7

Variability of spike trains and neural codes

The neuron models discussed in the previous chapters are deterministic and generate, for most choices of parameters, spike trains that look regular when driven by a constant stimulus. *In vivo* recordings of neuronal activity, however, are characterized by a high degree of irregularity. The spike train of an individual neuron is far from being periodic, and correlations between the spike timings of neighboring neurons are weak. If the electrical activity picked up by an extracellular electrode is made audible by a loudspeaker then what we basically hear is noise. The question whether this is indeed just noise or rather a highly efficient way of coding information cannot easily be answered. Indeed, listening to a computer modem or a fax machine might also leave the impression that this is just noise. Being able to decide whether we are witnessing the neuronal activity that is underlying the composition of a poem (or the electronic transmission of a love letter) and not just meaningless flicker is one of the most burning problems in neuroscience.

Several experiments have been undertaken to tackle this problem. It seems that a neuron *in vitro*, once it is isolated from the network, can react in a very reliable and reproducible manner to a fluctuating input current, and so can neurons in the sensory cortex *in vivo* when driven by a strong time-dependent signal. On the other hand, neurons produce irregular spike trains in the absence of any temporally structured stimuli. Irregular spontaneous activity, i.e., activity that is not related in any obvious way to external stimulation, and trial-to-trial variations in neuronal responses are often considered as noise.

The origin of this irregularity of neuronal dynamics *in vivo* is poorly understood. In integrate-and-fire models, noise is therefore often added explicitly to neuronal dynamics so as to mimic the unpredictability of neuronal recordings. How to add noise to neuron models is the topic of Chapters 8 and 9. The aim of the present chapter is a mere description and quantification of the variability of neuronal spike trains. We review in Section 7.1 some experimental evidence for noise in neurons and introduce in Sections 7.2–7.5 a statistical framework of spike-train analysis. In particular, we present the definitions of firing rate, interval distribution, power spectrum, and renewal statistics. In Section 7.6 we ask whether the firing rate, which is such a useful measure for quantification of spike trains, can also be considered as the code used by neurons in the brain.

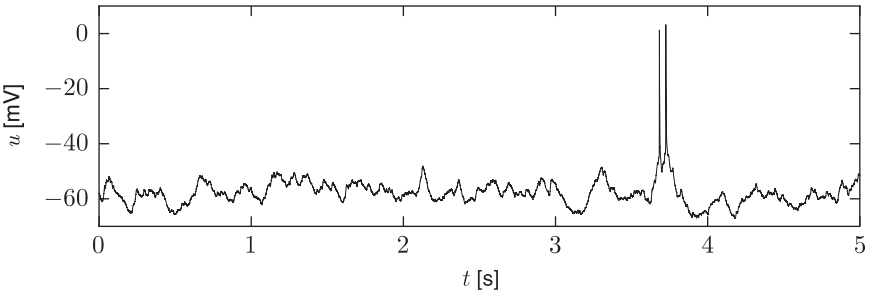

Fig. 7.1 Spontaneous activity *in vivo*. Sample of a voltage trace (whole-cell recording) of a cortical neuron when the animal receives no experimental stimulation. The neuron is from layer 2/3 of the C2 cortical column, a region of the cortex associated with whisker movement. The recording corresponds to a period of time where the mouse is awake and freely whisking. Data courtesy of Sylvain Crochet and Carl Petersen (Crochet *et al*., 2011).

7.1 Spike-train variability

If neuron models such as the Hodgkin–Huxley or the integrate-and-fire model are driven by a sufficiently strong constant current, they generate a regular sequence of spikes. In neuronal models with adaptation currents[1] there might be a short transient phase at the beginning, but then all interspike intervals are constant. Spike trains of typical neurons *in vivo* show much more irregular behavior. Whether the irregularity is the sign of thermal noise, microscopic chaos, or rather the signature of an intricate neural code is at present an open question. In the first subsection we review some evidence for neuronal variability and spike-train irregularity. We then discuss potential sources of noise.

7.1.1 Are neurons noisy?

Many *in vivo* experiments show noisy behavior of cortical neurons. The activity of neurons from the visual cortex, for example, can be recorded while a slowly moving bar is presented on a screen within the visual field of the animal. As soon as the bar enters the neuron's receptive field the firing rate goes up. The spike train, however, varies considerably from trial to trial, if the same experiment is repeated several times. Similarly, neurons in a region of the sensory cortex of rats or mice respond systematically to whisker movements, but the response is somewhat different between one trial and the next. Furthermore, the very same neuron occasionally emits a spontaneous spike, even if no external stimulus is applied. During spontaneous activity, the voltage trajectory fluctuates considerably and intervals between one spike and the next exhibit a large degree of variability (Fig. 7.1).

Are these experiments convincing evidence for ubiquitous noise in the central nervous system? The above observations refer to experiments on the neural system as a whole. The cortical neuron that is recorded from receives input not only from the sensors, but

[1] We neglect here intrinsically bursting and chaotic neurons.

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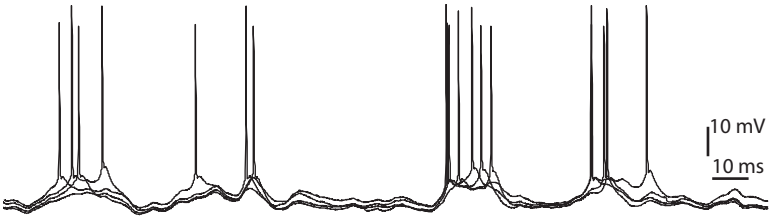

Fig. 7.2 Variability across four repetitions of the same stimulus *in vitro*. Sample voltage traces during stimulation with a time-dependent current. Modified from Naud and Gerstner (2012b) with kind permission from Springer Science and Business Media.

also from many other neurons in the brain. The effective input to this neuron is basically unknown. It is thus possible that there is a substantial fluctuation in the input current to cortical neurons, even though the external (e.g., visual or tactile) stimulus is always the same.

The advantage of experiments *in vitro* is that the stimulus injected into the neuron can be well controlled. If the stimulation consists of a known time-dependent current directly injected into the neuron, the neuronal response also varies from one trial to the next, even if the very same stimulation is repeated several times (Fig. 7.2). Is this an indication of "real" noise? The variability is visible only if the stimulating current is nearly constant (Fig. 7.3). In fact, when neurons are driven by a current with large-amplitude fluctuations of the input signal, neurons behave more or less deterministically (Bryant and Segundo, 1976; Mainen and Sejnowski, 1995).

Similarly, in the full and intact brain, neurons react much more reliably to a rapidly changing external stimulus than to constant or slowly moving stimuli. For example, spatially uniform random flicker of an image elicits more or less the same spike train in retinal ganglion cells if the same flicker sequence is presented again (Berry *et al*., 1997). A similar behavior has been reported for motion-sensitive neurons of the visual system in flies (de Ruyter van Steveninck *et al*., 1997) and monkey cortex (Bair and Koch, 1996); see Fig. 7.4 for an example of a cortical neuron. Whether a neuron behaves nearly deterministically or rather randomly thus depends, at least to a certain extent, on the stimulus.

In the following, we distinguish between intrinsic noise sources that generate stochastic behavior on the level of the *neuronal* dynamics and are present even in an isolated neuron *in vitro*; and extrinsic sources that arise from network effects and synaptic transmission naturally occurring *in vivo*.

7.1.2 Intrinsic noise sources

A source of noise which is literally omnipresent is thermal noise. Owing to the discrete nature of electric charge carriers, the voltage u across any electrical resistor R fluctuates at finite temperature (Johnson noise). The variance of the fluctuations at rest is $\langle \Delta u^2 \rangle \propto$

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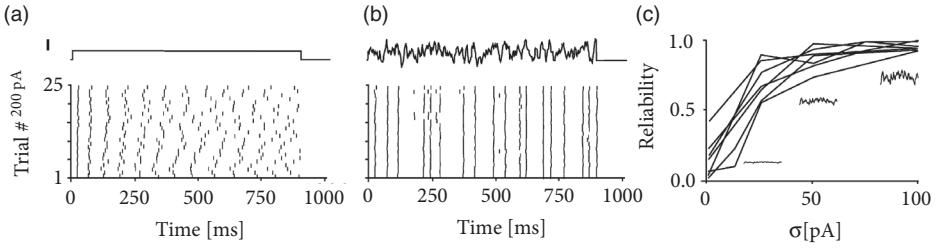

Fig. 7.3 Variability across repetitions of the same stimulus *in vitro*. (a) A constant stimulus leads to a large variability of spike timing between one trial and the next. (b) A stimulus with large-amplitude signal fluctuations generates reliable spike timing so that spike times vary across trials. (c) Reliability of spike timing (arbitrary units) as a function of the amplitude σ of signal fluctuations. Modified from Mainen and Sejnowski (1995) with permission from AAAS.

$RkTB$ where k is the Boltzmann constant, T the temperature and B the bandwidth of the system. Since neuronal dynamics is described by an equivalent electrical circuit containing resistors (see Chapter 2), the neuronal membrane potential fluctuates as well. Fluctuations due to Johnson noise are, however, of minor importance compared to other noise sources in neurons (Manwani and Koch, 1999).

Another source of noise that is specific to neuronal cells and present already in an isolated neuron arises from the finite number of ion channels in a patch of neuronal membrane. Most ion channels have only two states: they are either open or closed. The electrical conductivity of a patch of membrane for ion type i is proportional to the number of open ion channels. For a given constant membrane potential u, a fraction $P_i(u)$ of ion channel of type i is open *on average*. The actual number of open channels fluctuates around $N_i P_i(u)$ where N_i is the total number of ion channels of type i in that patch of membrane; see Fig. 2.5.

The formulation of the Hodgkin–Huxley equations in terms of ion channel conductivities (see Chapter 2) is implicitly based on the assumption of a large number of ion channels so that fluctuations can be neglected. Since, in reality, N_i is finite, the conductivity fluctuates and so does the potential. If the membrane potential is close to the threshold, channel noise can be critical for the generation of action potentials. Models that take the finite number of ion channels into account can reproduce the observed variability of real neurons with intracellular stimulation (Schneidman *et al.*, 1998; Chow and White, 1996). In particular, they show little spike jitter if the input current is rapidly changing, but are less reliable if the input current is constant.

7.1.3 Noise from the network

Apart from intrinsic noise sources at the level of an individual neuron there are also sources of noise that are due to signal transmission and network effects (extrinsic noise). Synaptic transmission failures, for instance, seem to impose a substantial limitation to signal transmission within a neuronal network. Experiments with double electrode recordings from

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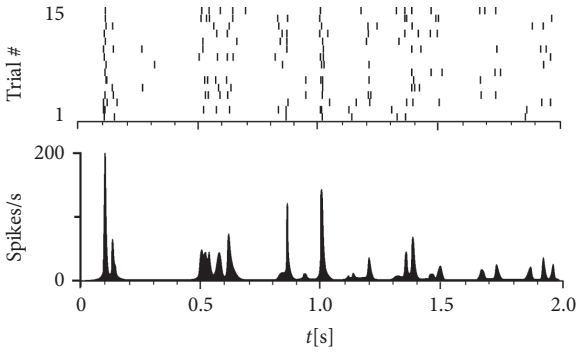

Fig. 7.4 Variability across repetitions of the same stimulus *in vivo*. Activity of a neuron in visual cortex (area MT) driven by a stimulus consisting of randomly moving dots. The same stimulus is repeated many times. Spikes in a single trial are shown as short vertical dashes along a horizontal line. Only 15 trials are shown. The peri-stimulus-time-histogram (accumulated over many more trials) is indicated at the bottom. Redrawn after Bair and Koch (1996), who show data from the Newsome lab (Newsome *et al*., 1989).

two synaptically connected neurons suggest that only 10–30% of presynaptic spikes generate a postsynaptic response (Hessler *et al*., 1993; Markram and Tsodyks, 1996).

Finally, an important part of the irregularity of neuronal spiking during spontaneous activity seems to be due to properties of the network – even if the network itself is completely deterministic. Model studies show that networks of excitatory and inhibitory neurons with fixed random connectivity can produce highly irregular spike trains – even in the absence of any source of noise. An example of variability in a deterministic network of leaky integrate-and-fire neurons with random excitatory and inhibitory interactions is shown in Fig. 7.5. We will discuss the underlying mechanisms in Part III of this book (see Sections 12.3.4 and 12.4.4). As a result of the network activity, each neuron receives as input an irregular spike sequence that can be described as stochastic spike arrival; see Chapter 8. The difference between the large variability of neurons *in vivo* compared to the variability during intracellular stimulation *in vitro* can therefore be, at least partially, attributed to network effects.

