the neuron is typically either silent or fires spontaneously with a low background firing

rate up to t_0 and after t_0 (and presumably some additional delay) the stimulus evokes some extra spikes, that would not occur otherwise. The following scenarios are compared in later sections:

1. *Absence of a spontaneous activity:*

The neuron is completely silent in the absence of stimulation.

- (a) *Instantaneous response* – The response, viewed as the random process generating spikes, starts immediately after t_0 , so that the first evoked spike can be observed arbitrary close to t_0 .
- (b) *Response with a delay* – Response starts after t_0 and a delay ω , which is a positive constant and has the meaning of the minimum reaction time due to finite transmission times of the involved electro-chemical processes. Therefore the first evoked spike cannot occur before $t_0 + \omega$.

2. *Presence of a spontaneous activity:*

In the absence of stimulation the neuron elicits spikes spontaneously. The response has a form of additional spikes observed on the top of the background spontaneous activity.

- (a) *Instantaneous response* – The response starts immediately after t_0 .
- (b) *Response with a delay* – The response starts after $t_0 + \omega$.

The spontaneous activity, whenever considered in this paper, is described by a Poisson process. This is based on results from [10], where the statistical properties of neuronal firing rate described by the classical Hodgkin-Huxley neuronal model with the inclusion of stochastic channel dynamics were analyzed and it was shown that the spontaneous activity arising from channel fluctuations is well described by the Poisson model. Besides that, the firing of the leaky integrate-and-fire model without input current but with stochastic fluctuations of the membrane potential can be also described by the Poisson spiking model ([39]). The main attention is given to the situation when both the spontaneous and the evoked response are Poissonian, nevertheless, a more general scenario, where the response is not a Poisson process, but a renewal process, is also briefly discussed for a comparison.

We are interested in the first-spike latency of the response, i.e., the time R elapsed from the stimulus onset at t_0 to the first evoked spike. However, if the neuron fires spikes spontaneously, there is no way how the first evoked spike can be experimentally distinguished from other eventual spikes resulting from the spontaneous activity. Therefore only the time to the first spike after t_0 , which is denoted by T , is measured, and it is taken into account that

$$T = \min\{W, R\}, \quad (1)$$

where W is the time to the first spontaneous spike after t_0 . Throughout all the paper it is assumed that W and R are independent. As W is given by the spontaneous activity, it must be also independent of the stimulation. This description of the time to the first observed spike was already used in [46, 55, 56]. An illustration of spike trains arising in the four scenarios introduced above is provided in Fig. 1. The realizations of R , W and T are also shown there.

When studying a neuronal response to a stimulation, the firing rate is typically investigated. A natural way how to estimate it from data is to divide the number of elicited spikes $N(t)$ observed in the time window $(t_0, t_0 + t)$, by the length of observation period t . Since it is assumed that the underlying point process generating spikes is at least locally stationary during the response, the following relationship

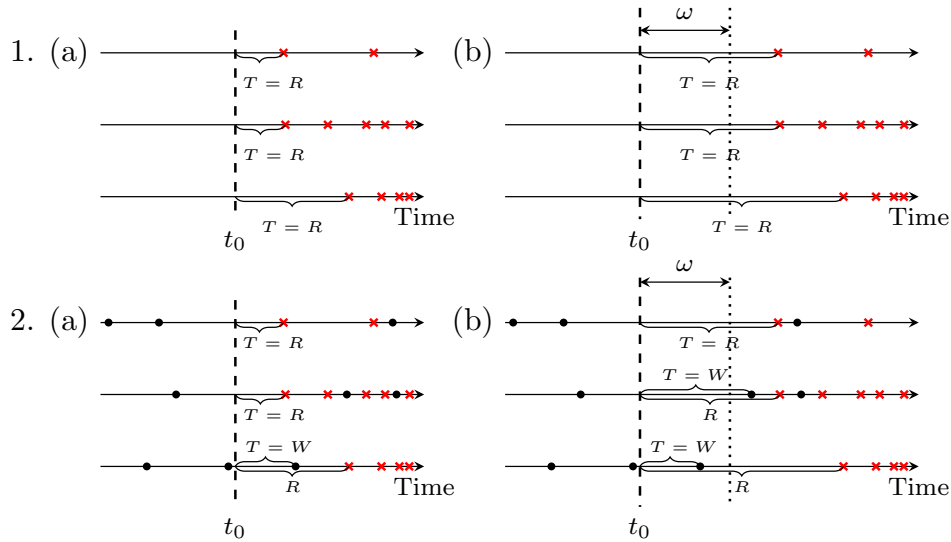


FIGURE 1. Spike trains generated according to the assumed scenarios. 1. No spontaneous activity; (a) response starts immediately after t_0 , (b) response starts after $t_0 + \omega$. 2. Spontaneous activity is present; (a) response starts immediately after t_0 , (b) response starts after $t_0 + \omega$. Spontaneous spikes are marked with black dots, evoked spikes with red crosses. W denotes the time from t_0 to the first subsequent spontaneous spike, R is the time to the first evoked spike and T is the time from t_0 to the first spike of any type, thus $T = \min\{W, R\}$. Spike times were simulated, so it is known if the first spike after t_0 is spontaneous ($T = W$) or evoked ($T = R$). Times of evoked and spontaneous spikes were generated separately and the same data are used for all subfigures. In 1.(a) only times of evoked spikes occur; in 1.(b) times of evoked spikes were shifted by ω ; in 2.(a) both times of spontaneous and evoked spikes are displayed together; in 2.(b) spontaneous spikes are displayed without any change and evoked spikes are shifted by ω .

between spike counts and interspike intervals (ISIs), denoted by X , holds (see [11])

$$\frac{E[N(t)]}{t} = \frac{1}{E(X)}. \quad (2)$$

This formula shows that the frequency of spikes and ISIs are closely related.

