Decoding Poisson Spike Trains by Gaussian Filtering

Sidney R. Lehky
sidney@salk.edu
Computational Neuroscience Lab, Salk Institute, La Jolla, CA 92037, U.S.A.

The temporal waveform of neural activity is commonly estimated by low-pass filtering spike train data through convolution with a gaussian kernel. However, the criteria for selecting the gaussian width $\sigma$ are not well understood. Given an ensemble of Poisson spike trains generated by an instantaneous firing rate function $\lambda(t)$, the problem was to recover an optimal estimate of $\lambda(t)$ by gaussian filtering. We provide equations describing the optimal value of $\sigma$ using an error minimization criterion and examine how the optimal $\sigma$ varies within a parameter space defining the statistics of inhomogeneous Poisson spike trains. The process was studied both analytically and through simulations. The rate functions $\lambda(t)$ were randomly generated, with the three parameters defining spike statistics being the mean of $\lambda(t)$, the variance of $\lambda(t)$, and the exponent $\alpha$ of the Fourier amplitude spectrum $1/f^\alpha$ of $\lambda(t)$. The value of $\sigma_{opt}$ followed a power law as a function of the pooled mean interspike interval $I$, $\sigma_{opt} = aI^b$, where $a$ was inversely related to the coefficient of variation CV of $\lambda(t)$, and $b$ was inversely related to the Fourier spectrum exponent $\alpha$. Besides applications for data analysis, optimal recovery of an analog signal waveform $\lambda(t)$ from spike trains may also be useful in understanding neural signal processing in vivo.

1 Introduction

Spike trains act as carriers by which information is transmitted from neuron to neuron. They typically form the raw data from perceptual, cognitive, and motor experiments using microelectrode techniques. Given a spike train, we would like to decode it by extracting some parameter that expresses its functional content in a more explicit form. Although what aspect of the spike train is the relevant information carrier is a matter of debate, we shall consider here estimation of the instantaneous spike rate.

We treat spike trains as being generated by an inhomogeneous Poisson process, in which the spike rate varies as a function of time in accord with an instantaneous firing rate function $\lambda(t)$. An example firing rate function is shown in Figure 1, together with a set of Poisson spike trains generated by that same rate function. The problem is to invert this process and estimate $\lambda(t)$ given a sample of spike trains. If one normalizes the area under $\lambda(t)$ to
one, it becomes a probability density function for the occurrence of a spike at time $t$. Hence, instantaneous firing rates and probabilistic spike timings are the same thing aside from a multiplicative constant. Here we discuss the problem using the firing rate formalism.

The temporal waveform of the instantaneous firing rate obviously conveys more information than average firing rate calculated over an extended period (Rieke, Warland, de Ruyter van Steveninck, & Bialek, 1997), with the amount of information dependent on the autocorrelation of $\lambda(t)$ (or, equivalently, on the frequency bandwidth of $\lambda(t)$). The extent to which this additional information is actually used is uncertain. Possibly the overall temporal pattern of the response may be functionally significant, or it may be just some particular aspect of the temporal pattern, such as neural latency or peak response time. In any case, when analyzing spike train data, one would often like to have an accurate estimate of the response at a higher temporal resolution than provided by the average response. Once the temporal aspect of the neural response is more accurately characterized, one may be in a better position to interpret that response in terms of the sensory stimuli or the behavioral activity producing it.

A common approach for estimating the time course of neural responses from spike trains is to construct a peristimulus time histogram (PSTH). A related but superior method that avoids the binning artifacts of histograms is kernel smoothing (Bowman & Azzalini, 1997; Silverman, 1986; Wand & Jones, 1995), in which the spike train is convolved with some kernel function. For a gaussian kernel, for example, this has the effect of replacing each spike (idealized as an instantaneous pulse) by a gaussian curve having unit area. The set of gaussians is then summed to produce the estimate of $\lambda(t)$ (see Figure 2). This kernel intensity estimate (instantaneous firing rate) becomes a kernel density estimate (probabilistic spike timing) when the area under the summed curve is normalized.

Kernel smoothing is the approach used in this study. Kernel smoothing also goes under the name of the Parzen window method, after its originator (Parzen, 1962). As this technique involves interpolating a continuous
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A problem with applying kernel smoothing is choosing the kernel width $\sigma$ (analogous to choosing bin size when plotting PSTHs), as the shape of the estimated $\lambda(t)$ will strongly depend on this parameter (see Figure 3). The primary concern in this study is to provide an objective basis for selecting an optimal kernel width that minimizes the error between actual and estimated $\lambda(t)$. Although automatic bandwidth selection algorithms exist (Jones, Marron, & Sheather, 1996), they are general-purpose statistical methods without any domain-specific knowledge built into them. A hope here is that by studying how various neurophysiological parameters affect the selection of bandwidth for spike train smoothing, a special-purpose model can be constructed that does better than the nonspecific methods.

A notable previous theoretical treatment of this problem was by Bialek, Rieke, de Ruyter van Steveninck, and Warland (1991), studying movement-sensitive neurons in the blowfly visual system. However, their approach to estimating the smoothing kernel is valid only for the special case in which there is a high correlation between the temporal waveform of the sensory stimulus and the temporal waveform of the sensory neuron response. Such would occur in a linear system or one with soft nonlinearities (saturation effects). For mammalian visual processing, for instance, that would limit applicability of those methods to relatively peripheral structures. As one moves centrally through multiple cortical areas (over 30 have been identified in the monkey visual system; Felleman & Van Essen, 1991), the waveform of the neural response becomes decorrelated from that of the stimulus through the influence of multiple layers of nonlinear recurrent interactions.

Figure 2: Recovering an estimated spike rate function $\hat{\lambda}(t)$ by gaussian smoothing. Each spike is convolved with a gaussian kernel (dotted lines) and the results summed to produce the estimate $\hat{\lambda}(t)$. Function between the events of a point process (spikes), it is an example of radial basis function interpolation when using a symmetric kernel such as a gaussian function.
Figure 3: The spike rate function $\hat{\lambda}(t)$ estimated from a set of spike trains depends on the width $\sigma$ of the gaussian smoothing kernel used. Shown are the actual $\lambda(t)$ (dotted line), as well as the estimated $\hat{\lambda}(t)$ generated by four different values of $\sigma$. Each estimated $\hat{\lambda}(t)$ was produced by convolving 100 spike trains, generated by the same $\lambda(t)$, with a gaussian kernel of the specified $\sigma$. The results for all trials were then averaged.