7.2 Mean firing rate

In the next few sections, we introduce some important concepts commonly used for the statistical description of neuronal spike trains. Central notions will be the interspike interval distribution (Section 7.3), the noise spectrum (Section 7.4), but most importantly the concept of "firing rate," which we discuss first.

A quick glance at the experimental literature reveals that there is no unique and well-defined concept of "mean firing rate." In fact, there are at least three different notions of rate, which are often confused and used simultaneously. The three definitions refer to three

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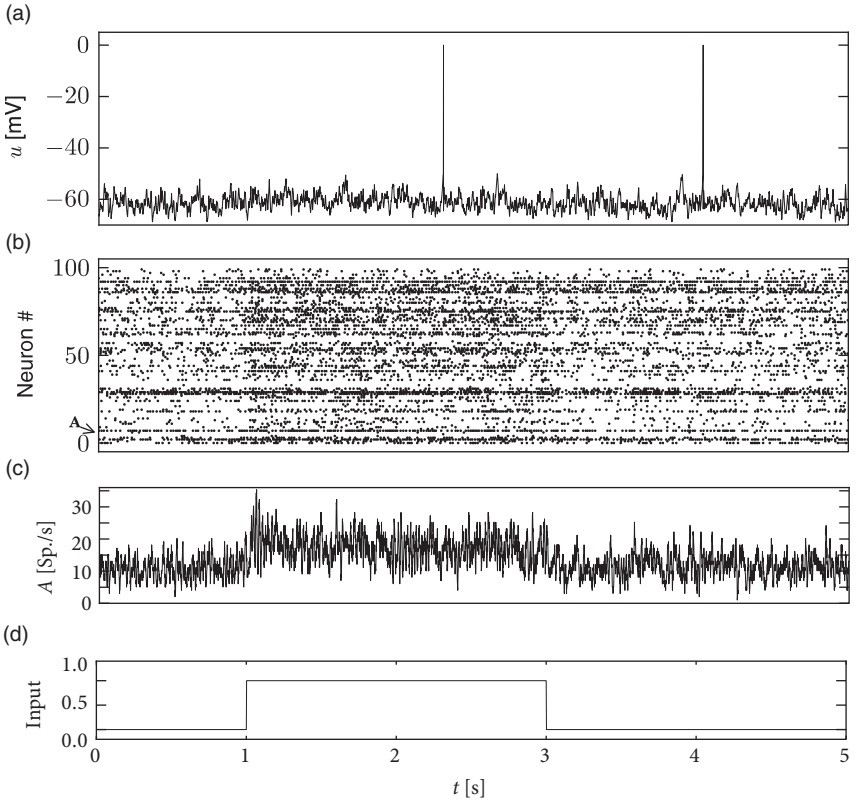

Fig. 7.5 Variability in a deterministic model network of 8000 excitatory and 2000 inhibitory neurons, both modeled as leaky integrate-and-fire neurons. (a) Voltage trace as a function of time for a single model neuron. Spikes (vertical lines) are generated whenever the membrane potential (solid line) hits the firing threshold. (b) Spike raster of 100 neurons in the network. Spike times (dots) of a single neuron appear along a horizontal line. (C) Population activity A as a function of time t, measured by averaging across the spikes of the subpopulation of 100 neurons shown in (b). From time $t = 1$ s to $t = 3$ s, all neurons in this population receive a nonzero input. (d) Input to the subpopulation of 100 neurons. Simulation results courtesy of F. Zenke and T. P. Vogels (Vogels *et al.*, 2011).

different averaging procedures: an average over time, or an average over several repetitions of the experiment, or an average over a population of neurons. The following three subsections will revisit in detail these three concepts.

7.2.1 Rate as a spike count and Fano factor

The first and most commonly used definition of a firing rate refers to a temporal average.

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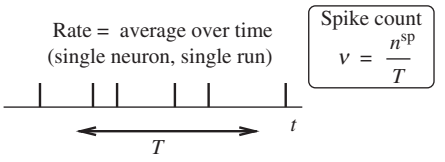

Fig. 7.6 The spike count measure: definition of the mean firing rate by temporal average.

An experimenter observes in trial k the spikes of a given neuron (see Fig. 7.6). The firing rate in trial k is the spike count n_k^{sp} in an interval of duration T divided by T

$$\nu_k = \frac{n_k^{sp}}{T} . \tag{7.1}$$

The length T of the time window is set by the experimenter and depends on the type of neuron and the stimulus. In practice, to get sensible averages, several spikes should occur within the time window. Typical values are $T = 100\,\text{ms}$ or $T = 500\,\text{ms}$, but the duration may also be longer or shorter.

This definition of rate has been successfully used in many preparations, particularly in experiments on sensory or motor systems. A classical example is the stretch receptor in a muscle spindle (Adrian, 1926). The number of spikes emitted by the receptor neuron increases with the force applied to the muscle.

If the same experiment is repeated several times, the measured spike count varies between one trial and the next. Let us denote the spike count in trial k by the variable n_k^{sp}, its mean by $\langle n^{sp} \rangle$ and deviations from the mean as $\Delta n_k^{sp} = n_k^{sp} - \langle n^{sp} \rangle$. Variability of the spike count measure is characterized by the Fano factor, defined as the variance of the spike count $\langle (\Delta n^{sp})^2 \rangle$ divided by its mean

$$F = \frac{\langle (\Delta n^{sp})^2 \rangle}{\langle n^{sp} \rangle} . \tag{7.2}$$

In experiments, the mean and variance are estimated by averaging over K trials $\langle n^{sp} \rangle = (1/K) \sum_{k=1}^{K} n_k^{sp}$ and $\langle (\Delta n^{sp})^2 \rangle = (1/K) \sum_{k=1}^{K} (\Delta n_k^{sp})^2$.

If we find on average $\langle n^{sp} \rangle$ spikes in a long temporal window of duration T, the mean interval between two subsequent spikes is $T/\langle n^{sp} \rangle$. Indeed, using the notion of interspike-interval distribution to be introduced below (Section 7.3), we can make the following statement: the firing rate defined here as spike count divided by the measurement time T is identical to the inverse of the mean interspike interval. We will come back to interspike intervals in Section 7.3.

It is tempting, but misleading, to consider the inverse interspike interval as a "momentary firing rate:" if a first spike occurs at time t^k and the next one at time t^{k+1}, we could artificially assign a variable $\tilde{\nu}(t) = 1/(t^{k+1} - t^k)$ for all times $t^k < t \le t^k$. However, the temporal average of $\tilde{\nu}(t)$ over a much longer time T is *not* the same as the mean rate ν defined here as spike count divided by T, simply because $1/\langle x \rangle \neq \langle (1/x) \rangle$. A practical definition of "instantaneous firing rate" will be given below in Section 7.2.2.

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Example: Homogeneous Poisson process

If the rate ν is defined via a spike count over a time window of duration T, the exact firing time of a spike does not matter. It is therefore tempting to describe spiking as a Poisson process where spikes occur independently and stochastically with a constant rate ν.

Let us divide the duration T (say 500 ms) into a large number of short segments Δt (say $\Delta t = 0.1$ ms). In a homogeneous Poisson process, the probability of finding a spike in a *short* segment of duration Δt is

$$P_F(t;t+\Delta t) = \nu \Delta t\,. \tag{7.3}$$

In other words, spike events are independent of each other and occur with a *constant* rate (also called stochastic intensity) defined as

$$\nu = \lim_{\Delta t \to 0} \frac{P_F(t;t+\Delta t)}{\Delta t}\,. \tag{7.4}$$

The expected number of spikes to occur in the measurement interval T is therefore

$$\langle n^{\rm sp} \rangle = \nu T, \tag{7.5}$$

so that the experimental procedure of (i) counting spikes over a time T and (ii) dividing by T gives an empirical estimate of the rate ν of the Poisson process.

For a Poisson process, the Fano factor is exactly 1. Therefore, measuring the Fano factor is a powerful test so as to find out whether neuronal firing is Poisson-like; see the discussion in Rieke *et al*. (1997).

7.2.2 Rate as a spike density and the peri-stimulus-time histogram

An experimenter records from a neuron while stimulating with some input sequence. The same stimulation sequence is repeated several times and the neuronal response is reported in a peri-stimulus-time histogram (PSTH) with bin width Δt; see Fig. 7.7. The time t is measured with respect to the start of the stimulation sequence and Δt defines the time bin for generating the histogram, it is typically of the order of milliseconds.

The number of occurrences of spikes $n_K(t;t+\Delta t)$ summed over all repetitions of the experiment divided by the number K of repetitions is a measure of the typical activity of the neuron between time t and $t+\Delta t$. A further division by the interval length Δt yields the spike density

$$\rho(t) = \frac{1}{\Delta t} \frac{n_K(t;t+\Delta t)}{K}\,. \tag{7.6}$$

Sometimes the result is smoothed to get a continuous (time-dependent) rate variable, usually reported in units of hertz. As an experimental procedure, the PSTH measure is a useful method to evaluate neuronal activity, in particular in the case of time-dependent stimuli; see Fig. 7.4. We call it the time-dependent firing rate.

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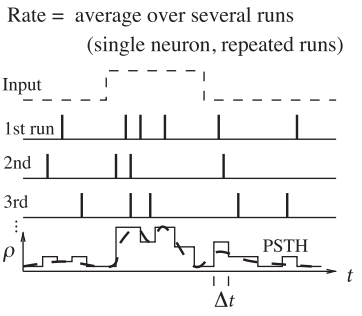

Spike density in PSTH
$\rho = \frac{1}{\Delta t}\frac{1}{K} n_K(t; t+\Delta t)$

Fig. 7.7 The peri-stimulus-time histogram (PSTH) and the time-dependent firing rate as an average over several runs of the experiment.

In order to see the relation of Eq. (7.6) to a time-dependent firing rate, we recall that spikes are formal events characterized by their firing time t^f where f counts the spikes. In Chapter 1 we have defined (Eq. (1.14)) the spike train as a sum of δ-functions:

$$S(t) = \sum_f \delta(t - t^f)\,. \tag{7.7}$$

If each stimulation can be considered as an independent sample from the identical stochastic process, we can define an *instantaneous firing rate* as an expectation over trials

$$\nu(t) = \langle S(t) \rangle. \tag{7.8}$$

An expectation value over δ-functions may look strange to the reader not used to seeing such mathematical objects. Let us therefore consider the experimental procedure to estimate the expectation value. First, in each trial k, we count the number of spikes that occur in a short time interval Δt by integrating the spike train over time, $n_k^{\rm sp}(t) = \int_t^{t+\Delta t} S_k(t')\mathrm{d}t'$ where the lower index k denotes the trial number. Note that integration removes the δ-function. Obviously, if the time bin Δt is small enough we will find at most one spike so that $n_k^{\rm sp}$ is either zero or 1. Second, we average over the K trials and divide by Δt in order to obtain the empirical estimate

$$\nu(t) = \frac{1}{K\,\Delta t} \sum_{k=1}^{K} n_k^{\rm sp}(t)\,. \tag{7.9}$$

The PSTH, defined as spike count per time bin averaged over several trials and divided by the bin length (the right-hand side of Eq. (7.9)), provides therefore an empirical estimate of the instantaneous firing rate (the left-hand side).

Example: Inhomogeneous Poisson process

An inhomogeneous Poisson process can be used to describe the spike density measured in a PSTH. In an inhomogeneous Poisson process, spike events are independent of each other and occur with an instantaneous firing rate

$$\nu(t) = \lim_{\Delta t \to 0} \frac{P_F(t; t+\Delta t)}{\Delta t}\,. \tag{7.10}$$

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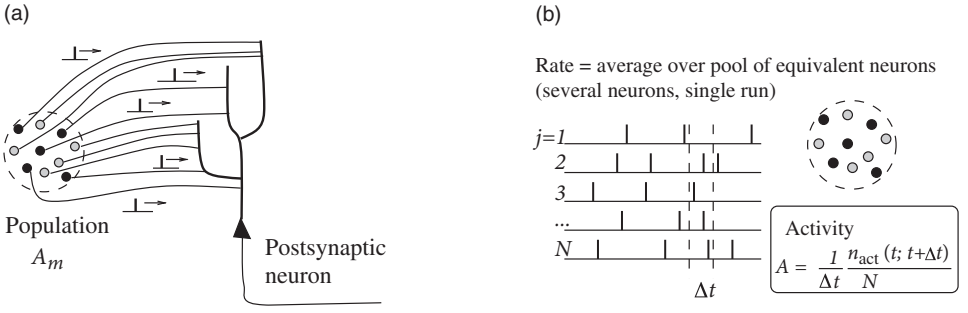

Fig. 7.8 (a) A postsynaptic neuron receives spike input from the population m with activity A_m. (b) The population activity is defined as the fraction of neurons that are active in a short interval $[t, t+\Delta t]$ divided by Δt.