3. Transfer function. There is an experimental evidence (e.g. [53]) that the mean of the time to the first spike, $E(T)$, depends on the strength of the stimulus, also called a stimulus level, s . Since W is completely independent of the stimulation, the dependence of $E(T)$ on s is a result of the relationship between $E(R)$ and s . Whenever it is needed to highlight that R or T is considered for a given signal level s , it is indicated by a lower index as R_s and T_s .

The relationship between the signal level s and $E(R_s)$ is described by a transfer function. A transfer function, in a broad sense, refers to a function that describes a

relationship between the stimulus level and any quantity of the model that changes with respect to the stimulation intensity. There is almost no experimental evidence about the relationship between the first spike latency and the stimulus intensity. When selecting an appropriate formula for the transfer function describing $E(R)$, we can come out of the usual form of a transfer function used for the firing rate. The experimentally obtained frequencies of spikes are often fitted to the Hill function ([2, 9, 15], for example). Its basic form is

$$f(x) = \frac{ax^b}{C^b + x^b}, \quad x \geq 0, \quad (3)$$

where x is the nonnegative stimulus intensity expressed in corresponding physical units on a linear scale, $f(x)$ is the number of spikes per unit of time and $a > 0$, $b > 0$, $C > 0$. However, instead of the original signal level x , its logarithm $s = \log x$ is often considered, which implies that the transformed signal level s is allowed to be positive as well as negative. The resulting transfer function for the firing frequency is then ([37, 44, 53])

$$f(s) = \frac{a}{1 + e^{-b(s-c)}}, \quad s \in (-\infty, \infty), \quad (4)$$

where $c = \log C$. The logistic function (4) is bounded by two asymptotes; zero for $s \rightarrow -\infty$ and a for $s \rightarrow \infty$ (the saturating level). The parameter b is responsible for the steepness of the curve and also affects the width of the region of predominant increase of the function, i.e., a range of signals for which the function changes significantly (a dynamical range); c corresponds to the inflection point where the slope is maximal. As was pointed out in [34], the choice of the stimulus scale is an integral part of the neural coding problem and may have a significant influence on the coding accuracy. Therefore it is crucial to work with a physiologically relevant scale, which is assumed in the rest of the paper.

The frequency can be viewed as the inverse of the mean ISI, as shown in (2). If we assume that $E(R)$ is proportional to $E(X)$, then $E(R)$ is inversely proportional to the firing rate and the transfer function for $E(R)$ may be approximated by the inverse of (3), yielding

$$E(R_x) = \theta_0 \left(1 + \frac{C^b}{x^b} \right), \quad x \geq 0. \quad (5)$$

where $\theta_0 = 1/a$ has the meaning of the minimum mean latency. Since the rate of spikes and the first-spike latency are not exactly inverse, the parameters in (3) and (5) do not have to be identical. If the latency is expressed for s on the log scale, $s = \log(x)$, by rescaling (5) or inverting (4) we get

$$E(R_s) = \theta_0 \left(1 + e^{-b(s-c)} \right), \quad s \in (-\infty, \infty). \quad (6)$$

This formula can be also supported by experimental data from frog olfactory receptor neurons in [53], where the function of the same form was reported as the best choice to fit the dependence of the measured first-spike latencies with respect to changing stimulus levels. The transfer functions (3)–(6) are illustrated in Fig. 2. All calculations in the following section are based on the transfer function (6).

When the rate coding is studied, the simplest and most intuitive way to determine the optimally detectable signal level is to identify s , for which the slope of the transfer function (4) is maximal, so that a small change in s implies a large change of the rate of elicited spikes. This suggests that the maximum of $\partial f(s)/\partial s$ may be