In inferotemporal cortex, a visual stimulus displayed temporally as an extended rectangular pulse typically elicits a complex multipeaked neural response. Furthermore, in central neurons, the temporal aspect of the neural response may not even in principle be coding the temporal aspect of the stimulus. For example, it has been suggested that the temporal waveforms of monkey inferotemporal neurons are encoding information about stimulus shape (Richmond, Optican, Podell, & Spitzer, 1987). Thus, for these reasons, the cross-correlational approach used by Bialek et al. (1991) is inadequate in the general case. In this study, we used a different procedure that attempts to estimate the rate function using information intrinsic to the neural signal, without knowledge of inputs from the external environment. Related theoretical treatments of spike train decoding include August and Levy (1996), Goldberg and Andreou (2007), and Paulin and Hoffman (2001).
2 Methods

Our approach was to examine the problem from an analytic perspective as well as to conduct simulations. For the simulations, Poisson spike trains were generated from a known $\lambda(t)$, and then a family of estimates $\hat{\lambda}(t|\sigma)$ was recovered from those spikes by gaussian smoothing, using a range of values for the kernel width $\sigma$. A global error measure $E_T(\sigma)$ was calculated dependent on the difference between actual and estimated $\lambda(t)$ for different values of $\sigma$. The minimum of the $E_T(\sigma)$ curve indicated the optimal $\sigma$. The shape of the $E_T(\sigma)$ curve (and therefore the optimal $\sigma$) depended on the stochastic characteristics of $\lambda(t)$, and the nature of that dependence is the major concern here. (See the appendix for a list of symbols.)

We held kernel shape fixed in the form of a gaussian curve and investigated only effects of kernel width, as kernel smoothing estimates are generally more sensitive to changes in kernel size than shape (Bowman & Azzalini, 1997). By using a gaussian kernel, we were performing acausal filtering, thus making these results more directly applicable to data analysis rather than a biophysical account of neural processing, though the general conceptual framework may transfer into in vivo situations.

Details of generating the Poisson spike train from $\lambda(t)$ have been discussed elsewhere (Lehky, 2004). The spike train was represented as a set of Dirac $\delta$ functions occurring at times $t_i$. Therefore, the shape and duration of biological spikes were abstracted away. For purposes of numerical simulations, time was discretized to 1 msec bins. That is, each 1 msec bin contained either a $\delta$ function pulse or a zero (in practice, mostly zeros with an occasional pulse). This is similar to the convention in systems neuroscience data files of representing spike trains as strings of ones and zeros, a one being recorded for each spike when the voltage of the spike first enters a particular voltage window. A 3 ms refractory period was included in the Poisson generation process, so that variability of the spike count in a trial was slightly lower than for a pure Poisson process (i.e., the Fano factor was less than one).

The mathematical form of the spike train representation was

$$S(t | t_i) = \sum_{t_i} \delta(t - t_i)$$

where $\delta(t - t_i)$ represented a spike occurring at time $t_i$, and the range of $t$ was 0 to 1000 ms, the duration of spike trains in the simulations. The gaussian smoothing kernel was

$$K(t | t_i, \sigma) = \frac{1}{\sigma \sqrt{2\pi}} e^{-\frac{(t-t_i)^2}{2\sigma^2}},$$
and the estimate of the instantaneous firing rate given by the convolution of the spike train by the smoothing kernel:

\[
\hat{\lambda}(t \mid t_i, \sigma) = S * K = \sum_{t_i} K(t \mid t_i, \sigma)
\] (2.3)

(taking advantage of the sifting property of the \(\delta\) impulse).

To deal with edge effects during the convolution, we used spike trains with reflecting boundaries. Appended to both ends of the spike trains were time-reflected copies of the train, forming an extended spike train. That was equivalent to reflecting the tail of the kernel back into the spike train period if it fell beyond that period. If the kernel was so broad that it went beyond even the extended spike train, the kernel tail was truncated, and the area under the truncated kernel was renormalized to one.

Estimating the rate function by convolving the spike train with a smoothing kernel is equivalent to low-pass-filtering the spike train. The transfer function of the gaussian kernel in the frequency domain is

\[
H(\omega \mid \sigma) = e^{-\frac{1}{2}(\sigma \omega/1000)^2},
\]

where \(\omega\) is radial frequency and \(\sigma\) is in milliseconds. The bandwidth (half-power) of the gaussian filtering is

\[
\omega_{BW} = \frac{1000\sqrt{\log(2)}}{\sigma}.
\]

Thus, there is an inverse relation between the width of the kernel in the time and frequency domains. Broad kernels in the time domain correspond to narrow-width low-pass filters.

The rate function \(\lambda(t)\) was characterized by three parameters: (1) the mean rate,

\[
\langle \lambda(t) \rangle_t = \frac{1}{t_D} \int_0^{t_D} \lambda(t) \, dt,
\]

where \(\langle \rangle_t\) is the mean value operator with respect to time and \(t_D\) is spike train duration; (2) the variance \(\text{Var}(\lambda(t))\); and (3) an exponent \(\alpha\) defining a power law Fourier amplitude spectrum for \(\lambda(t)\), which was proportional to \(1/f^\alpha\).

The rate function was computed by generating gaussian white noise followed by low-pass filtering in the frequency domain with the appropriate power law \(1/f^\alpha\). The spectrum was truncated to zero for frequencies above 100 Hz for biophysical reasons. The function was then returned to the time domain by an inverse Fourier transform. At this point, the function was
Figure 4: Example rate functions $\lambda(t)$ with different Fourier amplitude spectra. The Fourier spectra were proportional to $1/f^\alpha$, with the values of $\alpha$ indicated in each panel. Besides the Fourier spectral exponent $\alpha$, the other two parameters defining the randomly generated $\lambda(t)$ were their mean and variance.

linearily scaled to give the desired mean and variance. This procedure produced rate functions $\lambda(t)$ that were random functions in the form of colored noise, with $\alpha = 1$ being pink noise, $\alpha = 2$ being brown noise, and $\alpha = 3$ sometimes called black noise (Schroeder, 1991). Some example rate functions are shown in Figure 4 for different values of $\alpha$. In addition to a smaller high-frequency contribution, larger values of $\alpha$ lead to a broader autocorrelation function and can be considered “burstier.” Intracellular recordings show that neuronal firing rates can show rapid fluctuations similar to those seen in these rate functions, with the firing rates mirroring noisy current inputs to the cell (Carandini, Mechler, Leonard, & Movshon, 1996; Nowak, Sanchez-Vivez, & McCormick, 1997).

A simulation “experiment” consisted of $p$ trials, each trial using an identical rate function $\lambda(t)$ but with a different random spike train derived from that rate function (see Figure 1). This is analogous to the way the same stimulus is presented multiple times in actual experiments. The value of $p$ in simulations ranged from 1 to 256. The estimated rate function for an experiment, $\hat{\lambda}(t)$, was calculated by averaging the estimated rate functions for individual trials:

$$\hat{\lambda}(t) = \frac{1}{p} \sum_{k=1}^{p} \hat{\lambda}_k(t).$$ (2.7)

We shall be concerned exclusively with rate estimates based on entire experiments, $\hat{\lambda}(t)$, not individual trials, $\hat{\lambda}_k(t)$ (except for the special case $p = 1$).

Each experiment was replicated $m$ times with the same rate function $\lambda(t)$ to form a set called an experiment replication. Each experiment replication, in turn, was repeated $n$ times, each with a different $\lambda(t)$, to form an
experiment group. The \( m \) exemplars of \( \lambda(t) \) within each group were randomly generated using the same triplet of parameters (mean, variance, and spectral exponent \( \alpha \)). Thus, for each experimental group, we were interested in estimation errors associated with the statistical characteristics underlying \( \lambda(t) \), not with individual examples of \( \lambda(t) \). Each experimental group was therefore associated with one point in the statistical parameter space defining \( \lambda(t) \), and the parameter space was sampled with simulation data from a set of experimental groups.