Therefore, the probability of finding a spike in a *short* segment of duration Δt, say, a time bin of 1 ms, is $P_F(t;t+\Delta t) = \nu(t)\,\Delta t$. More generally, the expected number of spikes in an interval of finite duration T is $\langle n^{\rm sp}\rangle = \int_0^T \nu(t)\,{\rm d}t$ and the Fano factor is 1, as was the case for the homogeneous Poisson process.

Once we have measured a PSTH, we can always find an inhomogeneous Poisson process which reproduces the PSTH. However, this does not imply that neuronal firing is Poisson-like. A Poisson process has, for example, the tendency to generate spikes with very short interspike intervals, which cannot occur for real neurons because of refractoriness.

7.2.3 Rate as a population activity (average over several neurons)

The number of neurons in the brain is huge. Often many neurons have similar properties and respond to the same stimuli. For example, neurons in the primary visual cortex of cats and monkeys are arranged in columns of cells with similar properties (Hubel and Wiesel, 1962). Let us idealize the situation and consider a population of neurons with identical properties. In particular, all neurons in the population should have the same pattern of input and output connections. The spikes of the neurons in a population m are sent off to another population n. In our idealized picture, each neuron in population n receives input from all neurons in population m. The relevant quantity, from the point of view of the receiving neuron, is the proportion of active neurons in the presynaptic population m; see Fig. 7.8a. Formally, we define the population activity

$$A(t) = \frac{1}{\Delta t}\frac{n_{\rm act}(t;t+\Delta t)}{N} = \frac{1}{\Delta t}\frac{\int_t^{t+\Delta t}\sum_j\sum_f \delta(t-t_j^f)\,{\rm d}t}{N}, \qquad (7.11)$$

where N is the size of the population, $n_{\rm act}(t;t+\Delta t)$ is the number of spikes (summed over all neurons in the population) that occur between t and $t+\Delta t$, where Δt is a small time

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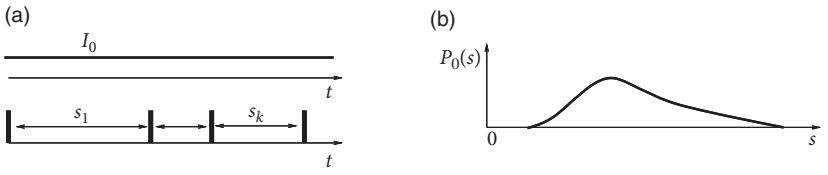

Fig. 7.9 Stationary interval distribution. (a) A neuron driven by a constant input produces spikes with variable intervals. (b) A histogram of the interspike intervals $s_1, s_2, \ldots$ can be used to estimate the interval distribution $P_0(s)$.

interval; see Fig. 7.8. Eq. (7.11) defines a variable with units inverse time – in other words, a rate.

As we can see from Fig. 7.5c, the population activity may vary rapidly and can reflect changes in the stimulus conditions nearly instantaneously. Before we discuss the problem of neural coding (Section 7.6), let us first study further statistical measures of spike train statistics.

7.3 Interval distribution and coefficient of variation

The estimation of interspike-interval (ISI) distributions from experimental data is a common method to study neuronal variability given a certain *stationary* input. In a typical experiment, the spike train of a single neuron (e.g., a neuron in the visual cortex) is recorded while driven by a constant stimulus. The stimulus might be an external input applied to the system (e.g., a visual contrast grating moving at constant speed); or it may be an intracellularly applied constant driving current. The spike train is analyzed and the distribution of intervals s_k between two subsequent spikes is plotted in a histogram. For a sufficiently long spike train, the histogram provides a good estimate of the ISI distribution, which we denote as $P_0(s)$; see Fig. 7.9. The interval distribution can be interpreted as a conditional probability density

$$P_0(s) = P(t^f + s | t^f), \tag{7.12}$$

where $\int_t^{t+\Delta t} P(t'|t^f)\,\mathrm{d}t'$ is the probability that the next spike occurs in the interval $[t, t+\Delta t]$ given that the last spike occurred at time t^f.

In order to extract the mean firing rate from a stationary interval distribution $P_0(s)$, we start with the definition of the mean interval,

$$\langle s \rangle = \int_0^\infty s P_0(s)\,\mathrm{d}s\,. \tag{7.13}$$

The mean firing rate is the inverse of the mean interval

$$\nu = \frac{1}{\langle s \rangle} = \left[\int_0^\infty s P_0(s)\,\mathrm{d}s \right]^{-1}. \tag{7.14}$$

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7.3.1 Coefficient of variation C_V

Interspike-interval distributions $P_0(s)$ derived from a spike train under stationary conditions can be broad or sharply peaked. To quantify the width of the interval distribution, neuroscientists often evaluate the coefficient of variation, C_V, defined as the ratio of the standard deviation and the mean. Therefore the square of the C_V is

$$C_V^2 = \frac{\langle \Delta s^2 \rangle}{\langle s \rangle^2}, \tag{7.15}$$

where $\langle s \rangle = \int_0^\infty s P_0(s)\,\mathrm{d}s$ and $\langle \Delta s^2 \rangle = \int_0^\infty s^2 P_0(s)\,\mathrm{d}s - \langle s \rangle^2$. A Poisson process produces distributions with $C_V = 1$. A value of $C_V > 1$ implies that a given spike train is less regular than a Poisson process with the same firing rate. If $C_V < 1$, then the spike train is more regular. Most deterministic integrate-and-fire neurons fire periodically when driven by a constant stimulus and therefore have $C_V = 0$. Intrinsically bursting neurons, however, can have $C_V > 1$.

Example: Poisson process with absolute refractoriness

We study a Poisson neuron with absolute refractory period Δ^{abs}. For times since the last spike larger than Δ^{abs}, the neuron is supposed to fire stochastically with rate r. The interval distribution of a Poisson process with absolute refractoriness (Fig. 7.10a) is given by

$$P_0(s) = \begin{cases} 0 & \text{for} \quad s < \Delta^{\mathrm{abs}}, \\ r \exp\left[-r\,(s - \Delta^{\mathrm{abs}})\right] & \text{for} \quad s > \Delta^{\mathrm{abs}}, \end{cases} \tag{7.16}$$

and has a mean $\langle s \rangle = \Delta^{\mathrm{abs}} + 1/r$ and variance $\langle \Delta s^2 \rangle = 1/r^2$. The coefficient of variation is therefore

$$C_V = 1 - \frac{\Delta^{\mathrm{abs}}}{\langle s \rangle}. \tag{7.17}$$

Let us compare the C_V of Eq. (7.17) with that of a homogeneous Poisson process of the same mean rate $\nu = \langle s \rangle^{-1}$. As we have seen, a Poisson process has $C_V = 1$. A refractory period $\Delta^{\mathrm{abs}} > 0$ lowers the C_V, because a neuron with absolute refractoriness fires more regularly than a Poisson neuron. If we increase Δ^{abs}, we must increase the instantaneous rate r in order to keep the same mean rate ν. In the limit of $\Delta^{\mathrm{abs}} \to \langle s \rangle$, the C_V approaches zero, since the only possible spike train is regular firing with period $\langle s \rangle$.

7.4 Autocorrelation function and noise spectrum

Suppose that, during a stationary input scenario, we observe a neuron i firing a first spike at time t. While the interval distribution $P_0(s)$ describes the probability that the *next* spike occurs at time $t + s$, the autocorrelation function $C(s)$ focuses on the probability of finding

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another spike at time $t+s$ – independent of whether this is the next spike of the neuron or not.

In order to make the notion of an autocorrelation function more precise, let us consider a spike train $S_i(t) = \sum_f \delta(t - t_i^f)$ of length T. The firing times t_i^f might have been measured in an experiment or else generated by a neuron model. We suppose that T is sufficiently long so that we can formally consider the limit $T \to \infty$. The autocorrelation function $C_{ii}(s)$ of the spike train is a measure for the probability of finding two spikes at a time interval s, i.e.,

$$C_{ii}(s) = \langle S_i(t)\, S_i(t+s) \rangle_t \,, \tag{7.18}$$

where $\langle \cdot \rangle_t$ denotes an average over time t,

$$\langle f(t) \rangle_t = \lim_{T\to\infty} \frac{1}{T} \int_{-T/2}^{T/2} f(t)\, \mathrm{d}t \,. \tag{7.19}$$

We note that the right-hand side of Eq. (7.18) is symmetric so that $C_{ii}(-s) = C_{ii}(s)$ holds. The calculation of the autocorrelation function for a stationary renewal process is the topic of Section 7.5.2.

It turns out that the autocorrelation function is intimately linked to the power spectrum of a neuronal spike train, also called the noise spectrum. The power spectrum (or power spectral density) of a spike train is defined as $\mathscr{P}(\omega) = \lim_{T\to\infty} \mathscr{P}_T(\omega)$, where $\mathscr{P}_T$ is the power of a segment of length T of the spike train,

$$\mathscr{P}_T(\omega) = \frac{1}{T} \left| \int_{-T/2}^{T/2} S_i(t)\, \mathrm{e}^{-i\omega t}\, \mathrm{d}t \right|^2 . \tag{7.20}$$

The power spectrum $\mathscr{P}(\omega)$ of a spike train is equal to the Fourier transform $\hat{C}_{ii}(\omega)$ of its autocorrelation function (Wiener–Khinchin theorem). To see this, we use the definition of the autocorrelation function

$$\begin{aligned}
\hat{C}_{ii}(\omega) &= \int_{-\infty}^{\infty} \langle S_i(t)\, S_i(t+s) \rangle\, \mathrm{e}^{-i\omega s}\, \mathrm{d}s \\
&= \lim_{T\to\infty} \frac{1}{T} \int_{-T/2}^{T/2} S_i(t) \int_{-\infty}^{\infty} S_i(t+s)\, \mathrm{e}^{-i\omega s}\, \mathrm{d}s\, \mathrm{d}t \\
&= \lim_{T\to\infty} \frac{1}{T} \int_{-T/2}^{T/2} S_i(t)\, \mathrm{e}^{+i\omega t}\, \mathrm{d}t \int_{-\infty}^{\infty} S_i(s')\, \mathrm{e}^{-i\omega s'}\, \mathrm{d}s' \\
&= \lim_{T\to\infty} \frac{1}{T} \left| \int_{-T/2}^{T/2} S_i(t)\, \mathrm{e}^{-i\omega t}\, \mathrm{d}t \right|^2 .
\end{aligned} \tag{7.21}$$

In the limit of $T \to \infty$, Eq. (7.20) becomes identical to (7.21) so that the assertion follows. The power spectral density of a spike train during spontaneous activity is called the noise spectrum of the neuron. Noise is a limiting factor to all forms of information transmission and in particular to information transmission by neurons. An important concept of the theory of signal transmission is the signal-to-noise ratio. A signal that is transmitted at a certain frequency ω should be stronger than (or at least of the same order of magnitude

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as) the noise at the same frequency. For this reason, the noise spectrum $\mathscr{P}(\omega)$ of the transmission channel is of interest. As we shall see in the next section, the noise spectrum of a stationary renewal process is intimately related to the interval distribution $P_0(s)$.

7.5 Renewal statistics

Poisson processes do not account for neuronal refractoriness and cannot be used to describe realistic interspike-interval distributions. In order to account for neuronal refractoriness in the stochastic description of spike trains, we need to switch from a Poisson processes to a renewal process. Renewal processes keep a memory of the last event (last firing time) $\hat{t}$, but not of any earlier events. More precisely, spikes are generated in a renewal process, with a stochastic intensity (or "hazard")

$$\rho(t|\hat{t}) = \rho_0(t-\hat{t}) \tag{7.22}$$

which depends on the time since the last spike. One of the simplest example of a renewal system is a Poisson process with absolute refractoriness which we have already encountered in the previous section; see Eq. (7.16).

