1

Introduction

The aim of this chapter is to introduce several elementary notions of neuroscience, in particular the concepts of action potentials, postsynaptic potentials, firing thresholds, and refractoriness. Based on these notions, a first phenomenological model of neuronal dynamics is built that will be used as a starting point for a discussion of neuronal coding. Due to the limitations of space we cannot – and do not want to – give a comprehensive introduction into such a complex field as neurobiology. The presentation of the biological background in this chapter is therefore highly selective and simplistic. For an in-depth discussion of neurobiology we refer the reader to the literature mentioned at the end of this chapter. Nevertheless, we try to provide the reader with a minimum of information necessary to appreciate the biological background of the theoretical work presented in this book.

1.1 Elements of neuronal systems

Over the past hundred years, biological research has accumulated an enormous amount of detailed knowledge about the structure and function of the brain. The elementary processing units in the central nervous system are neurons which are connected to each other in an intricate pattern. A tiny portion of such a network of neurons is sketched in Fig. 1.1 which shows a drawing by Ramón y Cajal, one of the pioneers of neuroscience around 1900. We can distinguish several neurons with triangular or circular cell bodies and long wire-like extensions. This picture can only give a glimpse of the network of neurons in the cortex. In reality, cortical neurons and their connections are packed into a dense network with more than 10^4 cell bodies and several kilometers of "wires" per cubic millimeter. In other areas of the brain the wiring pattern may look different. In all areas, however, neurons of different sizes and shapes form the basic elements.

The cortex does not consist exclusively of neurons. Beside the various types of neuron there is a large number of "supporter" cells, so-called glia cells, that are

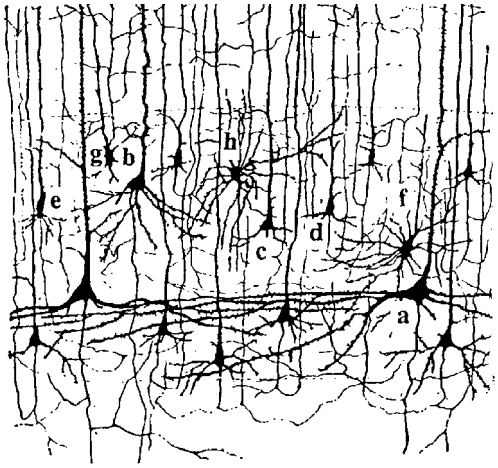

Fig. 1.1. This reproduction of a drawing of Ramón y Cajal shows a few neurons in the mammalian cortex that he observed under the microscope. Only a small portion of the neurons contained in the sample of cortical tissue have been made visible by the staining procedure; the density of neurons is in reality much higher. Cell b is a nice example of a pyramidal cell with a triangularly shaped cell body. Dendrites, which leave the cell laterally and upwards, can be recognized by their rough surface. The axons are recognizable as thin, smooth lines which extend downwards with a few branches to the left and right. From Ramón y Cajal (1909).

required for energy supply and structural stabilization of brain tissue. Since glia cells are not directly involved in information processing, we will not discuss them any further. We will also neglect a few rare subtypes of neuron, such as analog neurons in the mammalian retina. Throughout this book we concentrate on spiking neurons only.

1.1.1 The ideal spiking neuron

A typical neuron can be divided into three functionally distinct parts, called dendrites, soma, and axon; see Fig. 1.2. Roughly speaking, the dendrites play the role of the "input device" that collects signals from other neurons and transmits them to the soma. The soma is the "central processing unit" that performs an important nonlinear processing step. If the total input exceeds a certain threshold, then an output signal is generated. The output signal is taken over by the "output device", the axon, which delivers the signal to other neurons.

The junction between two neurons is called a synapse. Let us suppose that a neuron sends a signal across a synapse. It is common to refer to the sending neuron as the presynaptic cell and to the receiving neuron as the postsynaptic cell. A single neuron in vertebrate cortex often connects to more than 10^4 postsynaptic neurons.