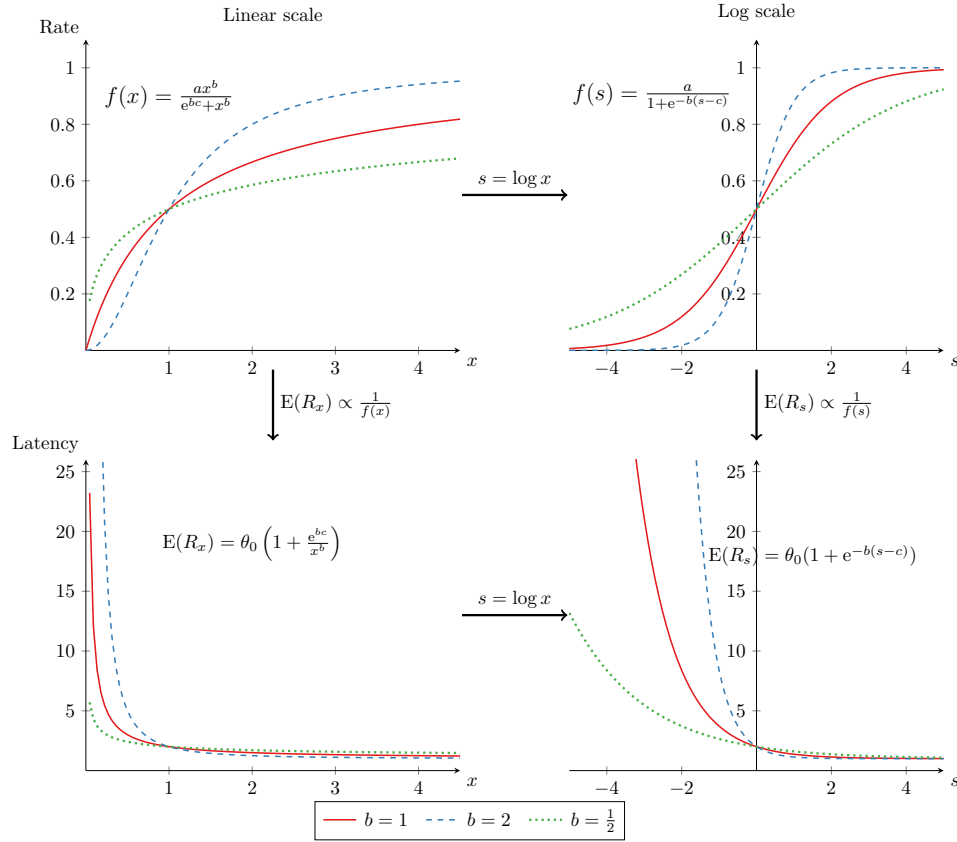


FIGURE 2. Transfer functions for the rate of spikes on the linear ($f(x)$) and the log scale ($f(s)$) and their counterparts for the latency obtained as their inversions $E(R_x)$ and $E(R_s)$. Three different values of b are used, $b = 1$ (full red line), $b = 2$ (dashed blue line) and $b = 1/2$ (dotted green line). In all the graphs, $a = 1$, $c = 0$, $\theta_0 = 1$.

an indicator of the optimally detectable signal level with respect to the rate coding. If the same idea is applied for the latency coding, then the slope of (6) would be investigated and the optimality measure would be

$$J_s^{(0)}(s) = \left| \frac{\partial E(R_s)}{\partial s} \right|. \tag{7}$$

Recall that $E(R_s)$ as given in Eq. (6) is independent of which of the models is assumed. The maximal slope of $E(R_s)$ is reached for $s = -\infty$ and thus this optimality measure suggests that the weakest possible signal is optimal for all of the models 1.(a)–2.(b).

4. Fisher information. The measure $J_s^{(0)}$ does not take into account the randomness of R_s and the fact that not only the mean of R_s , but also its variability may change with respect to s , making thus the identification of the signal level for some s more difficult than for others. The whole distribution of R should be therefore

taken into account. Fisher information is a more complex measure that overcomes this problem. Another difficulty arises in the presence of spontaneous activity when R is not directly observed and the signal level detection is based on observations of T , from which the distribution of R has to be deduced.

Fisher information reflects, how well a parameter can be estimated from available data, if the distribution family is known. The Cramer-Rao inequality states that, under some regularity conditions, the variance of an unbiased estimator \hat{s} of the signal level s based on observations of T_s cannot be smaller than the inverse of the Fisher information. Obviously, the higher the Fisher information, the smaller the lower bound on variance and the more accurate estimate of s can be reached. This rule also implies that the higher the Fisher information, the less neurons are needed to get an equally accurate estimate.

Fisher information about a generic parameter α in one observation of T can be calculated according to the formula

$$J_\alpha(\alpha) = \mathbb{E} \left(\frac{\partial}{\partial \alpha} \log f_T(T; \alpha) \right)^2 = \int \frac{1}{f_T(t)} \left(\frac{\partial}{\partial \alpha} f_T(t; \alpha) \right)^2 dt. \quad (8)$$

If the parameter α is a function of s , the Fisher information can be easily reparameterized, yielding the Fisher information about s as

$$J_s(s) = J_\alpha(\alpha(s)) \left(\frac{\partial}{\partial s} \alpha(s) \right)^2. \quad (9)$$

The following lower bound for J_s can be obtained from the Cauchy-Schwarz inequality ([54]),

$$J_s^{(2)}(s) = \frac{1}{\text{Var}(T_s)} \left(\frac{\partial \mathbb{E}(T_s)}{\partial s} \right)^2, \quad (10)$$

where $\text{Var}(T_s)$ is the variance of the random variable T_s . In experimental works, this quantity is often used and referred to as Fisher information, e.g. in [13, 30, 45]. If $\text{Var}(T_s)$ is constant for all s and $\partial \mathbb{E}(T_s)/\partial s$ is proportional to $\partial \mathbb{E}(R_s)/\partial s$, then $J_s^{(2)}(s) \propto [J_s^{(0)}(s)]^2$. Thus the optimal signal level deduced from $J^{(0)}(s)$ can be regarded as a crude approximation of the optimal signal level based on the Fisher information J_s .

When thinking about efficient neuronal decoding, one would require not only the information about stimulus to be estimated with maximal accuracy (as can be expressed in terms of Fisher information), but also that the decoding process is as fast as possible. Thus the time necessary to observe the first spike after t_0 should be also taken into account and signal levels leading on average to long waiting times ought to be penalized. The following normalized Fisher information was used in [36, 38],

$$I_s(s) = \frac{J_s(s)}{\mathbb{E}(T_s)}. \quad (11)$$

It can be considered as an alternative criterion of optimality and its maximum represents a stimulus with the maximal Fisher information per unit of time.

5. Results. This section is devoted to the inspection of Fisher information about the signal level contained in the latency for the scenarios outlined in Section 2. Although values of optimal signals from the perspective of a particular optimality measure are provided whenever it is possible, the primary aim lies not in the specific

values of optimal s , but in their comparison under different conditions and for different optimality measures.

5.1. Fisher information in a Poissonian model. At first, assume the simplest of neuronal responses, when the stimulation evokes a sequence of spikes following a Poisson process, there is no spontaneous activity and no delay (scenario 1.(a), see Fig. 1). The first observed spike is thus identical with the first spike evoked by the stimulation, $T = R$. When the underlying Poisson process has parameter $\lambda > 0$, the time to the first spike is exponentially distributed with mean $1/\lambda$. Thus $T \sim \text{Exp}(\lambda)$ and its pdf is $f_T(t) = \lambda e^{-\lambda t}$, $t \geq 0$. The mean $E(R) = 1/\lambda$ depends on the signal level s as described by (6), therefore

$$\lambda(s) = \frac{1}{\theta_0(1 + e^{-b(s-c)})}. \quad (12)$$

Note that $\lambda(s)$ is identical with the transfer function for spike frequency (4). The Fisher information about λ and s conveyed in one observation of T is then