Renewal processes are a class of stochastic point processes that describe a sequence of events in time (Cox, 1962; Papoulis, 1991). Renewal systems in the *narrow* sense (stationary renewal processes), presuppose stationary input and are defined by the fact that the state of the system, and hence the probability of generating the next event, depends only on the "age" $t-\hat{t}$ of the system, i.e., the time that has passed since the last event (last spike). The central assumption of renewal theory is that the state does not depend on earlier events (i.e., earlier spikes of the same neuron). The aim of renewal theory is to predict the probability of the next event given the age of the system. In other words, renewal theory allows us to calculate the interval distribution

$$P_0(s) = P(t^f + s|t^f), \tag{7.23}$$

i.e., the probability density that the next event occurs at time $t^f + s$ given that the last event was observed at time t^f.

While for a Poisson process all events occur independently, in a renewal process generation of events (spikes) depends on the previous event, so that events are *not* independent. However, since the dependence is restricted to the most recent event, *intervals between subsequent events are independent*. Therefore, an efficient way of generating a spike train of a renewal system is to draw interspike intervals from the distribution $P_0(s)$.

Example: Light bulb failure as a renewal system

A generic example of a renewal system is a light bulb. The event is the failure of the bulb and its subsequent exchange. Obviously, the state of the system only depends on the age of the current bulb, and not on that of any previous bulb that has already been

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exchanged. If the usage pattern of the bulbs is stationary (e.g., the bulb is switched on for 10 hours each night) then we have a stationary renewal process. The aim of renewal theory is to calculate the probability of the next failure given the age of the bulb.

7.5.1 Survivor function and hazard

The interval distribution $P(t|\hat{t})$ as defined above is a probability *density*. Thus, integration of $P(t|\hat{t})$ over time yields a probability. For example, $\int_{\hat{t}}^{t} P(t'|\hat{t})\,\mathrm{d}t'$ is the probability that a neuron which has emitted a spike at $\hat{t}$ fires the next action potential between $\hat{t}$ and t. Thus

$$S(t|\hat{t}) = 1 - \int_{\hat{t}}^{t} P(t'|\hat{t})\,\mathrm{d}t' \tag{7.24}$$

is the probability that the neuron stays quiescent between $\hat{t}$ and t. $S(t|\hat{t})$ is called the *survivor function*: it gives the probability that the neuron "survives" from $\hat{t}$ to t without firing.

The survivor function $S(t|\hat{t})$ has an initial value $S(\hat{t}|\hat{t}) = 1$ and decreases to zero for $t \to \infty$. The rate of decay of $S(t|\hat{t})$ will be denoted by $\rho(t|\hat{t})$ and is defined by

$$\rho(t|\hat{t}) = -\frac{\frac{\mathrm{d}}{\mathrm{d}t}S(t|\hat{t})}{S(t|\hat{t})} = \frac{P(t|\hat{t})}{1 - \int_{\hat{t}}^{t} P(t'|\hat{t})\,\mathrm{d}t'}\,. \tag{7.25}$$

In the language of renewal theory, $\rho(t|\hat{t})$ is called the "age-dependent death rate" or "hazard" (Cox, 1962; Cox and Lewis, 1966).

Integration of the differential equation $\mathrm{d}S/\mathrm{d}t = -\rho\,S$ [see the first identity in Eq. (7.25)] yields the survivor function

$$S(t|\hat{t}) = \exp\left[-\int_{\hat{t}}^{t} \rho(t'|\hat{t})\,\mathrm{d}t'\right]. \tag{7.26}$$

According to the definition of the survivor function in Eq. (7.24), the interval distribution is given by

$$P(t|\hat{t}) = -\frac{\mathrm{d}}{\mathrm{d}t}S(t|\hat{t}) = \rho(t|\hat{t})\,S(t|\hat{t})\,, \tag{7.27}$$

which has a nice intuitive interpretation: In order to emit its *next* spike at t, the neuron has to survive the interval $(\hat{t},t)$ without firing and then fire at t. The survival probability is $S(t|\hat{t})$ and the hazard of firing a spike at time t is $\rho(t|\hat{t})$. Multiplication of the survivor function S with the momentary hazard ρ gives the two factors on the right-hand side of Eq. (7.27). Inserting Eq. (7.26) in (7.27), we obtain an explicit expression for the interval distribution in terms of the hazard:

$$P(t|\hat{t}) = \rho(t|\hat{t})\,\exp\left[-\int_{\hat{t}}^{t} \rho(t'|\hat{t})\,\mathrm{d}t'\right]. \tag{7.28}$$

On the other hand, given the interval distribution we can derive the hazard from Eq. (7.25). Thus, each of the three quantities $\rho(t|\hat{t})$, $P(t|\hat{t})$, and $S(t|\hat{t})$ is sufficient to describe the

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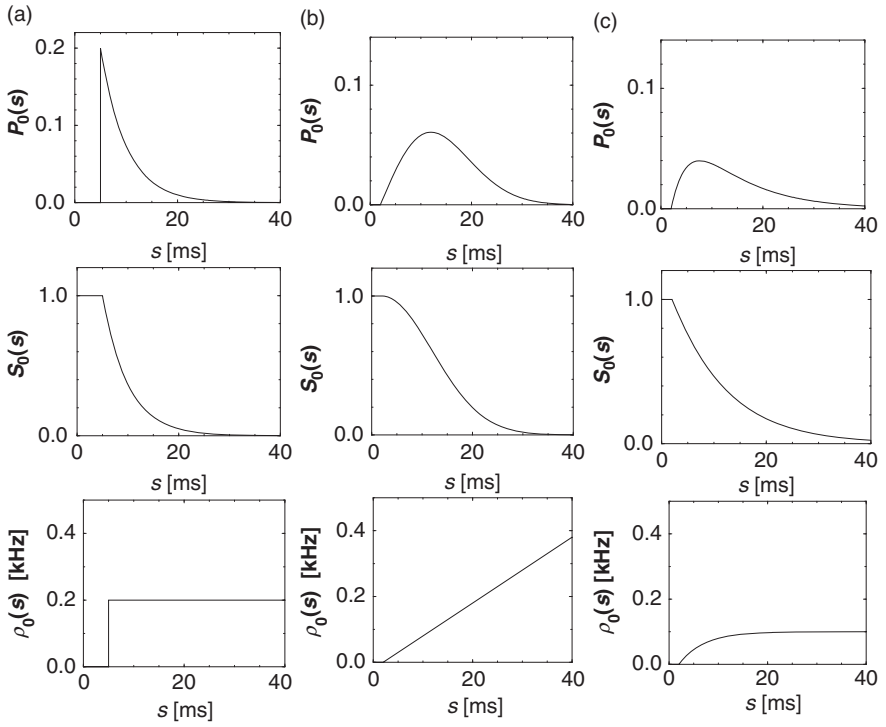

Fig. 7.10 Interval distribution $P_0(s)$ (top), survivor function $S_0(s)$ (middle) for three different hazard functions (bottom). (a) Hazard function corresponds to a Poisson neuron with absolute refractoriness of 5 ms. (b) Hazard function defined by $\rho_0(s) = a_0\,(s-\Delta^{\rm abs})\,\Theta(s-\Delta^{\rm abs})$ with $a_0 = 0.01\,{\rm ms}^{-2}$ and $\Delta^{\rm abs} = 2\,{\rm ms}$. (c) Hazard function defined by $\rho_0(s) = \nu\{1-\exp[-\lambda\,(s-\Delta^{\rm abs})]\}\,\Theta(s-\Delta^{\rm abs})$ with $\nu = 0.1\,{\rm kHz}$, $\lambda = 0.2\,{\rm kHz}$, and $\Delta^{\rm abs} = 2\,{\rm ms}$.

statistical properties of a renewal system. Since we focus on stationary renewal systems, the notation can be simplified and Eqs. (7.24)–(7.28) hold with the replacement

$$P(t|\hat{t}) = P_0(t-\hat{t}), \tag{7.29}$$

$$S(t|\hat{t}) = S_0(t-\hat{t}), \tag{7.30}$$

$$\rho(t|\hat{t}) = \rho_0(t-\hat{t})\,. \tag{7.31}$$

Eqs. (7.24)–(7.28) are standard results of renewal theory. The notation that we have chosen in Eqs. (7.24)–(7.28) will turn out to be useful in later chapters and highlights the fact that these quantities are conditional probabilities, probability densities, or rates.

Example: From interval distribution to hazard function

Let us suppose that we have found under stationary experimental conditions an inter-

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val distribution that can be approximated as

$$P_0(s) = \begin{cases} 0 & \text{for} \quad s \le \Delta^{\text{abs}}, \\ a_0 \, (s - \Delta^{\text{abs}}) \, , e^{-\frac{a_0}{2}(s-\Delta^{\text{abs}})^2} & \text{for} \quad s > \Delta^{\text{abs}}, \end{cases} \tag{7.32}$$

with a constant $a_0 > 0$; see Fig. 7.10b. From Eq. (7.25), the hazard is found to be

$$\rho_0(s) = \begin{cases} 0 & \text{for} \quad s \le \Delta^{\text{abs}}, \\ a_0 \, (s - \Delta^{\text{abs}}) & \text{for} \quad s > \Delta^{\text{abs}} . \end{cases} \tag{7.33}$$

Thus, during an interval Δ^{abs} after each spike the hazard vanishes. We may interpret Δ^{abs} as the absolute refractory time of the neuron. For $s > \Delta^{\text{abs}}$ the hazard increases linearly, i.e., the longer the neuron waits the higher its probability of firing. In Chapter 9, the hazard of Eq. (7.33) can be interpreted as the instantaneous rate of a non-leaky integrate-and-fire neuron subject to noise.

7.5.2 Renewal theory and experiments

Renewal theory is usually associated with stationary input conditions. The interval distribution P_0 can then be estimated experimentally from a single long spike train. The applicability of renewal theory relies on the hypothesis that a memory back to the last spike suffices to describe the spike statistics. In particular, there should be no correlation between one interval and the next. In experiments, the renewal hypothesis can be tested by measuring the correlation between subsequent intervals. Under some experimental conditions, correlations are small, indicating that a description of spiking as a stationary renewal process is a good approximation (Goldberg *et al.*, 1964); however, under experimental conditions where neuronal adaptation is strong, intervals are *not* independent (Fig. 7.11). Given a time series of events with variable intervals s_j, a common measure of memory effects is the serial correlation coefficients

$$c_k = \frac{\langle s_{j+k} s_j \rangle_j - \langle s_j \rangle_j^2}{\langle s_j^2 \rangle - \langle s_j \rangle^2}. \tag{7.34}$$

Spike-frequency adaptation causes a negative correlation between subsequent intervals ($c_1 < 0$). Long intervals are most likely followed by short ones, and vice versa, so that the assumption of renewal theory does not hold (Schwalger *et al.*, 2010; Ratnam and Nelson, 2000; Chacron *et al.*, 2000).

The notion of stationary input conditions is a mathematical concept that cannot be easily translated into experiments. With intracellular recordings under *in vitro* conditions, constant input current can be imposed and thus the renewal hypothesis can be tested directly. Under *in vivo* conditions, the assumption that the input current to a neuron embedded in a large neural system is constant (or has stationary statistics) is questionable; see (Perkel

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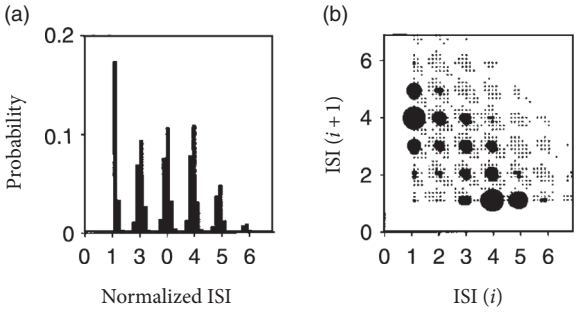

Fig. 7.11 Limitations of the renewal assumption. (a) The interval distribution $P_0(s)$ of an afferent sensory fiber in the weakly electric fish exhibits periodic peaks, which are associated to the background oscillation normalized to period $T = 1$. The most likely interval is exactly one period, but longer intervals are possible. (b) Testing for renewal in a plot of the joint density of the interval i (horizontal axis) and the next interval $i+1$ (vertical axis). Size of symbol indicates probability of occurrence. The most likely sequence is that an interval of length 4 is followed by an interval of length 1; moreover, a short interval of length 1 is most likely followed by a long interval of length 4. Modified from Ratnam and Nelson (2000).

et al., 1967a,b) for a discussion. While the externally controlled stimulus can be made stationary (e.g., a grating drifting at constant speed), the input to an individual neuron is out of control.