The total error function was the mean integrated square error (MISE) between actual and estimated rate functions:

\[
E_T(\sigma) = \frac{1}{n} \sum_{i=1}^{n} \left( \frac{1}{m} \sum_{j=1}^{m} \left( \int_{t=0}^{t_D} \left( \lambda_i(t) - \hat{\lambda}_{ij}(t | \sigma) \right)^2 dt \right) \right),
\]

(2.8)

where \( t_D \) was the duration of the spike train. Taking advantage of the ergodicity of \( \lambda(t) \), total error in practice was calculated across time rather than across an ensemble at a point in time.

3 Results

Plots of example total error curves \( E_T(\sigma) \) are shown in Figure 5, with a different value of mean rate \( \langle \lambda(t) \rangle \) in each panel. The curves generally have a dipper shape, first declining and then either increasing or remaining at a plateau. The error curves within each panel change shape as the number of trials per experiment \( p \) is increased. The initial descending portion of the curve shifts downward proportionally to \( p \). The ascending portion of the curve shifts downward to an asymptotic limit as \( p \to \infty \).

Total error can be expressed as the sum of components related to variance error and bias squared error (Silverman, 1986):

\[
E_T(\sigma) = E_V(\sigma) + E_B(\sigma).
\]

(3.1)

\( E_V(\sigma) \) is the integrated variance error,

\[
E_V(\sigma) = \frac{1}{n} \sum_{i=1}^{n} \left( \frac{1}{m} \sum_{j=1}^{m} \left( \int_{t=0}^{t_D} \text{Var}(\hat{\lambda}_{ij}(t | \sigma)) dt \right) \right),
\]

(3.2)

averaged over \( m \) instantiations of spike trains from the same \( \lambda(t) \), as well as \( n \) exemplars of different \( \lambda(t) \) functions randomly generated using the same triplet of parameter values. Variance here refers to variance across an
Figure 5: Error between actual rate function $\lambda(t)$ and estimated rate function $\hat{\lambda}(t)$ as a function of the width $\sigma$ of the gaussian smoothing kernel used. Error was defined as mean integrated square error (MISE), with units of (spikes/sec)$^2$. Curves were generated through simulations. Each panel shows error curves for a different mean firing rate of $\lambda(t)$. Within individual panels, each curve corresponds to a different number of trials per experiment $p$, with the curve reflecting estimation error after pooling the $p$ replications. In all cases, variance of $\lambda(t)$ was equal to 0.1 times the mean firing rate, with Fourier exponent $\alpha = 2$. Dotted lines are asymptotic bias error curves as $p \to \infty$.

ensemble of $\hat{\lambda}(t)$ at each point in time. $E_B(\sigma)$ is the integrated bias squared error,

$$E_B(\sigma) = \frac{1}{n} \sum_{i=1}^{n} \left( \int_{t_D}^{t_B} \left( \lambda_i(t) - \frac{1}{m} \sum_{j=1}^{m} \hat{\lambda}_{ij}(t | \sigma) \right)^2 \, dt \right),$$

(3.3)
Figure 6: Decomposition of total error curves (as in Figure 5) into a variance error component and a bias error component. Each panel shows curves corresponding to a different mean firing rate of \( \lambda(t) \). In all cases, variance of \( \lambda(t) \) was equal to 0.1 times the mean firing rate, with Fourier exponent \( \alpha = 2 \) and the number of replication trials per experiment \( p = 16 \). The empty circle symbol toward the right of each curve is the error if \( \lambda(t) \) is estimated as the mean firing rate over trial duration (effectively setting \( \sigma \to \infty \)).

averaged in the same way, again based on ensemble calculations. For convenience, we shall refer to \( E_V(\sigma) \) and \( E_B(\sigma) \) by the shorthand expressions “variance error” and “bias error,” keeping in mind that we are actually referring to integrated errors. Example \( E_T(\sigma) \) curves decomposed into their \( E_V(\sigma) \) and \( E_B(\sigma) \) components are shown in Figure 6. The variance error is associated with the descending portion of the \( E_T(\sigma) \) curve to the left, while
the bias error is associated with the flat or ascending portion of the curve to the right.

An analytic expression for \( E_V(\sigma) \) can be derived. Consider a spike train of duration \( t_D \) with a single spike at time \( t_i \) that has been smoothed by a gaussian kernel with width \( \sigma \). The smoothed spike train (estimated rate function \( \hat{\lambda}(t) \)) is then given by

\[
\hat{\lambda}(t | \sigma) = \frac{1}{\sigma \sqrt{2\pi}} e^{-\frac{(t-t_i)^2}{2\sigma^2}}, \quad t = [0, t_D]. \tag{3.4}
\]

For the \( E_V(\sigma) \) curve, we want to know the integrated \( \text{Var}(\hat{\lambda}(t | \sigma)) \) as a function of \( \sigma \). Note we are taking the variance of gaussian curve values with respect to the vertical axis. A standard formula for variance is

\[
\text{Var}(\hat{\lambda}) = \langle \hat{\lambda}^2 \rangle_t - \langle \hat{\lambda} \rangle_t^2 \tag{3.5}
\]

(taking advantage of the ergodicity of \( \lambda(t) \) to go from ensemble averages to time averages). For \( \sigma \) small relative to \( t_D \) in equation 3.4, \( \langle \hat{\lambda}^2 \rangle_t \gg \langle \hat{\lambda} \rangle_t^2 \). Therefore,

\[
\text{Var}(\hat{\lambda}) \approx \langle \hat{\lambda}^2 \rangle_t. \tag{3.6}
\]

For an experiment (see equation 2.7) averaging data from \( p \) one-spike trials with the spike at random \( t_i \) for each trial, the resulting \( \epsilon \hat{\lambda}(t) \) is the sum of \( p \) gaussian curves, each gaussian being attenuated in height by a factor of \( 1/p \) (variance of each gaussian attenuated by a factor of \( 1/p^2 \)). That gives

\[
\text{Var}(\epsilon \hat{\lambda}) \approx p \left( \frac{1}{p^2} \langle \hat{\lambda}^2 \rangle_t \right) = \frac{1}{p} \langle \hat{\lambda}^2 \rangle_t, \tag{3.7}
\]

assuming that the firing rate and kernel width are both small enough such that the \( p \) gaussians do not substantially overlap. Inserting this expression into equation 3.2,

\[
E_V(\sigma) = \frac{1}{n} \sum_{i=1}^{n} \left( \frac{1}{m} \sum_{j=1}^{m} \left( \frac{1}{p} \int_{t=0}^{t_D} \langle \hat{\lambda}^2 \rangle_t dt \right) \right). \tag{3.8}
\]

Developing an expression for \( \langle \hat{\lambda}^2 \rangle_t \) inside the integral, we square equation 3.4:

\[
\hat{\lambda}(t | \sigma)^2 = \frac{1}{2\pi \sigma^2} e^{-\frac{(t-t_i)^2}{2\sigma^2}}. \tag{3.9}
\]
The value of \( \langle \hat{\lambda}^2 \rangle_t \), or mean value of \( \hat{\lambda}(t | \sigma)^2 \), is the area under \( \hat{\lambda}(t | \sigma)^2 \) divided by the length of the time period \( t_D \):

\[
\langle \hat{\lambda}(t | \sigma)^2 \rangle_t = \frac{1}{2\pi t_D} \int_{t=0}^{t_D} \frac{1}{\sigma^2} e^{-\frac{(t-t_i)^2}{\sigma^2}} \, dt.
\]