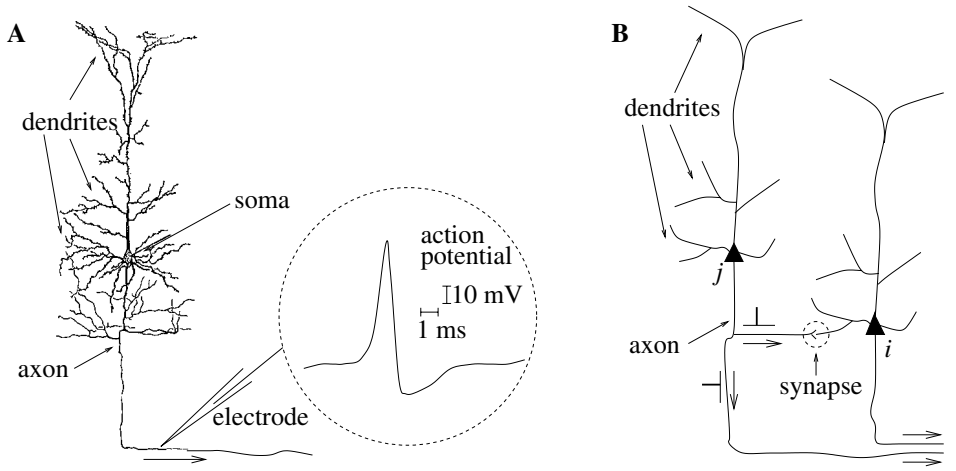

Fig. 1.2. **A**. Single neuron in a drawing by Ramón y Cajal. Dendrite, soma, and axon can be clearly distinguished. The inset shows an example of a neuronal action potential (schematic). The action potential is a short voltage pulse of 1–2 ms duration and an amplitude of about 100 mV. **B**. Signal transmission from a presynaptic neuron j to a postsynaptic neuron i. The synapse is marked by the dashed circle. The axons at the lower right end lead to other neurons (schematic figure).

Many of its axonal branches end in the direct neighborhood of the neuron, but the axon can also stretch over several centimeters so as to reach to neurons in other areas of the brain.

1.1.2 Spike trains

The neuronal signals consist of short electrical pulses and can be observed by placing a fine electrode close to the soma or axon of a neuron; see Fig. 1.2. The pulses, so-called action potentials or spikes, have an amplitude of about 100 mV and typically a duration of 1–2 ms. The form of the pulse does not change as the action potential propagates along the axon. A chain of action potentials emitted by a single neuron is called a spike train – a sequence of stereotyped events which occur at regular or irregular intervals. Since all spikes of a given neuron look alike, the form of the action potential does not carry any information. Rather, it is the number and the timing of spikes which matter. The action potential is the elementary unit of signal transmission.

Action potentials in a spike train are usually well separated. Even with very strong input, it is impossible to excite a second spike during or immediately after a first one. The minimal distance between two spikes defines the absolute refractory period of the neuron. The absolute refractory period is followed by a phase of

relative refractoriness where it is difficult, but not impossible, to excite an action potential.

1.1.3 Synapses

The site where the axon of a presynaptic neuron makes contact with the dendrite (or soma) of a postsynaptic cell is the synapse. The most common type of synapse in the vertebrate brain is a chemical synapse. At a chemical synapse, the axon terminal comes very close to the postsynaptic neuron, leaving only a tiny gap between pre- and postsynaptic cell membranes, called the synaptic cleft. When an action potential arrives at a synapse, it triggers a complex chain of biochemical processing steps that lead to the release of neurotransmitter from the presynaptic terminal into the synaptic cleft. As soon as transmitter molecules have reached the postsynaptic side, they will be detected by specialized receptors in the postsynaptic cell membrane and open (either directly or via a biochemical signaling chain) specific channels so that ions from the extracellular fluid flow into the cell. The ion influx, in turn, leads to a change of the membrane potential at the postsynaptic site so that, in the end, the chemical signal is translated into an electrical response. The voltage response of the postsynaptic neuron to a presynaptic action potential is called the postsynaptic potential.