Let us suppose that, for a given experiment, we have checked that the renewal hypothesis holds to a reasonable degree of accuracy. From the experimental interval distribution P_0 we can then calculate the survivor function S_0 and the hazard ρ_0 via Eqs. (7.24) and (7.25). If some additional assumptions regarding the nature of the noise are made, the form of the hazard $\rho_0(t|\hat{t})$ can be interpreted in terms of neuronal dynamics. In particular, a reduced hazard immediately after a spike is a signature of neuronal refractoriness (Goldberg *et al.*, 1964; Berry and Meister, 1998).

Example: Plausible hazard function and interval distributions

Interval distributions and hazard functions have been measured in many experiments. For example, in auditory neurons of the cat driven by stationary stimuli, the hazard function $\rho_0(t-\hat{t})$ increases, after an absolute refractory time, to a constant level (Goldberg *et al.*, 1964). We approximate the time course of the hazard function as

$$\rho_0(s) = \begin{cases} 0 & \text{for} \quad s \le \Delta^{\text{abs}}, \\ \nu\,[1 - \mathrm{e}^{-\lambda\,(s-\Delta^{\text{abs}})}] & \text{for} \quad s > \Delta^{\text{abs}}, \end{cases} \tag{7.35}$$

with parameters $\Delta^{\text{abs}}, \lambda$, and ν; Fig. 7.10c. In Chapter 9 we shall see how the hazard (7.35) can be related to neuronal dynamics. Given the hazard function, we can calculate

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the survivor function and interval distributions. Application of Eq. (7.26) yields

$$S_0(s) = \begin{cases} 1 & \text{for} \quad s < \Delta^{\text{abs}}, \\ \mathrm{e}^{-\nu\,(s-\Delta^{\text{abs}})}\,\mathrm{e}^{\rho_0(s)/\lambda} & \text{for} \quad s > \Delta^{\text{abs}}. \end{cases} \tag{7.36}$$

The interval distribution is given by $P_0(s) = \rho_0(s)\,S_0(s)$. Interval distribution, survivor function, and hazard are shown in Fig. 7.10c.

We may compare the above hazard function and interval distribution with that of the Poisson neuron with absolute refractoriness. The main difference is that the hazard in Eq. (7.16) jumps from the state of absolute refractoriness to a constant firing rate, whereas in Eq. (7.35) the transition is smooth.

7.5.3 Autocorrelation and noise spectrum of a renewal process (*)

In case of a stationary renewal process, the interval distribution P_0 contains *all* the statistical information so that the autocorrelation function and noise spectrum can be derived. In this section we calculate the noise spectrum of a stationary renewal process. As we have seen above, the noise spectrum of a neuron is directly related to the autocorrelation function of its spike train. Both noise spectrum and autocorrelation function are experimentally accessible.

Let $\nu_i = \langle S_i \rangle$ denote the mean firing rate (expected number of spikes per unit time) of the spike train. Thus the probability of finding a spike in a short segment $[t, t+\Delta t]$ of the spike train is $\nu\,\Delta t$. For large intervals s, firing at time $t+s$ is independent of whether or not there was a spike at time t. Therefore, the expectation of finding a spike at t and another spike at $t+s$ approaches for $s \to \infty$ a limiting value $\lim_{s\to\infty}\langle S_i(t)\,S_i(t+s)\rangle = \lim_{s\to\infty} C_{ii}(s) = \nu_i^2$. It is convenient to subtract this baseline value and introduce a "normalized" autocorrelation,

$$C_{ii}^0(s) = C_{ii}(s) - \nu_i^2\,, \tag{7.37}$$

with $\lim_{s\to\infty} C_{ii}^0(s) = 0$. The Fourier transform of Eq. (7.37) yields

$$\hat{C}_{ii}(\omega) = \hat{C}_{ii}^0(\omega) + 2\pi\nu_i^2\,\delta(\omega)\,. \tag{7.38}$$

Thus $\hat{C}_{ii}(\omega)$ diverges at $\omega = 0$; the divergence is removed by switching to the normalized autocorrelation. In the following we will calculate the noise spectrum $\hat{C}_{ii}(\omega)$ for $\omega \neq 0$.

In the case of a stationary renewal process, the autocorrelation function is closely related to the interval distribution $P_0(s)$. This relation will now be derived. Let us suppose that we have found a first spike at t. To calculate the autocorrelation we need the probability density for a spike at $t+s$. Let us construct an expression for $C_{ii}(s)$ for $s > 0$. The correlation function for positive s will be denoted by $\nu_i\,C_+(s)$ or

$$C_+(s) = \frac{1}{\nu_i}\,C_{ii}(s)\,\Theta(s)\,. \tag{7.39}$$

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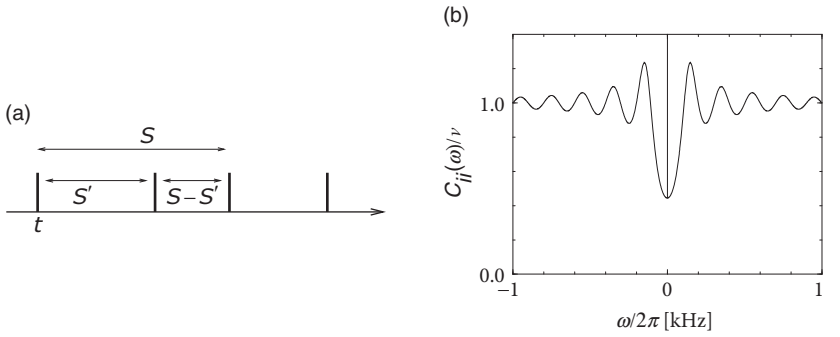

Fig. 7.12 (a) The autocorrelation of a spike train describes the chance to find two spikes at a distance s, independent of the number of spikes that occur in between. (b) Fourier transform of the autocorrelation function C_{ii} of a Poisson neuron with absolute refractoriness ($\Delta^{\rm ax} = 5\,$ms) and constant stimulation ($\nu = 100\,$Hz).

The factor ν_i in Eq. (7.39) takes care of the fact that we expect a first spike at t with rate ν_i; $C_+(s)$ gives the *conditional* probability density that, given a spike at t, we will find another spike at $t+s > t$. The spike at $t+s$ can be the first spike after t, or the second one, or the nth one; see Fig. 7.12. Thus for $s > 0$

$$C_+(s) = P_0(s) + \int_0^\infty P_0(s')\,P_0(s-s')\,{\rm d}s' + \int_0^\infty \int_0^\infty P_0(s')\,P_0(s'')\,P_0(s-s'-s'')\,{\rm d}s'\,{\rm d}s'' + \cdots \tag{7.40}$$

or

$$C_+(s) = P_0(s) + \int_0^\infty P_0(s')\,C_+(s-s')\,{\rm d}s' \tag{7.41}$$

as can be seen by inserting Eq. (7.40) on the right-hand side of (7.41); see Fig. 7.13.

Owing to the symmetry of C_{ii}, we have $C_{ii}(s) = \nu C_+(-s)$ for $s < 0$. Finally, for $s = 0$, the autocorrelation has a δ peak reflecting the trivial autocorrelation of each spike with itself. Hence,

$$C_{ii}(s) = \nu_i\,[\delta(s) + C_+(s) + C_+(-s)]\,. \tag{7.42}$$

In order to solve Eq. (7.41) for C_+ we take the Fourier transform of Eq. (7.41) and find

$$\hat{C}_+(\omega) = \frac{\hat{P}_0(\omega)}{1-\hat{P}_0(\omega)}\,. \tag{7.43}$$

Together with the Fourier transform of Eq. (7.42), $\hat{C}_{ii} = \nu_i\,[1 + 2\,{\rm Re}\{\hat{C}_+(\omega)\}]$, we obtain

$$\hat{C}_{ii}(\omega) = \nu_i\,{\rm Re}\left\{\frac{1+\hat{P}_0(\omega)}{1-\hat{P}_0(\omega)}\right\} \quad \text{for} \quad \omega \neq 0\,. \tag{7.44}$$

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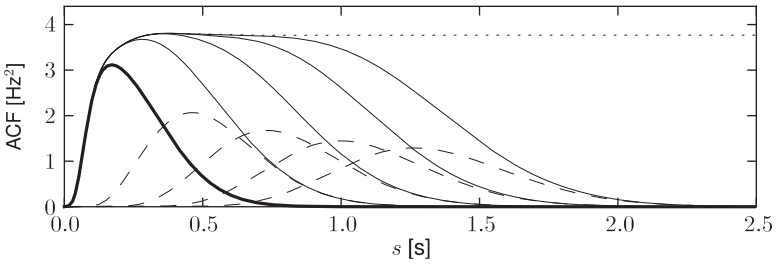

Fig. 7.13 The autocorrelation function (ACF) is a sum of interspike-interval distributions convolved with itself (graphical representation of Eq. (7.40)). The interspike-interval distribtion ($P_0(s)$, thick line) is added sequentially to self-convolutions such as $\int_0^\infty P_0(s')P_0(s-s')\mathrm{d}s'$ (dashed lines). The partial sums (solid lines) gradually converge to the autocorrelation function ($C_+(s)$, dotted line).

For $\omega = 0$, the Fourier integral over the right-hand side of Eq. (7.40) diverges, since $\int_0^\infty P_0(s)\mathrm{d}s = 1$. If we add the diverging term from Eq. (7.38), we arrive at

$$\hat{C}_{ii}(\omega) = \nu_i \,\mathrm{Re}\left\{\frac{1+\hat{P}_0(\omega)}{1-\hat{P}_0(\omega)}\right\} + 2\pi\,\nu_i^2\,\delta(\omega). \tag{7.45}$$

This is a standard result of stationary renewal theory (Cox and Lewis, 1966) which has been repeatedly applied to neuronal spike trains (Edwards and Wakefield, 1993; Bair *et al.*, 1994).

Example: Stationary Poisson process

In Sections 7.2.1 and 7.5 we have already discussed the Poisson neuron from the perspective of mean firing rate and renewal theory, respectively. The autocorrelation of a Poisson process is

$$C_{ii}(s) = \nu\,\delta(s) + \nu^2. \tag{7.46}$$

We want to show that Eq. (7.46) follows from Eq. (7.40).

Since the interval distribution of a Poisson process is exponential [see Eq. (7.16) with $\Delta^{\mathrm{abs}} = 0$], we can evaluate the integrals on the right-hand side of Eq. (7.40) in a straightforward manner. The result is

$$C_+(s) = \nu\,\mathrm{e}^{-\nu s}\left[1 + \nu s + \frac{1}{2}(\nu s)^2 + \cdots\right] = \nu\,. \tag{7.47}$$

Hence, with Eq. (7.42), we obtain the autocorrelation function (7.46) of a homogeneous Poisson process. The Fourier transform of Eq. (7.46) yields a flat spectrum with a δ peak at zero:

$$\hat{C}_{ii}(\omega) = \nu + 2\pi\,\nu^2\,\delta(\omega)\,. \tag{7.48}$$

The result could have also been obtained by evaluating Eq. (7.45).

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Example: Poisson process with absolute refractoriness

We return to the Poisson process with absolute refractoriness defined in Eq. (7.16). Apart from an absolute refractory time $\Delta^{\rm abs}$, the neuron fires with rate r. For $\omega \neq 0$, Eq. (7.45) yields the noise spectrum

$$\hat{C}_{ii}(\omega) = \nu \left\{ 1 + 2\frac{\nu^2}{\omega^2}[1-\cos(\omega\Delta^{\rm abs})] + 2\frac{\nu}{\omega}\sin(\omega\Delta^{\rm abs}) \right\}^{-1}; \tag{7.49}$$

see Fig. 7.12b. In contrast to the stationary Poisson process Eq. (7.46), the noise spectrum of a neuron with absolute refractoriness $\Delta^{\rm abs} > 0$ is no longer flat. In particular, for $\omega \to 0$, the noise spectrum is *decreased* by a factor $[1 + 2(\nu\Delta^{\rm abs}) + (\nu\Delta^{\rm abs})^2]^{-1}$. Eq. (7.49) and generalizations thereof have been used to fit the power spectrum of, e.g., auditory neurons (Edwards and Wakefield, 1993) and MT (middle temporal) neurons (Bair *et al.*, 1994).