(3.10)

Equation 3.10 in turn is equal to

\[
\langle \hat{\lambda}(t | \sigma)^2 \rangle_t = \frac{\text{erf} \left( \frac{t_D-t_i}{\sigma} \right) + \text{erf} \left( \frac{t_i}{\sigma} \right)}{4\sqrt{\pi t_D \sigma}} \approx \frac{1}{2\sqrt{\pi t_D \sigma}}
\]

(3.11)

as the error function \( \text{erf} \) approaches one for \( \sigma \) small relative to \( t_D - t_i \) and \( t_i \). If we have a spike train with \( s \) spikes instead of one, then equation 3.11 becomes

\[
\langle \hat{\lambda}(t | \sigma)^2 \rangle_t \approx \frac{s}{2\sqrt{\pi t_D \sigma}},
\]

(3.12)

assuming the spike rate is low enough that convolution kernels for the spikes do not substantially overlap. Substituting equation 3.12 into equation 3.8 and moving constant terms out of the integral,

\[
E_V(\sigma) = \left( \frac{1}{2\sqrt{\pi p \sigma}} \right) \frac{1}{n} \sum_{i=1}^{n} \left( \frac{1}{m} \sum_{j=1}^{m} \left( s_{ij} \int_{t=0}^{t_D} \, dt \right) \right)
\]

\[
= \left( \frac{t_D}{2\sqrt{\pi p \sigma}} \right) \frac{1}{n} \sum_{i=1}^{n} \left( \frac{1}{m} \sum_{j=1}^{m} \left( s_{ij} \right) \right).
\]

(3.13)

The expected value of \( s_{ij}/t_D \) (spikes per unit time) is equal to the mean of the rate function \( \langle \lambda(t) \rangle_t \), giving us the final result for the variance error curve:

\[
E_V(\sigma) = \frac{t_D \langle \lambda(t) \rangle_t}{2\sqrt{\pi p \sigma}} \cdot \frac{1}{\sigma}.
\]

(3.14)

The variance error proportionality constant is

\[
\beta_V = \frac{t_D \langle \lambda(t) \rangle_t}{2\sqrt{\pi p}}.
\]

(3.15)

The inverse relation between variance error and \( \sigma \) seen in equation 3.14 is an idealization that is perturbed by two factors in real situations: edge effects from a finite duration spike train and overlap between kernels as the
Table 1: Fitted Parameter Values for the Empirical Variance Error Curve, Equation 3.16, for Different Mean Firing Rates \( \langle \lambda(t) \rangle_t \).

<table>
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<tr>
<th>( \langle \lambda(t) \rangle_t )</th>
<th>( \eta_0 )</th>
<th>( \eta_1 )</th>
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<th>( \eta_3 )</th>
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</table>

spike rate increases. The idealization holds for \( \sigma \) small relative to the spike train duration \( t_D \), and for low spike rates such that \( \sigma \) is small relative to the mean interspike interval. In a log-log plot, the ideal \( EV(\sigma) \) is a straight line with a slope of \(-1\). In the \( EV(\sigma) \) plots of Figure 6, we see deviations from this ideal for large \( \sigma \). An empirical expression for the actual \( EV(\sigma) \) is given by

\[
\hat{E}_v(\sigma) = \beta_V \exp \left( \sum_{i=0}^{4} \eta_i \log(\sigma)^i \right), \tag{3.16}
\]

with values of \( \eta_i \) in Table 1 fitted from simulations by nonlinear regression. This is a polynomial in log-log space. Deviations from the ideal in the empirical \( EV(\sigma) \) curve are specific for the particular boundary conditions in effect.

The right side of the total error curve \( ET(\sigma) \), which is dominated by bias error, approaches a limit as the number of trials per experiment \( p \to \infty \) (dashed lines in Figure 5). That limit is the asymptotic bias error, given by

\[
E_{asyB}(\sigma) = \frac{1}{n} \sum_{i=1}^{n} \left( \int_{t=0}^{t_D} (\lambda_i(t) - \lambda_i(t) \ast K(t | \sigma))^2 \, dt \right), \tag{3.17}
\]

where \( K(t | \sigma) \) is the smoothing kernel with width \( \sigma \). Essentially \( E_{asyB}(\sigma) \) is the integrated bias squared error between \( \lambda(t) \) and a smoothed version of itself. The equation for asymptotic bias is analogous to that of the regular bias \( E_B(\sigma) \), except that smoothing is performed directly on \( \lambda(t) \) and not on the spike trains generated from \( \lambda(t) \). As there is no stochastic mapping from \( \lambda(t) \) to spike trains in this case, the averaging over \( m \) experiment replications can be omitted.

\( E_{asyB}(\sigma) \) curves have a sigmoidal form whose shape depends entirely on Fourier spectral exponent \( \alpha \) of \( \lambda(t) \), and not on \( \langle \lambda(t) \rangle_t \) or \( \text{Var}(\lambda(t)) \). Plots of \( E_{asyB}(\sigma) \) for different values of \( \alpha \) are given in Figure 7, normalized on a
Table 2: Fitted Parameter Values for the Asymptotic Bias Error Curve, Equation 3.18, for Different Values of the Fourier Spectral Exponent $\alpha$.

<table>
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</tbody>
</table>

Figure 7: Asymptotic bias error curves, showing how curve shape changes as a function of Fourier spectral exponent $\alpha$. These curves have been normalized to a height of one. The asymptotic bias error curves indicate the limit of bias error as the number of trials per experiment $p \to \infty$ (see the dotted curves in Figure 5).

The $E_{asyB}(\sigma)$ curves are empirically approximated by the following equation:

$$E_{asyB}(\sigma) = \beta_{asyB} \left[ \frac{\nu_1}{\nu_3 \sqrt{2\pi}} \int_{x=0}^{\sigma} \frac{1}{x} e^{-\frac{(\ln x - \nu_2)^2}{2\nu_3^2}} dx + \frac{1 - \nu_1}{\nu_5 \Gamma(\nu_4)} \int_{x=0}^{\sigma} x^{\nu_4 - 1} e^{-\frac{x}{\nu_5^2}} dx \right],$$

(3.18)

where $\Gamma$ is the gamma function. The parameters $\nu_1, \ldots, 5$ for the curves, found by nonlinear regression of equation 3.18 on the simulations, are given in Table 2. This equation is the weighed sum of the equations for the log-normal cumulative distribution function (cdf) and the gamma cdf. Those cdfs have no probabilistic interpretation here but were empirically chosen for their ability to fit the sigmoid $E_{asyB}(\sigma)$ curves that arose through simulation.
The proportionality constant $\beta_{asyB}$ in equation 3.18 can be derived analytically. The value of $\beta_{asyB}$ is $\lim_{\sigma \to \infty} E_{asyB}(\sigma)$. As the width of the gaussian kernel approaches infinity, convolving $\lambda(t)$ with the kernel produces the mean of $\lambda(t)$:

$$\lim_{\sigma \to \infty} [\lambda(t) * K(t | \sigma)] = \langle \lambda(t) \rangle_t.$$  \hfill (3.19)