$$J_\lambda(\lambda) = \frac{1}{\lambda^2}, \quad (13)$$

$$J_s(s) = \frac{b^2 e^{-2b(s-c)}}{(1 + e^{-b(s-c)})^2}, \quad (14)$$

$$I_s(s) = \frac{b^2 e^{-2b(s-c)}}{\theta_0(1 + e^{-b(s-c)})^3}. \quad (15)$$

The transfer function $\lambda(s)$ together with J_λ , J_s and I_s are illustrated in Fig. 3. As we can see, the Fisher information J_s is bounded on the interval $[0, b^2]$ and is decreasing for increasing s . It means that the stronger is the stimulus, the less accurate estimate of s in terms of the mean squared error can be obtained. The normalized Fisher information does not favour small values of s and suggests the optimal signal level

$$s = c - \frac{1}{b} \log 2. \quad (16)$$

5.1.1. Effect of a delayed response. In the scenario 1.(b) a delay ω for the response is introduced (see Fig. 1). Note that ω represents a substantially different quantity from θ_0 , because θ_0 is a lower limit for $E(R_s)$, whereas ω is the lower limit for any realization of R . The time to the first spike follows now a shifted exponential distribution with rate λ and shift ω , $T \sim \text{shExp}(\lambda, \omega)$. Its pdf is thus $f_T(t) = \lambda e^{-\lambda(t-\omega)}$, $t \geq \omega$, and the mean is $E(T) = E(R) = \omega + 1/\lambda$. In order to ensure that $E(R)$ is not in contradiction with the transfer function (6), namely that the lower asymptote of $E(R_s)$ is not higher than θ_0 , it must hold that $\omega \leq \theta_0$.

Since ω describes an intrinsic property of the neuron, it is treated as a constant regardless of the applied stimulus. The only parameter depending on the stimulus level is λ . The Fisher information about λ is the same as in the previous model, see (13), because the shift ω has no impact on the value of the integral in (8). However, we must modify the dependence of λ on s , which is now

$$\lambda(s) = \frac{1}{\theta_0(1 + e^{-b(s-c)}) - \omega}. \quad (17)$$

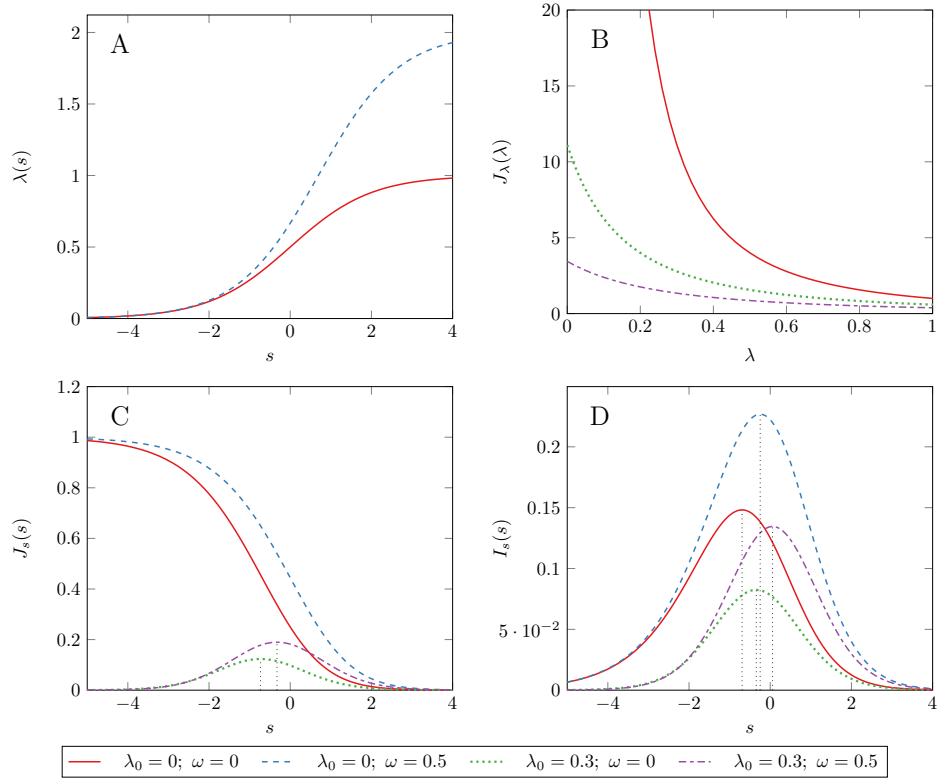


FIGURE 3. Fisher information for the Poissonian response. A: Response rate λ as a function of stimulus intensity s ; B: Fisher information about λ ; C: Fisher information about s ; D: normalized Fisher information about s . Results for the four different scenarios are shown: no spontaneous activity and no delay (full red line), no spontaneous activity and nonzero delay (dashed blue line), presence of spontaneous activity and no delay (dotted green line), presence of spontaneous activity and nonzero delay (dash-dotted purple line). Optimal stimulus levels given by maxima of J_s and I_s , respectively, are marked with vertical dotted lines. Presence or absence of spontaneous activity plays no role in the first subfigure. All the other parameters apart from the delay and the level of spontaneous activity are fixed to $\theta_0 = 1$, $b = 1$ and $c = 0$.