Can we understand the decrease in the noise spectrum for $\omega \to 0$? The mean interval of a Poisson neuron with absolute refractoriness is $\langle s \rangle = \Delta^{\rm abs} + r^{-1}$. Hence the mean firing rate is

$$\nu = \frac{r}{1 + \Delta^{\rm abs} r}. \tag{7.50}$$

For $\Delta^{\rm abs} = 0$ we retrieve the stationary Poisson process Eq. (7.3) with $\nu = r$. For finite $\Delta^{\rm abs}$ the firing is more regular than that of a Poisson process with the same mean rate ν. We note that, for finite $\Delta^{\rm abs} > 0$, the mean firing rate remains bounded even if $r \to \infty$. The neuron then fires regularly with period $\Delta^{\rm abs}$. Because the spike train of a neuron with refractoriness is more regular than that of a Poisson neuron with the same mean rate, the spike count over a long interval, and hence the spectrum for $\omega \to 0$, is less noisy. This means that Poisson neurons with absolute refractoriness can transmit slow signals more reliably than a simple Poisson process.

7.5.4 Input-dependent renewal theory (*)

It is possible to use the renewal concept in a broader sense and define a renewal process as a system where the state at time t (and hence the probability of generating an event at t), depends both on the time that has passed since the last event (i.e., the firing time $\hat{t}$) *and* the input $I(t')$, $\hat{t} < t' < t$, that the system received since the last event. Input-dependent renewal systems are also called modulated renewal processes (Reich *et al.*, 1998), non-stationary renewal systems (Gerstner, 1995, 2000), or inhomogeneous Markov interval processes (Kass and Ventura, 2001). The aim of a theory of input-dependent renewal systems is to predict the probability density

$$P_I(t|\hat{t}) \tag{7.51}$$

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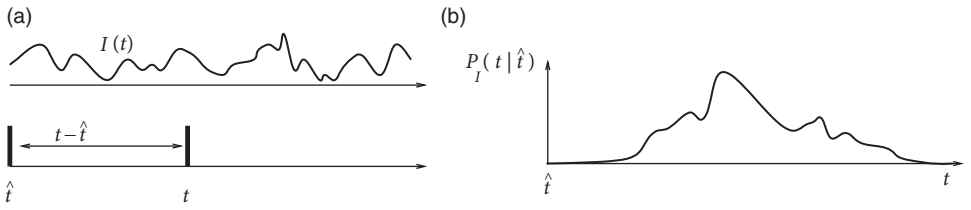

Fig. 7.14 Input-dependent interval distribution. (a) A neuron, stimulated by the current $I(t)$ has emitted a first spike at $\hat{t}$. (b) The interval distribution $P_I(t|\hat{t})$ gives the probability density that the next spike occurs after an interval $t-\hat{t}$.

of the next event to occur at time t, given the timing $\hat{t}$ of the last event *and* the input $I(t')$ for $\hat{t} < t' < t$; see Fig. 7.14. The relation between hazard, survivor function, and interval distribution for the input-dependent case is the same as the one given in Eqs. (7.25)–(7.28). The generalization to a time-dependent renewal theory will be useful later on, in Chapter 9.

The lower index I of $P_I(t|\hat{t})$ is intended to remind the reader that the probability density $P_I(t|\hat{t})$ depends on the time course of the input $I(t')$ for $t' < t$. Since $P_I(t|\hat{t})$ is conditioned on the spike at $\hat{t}$, it can be called a spike-triggered spike density. We interpret $P_I(t\,|\,\hat{t})$ as the distribution of interspike intervals in the presence of an input current I or as the *input-dependent interval distribution*. For stationary input, $P_I(t|\hat{t})$ reduces to $P_0(t-\hat{t})$.

7.6 The problem of neural coding

We have discussed in the preceding sections measures to quantify neural spike train data. This includes measures of interval distribution, autocorrelation, noise spectrum, but also simple measures such as the firing rate. All of these measures are useful tools for an experimenter who plans to study a neural system. A completely different question, however, is whether neurons transmit information by using any of these quantities as a neural code.

In this section we critically review the notion of rate codes, and contrast rate coding schemes with spike codes.

7.6.1 Limits of rate codes

The successful application of rate concepts to neural data does not necessarily imply that the neuron itself uses a rate code. Let us look at the limitations of the spike count measure and the PSTH.

Limitations of the spike count code

An experimenter as an external observer can evaluate and classify neuronal firing by a spike count measure – but is this really the code used by neurons in the brain? In other

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words, is a cortical neuron which receives signals from a sensory neuron only looking at and reacting to the number of spikes it receives in a time window of, say, 500 ms? We will approach this question from a modeling point of view later on in the book. Here we discuss some critical experimental evidence.

From behavioral experiments it is known that reaction times are often rather short. A fly can react to new stimuli and change the direction of flight within 30–40 ms; see the discussion in (Rieke *et al.*, 1997). This is not long enough for counting spikes and averaging over some long time window. The fly has to respond after a postsynaptic neuron has received one or two spikes. Humans can recognize visual scenes in just a few hundred milliseconds (Thorpe *et al.*, 1996), even though recognition is believed to involve several processing steps. Again, this does not leave enough time to perform temporal averages on each level.

From the point of view of rate coding, spikes are just a convenient way to transmit the analog output variable ν over long distances. In fact, the best coding scheme to transmit the value of the rate ν would be by a regular spike train with intervals $1/\nu$. In this case, the rate could be reliably measured after only two spikes. From the point of view of rate coding, the irregularities encountered in real spike trains of neurons in the cortex must therefore be considered as noise. In order to get rid of the noise and arrive at a reliable estimate of the rate, the experimenter has to average over a larger number of spikes.

Temporal averaging can work well in cases where the stimulus is constant or slowly varying and does not require a fast reaction of the organism – and this is the situation encountered in many experimental protocols. Real-world input, however, is rarely stationary, but often changing on a fast time scale. For example, even when viewing a static image, humans perform saccades, rapid changes of the direction of gaze. The image projected onto the retinal photo receptors changes therefore every few hundred milliseconds – and with each new image the retinal photo receptors change the response (Fig. 7.16c). Since, in a changing environment, a postsynaptic neuron does not have the time to perform a temporal average over many (noisy) spikes, we consider next whether the PSTH could be used by a neuron to estimate a time-dependent firing rate.

Limitations of the PSTH

The obvious problem with the PSTH is that it needs several trials to build up. Therefore it cannot be the decoding scheme used by neurons in the brain. Consider, for example, a frog that wants to catch a fly. It cannot wait for the insect to fly repeatedly along exactly the same trajectory. The frog has to base its decision on a single run – each fly and each trajectory is different.

Nevertheless, the PSTH measure of the instantaneous firing rate can make sense if there are large populations of similar neurons that receive the same stimulus. Instead of recording from a population of N neurons in a single run, it is experimentally easier to record from a single neuron and average over N repeated runs. Thus, a neural code based on the PSTH relies on the implicit assumption that there are always populations of neurons with similar properties.

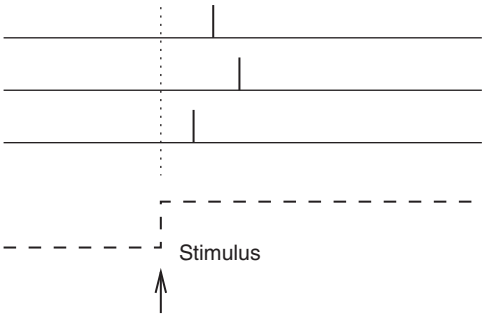

Fig. 7.15 Time-to-first-spike. The spike train of three neurons are shown. The third neuron from the top is the first one to fire a spike after the stimulus onset (arrow). The dashed line indicates the time course of the stimulus.

Limitations of rate as a population average

A potential difficulty with the definition (7.11) of the firing rate as an average over a population of neurons is that we have formally required a homogeneous population of neurons with identical connections, which is hardly realistic. Real populations will always have a certain degree of heterogeneity both in their internal parameters and in their connectivity pattern. Nevertheless, rate as a population activity (of suitably defined pools of neurons) may be a useful coding principle in many areas of the brain.

For inhomogeneous populations, the definition (7.11) may be replaced by a weighted average over the population. To give an example of a weighted average in an inhomogeneous population, we suppose that we are studying a population of neurons which respond to a stimulus $\boldsymbol{x}$. We may think of $\boldsymbol{x}$ as the location of the stimulus in input space. Neuron i responds best to stimulus $\boldsymbol{x}_i$, another neuron j responds best to stimulus $\boldsymbol{x}_j$. In other words, we may say that the spikes of a neuron i "represent" an input vector $\boldsymbol{x}_i$ and those of j an input vector $\boldsymbol{x}_j$. In a large population, many neurons will be active simultaneously when a new stimulus $\boldsymbol{x}$ is represented. The location of this stimulus can then be estimated from the weighted population average

$$\boldsymbol{x}^{\text{est}}(t) = \frac{\int_t^{t+\Delta t} \sum_j \sum_f \boldsymbol{x}_j \, \delta(t - t_j^f) \, \mathrm{d}t}{\int_t^{t+\Delta t} \sum_j \sum_f \delta(t - t_j^f) \, \mathrm{d}t} \,. \tag{7.52}$$

Both numerator and denominator are closely related to the population activity (7.11). The estimate (7.52) has been successfully used for an interpretation of neuronal activity in primate motor cortex (Georgopoulos *et al*., 1986) and hippocampus (Wilson and McNaughton, 1993). It is, however, not completely clear whether postsynaptic neurons really evaluate the fraction (7.52) – a potential problem for a neuronal coding and decoding scheme lies in the normalization by division.

7.6.2 Candidate temporal codes

Rate coding in the sense of a population average is one of many candidate coding schemes that could be implemented and used by neurons in the brain. In this section, we introduce some potential coding strategies based on spike timing.

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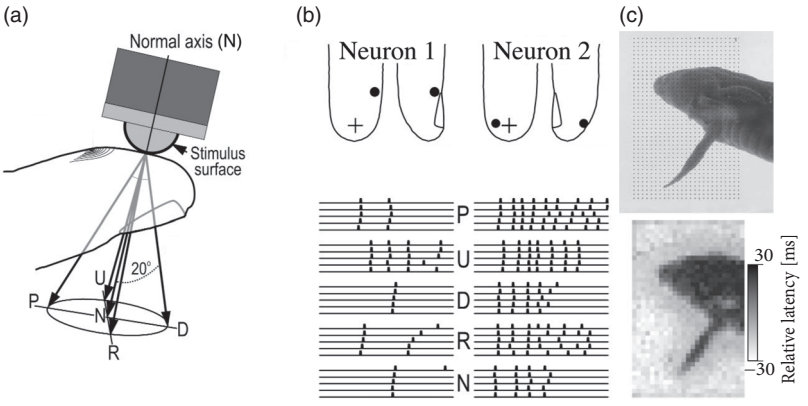

Fig. 7.16 Time-to-first-spike. (a) Touching the finger tip with a sharp object can be quantified by a force vector with total strength in the normal direction (N), possibly superimposed with a tangential component in one of four possible directions (P, U, D, R). (b) Spike response to onset of touch force in the five possible direction (P, U, D, R, N). Different stimuli yield different spike latencies which are consistent across the five repetitions. Different neurons have different response patterns (two selected neurons are shown). The location where stimulation yields maximal response is shown with a filled circle. (c) (Top) Presentation of an image on the retina. The grid of recording electrodes is indicated by dots. (Bottom) The latency of the first spike detected at each electrode reflects the original image. Each pixel corresponds to one recorded neuron. (a) and (b) modified from Johansson and Birznieks (2004), (c) is modified from Gollisch and Meister (2008) with permission from AAAS.

Time-to-first-spike: latency code

Let us study a neuron which abruptly receives a new constant input at time t_0. For example, a neuron might be driven by an external stimulus which is suddenly switched on at time t_0. This seems to be somewhat artificial, but even in a realistic situation abrupt changes in the input are quite common. When we look at a picture, our gaze jumps from one point to the next. After each saccade, the photo receptors in the retina receive a new visual input. Information about the onset of a saccades should easily be available in the brain and could serve as an internal reference signal. We can then imagine a code where for each neuron the timing of the *first* spike after the reference signal contains all information about the new stimulus. A neuron which fires shortly after the reference signal is interpreted as a strong stimulation of this neuron, whereas firing somewhat later would signal a weaker stimulation; see Fig. 7.15.