Apart from chemical synapses neurons can also be coupled by electrical synapses, so-called gap junctions. Specialized membrane proteins make a direct electrical connection between the two neurons. Not very much is known about the functional aspects of gap junctions, but they are thought to be involved in the synchronization of neurons.

1.2 Elements of neuronal dynamics

The effect of a spike on the postsynaptic neuron can be recorded with an intracellular electrode which measures the potential difference $u(t)$ between the interior of the cell and its surroundings. This potential difference is called the membrane potential. Without any spike input, the neuron is at rest corresponding to a constant membrane potential. After the arrival of a spike, the potential changes and finally decays back to the resting potential, cf. Fig. 1.3A. If the change is positive, the synapse is said to be excitatory. If the change is negative, the synapse is inhibitory.

At rest, the cell membrane already has a strong negative polarization of about -65 mV. An input at an excitatory synapse reduces the negative polarization of the membrane and is therefore called depolarizing. An input that increases the negative polarization of the membrane even further is called hyperpolarizing.

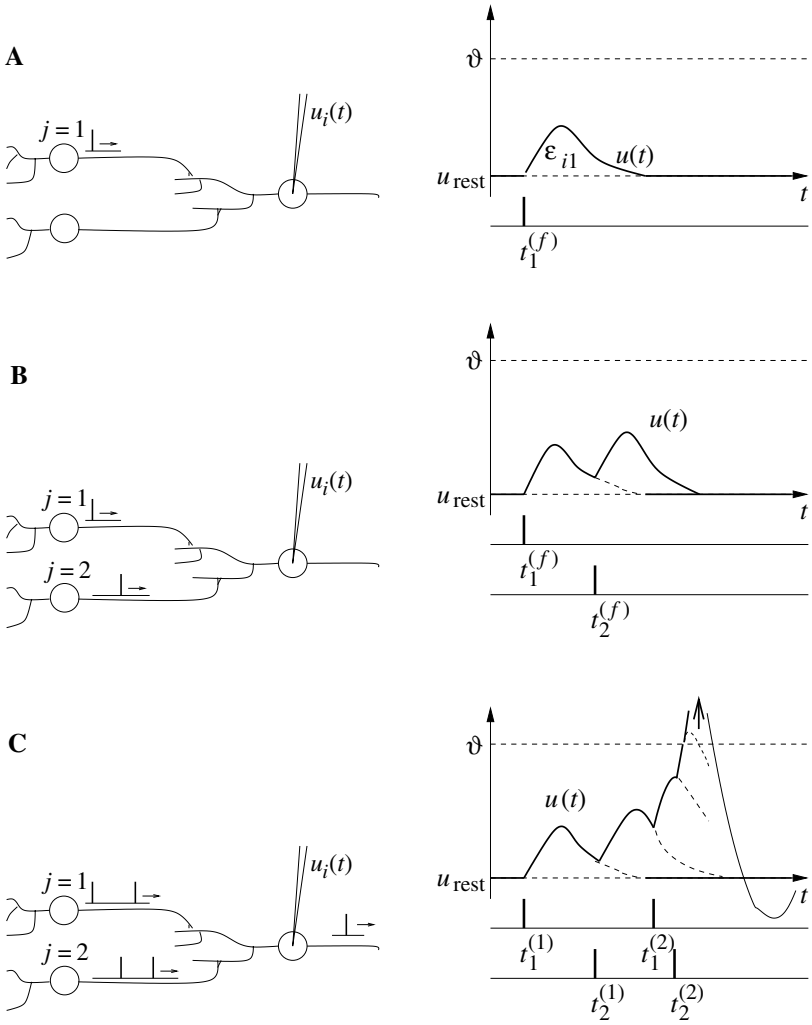

Fig. 1.3. A postsynaptic neuron i receives input from two presynaptic neurons $j = 1, 2$. **A**. Each presynaptic spike evokes an excitatory postsynaptic potential (EPSP) that can be measured with an electrode as a potential difference $u_i(t) - u_{\rm rest}$. The time course of the EPSP caused by the spike of neuron $j = 1$ is $\epsilon_{i1}(t - t_1^{(f)})$. **B**. An input spike from a second presynaptic neuron $j = 2$ that arrives shortly after the spike from neuron $j = 1$ causes a second postsynaptic potential that adds to the first one. **C**. If $u_i(t)$ reaches the threshold ϑ, an action potential is triggered. As a consequence, the membrane potential starts a large positive pulse-like excursion (arrow). On the voltage scale of the graph, the peak of the pulse is out of bounds. After the pulse the voltage returns to a value below the resting potential.

1.2.1 Postsynaptic potentials

Let us formalize the above observation. We study the time course $u_i(t)$ of the membrane potential of neuron i. Before the input spike has arrived, we have $u_i(t) = u_{\rm rest}$. At $t = 0$ the presynaptic neuron j fires its spike. For $t > 0$, we see at the electrode a response of neuron i

$$u_i(t) - u_{\rm rest} = \epsilon_{ij}(t)\,. \tag{1.1}$$