This converts equation 3.17 to

$$\lim_{\sigma \to \infty} E(\sigma) = \beta_{asyB} = \frac{1}{n} \sum_{i=1}^{n} \left( \int_{t=0}^{tD} (\lambda_i(t) - \langle \lambda_i(t) \rangle_t)^2 dt \right).$$  \hfill (3.20)

Multiplying equation 3.20 by $t_D/t_D = 1$,

$$\beta_{asyB} = \frac{1}{n} \sum_{i=1}^{n} \left( t_D \left( \frac{1}{t_D} \int_{t=0}^{tD} (\lambda_i(t) - \langle \lambda_i(t) \rangle_t)^2 dt \right) \right).$$  \hfill (3.21)

The term in the inner parentheses is the mean of $(\lambda_i(t) - \langle \lambda_i(t) \rangle_t)^2$, so

$$\beta_{asyB} = \frac{1}{n} \sum_{i=1}^{n} (t_D \langle (\lambda_i(t) - \langle \lambda_i(t) \rangle_t)^2 \rangle_t).$$  \hfill (3.22)

From the definition of variance, equation 3.22 becomes

$$\beta_{asyB} = \frac{1}{n} \sum_{i=1}^{n} (t_D \text{Var}(\lambda_i(t))).$$  \hfill (3.23)

As all $\lambda_i(t)$ are defined to have identical variance, we get the final result:

$$\beta_{asyB} = t_D \text{Var}(\lambda(t)).$$  \hfill (3.24)

Empirically, we shall treat the bias error curve as having the same shape as the asymptotic bias error curve but translated upward. This amounts to replacing in equation 3.18 the proportionality constant $\beta_{asyB}$ by $\beta_B$:

$$\hat{E}_B(\sigma) = \beta_B \left[ \frac{\beta_1}{\beta_3 \sqrt{2\pi}} \int_{x=-\infty}^{\sigma} \frac{1}{x} e^{-\frac{(x+\beta_2)^2}{2\beta_3^2}} dx + \frac{1 - \beta_1}{\beta_4^{\beta_5} \Gamma(\beta_4)} \int_{x=-\infty}^{\sigma} x^{\beta_4-1} e^{\frac{x^2}{\beta_5}} dx \right].$$  \hfill (3.25)
An analytic expression can be derived for $\beta_B$, which is equal to
\[
\lim_{\sigma \to \infty} E_B(\sigma) = \lim_{\sigma \to \infty} E_T(\sigma).
\]
As $\sigma \to \infty$, the variance error $E_B(\sigma)$ goes to zero (see equation 3.14), so that by equation 3.1, $\lim_{\sigma \to \infty} E_B(\sigma) = \lim_{\sigma \to \infty} E_T(\sigma)$. From the expression for $E_T(\sigma)$ in equation 2.8,

\[
\beta_B = \lim_{\sigma \to \infty} E_B(\sigma) = \lim_{\sigma \to \infty} E_T(\sigma)
= \lim_{\sigma \to \infty} \left( \frac{1}{n} \sum_{i=1}^{n} \left( \frac{1}{m} \sum_{j=1}^{m} \left( \int_{t=0}^{t_D} (\lambda_i(t) - \lambda_{ij}(t | \sigma))^2 d\tau \right) \right) \right). \tag{3.26}
\]

As the width of the gaussian kernel approaches infinity, convolving the spike train $S(t | t_i)$ with the kernel $K(t | \sigma)$ produces the mean of $S(t | t_i)$, which is equal to the number of spikes on the $k$th trial $s_k$ divided by the spike train duration $t_D$, or the mean rate $r_k$ for trial $k$:

\[
\lambda(t | t_i, \sigma) = S * K = \langle S(t | t_i) \rangle = \frac{s_k}{t_D} = r_k. \tag{3.27}
\]

Taking $\epsilon_{rij}$ as the mean of $r_k$ over $p$ trials in the $i, j$th experiment converts equation 3.26 to

\[
\beta_B = \frac{1}{n} \sum_{i=1}^{n} \left( \frac{1}{m} \sum_{j=1}^{m} \left( \int_{t=0}^{t_D} (\lambda_i(t) - \langle \lambda_i(t) \rangle_t)^2 d\tau \right) \right). \tag{3.28}
\]

Adding the term $\langle \lambda_i(t) \rangle_t - \langle \lambda_i(t) \rangle_t = 0$ into equation 3.28 and rearranging gives

\[
\beta_B = \frac{1}{n} \sum_{i=1}^{n} \left( \frac{1}{m} \sum_{j=1}^{m} \left( \int_{t=0}^{t_D} \left[ (\lambda_i(t) - \langle \lambda_i(t) \rangle_t) - (\epsilon_{rij} - \langle \lambda_i(t) \rangle_t)^2 \right] d\tau \right) \right). \tag{3.29}
\]

Expanding the square within the integral,

\[
\beta_B = \frac{1}{n} \sum_{i=1}^{n} \left( \frac{1}{m} \sum_{j=1}^{m} \left( \int_{t=0}^{t_D} (\lambda_i(t) - \langle \lambda_i(t) \rangle_t)^2 d\tau - 2 \int_{t=0}^{t_D} (\lambda_i(t) - \langle \lambda_i(t) \rangle_t) (\epsilon_{rij} - \langle \lambda_i(t) \rangle_t)^2 d\tau \right) \right) \times (\epsilon_{rij} - \langle \lambda_i(t) \rangle_t) d\tau + \int_{t=0}^{t_D} (\epsilon_{rij} - \langle \lambda_i(t) \rangle_t)^2 d\tau \right) \right). \tag{3.30}
\]
The $r_{ij} - \langle \lambda_i(t) \rangle_t$ term in the middle integral is a constant, and the $\lambda_i(t) - \langle \lambda_i(t) \rangle_t$ term integrates to zero, so the middle integral disappears, leaving

$$
\beta_B = \frac{1}{n} \sum_{i=1}^{n} \left( \frac{1}{m} \sum_{j=1}^{m} \left( \int_{t=0}^{t_D} (\lambda_i(t) - \langle \lambda_i(t) \rangle_t)^2 d t \right) \right) + \int_{t=0}^{t_D} (r_{ij} - \langle \lambda_i(t) \rangle_t)^2 d t \right) \right).
$$

(3.31)

The first integral in equation 3.31 is $\beta_{asyB}$ (see equations 3.20 and 3.24), so:

$$
\beta_B = \beta_{asyB} + \frac{1}{n} \sum_{i=1}^{n} \left( \frac{1}{m} \sum_{j=1}^{m} \left( \int_{t=0}^{t_D} (r_{ij} - \langle \lambda_i(t) \rangle_t)^2 d t \right) \right)
$$

$$
= t_D \text{Var}(\lambda(t)) + \frac{1}{n} \sum_{i=1}^{n} \left( \frac{1}{m} \sum_{j=1}^{m} \left( \int_{t=0}^{t_D} (r_{ij} - \langle \lambda_i(t) \rangle_t)^2 d t \right) \right).
$$