Using this and the formula (9), we get the Fisher information about s as follows

$$J_s(s) = \frac{\theta_0^2 b^2 e^{-2b(s-c)}}{\left[\theta_0 (1 + e^{-b(s-c)}) - \omega \right]^2}, \quad (18)$$

$$I_s(s) = \frac{\theta_0 b^2 e^{-2b(s-c)}}{(1 + e^{-b(s-c)}) \left[\theta_0 (1 + e^{-b(s-c)}) - \omega \right]^2}. \quad (19)$$

The only change in J_s , when compared with the previous scenario without a delay, is that now the squared expression in the denominator is lowered by ω . Thus, although still decreasing and bounded on the range $[0, b^2]$, J_s in the scenario 1.(b) is greater for all s . This is not surprising, because the constant shift ω allows $\lambda(s)$ to reach higher values and leads to a wider dynamical range. The normalized Fisher information shows an optimum for

$$s = c - \frac{1}{b} \log \left(\frac{\theta_0 - \omega + \sqrt{(\theta_0 - \omega)(9\theta_0 - \omega)}}{2\theta_0} \right). \quad (20)$$

The transfer function $\lambda(s)$ together with J_λ , J_s and I_s are illustrated in Fig. 3.

5.1.2. *Effect of spontaneous activity.* Assume now that the neuron fires spikes spontaneously even in the absence of stimulation and the stimulation modulates the ongoing neuronal activity. For now the possibility of a delay is not taken into account (scenario 2.(a) in Fig. 1). Identification of latency in such situation was discussed in [46]. For simplicity, the spontaneous activity is considered as Poisson process with rate λ_0 and the stimulation causes emission of extra spikes according to Poisson process with rate λ . Thus the overall activity of the neuron during the response is given by Poisson process with rate $\lambda_0 + \lambda$. As a result, we have $W \sim \text{Exp}(\lambda_0)$ and $R \sim \text{Exp}(\lambda)$ and we get the pdf of T as $f_T(t) = (\lambda_0 + \lambda)e^{-(\lambda_0 + \lambda)t}$, $t > 0$, which is a pdf of the exponential distribution with rate parameter $\lambda_0 + \lambda$.

The parameter of the spontaneous activity λ_0 remains fixed, while λ depends on s , so we are interested in the Fisher information about λ , which is

$$J_\lambda(\lambda) = \frac{1}{(\lambda_0 + \lambda)^2}. \quad (21)$$

In comparison with (13) we see that $\lambda_0 > 0$ results in a decrease of J_λ for every possible λ , so the presence of noise complicates the information decoding. The rate parameter λ depends on s as stated in (12) and, after applying (9), this yields

$$J_s(s) = \frac{b^2 e^{-2b(s-c)}}{(1 + e^{-b(s-c)})^2 [\lambda_0 \theta_0 (1 + e^{-b(s-c)}) + 1]^2}, \quad (22)$$

$$I_s(s) = \frac{b^2 e^{-2b(s-c)}}{\theta_0 (1 + e^{-b(s-c)})^3 [\lambda_0 \theta_0 (1 + e^{-b(s-c)}) + 1]}. \quad (23)$$

Interestingly, J_s is nonmonotone (see Fig. 3). For $s \rightarrow -\infty$ the Fisher information J_s approaches zero, because the response is almost completely covered by the spontaneous activity. As s increases, the noise induced by the spontaneous firing plays smaller and smaller role and consequently J_s rises. Simultaneously, the inherent decreasing tendency of J_s , as shown for the scenarios without spontaneous activity (14), gradually comes in and after the maximum is reached for

$$s_1 = c - \frac{1}{2b} \log \left(\frac{\lambda_0 \theta_0 + 1}{\lambda_0 \theta_0} \right), \quad (24)$$

it completely prevails and J_s decreases to zero. The normalized Fisher information I_s has a similar shape, but the maximum is reached for a different value of s

$$s_2 = c - \frac{1}{b} \log \left(\frac{-1 + \sqrt{1 + 16\lambda_0 \theta_0 (1 + \lambda_0 \theta_0)}}{4\lambda_0 \theta_0} \right). \quad (25)$$

The optimal level suggested by I_s is higher, which is in agreement with the expectation, because I_s penalizes weak signals with long latencies in general. The difference between s_1 and s_2 depends on the level of spontaneous activity, as shown in Fig. 4, and decreases with increasing spontaneous activity. In the limit when $\lambda_0 \rightarrow \infty$ both optimal levels are equal.

5.1.3. *Mutual effect of a delayed response and spontaneous activity.* Consider again that the evoked activity is observed on top of a background spontaneous activity, but now we allow for a delay for the first evoked spike (scenario 2.(b) in Fig. 1). Consequently, R follows a shifted exponential distribution, $R \sim \text{sh Exp}(\lambda(s), \omega)$, while W remains unchanged. Several methods for the estimation of the delay ω in such a case were shown in [55, 56]. The pdf of T is

$$f_T(t) = \begin{cases} \lambda_0 e^{-\lambda_0 t} & 0 < t < \omega \\ (\lambda_0 + \lambda) e^{-\lambda_0 t - \lambda(t-\omega)} & t \geq \omega. \end{cases} \quad (26)$$

Assume again that all the parameters except λ does not depend on the stimulus level. The Fisher information about λ is

$$J_\lambda(\lambda) = \frac{e^{-\lambda_0 \omega}}{(\lambda_0 + \lambda)^2}. \quad (27)$$

In comparison with the previous case without a delay (21), J_λ is multiplied by the factor $\exp(-\lambda_0 \omega) = \mathbb{P}(T > \omega) < 1$, which rules out all the cases when $W \leq \omega$ and therefore T carries no information about the stimulus. After employing (17) we get

$$J_s(s) = \frac{\theta_0^2 b^2 e^{-\lambda_0 \omega - 2b(s-c)}}{\left[\lambda_0 \theta_0 (1 + e^{-b(s-c)}) - \lambda_0 \omega + 1 \right]^2 \left[\theta_0 (1 + e^{-b(s-c)}) - \omega \right]^2}, \quad (28)$$

$$I_s(s) = \frac{\lambda_0 \theta_0^2 b^2 e^{-\lambda_0 \omega - 2b(s-c)}}{\left[\theta_0 (1 + e^{-b(s-c)}) - \omega \right]^2 \left[\lambda_0 [\theta_0 (1 + e^{-b(s-c)}) - \omega] + 1 \right] \left[\lambda_0 [\theta_0 (1 + e^{-b(s-c)}) - \omega] + 1 - e^{-\lambda_0 \omega} \right]}. \quad (29)$$

All the results are illustrated in Fig. 3.