The right-hand side of Eq. (1.1) defines the postsynaptic potential (PSP). If the voltage difference $u_i(t) - u_{\rm rest}$ is positive (negative) we have an excitatory (inhibitory) PSP or short EPSP (IPSP). In Fig. 1.3A we have sketched the EPSP caused by the arrival of a spike from neuron j at an excitatory synapse of neuron i.

1.2.2 Firing threshold and action potential

Consider two presynaptic neurons $j = 1, 2$, which both send spikes to the postsynaptic neuron i. Neuron $j = 1$ fires spikes at $t_1^{(1)}, t_1^{(2)}, \ldots$, similarly neuron $j = 2$ fires at $t_2^{(1)}, t_2^{(2)}, \ldots$. Each spike evokes a PSP ϵ_{i1} or ϵ_{i2}, respectively. As long as there are only few input spikes, the total change of the potential is approximately the sum of the individual PSPs,

$$u_i(t) = \sum_j \sum_f \epsilon_{ij}(t - t_j^{(f)}) + u_{\rm rest}\,, \tag{1.2}$$

i.e., the membrane potential responds linearly to input spikes; see Fig. 1.3B.

However, linearity breaks down if too many input spikes arrive during a short interval. As soon as the membrane potential reaches a critical value ϑ, its trajectory shows a behavior that is quite different from a simple summation of PSPs: the membrane potential exhibits a pulse-like excursion with an amplitude of about 100 mV, viz., an action potential. This action potential will propagate along the axon of neuron i to the synapses of other neurons. After the pulse the membrane potential does not directly return to the resting potential, but passes through a phase of hyperpolarization below the resting value. This hyperpolarization is called "spike-afterpotential".

Single EPSPs have amplitudes in the range of 1 mV. The critical value for spike initiation is about 20–30 mV above the resting potential. In most neurons, four spikes – as shown schematically in Fig. 1.3C – are thus not sufficient to trigger an action potential. Instead, about 20–50 presynaptic spikes have to arrive within a short time window before postsynaptic action potentials are triggered.

1.3 A phenomenological neuron model

In order to build a phenomenological model of neuronal dynamics, we describe the critical voltage for spike initiation by a formal threshold ϑ. If $u_i(t)$ reaches ϑ from below we say that neuron i fires a spike. The moment of threshold crossing defines the firing time $t_i^{(f)}$. The model makes use of the fact that action potentials always have roughly the same form. The trajectory of the membrane potential during a spike can hence be described by a certain standard time course denoted by $\eta(t - t_i^{(f)})$.