(3.32)

Both $r_{ij}$ and $\langle \lambda_i(t) \rangle_t$ are constants as a function of time, so they may be taken outside the integral, producing

$$
\beta_B = t_D \text{Var}(\lambda(t)) + t_D \frac{1}{n} \sum_{i=1}^{n} \left( \frac{1}{m} \sum_{j=1}^{m} (r_{ij} - \langle \lambda_i(t) \rangle_t)^2 \right).
$$

(3.33)

As the mean rate $\langle \lambda_i(t) \rangle_t$ is defined as identical for all $i$, the expected value of $\langle r \rangle_t = \langle \lambda_i(t) \rangle_t$, where $\langle r \rangle_t$ is the observed mean firing rate over $m \cdot n$ experiments. Therefore:

$$
\beta_B = t_D \text{Var}(\lambda(t)) + t_D \frac{1}{n} \sum_{i=1}^{n} \left( \frac{1}{m} \sum_{j=1}^{m} (r_{ij} - \langle r \rangle_t)^2 \right)
$$

$$
= t_D \text{Var}(\lambda(t)) + t_D \langle \text{Var}(r) \rangle_t
$$

$$
= t_D \text{Var}(\lambda(t)) + t_D \text{Var}(r),
$$

(3.34)

where $\text{Var}(r)$ is the variance of the mean firing rate among replicated experiments. Since $\text{Var}(r)$ results from averaging over $p$ trials per experiment, in terms of a single-trial $r$, equation 3.34 becomes

$$
\beta_B = t_D \text{Var}(\lambda(t)) + t_D \frac{\text{Var}(r)}{p},
$$

(3.35)

where $\text{Var}(r)$ is the variance of the mean rate between individual trials.
Var(r) in the above expression can be reexpressed in terms of mean rate \( \langle r \rangle_t \) using the Fano factor. The Fano factor with respect to the number of spikes per trial \( s \) is

\[
F_s = \frac{\text{Var}(s)}{\langle s \rangle_t}. \tag{3.36}
\]

For a \( k \)th-order gamma process, \( F_s = 1/k \), with Poisson processes being a special case with \( k = 1 \). It should be emphasized that this is the Fano factor for the underlying stochastic spiking process and not the rate function \( \lambda(t) \). In other words, it is the Fano factor for a spike train when the spike rate is constant over the entire trial. Going to the Fano factor for spike count (\( F_r \)) from the Fano factor for spike rate (\( F_s \)) gives

\[
F_r = \frac{\text{Var}(r)}{\langle r \rangle_t} = \frac{\text{Var}(s/t_D)}{\langle s/t_D \rangle_t} = \frac{1}{t_D} \frac{\text{Var}(s)}{\langle s \rangle_t} = \frac{F_s}{t_D}. \tag{3.37}
\]

From equation 3.37,

\[
\text{Var}(r) = F_r \langle r \rangle_t = \frac{F_s}{t_D} \langle r \rangle_t. \tag{3.38}
\]

Substituting equation 3.38 into equation 3.35 produces

\[
\beta_B = t_D \text{Var}(\lambda(t)) + \frac{F_s}{p} \langle r \rangle_t. \tag{3.39}
\]

The expected value of the mean firing rate \( \langle r \rangle_t \) estimated over \( m \cdot n \cdot p \) trials is equal to the actual mean firing rate \( \langle \lambda(t) \rangle_t \), giving the final result:

\[
\beta_B = t_D \text{Var}(\lambda(t)) + \frac{F_s}{p} \langle \lambda(t) \rangle_t. \tag{3.40}
\]

From an examination of equations 3.24 and 3.40, as trials per experiment \( p \to \infty \), \( \beta_B \to \beta_{\text{asyB}} \), consistent with the simulations shown in Figure 5.

At this point we introduce the concept of the spike density of an experiment. As described earlier, each experiment consists of \( p \) trials, with all trials having an identical rate function \( \lambda(t) \) with mean \( \langle \lambda(t) \rangle_t \). The expected spike density \( \delta \) for the experiment is

\[
\delta = p \cdot \langle \lambda(t) \rangle_t. \tag{3.41}
\]
Spike density is associated with an experiment as a whole, whereas spike rate is associated with individual trials. The inverse of spike density is the pooled mean interspike interval $I$ for an experiment:

$$I = \frac{1}{\delta}. \quad (3.42)$$

Given that bit of nomenclature, we can now turn to the issue of the optimal value of $\sigma$, which minimizes the $E_T(\sigma)$ curve.

Under certain conditions, changing mean rate $\langle \lambda(t) \rangle_t$ translates the total error curve $E_T(\sigma)$ vertically while leaving its shape invariant under a logarithmic scale. The significance of maintaining the shape invariance of $E_T(\sigma)$ is that the value of $\sigma$ that minimizes $E_T(\sigma)$, $\sigma_{opt}$, remains constant. For error curve shape invariance to happen, the ratio of the variance error and bias error proportionality constants, $\beta_B / \beta_V$, must be constant as a function of $\langle \lambda(t) \rangle_t$. Using the definition of spike density $\delta$ (see equation 3.41), the proportionality constants $\beta_V$ (see equation 3.15) and $\beta_B$ (see equation 3.40) become

$$\beta_V = \frac{t_D}{2\sqrt{\pi}} \frac{\langle \lambda(t) \rangle_t^2}{\delta} \quad (3.43)$$

$$\beta_B = t_D \text{Var}(\lambda(t)) + F_n \frac{(\langle \lambda(t) \rangle_t)^2}{\delta}. \quad (3.44)$$

Their ratio is

$$\frac{\beta_B}{\beta_V} = 2\sqrt{\pi} \left( \frac{\delta \text{Var}(\lambda(t))}{\langle \lambda(t) \rangle_t^2} + \frac{F_n}{t_D} \right)$$

$$= 2\sqrt{\pi} \left( \delta \left( \frac{\text{Std}(\lambda(t))}{\langle \lambda(t) \rangle_t} \right)^2 + \frac{F_n}{t_D} \right). \quad (3.45)$$

The term within the inner bracket, the ratio of the standard deviation to the mean of $\lambda(t)$, is the coefficient of variation of $\lambda(t)$:

$$C_V(\lambda) = \frac{\text{Std}(\lambda(t))}{\langle \lambda(t) \rangle_t}. \quad (3.46)$$

By substitution, equation 3.45 becomes

$$\frac{\beta_B}{\beta_V} = 2\sqrt{\pi} \left( \delta C_V^2 + \frac{F_n}{t_D} \right). \quad (3.47)$$
Figure 8: A set of error curves produced when the following three parameters were held constant: the spike density $\delta$ of the data set, the coefficient of variation $C_V$, and the Fourier exponent $\alpha$ of the rate function. This shows that the shapes of error curves are nearly invariant when these parameters are held constant, and consequently have their minima $\sigma_{opt}$ at approximately the same values. Curves are vertically shifted from each other as a function of mean firing rate. Spike density is the mean of the firing rate function $\langle \lambda(t) \rangle_t$ times the number of trials per experiment $p$. For all three curves, spike density was fixed at 1024 spikes/sec. The coefficient of variation $C_V$ of $\lambda(t)$ was set to 0.1 for these curves, and the Fourier exponent $\alpha$ was 2.