The function J_s is nonmonotonic again and reaches its maximum at

$$s = c - \frac{1}{2b} \log \left[\frac{(\theta_0 - \omega)(1 + \lambda_0(\theta_0 - \omega))}{\lambda_0 \theta_0^2} \right]. \quad (30)$$

Note the difference between J_s with and without an incorporated delay (Eqs. (22) and (28)). The effect of the delay manifests itself in two opposite ways. First, there is a multiplying constant $e^{-\lambda_0 \omega} < 1$ in the numerator of (28), which decreases the value of the Fisher information. Secondly, the denominator is lowered by the delay, which increases the Fisher information. Whether the overall effect of the delay for given s results in an increase or a decrease of J_s depends on the actual values of the parameters.

The optimal signal level according to I_s is not shown because the formula is too complicated and provides no useful insight. Fig. 4 shows how it changes with respect to λ_0 . Again, the optimal signal level given by I_s is higher than the optimal signal level given by the classical Fisher information J_s , but this difference decreases with increasing λ_0 and tends to zero.

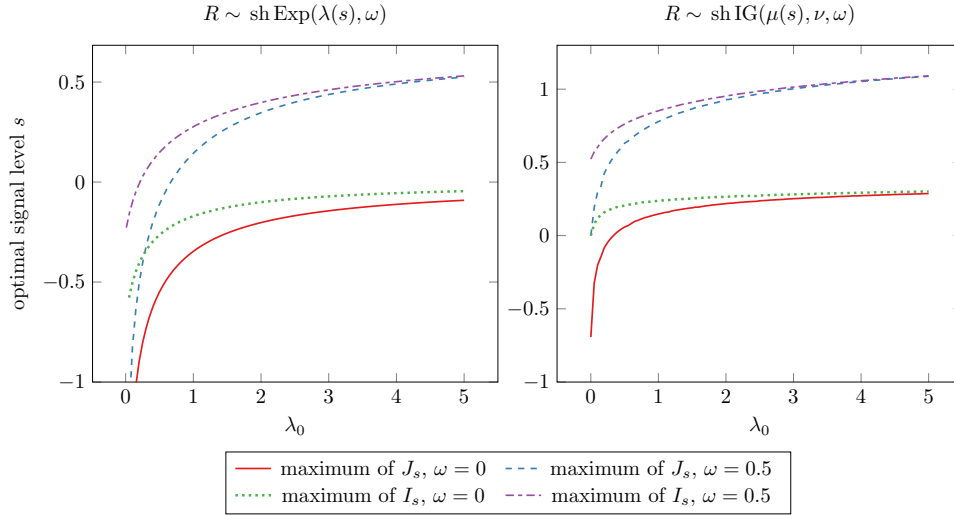


FIGURE 4. Dependence of the optimal signal level s determined by the maximum of the Fisher information J_s and its normalized version I_s on the level of spontaneous activity λ_0 . Left: response is given by Poisson process; right: R follows inverse Gaussian distribution.

5.2. Inverse Gaussian distribution of the first-spike latency. Poisson process is memoryless and one might argue that it possibly does not reflect the key properties of a response adequately. Therefore an example of a slightly different model based on Eq. (1) is briefly presented. The eventual spontaneous activity is still presumed to be given by a Poisson process, but for R the inverse Gaussian distribution is now used. It is one of commonly applied distributions in neuroscience [27]. One of the reasons is that it can be obtained as a distribution of the first time, when a Wiener process $V(t)$ with drift μ and diffusion parameter σ , defined as

$$V(t) = \mu dt + \sigma dW(t), \quad V(0) = 0, \quad (31)$$

reaches a threshold $B > 0$, where $W(t)$ denotes the standard Wiener process, μ and σ are positive constants. This process can be used as a description of membrane potential in the perfect integrate-and-fire model ([21]).

Throughout this section, the parametrization by Tweedie ([57]) is used. Inverse Gaussian distribution is characterized by two parameters, mean parameter $\alpha = B/\mu$ and shape parameter $\beta = B^2/\sigma^2$, so that $E(R) = \alpha$ and $\text{Var}(R) = \alpha^3/\beta$. Results for J_s and I_s are invariant with respect to reparametrization.

The pdf of R , if the response starts after a delay $\omega \geq 0$, is

$$f_R(t) = \sqrt{\frac{\beta}{2\pi(t-\omega)^3}} \exp\left(-\frac{\beta(t-\omega-\alpha)^2}{2\alpha^2(t-\omega)}\right), \quad t \geq \omega. \quad (32)$$

$$(33)$$

From $E(R_s) = \omega + \alpha(s)$ we get the transfer function

$$\alpha(s) = \theta_0 \left[1 + e^{-b(s-c)}\right] - \omega, \quad (34)$$

β is treated as a constant. If a delay is not considered, we set $\omega = 0$. T is equal to R in the absence of spontaneous activity (scenarios 1.(a) and (b)) and we get

$$J_\alpha(\alpha) = \frac{\beta}{\alpha^3}, \quad (35)$$

$$J_s(s) = \frac{\beta\theta_0^2 b^2 e^{-2b(s-c)}}{\left[\theta_0(1 + e^{-b(s-c)}) - \omega\right]^3}, \quad (36)$$

$$I_s(s) = \frac{\beta\theta_0 b^2 e^{-2b(s-c)}}{(1 + e^{-b(s-c)}) \left[\theta_0(1 + e^{-b(s-c)}) - \omega\right]^3}. \quad (37)$$