In a pure version of this coding scheme, each neuron needs to fire only a single spike to transmit information. If it emits several spikes, only the first spike after the reference signal counts. All following spikes would be irrelevant. To implement a clean version of such a coding scheme, we imagine that each neuron is shut off by inhibition as soon as it has fired a spike. Inhibition ends with the onset of the next stimulus (e.g., after the next saccade). After the release from inhibition the neuron is ready to emit its next spike, which now transmits information about the new stimulus. Since each neuron in such a scenario

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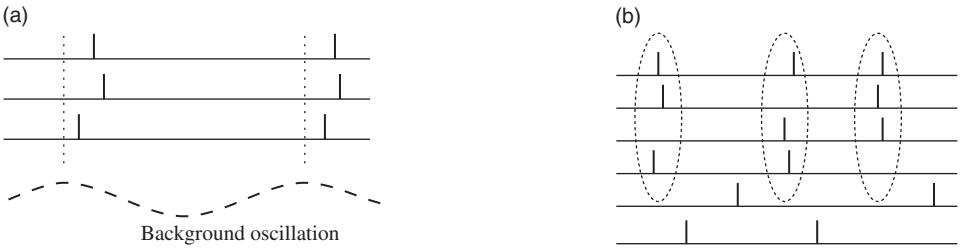

Fig. 7.17 Phase and synchrony. (a) Phase coding: the neurons fire at different phases with respect to the background oscillation (dashed). The phase could code relevant information. (b) Coding by synchrony: the upper four neurons are nearly synchronous: two other neurons at the bottom are not synchronized with the others.

transmits exactly one spike per stimulus, it is clear that only the timing conveys information and not the number of spikes.

Experimental evidence indicates that a coding scheme based on the latency of the first spike transmit a large amount of information. For example, touch sensors in the finger tip encode the strength and direction of the touch in the timing of the first spike emitted by each neuron (Fig. 7.16). Similarly, the relative latency of first spikes of retinal neurons encode the image projected on the retina (Fig. 7.16c). In a slightly different context coding by first spikes has been discussed by Thorpe *et al*. (1996). Thorpe argues that the brain does not have time to evaluate more than one spike from each neuron per processing step. Therefore the first spike should contain most of the relevant information, which is read out by neurons further down the processing chain. Using information-theoretic measures on their experimental data, several groups have shown that most of the information about a new stimulus is indeed conveyed during the first 20 or 50 milliseconds after the onset of the neuronal response (Optican and Richmond, 1987; Tovee and Rolls, 1995).

Phase

We can apply a code by "time to first spike" also in the situation where the reference signal is not a single event, but a periodic signal. In the hippocampus, in the olfactory system, and also in other areas of the brain, oscillations of some global variable (for example the population activity) are quite common. These oscillations could serve as an internal reference signal. Neuronal spike trains could then encode information in the phase of a pulse with respect to the background oscillation. If the input does not change between one cycle and the next, then the same pattern of phases repeats periodically; see Fig. 7.17a.

The concept of coding by phases has been studied by several different groups. There is, for example, evidence that the phase of a spike during an oscillation in the hippocampus of the rat conveys information on the spatial location of the animal which is not fully accounted for by the firing rate of the neuron (O'Keefe and Recce, 1993).

Correlations and synchrony

We can also use spikes from other neurons as the reference signal for a spike code. For example, synchrony of a pair or of many neurons could signify special events and convey information which is not contained in the firing rate of the neurons; see Fig. 7.17b. One famous idea is that synchrony could mean "belonging together." Consider, for example, a complex scene consisting of several objects. It is represented in the brain by the activity of a large number of neurons. Neurons that represent the same object could be "labeled" by the fact that they fire synchronously (von der Malsburg, 1981; Eckhorn *et al*., 1988; Gray and Singer, 1989).

More generally, not only synchrony but any precise spatio-temporal pulse pattern could be a meaningful event. For example, a spike pattern of three neurons, where neuron 1 fires at some arbitrary time t_1 followed by neuron 2 at time $t_1 + \delta_{12}$ and by neuron 3 at $t_1 + \delta_{13}$, might represent a certain stimulus condition. The same three neurons firing with different relative delays might signify a different stimulus. The relevance of precise spatio-temporal spike patterns has been studied intensively by Abeles (1991). Similarly, but on a somewhat coarse time scale, correlations of auditory and visual neurons are found to be stimulus dependent and might convey information beyond that contained in the firing rate alone (deCharms and Merzenich, 1996; Steinmetz *et al*., 2000).

Stimulus reconstruction and reverse correlation

Let us consider a neuron which is driven by a time-dependent stimulus $s(t)$. Every time a spike occurs, we note the time course of the stimulus in a time window of about 100 ms immediately before the spike. Averaging the results over several spikes yields the typical time course of the stimulus just before a spike (de Boer and Kuyper, 1968). Such a procedure is called a "reverse correlation" approach; see Fig. 7.18. In contrast to the PSTH experiment sketched in Section 7.2.2 where the experimenter averages the neuron's response over several trials with the same stimulus, reverse correlation means that the experimenter averages the input under the condition of an identical response, i.e., a spike. In other words, it is a spike-triggered average (see, e.g., de Ruyter van Stevenhick and Bialek 1988; Rieke *et al*. 1997). The results of the reverse correlation, i.e., the typical time course of the stimulus that has triggered a spike, can be interpreted as the "meaning" of a single spike. Reverse correlation techniques have made it possible to measure, for example, the spatio-temporal characteristics of neurons in the visual cortex (Eckhorn *et al*., 1993; DeAngelis *et al*., 1995).

With a somewhat more elaborate version of this approach, W. Bialek and his coworkers have been able to "read" the neural code of the H1 neuron in the fly and to reconstruct a time-dependent stimulus (Bialek *et al*., 1991; Rieke *et al*., 1997). Here we give a simplified version of their argument.

Results from reverse correlation analysis suggest that each spike signifies the time course of the stimulus preceding the spike. If this is correct, a reconstruction of the complete time course of the stimulus $s(t)$ from the set of firing times $\mathscr{F} = \{t^{(1)}, \ldots t^{(n)}\}$ should be

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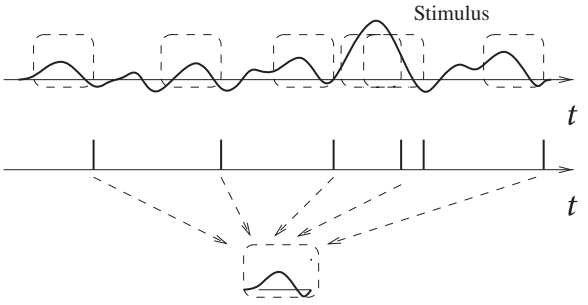

Fig. 7.18 Reverse correlation technique (schematic). The stimulus in the top trace has caused the spike train shown immediately below. The time course of the stimulus just before the spikes (dashed boxes) has been averaged to yield the typical time course (bottom).

possible; see Fig. 7.19. As a simple test of this hypothesis, Bialek and coworkers have studied a linear reconstruction. A spike at time t^f gives a contribution $\kappa(t-t^f)$ to the estimation $s^{\rm est}(t)$ of the time course of the stimulus. Here, $t^f \in \mathscr{F}$ is one of the firing times and $\kappa(t-t^f)$ is a kernel which is nonzero during some time before and around t^f; see Fig. 7.19b. A linear estimate of the stimulus is

$$s^{\rm est}(t) = \sum_{f=1}^{n} \kappa(t-t^f)\,. \tag{7.53}$$

The form of the kernel κ was determined through optimization so that the average reconstruction error $\int {\rm d}t[s(t)-s^{\rm est}(t)]^2$ was minimal. The quality of the reconstruction was then tested on additional data which was not used for the optimization. Surprisingly enough, the simple linear reconstruction (7.53) gave a fair estimate of the time course of the stimulus even though the stimulus varied on a time scale comparable to the typical interspike interval (Bialek *et al*., 1991; Rieke *et al*., 1997). This reconstruction method shows nicely that information about a time-dependent input can indeed be conveyed by spike timing. Chapter 11 will revisit the spike train decoding in the presence of refractoriness and adaptation.

Rate versus temporal codes (*)

The dividing line between spike codes and firing rates is not always as clearly drawn as it may seem at first sight. Some codes which were first proposed as pure examples of pulse codes have later been interpreted as variations of rate codes. For example, the stimulus reconstruction (7.53) with kernels seems to be a clear example of a spike code. Nevertheless, it is also not so far from a rate code based on spike counts (Abbott, 1994; Theunissen and Miller, 1995). To see this, consider a spike count measure with a running time window $K(.)$. We can estimate the rate ν at time t by

$$\nu(t) = \frac{\int K(\tau)\,S(t-\tau){\rm d}\tau}{\int K(\tau){\rm d}\tau}\,, \tag{7.54}$$

where $S(t)=\sum_{f=1}^{n}\delta(t-t^f)$ is the spike train under consideration. The integrals run from minus to plus infinity. For a rectangular time window $K(\tau)=1$ for $-T/2<\tau<T/2$ and zero otherwise, (7.54) reduces exactly to our definition of a rate as a spike count measure in Eq. (7.1).

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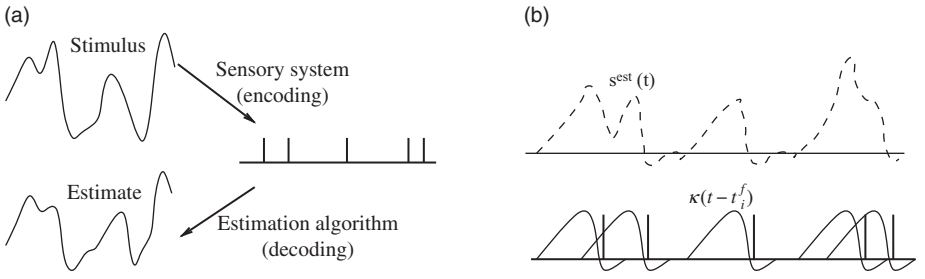

Fig. 7.19 Reconstruction of a stimulus (schematic). (a) A stimulus evokes a spike train of a neuron. The time course of the stimulus may be estimated from the spike train; redrawn after Rieke et al., (1996). (b) In the framework of linear stimulus reconstruction, the estimation $s^{\text{est}}(t)$ (dashed) is the sum of the contributions κ (solid lines) of all spikes.

The time window in (7.54) can be made rather short so that at most a few spikes fall into the interval T. Furthermore, there is no need for the window $K(.)$ to be symmetric and rectangular. We might just as well take an asymmetric time window with smooth borders. Moreover, we can perform the integration over the δ-function, which yields

$$\nu(t) = c \sum_{f=1}^{n} K(t - t^f), \tag{7.55}$$

where $c = [\int K(s)\mathrm{d}s]^{-1}$ is a constant. Except for the constant c (which sets the overall scale to units of 1 over time), the generalized rate formula (7.55) is now identical to the reconstruction formula (7.53). In other words, the linear reconstruction is just the firing rate measured with a cleverly optimized time window.

Similarly, a code based on the "time-to-first-spike" is also consistent with rate coding. If, for example, the mean firing rate of a neuron is high for a given stimulus, then the first spike is expected to occur early. If the rate is low, the first spike is expected to occur later. Thus the timing of the first spike contains a lot of information about the underlying rate.

The discussion of whether or not to call a given code a rate code is still ongoing. What is important, in our opinion, is to have a coding scheme which allows neurons to quickly respond to stimulus changes. A naïve spike count code with a long time window is unable to do this, but a code based on population activities introduced above and many of the other codes are. The name of such a code, whether it is deemed a rate code or not is of minor importance.

Example: Towards a definition of rate codes

We have seen above in Eq. (7.55) that stimulus reconstruction with a linear kernel can be seen as a special instance of a rate code. This suggests a formal definition of a

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rate code via the reconstruction procedure: if all information contained in a spike train can be recovered by the linear reconstruction procedure of Eq. (7.53), then the neuron is, by definition, using a rate code. Spike codes would then be codes where a linear reconstruction is not successful. Theunissen and Miller have proposed a definition of rate coding that makes the above ideas more precise (Theunissen and Miller, 1995).