Thus, a condition for shape invariance of the $E_T(\sigma)$ curve at different mean firing rates is for the spike density $\delta$ (or, equivalently, its inverse $1/\delta$) to be constant as well as for $C_V$ of $\lambda(t)$ to be constant. In addition to these two parameters, which affect the shape of $E_T(\sigma)$ by vertically shifting the relative positions of the underlying bias and variance error components without changing the shapes of the component curves themselves, there is a third parameter (not included in equation 3.47) that affects $E_T(\sigma)$ by changing the shape of the $E_B(\sigma)$ component. That third parameter is the Fourier spectral exponent $\alpha$ of $\lambda(t)$, which should also be constant in order to hold the shape of $E_T(\sigma)$ constant. These three variables controlling the shape of the $E_T(\sigma)$ curve ($\delta$, $C_V$, and $\alpha$) are all parameters describing the spike rate function $\lambda(t)$. In addition, from equation 3.47, we see that the Fano factor $F_n$ of the spike generation process (whether it is a Poisson process, gamma process, or something else) also affects the $E_T(\sigma)$ curve shape, independent of the characteristics of $\lambda(t)$, although it will be shown below that this parameter has a relatively small effect.

Shape invariance of $E_T(\sigma)$ is illustrated in Figure 8, where the mean rate $\langle \lambda(t) \rangle_t$ is varied while $\delta$, $C_V$, and $\alpha$ are held constant (using a Poisson spike-generation process). The shape invariance is approximate due to deviations from the ideal of both the $E_V(\sigma)$ and $E_B(\sigma)$ components of $E_T(\sigma)$ at higher spike rates. By determining the parameters that control the shape of the
Figure 9: The optimal value of the gaussian width $\sigma_{opt}$ plotted as a function of the pooled mean interspike time $I$. The pooled mean interspike time was calculated after combining multiple replication trials in an experiment and is the reciprocal of spike density. (a) Three $\sigma_{opt}$ versus $I$ curves generated by changing the coefficient of variation $C_V$ of the rate function $\lambda(t)$. (b) Three $\sigma_{opt}$ versus $I$ curves generated by changing the Fourier spectral exponent $\alpha$ of the rate function $\lambda(t)$. In both panels, the curves show a discontinuity to $\sigma_{opt} \to \infty$ at the point when the intermediate dip in the error curves disappears, and instead they monotonically decline to some asymptotic value.

The total error curve $E_T(\sigma)$, we therefore know the parameters that potentially affect the value of $\sigma$ where the curve minimum is located, which is $\sigma_{opt}$. Thus, we have identified three parameters that may affect $\sigma_{opt}$: which are $\delta$ (or $I$), $C_V$, and $\alpha$.

The value of $\sigma_{opt}$ from simulation data is plotted in Figure 9 as a function of the pooled mean interspike interval $I$. The straight lines in the log-log plot indicate a power law relationship:

$$\sigma_{opt} = a I^b.$$  

(3.48)
Table 3: Functional Relationships Underlying the Power Law \( \sigma_{\text{opt}} = aI^b \) Governing the Optimal Smoothing Width, Equation 3.48, for First-Order (Poisson process), Second-Order, and Third-Order Gamma Processes.

<table>
<thead>
<tr>
<th>Order</th>
<th>( a )</th>
<th>( b )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.41C^{-1.17}</td>
<td>0.87( \alpha )^{-0.57}</td>
</tr>
<tr>
<td>2</td>
<td>5.54C^{-1.24}</td>
<td>0.84( \alpha )^{-0.57}</td>
</tr>
<tr>
<td>3</td>
<td>4.52C^{-1.16}</td>
<td>0.88( \alpha )^{-0.51}</td>
</tr>
</tbody>
</table>

Figure 9a illustrates that \( a \) is primarily a function of \( C_V \) and is inversely proportional to it, although the Fourier spectral exponent \( \alpha \) also affects it to a lesser extent. Figure 9b illustrates that \( b \) primarily is a function of \( \alpha \) and is inversely proportional to it, although affected to a lesser extent by \( C_V \).

Formulas for \( a \) and \( b \) in equation 3.48 were estimated through nonlinear fitting of the simulation data and are given in Table 3. That includes results for a Poisson process (first-order gamma process), as well as second- and third-order gamma processes.

The results in Table 3 show that different renewal processes lead to similar functions for \( \sigma_{\text{opt}} \), suggesting that the characteristics of the spike generation process are of much less importance for setting \( \sigma_{\text{opt}} \) than the statistics of the rate function \( \lambda(t) \). That is not surprising when one considers that none of the analytic expressions derived here is dependent on the nature of the spike generation process, with the exception of the Fano factor in the equation for \( \beta_B \)—equation 3.39.

If \( \sigma_{\text{opt}} \) is indeed largely independent of the spike generation process, then it would be expected that the power law estimates provided here would also be valid if there was a deterministic relationship between spike timing and membrane voltage (Mainen & Sejnowski, 1995; Tiesinga, Fellous, & Sejnowski, 2008) rather than a stochastic one. In any case, even with a deterministic spike generation process, responses of a neuron to repeated trials of the same stimulus would remain effectively stochastic due to variations in the dynamical state of the large-scale network in which the neuron is embedded (Arieli, Sterkin, Grinvald, & Aertsen, 1996).

Although the power law in equation 3.48 is an approximation, even substantial uncertainties in estimating \( \sigma_{\text{opt}} \) will generally not lead \( E_T(\sigma) \) values far from the minimum, because \( E_T(\sigma) \) curves are very broad and shallow (see Figure 5). A noteworthy aspect of equation 3.48 is that \( \sigma_{\text{opt}} \) can be either greater than or less than the pooled mean interspike interval \( I \), depending on parameter values.

Equation 3.48 breaks down for small values of \( \beta_B / \beta_V \), which, for example, would occur for data with small spike densities. For \( \beta_B / \beta_V > 0.012 \) (using the ideal equation for \( \beta_V \), equation 3.15), the intermediate minima
seen in the curves of Figure 8 disappear, so that the curves monotonically decline to some asymptote. (Examples of monotonically declining curves can be seen in Figure 5.) That leads to a discontinuity from the relationship between $\sigma_{\text{opt}}$ and $I$, causing $\sigma_{\text{opt}}$ to go to infinity abruptly. When the empirical equation for $\beta_V$ is used (see equation 3.16), the breakdown is more gradual and occurs for approximately $\beta_B/\beta_V > 0.005$. These discontinuities are indicated in Figure 9, occurring when the pooled mean interspike interval becomes sufficiently large.

The estimates of $\sigma_{\text{opt}}$ in Figure 9 are based on simulations that generated entire error curves as a function of $\sigma$ and then found the minima of those curves. However, there exist algorithms for estimating the optimal width of the smoothing kernel directly from a single data sample, of which the Sheather-Jones algorithm (Sheather & Jones, 1991) is currently among the most widely used. A comparison of our simulation results with the output of the Sheather-Jones algorithm is shown in Figure 10. The comparison indicates that the Sheather-Jones algorithm underestimates $\sigma_{\text{opt}}$, and the underestimation become more pronounced as the pooled mean interspike interval of the data increases (spike density decreases). Moreover, the Sheather-Jones algorithm fails to pick up the discontinuity at very low spike densities where $\sigma_{\text{opt}} \rightarrow \infty$, at which point the best estimate of the temporal waveform of $\lambda(t)$ is a constant equal to its mean $\langle \lambda(t) \rangle_t$.