As illustrated in Fig. 5, J_s is nonmonotone, which is in contrast to the analogous case in the Poissonian model (14), where J_s is decreasing. The maximum of J_s is located at

$$s_1 = c - \frac{1}{b} \log\left(\frac{2(\theta_0 - \omega)}{\theta_0}\right). \quad (38)$$

The nonmonotone shape of J_s can be easily explained using the formula (9). For weak signals, $\alpha(s)$ is very high and thus $J_\alpha(\alpha(s))$ is near to zero. With increasing s , $J_\alpha(\alpha(s))$ rises, leading to the growth of J_s . However, the absolute value of the derivative of $\alpha(s)$ is decreasing and after s reaches the critical value s_1 , its influence prevails and makes J_s decrease. I_s is also nonmonotone and reaches its maximum at

$$s_2 = c - \frac{1}{b} \log\left(\frac{\sqrt{\omega^2 + 16\theta_0(\theta_0 - \omega)} - \omega}{4\theta_0}\right). \quad (39)$$

Now let us look on the effect of spontaneous activity (scenarios 2.(a) and (b) in Fig. 1). Assume again that the spontaneous activity is given by Poisson process with rate λ_0 . The pdf of T is then

$$f_T(t) = \begin{cases} \lambda_0 e^{-\lambda_0 t} & t \leq \omega, \\ \lambda_0 e^{-\lambda_0 t} (1 - F_R(t)) + e^{-\lambda_0 t} f_R(t) & t > \omega, \end{cases} \quad (40)$$

where $F_R(t)$ is the cumulative distribution function of R , which follows inverse Gaussian distribution shifted by ω . The mean of T can be calculated from the following formula derived in [55],

$$E(T) = E(W) [1 - e^{-\lambda_0 \omega} \mathcal{L}_{R-\omega}(\lambda_0)], \quad (41)$$

where $\mathcal{L}_{R-\omega}(s)$ is the Laplace transform of $F_R(t)$ with $\omega = 0$. This yields

$$E(T) = \frac{1}{\lambda_0} \left[1 - \exp\left(-\lambda_0 \omega + \frac{\beta}{\alpha} - \sqrt{\beta \left(\frac{\beta}{\alpha^2} + 2\lambda_0\right)}\right) \right]. \quad (42)$$

In the presence of a spontaneous activity, J_s and I_s are not available in a closed form. Results obtained by numerical methods are shown in Figs. 4 and 5 together with the results given in (35)–(37). We can see that for all the scenarios the Fisher information is increasing at first, but then decreases to zero again. The effect of a delay and the presence of spontaneous activity is analogous to the model with Poissonian response, i.e. the spontaneous activity decreases and the delay mostly increases the Fisher information, though the mutual effect of the delay and spontaneous activity is ambiguous.

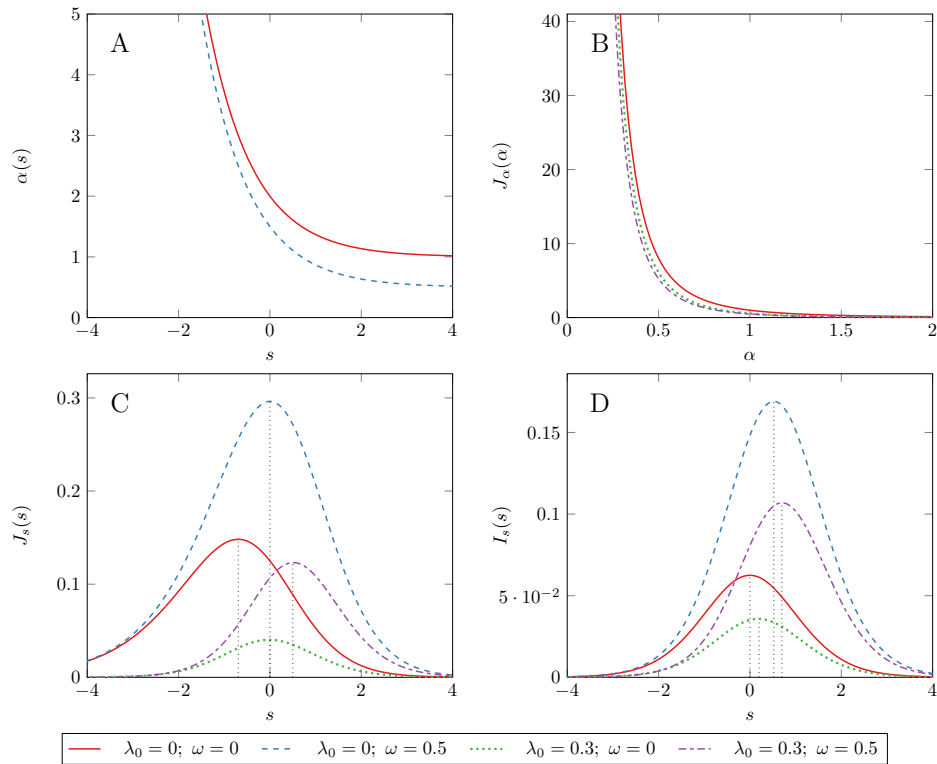


FIGURE 5. Fisher information if R follows inverse Gaussian distribution. A: the mean of R as a function of a stimulus intensity s ; B: the Fisher information about α ; C: the Fisher information about s ; D: the normalized Fisher information about s . Results for the four different scenarios are shown: no spontaneous activity and no delay (red), no spontaneous activity and nonzero delay (blue), presence of spontaneous activity and no delay (green), presence of spontaneous activity and nonzero delay (purple). The presence or the absence of spontaneous activity plays no role in the first sub-figure. All the parameters except λ_0 , ω are fixed; $\beta = 1$, $\theta_0 = 1$, $b = 1$ and $c = 0$.