To see how their definition works, we have to return to the reconstruction formula (7.53). It is, in fact, the first term of a systematic Volterra expansion for the estimation of the stimulus from the spikes (Bialek *et al*., 1991)

$$s^{\text{est}}(t) = \sum_f \kappa_1(t - t^f) + \sum_{f,f'} \kappa_2(t - t^f, t - t^{f'}) + \cdots . \tag{7.56}$$

For a specific neuron, inclusion of higher-order terms $\kappa_2, \kappa_3, \ldots$ may or may not improve the quality of the estimation. For most neurons where the reconstruction has been carried through, it seems that the higher-order terms do not contribute a large amount of information (Rieke *et al*., 1997). The neurons would then be classified as rate coding.

Let us now suppose that the reconstruction procedure indicates a significant contribution of the second-order term. Does this exclude rate coding? Unfortunately this is not the case. We have to exclude two other possibilities. Firstly, we might have chosen a suboptimal stimulus. A neuron might, for example, encode the variable x by a rate code, so that a nearly perfect linear reconstruction of x would be possible,

$$x(t) \approx x^{\text{est}} = \sum_{f=1}^{n} \kappa_1(t - t^f) . \tag{7.57}$$

But if we chose a stimulus $s = x^2$ instead of x, then the reconstruction for s^{est} would involve second-order terms, even though the neuron is really using rate code.

Secondly, according to Theunissen and Miller (1995) a spike code should show a temporal structure that is more precise than the temporal structure of the stimulus. The fact that neurons show precise and reliable spike timing as such is, for them, not sufficient to classify the neuron as a temporal encoder, since the neuronal precision could just be the image of precise temporal input. For a more quantitative treatment, let us consider a stimulus with cut-off frequency ω. In order to exclude the possibility that the timing is induced by the stimulus, Theunissen and Miller propose to consider the Fourier spectrum of the higher-order reconstruction kernels. If the Fourier transform of the higher-order kernels contains frequencies less than ω only, then the code is a rate code. If higher-order kernels are significant and contain frequencies above ω, then the information is encoded temporally. A positive example of a spike code (or of "temporal encoding") according to this definition would be the code by correlation and synchrony introduced above. Another example would be the phase code, in particular if the number of spikes per cycle is independent of the stimulus strength.

7.7 Summary

Variability of spike timing is a common phenomenon in biological neurons. Variability can be quantified by the C_V value of interval distributions, by the Fano factor of the spike count, or by the repeatability of spike timings between one trial and the next. Whether the variability represents noise or uncontrolled components of a signal which is not well characterized is a topic of debate. Experiments show that a neuron *in vitro*, or in one of the sensory areas *in vivo*, shows highly reliable spike timings if driven by a strong stimulus with large-amplitude fluctuations of the signal. Spontaneous activity *in vivo*, however, is unreliable and exhibits large variability of interspike intervals and spike counts.

The simplest stochastic description of neuronal firing is a Poisson process. However, since each spike firing in a Poisson process is independent of earlier spikes, Poisson firing cannot account for refractoriness. In renewal processes, the probability of firing depends on the time since the last spike. Therefore refractoriness is taken care of. The independent events are the interspike intervals which are drawn from an interval distribution $P_0(s)$. Knowledge of $P_0(s)$ is equivalent to knowing the survivor function $S_0(s)$ or the hazard $\rho_0(s)$. In neurons showing strong adaptation, interspike intervals are *not* independent so that renewal theory is not sufficient. Moreover, standard renewal theory is limited to stationary stimuli, whereas real-world stimuli have a strong temporal component – the solution is then a time-dependent generalization of renewal theory which we will encounter in Chapter 14.

A description of neuronal spike trains in terms of firing rates or interval distributions does not imply that neurons use the firing rate (or interval distribution) to transmit signals. In fact, neither the spike count (averaging over time) nor the time-dependent rate of the PSTH (averaging over trials) can be the neural code of sensory processing because they are too slow given known reaction times. A firing rate in the sense of a population activity, defined as the instantaneous average of spikes across a population of neurons with similar properties, is, however, a candidate neural code. Other candidate codes, with some experimental support are a latency code (time-to-first-spike), or a phase code.

In models, noise is usually added ad hoc to account for the observed variability of neural spike trains: two standard ways of adding noise to neuron models will be presented in the next two chapters. But even without explicit noise source, neural activity may look noisy if the neuron is embedded in a large deterministic network with fixed random connectivity. The analysis of such networks will be the topic of Part III.

Literature

A review of noise in the nervous system with a focus on internal noise sources can be found in Faisal *et al*. (2008). Analysis of spike trains in terms of stochastic point processes has a long tradition (Perkel *et al*., 1967a; Gerstein and Perkel, 1972) and often involves concepts

from renewal theory (Cox and Lewis, 1966). Some principles of spike-train analysis with an emphasis on modern results have been reviewed by Gabbiani and Koch (1998) and Rieke *et al*. (1997). For a discussion of the variability of interspike intervals see the debate of Shadlen and Newsome (1994), Softky (1995), and Bair and Koch (1996); these papers also give a critical discussion of the concept of temporal averaging. An accessible mathematical treatment of the inhomogeneous Poisson model in the context of neuronal signals is given in Rieke *et al*. (1997). The same book can also be recommended for its excellent discussion of rate codes, and their limits, as well as the method of stimulus reconstruction (Rieke *et al*., 1997).

Exercises

1. **Poisson process in discrete and continuous time**. *We consider a Poisson neuron model in discrete time. In every small time interval Δt, the probability that the neuron fires is given by $\nu\,\Delta t$. Firing in different time intervals is independent. The limit $\Delta t \to 0$ will be taken only at the end.*
   (a) What is the probability that the neuron does not fire during a time of arbitrarily large length $t = N\Delta t$?
   Hint: Consider first the probability of not firing during a single short interval Δt, and then extend your reasoning to N time steps.
   (b) Suppose that the neuron has fired at time $t = 0$. Calculate the distribution of intervals $P(t)$, i.e., the probability density that the neuron fires its next spike at a time $t = N\Delta t$.
   (c) Start from your results in (a) and (b) and take the limit $N \to \infty$, $\Delta t \to 0$, while keeping t fixed. What is the resulting survivor function $S_0(t)$ and the interval distribution $P_0(s)$ in continuous time?
   (d) Suppose that the neuron is driven by some input. For $t < t_0$, the input is weak, so that its firing rate is $\nu = 2\,\mathrm{Hz}$. For $t_0 < t < t_1 = t_0 + 100$ ms, the input is strong and the neuron fires at $\nu = 20\,\mathrm{Hz}$. Unfortunately, however, the onset time t_0 of the strong input is unknown; can an observer, who is looking at the neurons output, detect the period of strong input? How reliably?
   Hint: Calculate the interval distributions for weak and strong stimuli. What is the probability of having a burst consisting of two intervals of less than 20 ms each if the input is weak/strong?
2. **Autocorrelation of a Poisson process in discrete time**. *The autocorrelation*

$$C_{ii}(s) = \langle S_i(t)\, S_i(t+s)\rangle_t \tag{7.58}$$

   is defined as the joint probability density of finding a spike at time t **and** *a spike at time $t + s$. In Eq. (7.46) we have stated the autocorrelation of the homogeneous Poisson process in continuous time. Derive this result by starting with a Poisson process in discrete time where the probability of firing in a small time interval Δt is given by $\nu\,\Delta t$. To do so, take the following steps:*
   (a) What is the joint probability of finding a spike in the bin $[t, t+\Delta t]$ AND in the bin $[t', t'+\Delta t]$ where $t \neq t'$?
   (b) What is the joint probability of finding a spike in the bin $[t, t+\Delta t]$ AND in the bin $[t', t'+\Delta t]$ where $t = t'$?
   (c) What is the probability of finding two spikes in the bin $[t, t+\Delta t]$? Why can this term be neglected in the limit $\Delta t \to 0$?
   (d) Take the limit $\Delta t \to 0$ while keeping t and t' fixed so as to find the autocorrelation function $C_0(s)$ in continuous time.
3. **Repeatability and random coincidences**. *Suppose that a Poisson neuron with a constant rate of 20 Hz emits, in a trial of 5-second duration, 100 spikes at times $t^{(1)}; t^{(2)}; \ldots t^{(100)}$. Afterward, the experiment is repeated and a second spike train with a duration of 5 seconds is observed. How many spikes in the first trial can be expected to coincide with a spike in the second trial? More generally, what percentage of spikes coincide between two trials of a Poisson neuron with arbitrary rate ν_0 under the assumption that trials are sufficiently long?*

https://doi.org/10.1017/CBO9781107447615.009 Published online by Cambridge University Press

4. **Spike count and Fano factor**. *A homogeneous Poisson process has a probability to fire in a very small interval Δt equal to $\nu \Delta t$.*
(a) Show that the probability of observing exactly k spikes in the time interval $T = N\Delta t$ is $P_k(T) = [1/k!]\,(\nu T)^k \exp(-\nu T)$.
Hint: Start in discrete time and write the probability of observing k events in N slots using the binomial distribution: $P(k;N) = [N!/k!(N-k)!]\,p^k\,(1-p)^{N-k}$ where p is the probability of firing in a time bin of duration Δt. Take the continuous time limit with Stirling's formula $N! \approx (N/e)^N$.
(b) Repeat the above argument for an inhomogeneous Poisson process.
(c) Show for the inhomogeneous Poisson process that the mean spike count in an interval of duration T is $\langle k \rangle = \int_0^T \nu(t)\,\mathrm{d}t$.
(d) Calculate the variance of the spike count and the Fano factor for the inhomogeneous Poisson process.
5. **From interval distribution to hazard**. *During stimulation with a stationary stimulus, interspike intervals in a long spike train are found to be independent and given by the distribution*

$$P(t|t') = \frac{(t-t')}{\tau^2} \exp\left(-\frac{t-t'}{\tau}\right) \tag{7.59}$$

for $t > t'$.
(a) Calculate the survivor function $S(t|t')$, i.e., the probability that the neuron survives from time t' to t without firing.
Hint: You can use $\int_0^y x\mathrm{e}^{ax}\mathrm{d}x = e^{ay}[ay-1]/a^2$.
(b) Calculate the hazard function $\rho(t|t')$, i.e., the stochastic intensity that the neuron fires, given that its last spike was at t' and interpret the result: what are the signs of refractoriness?
(c) A spike train starts at time 0 and we have observed a first spike at time t_1. We are interested in the probability that the nth spike occurs around time $t_n = t_1 + s$. With this definition of spike labels, calculate the probability density $P(t_3|t_1)$ that the third spike occurs around time t_3.
6. **Gamma distribution**. *Stationary interval distributions can often be fitted by a Gamma distribution (for $s > 0$)*

$$P(s) = \frac{1}{(k-1)!}\,\frac{s^{k-1}}{\tau^k}\,\mathrm{e}^{-s/\tau}, \tag{7.60}$$

where k is a positive natural number. We consider in the following $k = 1$.
(a) Calculate the mean interval $\langle s \rangle$ and the mean firing rate.
(b) Assume that intervals are independent and calculate the power spectrum.
Hint: Use Eq. (7.45).
7. **C_V value of Gamma distribution**. *Stationary interval distributions can often be fitted by a Gamma distribution*

$$P(s) = \frac{1}{(k-1)!}\,\frac{s^{k-1}}{\tau^k}\,\mathrm{e}^{-s/\tau}, \tag{7.61}$$

where k is a positive natural number.
Calculate the coefficient of variation C_V for $k = 1, 2, 3$. Interpret your result.
8. **Poisson with dead time as a renewal process**. *Consider a process where spikes are generated with rate ρ_0, but after each spike there is a dead time of duration Δ^{abs}. More precisely, we have a renewal process*

$$\rho(t|\hat{t}) = \rho_0 \quad \text{for} t > \hat{t} + \Delta^{\mathrm{abs}}, \tag{7.62}$$

and zero otherwise.
(a) Calculate the interval distribution, using Eqs. ((7.26)) and ((7.27)).
(b) Calculate the Fano factor.
(c) If a first spike occurred at time $t = 0$, what is the probability that a further spike (there could be other spikes in between) occurs at $t = x\Delta^{\mathrm{abs}}$ where $x = 0.5, 1.5, 2.5$.

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