4 Conclusion

It has been generally understood in the past that $\sigma_{\text{opt}}$ is directly related to mean interspike interval (or modifying that concept here, the pooled mean
interspike spike interval of a multtrial experiment. Refining that, we show
here a power law relationship between $\sigma_{opt}$ and the interspike interval
$I$, and highlight two additional parameters affecting $\sigma_{opt}$: the coefficient
of variation $C_V$ and the Fourier spectral exponent $\alpha$ of the rate function
$\lambda(t)$. Of the three parameters, $I$ and $C_V$ can be estimated from the spike
train data set itself. The third one, $\alpha$, would need auxiliary data to assign
typical values, possibly based on the Fourier spectra of somal membrane
voltages obtained using the whole-cell patch clamping technique (Ferster

A limitation of this analysis is that it treats $\lambda(t)$ as if it were statistically
homogeneous (i.e., the statistical parameters underlying the rate function
do not vary as a function of time). In reality, $\lambda(t)$ may change its position
in parameter space if the functional state of the neuron (and the network
in which it is embedded) changes, as might occur for changed perceptual
input, cognitive state, or motor output of the organism. An approach to
dealing with this would be to select the kernel width $\sigma$ adaptively so that it
is no longer a constant but becomes $\sigma(t)$. That requires that trials be broken
into multiple time periods and $\sigma(t)$ chosen based on local conditions within
each period. Implicit in the use of low $C_V$ values in this study (ranging from
0.05 to 0.2) was the assumption of a local analysis. An entire trial in which
the firing rate ranged from spontaneous activity to a vigorous response
would typically have a much higher $C_V$.

Although the emphasis here has been on accurately recovering the
temporal waveform of a neural response for data analysis purposes, the
same conceptual framework might be transferable to issues in neural sig-
nal transmission in vivo. The overall transfer function between a spike
train and the postsynaptic dendritic voltage waveform, lumping together
multiple elements of the synaptic transmission process, can be treated as
a low-pass filter or, equivalently, convolution of the spike train by some
smoothing kernel (neglecting active membrane properties, if any, within
the dendrite). That is analogous to the process we have been studying
here. Within this framework, one question to ask is, How accurately is
the somatic voltage waveform of the presynaptic cell recovered in the
dendritic voltage waveform? A related question is, What are the char-
acteristics of the optimal synaptic transfer function (smoothing kernel)
that minimizes error in communicating analog signals between neurons
through an intervening spike train (granting that analog signals aris-
ing from nearby synapses may interact nonlinearly within the dendritic
tree)?

By use of both simulations and mathematical analysis, we have gained a
greater understanding of how to optimally recover the analog rate function
underlying an ensemble of spike trains using kernel smoothing. This has
practical applications for data analysis of spike train data and may also be
relevant to understanding neural signal processing in vivo.
Appendix: Symbols Used

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\sigma$</td>
<td>Width of gaussian smoothing kernel</td>
</tr>
<tr>
<td>$\sigma_{opt}$</td>
<td>Optimal smoothing width</td>
</tr>
<tr>
<td>$\lambda(t)$</td>
<td>Instantaneous spike rate as a function of time</td>
</tr>
<tr>
<td>$\hat{\lambda}(t, \sigma)$</td>
<td>Estimated spike rate function using kernel width $\sigma$</td>
</tr>
<tr>
<td>$\hat{\lambda}(t, \sigma)$</td>
<td>Estimated spike rate function for an experiment $\epsilon$, averaging over multiple trials</td>
</tr>
<tr>
<td>$f$</td>
<td>Frequency (Hz)</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>Exponent of the power law describing the Fourier amplitude spectrum of $\lambda(t)$</td>
</tr>
<tr>
<td>$E_T(\sigma)$</td>
<td>Mean integrated square error (total error) between actual and estimated spike rate functions, as a function of kernel width $\sigma$</td>
</tr>
<tr>
<td>$E_V(\sigma)$</td>
<td>Integrated variance error component of total error</td>
</tr>
<tr>
<td>$E_B(\sigma)$</td>
<td>Integrated bias squared error component of total error</td>
</tr>
<tr>
<td>$E_{asyB}(\sigma)$</td>
<td>Integrated asymptotic bias squared error</td>
</tr>
<tr>
<td>$S(t</td>
<td>t_i)$</td>
</tr>
<tr>
<td>$s$</td>
<td>Spike count for a spike train</td>
</tr>
<tr>
<td>$r_k$</td>
<td>Mean spike rate for trial $k$ of an experiment</td>
</tr>
<tr>
<td>$K(t</td>
<td>\sigma)$</td>
</tr>
<tr>
<td>$H(\omega</td>
<td>\sigma)$</td>
</tr>
<tr>
<td>$t$</td>
<td>Time</td>
</tr>
<tr>
<td>$t_D$</td>
<td>Spike train duration (or trial duration) in seconds</td>
</tr>
<tr>
<td>$p$</td>
<td>Number of trials per experiment, using the same $\lambda(t)$ in each trial</td>
</tr>
<tr>
<td>$m$</td>
<td>Number of experiment replications, using the same $\lambda(t)$ for each replication</td>
</tr>
<tr>
<td>$n$</td>
<td>Number of experiment groups, using different $\lambda(t)$ for each group</td>
</tr>
<tr>
<td>$\beta_V$</td>
<td>Integrated variance error proportionality constant</td>
</tr>
<tr>
<td>$\eta_i$</td>
<td>Parameters for the empirical variance error function</td>
</tr>
<tr>
<td>$\beta_B$</td>
<td>Integrated bias error proportionality constant</td>
</tr>
<tr>
<td>$\beta_{asyB}$</td>
<td>Integrated asymptotic bias error proportionality constant</td>
</tr>
<tr>
<td>$v_i$</td>
<td>Parameters for the empirical asymptotic bias error function</td>
</tr>
<tr>
<td>$F_s$</td>
<td>Fano factor of spike generation process with respect to spike count</td>
</tr>
<tr>
<td>$F_r$</td>
<td>Fano factor of spike generation process with respect to spike rate</td>
</tr>
<tr>
<td>$\delta$</td>
<td>Pooled spike density in spikes/sec, adding (not averaging) data from multiple trials in an experiment</td>
</tr>
<tr>
<td>$I$</td>
<td>Pooled mean interspike interval, equal to $1/\delta$</td>
</tr>
<tr>
<td>$C_V$</td>
<td>Coefficient of variation of $\lambda(t)$</td>
</tr>
<tr>
<td>$\langle \rangle_t$</td>
<td>Mean value operator with respect to time</td>
</tr>
<tr>
<td>Var()</td>
<td>Variance</td>
</tr>
<tr>
<td>Std()</td>
<td>Standard deviation</td>
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References


Received July 22, 2008; accepted September 14, 2009.