6. Discussion. All the models in the paper are constructed as a superposition of an eventual process generating spontaneous spikes and another process generating evoked spikes, so the models are explicitly designed for an excitatory response. Nevertheless, an inhibitory response can be also incorporated into the purely Poissonian model, provided that a spontaneous activity is present. In this model, the stimulation causes that the generation of spikes after $t_0 + \omega$ is given by a Poisson process with rate $\lambda_0 + \lambda(s)$. An inhibitory response can be easily captured if $\lambda(s) \in (-\lambda_0, 0)$. However, a similar thing cannot be easily done in the model with non-exponential distribution of R . A more elaborate way of combining the spontaneous and the evoked activity would be needed there, some examples can be found in [40].

The spike train model based on pooling of the spontaneous and evoked activity should not be understood as that there really exist two different types of spikes

TABLE 1. Distributions of nonnegative random variables frequently used for spiking data and the relationship between the mean and the variance, if one of the parameters varies with s .

Distribution	Parameters		Mean-variance relation
	Variable	Fixed	
Exponential λ - rate	$\lambda(s)$		$\text{Var}(T_s) = [\text{E}(T_s)]^2$
Gamma k - shape, λ - rate	$\lambda(s)$	k	$\text{Var}(T_s) = \frac{1}{k} [\text{E}(T_s)]^2$
	$k(s)$	λ	$\text{Var}(T_s) = \frac{1}{\lambda} \text{E}(T_s)$
Inverse Gaussian α - mean, β - shape	$\alpha(s)$	β	$\text{Var}(T_s) = \frac{1}{\beta} [\text{E}(T_s)]^3$
Lognormal μ - location, σ^2 - variance	$\mu(s)$	σ^2	$\text{Var}(T_s) = \sigma^2 [\text{E}(T_s)]^2$

arising from two independent sources. Nevertheless, the discrimination between spontaneous and evoked activity is well-founded for the first spike after t_0 . Furthermore, although the assumed response is characterized by a whole random point process, only the time to the first evoked spike is essential for the analysis. Therefore the results stay valid also for more complicated responses as far as the distribution of T is preserved.

It was mentioned in Introduction that the necessary condition for decoding through synchronization of first spikes is that the mean and the variance of the latency are directly proportional. Although the author is not aware of any general proof that a shorter mean latency implies a smaller variance, it seems to hold at least for unimodal distributions of nonnegative variables. The explanation is that the decreasing mean is equivalent to the mass of the distribution shifting towards zero, which means that the mode must increase and this leads simultaneously to the inevitable decline of variance. For instance, let R_{s_0} be the latency for the weakest stimulus, which is able to evoke a response, and let us assume that the latency for stronger stimuli is scaled as follows

$$R_s = k(s - s_0)R_{s_0}, \quad (43)$$

where $k(x)$ is a multiplying constant from the interval $[0, 1]$ that is a decreasing function of x , $x > 0$. Then we have

$$\begin{aligned} \text{E}(R_s) &= k(s - s_0)\text{E}(R_{s_0}) \\ \text{Var}(R_s) &= [k(s - s_0)]^2 \text{Var}(R_{s_0}), \end{aligned} \quad (44)$$

so both the mean and the variance are decreasing with respect to s . Many common distributions of nonnegative random variables have the same property that the mean and the variance evolve in the same direction with respect to a varying parameter of the distribution (see Table 1) and an analogous relation has been shown for the first-spike latency in Morris-Lecar model with a channel noise [23]. This phenomenon was observed also in experimental data, e.g. for retinal cells [5].

7. Conclusions. It was pointed out in Section 3 that the measure $J_s^{(0)}$, when applied on latency coding as described in this paper, suggests in all the models that the weakest possible signal is optimal. This is in most cases a substantially different result from the optimal stimulus level given by the exact Fisher information. In most cases J_s has a distinct maximum, indicating that a specific signal level can be discriminated best. If the normalized Fisher information I_s is applied as an optimality measure, a particular optimal signal level is identified in all the cases.

The models 1.(a), 1.(b) and 2.(a), although presented separately, are subcases of the model 2.(b), with the level of spontaneous activity, the delay or both of them equal to zero. Thus all the Fisher informations and normalized Fisher informations in the Poissonian model can be obtained from Eqs. (28) and (29) after choosing $\lambda_0 = 0$, $\omega = 0$ (case 1.(a)), $\lambda_0 = 0$ (case 1.(b)) or $\omega = 0$ (case 2.(a)).

The impact of spontaneous activity on the Fisher information is in agreement with a common intuition. The higher the spontaneous activity, the less accurate estimates we would get for all s . Besides that, the optimal signal level moves to higher values of s , because a stronger signal is necessary to achieve a sufficient contrast with the background activity. On the contrary, the effect of a delay is less straightforward. On one hand, in the presence of spontaneous activity it results in a lower probability that an observation of T carries information about the stimulus level. On the other hand, it broadens the range, on which the parameter depending on the stimulus level can vary, and thus improves the discriminability.

The parameters b and c of the transfer function $E(R_s)$ play only a quantitative role. The parameter c is responsible for shifts of the whole Fisher information function. The parameter b scales the Fisher information and thus influences its maximal value and slope, but affects also the location of the maximum. The impact of these two parameters on the optimal signal level follows the same pattern for all the scenarios

$$\begin{aligned} \arg \max_{s \in \mathbb{R}} J_s(s) &= c - \frac{K(\lambda_0, \theta_0, \omega)}{b} \\ \arg \max_{s \in \mathbb{R}} I_s(s) &= c - \frac{L(\lambda_0, \theta_0, \omega)}{b}, \end{aligned}$$

where $K(\lambda_0, \theta_0, \omega)$, $L(\lambda_0, \theta_0, \omega)$ are expressions independent of b and c . By contrast, the locations of the maxima of J_s and I_s are crucially affected by the shape of the transfer function, namely its first derivative. If the transfer function for $E(R_s)$ is derived from a slightly different formula for $f(s)$ than (4), this change could lead to a substantial shift of the optimum.

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