1.3.1 Definition of the model SRM$_0$

Putting all elements together we have the following description of neuronal dynamics. The variable u_i describes the momentary value of the membrane potential of neuron i. It is given by

$$u_i(t) = \eta(t - \hat{t}_i) + \sum_j \sum_f \epsilon_{ij}(t - t_j^{(f)}) + u_{\rm rest}, \tag{1.3}$$

where $\hat{t}_i$ is the last firing time of neuron i, i.e., $\hat{t}_i = \max\{t_i^{(f)} \,|\, t_i^{(f)} < t\}$. Firing occurs whenever u_i reaches the threshold ϑ from below,

$$u_i(t) = \vartheta \;\text{ and }\; \frac{\rm d}{{\rm d}t} u_i(t) > 0 \quad \Longrightarrow \quad t = t_i^{(f)}. \tag{1.4}$$

The term ϵ_{ij} in Eq. (1.3) describes the response of neuron i to spikes of a presynaptic neuron j. The term η in Eq. (1.3) describes the form of the spike and the spike-afterpotential.

Note that we are only interested in the potential *difference*, viz., the distance from the resting potential. By an appropriate shift of the voltage scale, we can always set $u_{\rm rest} = 0$. The value of $u(t)$ is then directly the distance from the resting potential. This is implicitly assumed in most neuron models discussed in this book.

The model defined in Eqs. (1.3) and (1.4) is called SRM$_0$ where SRM is short for Spike Response Model (Gerstner, 1995). The subscript zero is intended to remind the reader that it is a particularly simple "zero order" version of the full model that will be introduced in Chapter 4. Phenomenological models of spiking neurons similar to the models SRM$_0$ have a long tradition in theoretical neuroscience (Hill, 1936; Stein, 1965; Geisler and Goldberg, 1966; Weiss, 1966). Some important limitations of the model SRM$_0$ are discussed below in Section 1.3.2. Despite the limitations, we hope to be able to show in the course of this book that spiking neuron models such as the SR Model are a useful conceptual framework for the analysis of neuronal dynamics and neuronal coding.

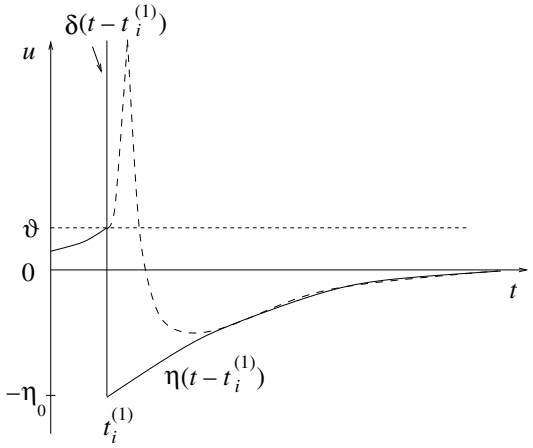

Fig. 1.4. In formal models of spiking neurons the shape of an action potential (dashed line) is usually replaced by a δ pulse (vertical line). The negative overshoot (spike-afterpotential) after the pulse is included in the kernel $\eta(t - t_i^{(1)})$ (thick line) which takes care of "reset" and "refractoriness". The pulse is triggered by the threshold crossing at $t_i^{(1)}$. Note that we have set $u_{\rm rest} = 0$.

Example: formal pulses

In a simple model, we may replace the exact form of the trajectory η during an action potential by, e.g., a square pulse, followed by a negative spike-afterpotential,

$$\eta(t - t_i^{(f)}) = \begin{cases} 1/\Delta t & \text{for } \; 0 < t - t_i^{(f)} < \Delta t \\ -\eta_0 \, \exp\left(-\dfrac{t - t_i^{(f)}}{\tau}\right) & \text{for } \; \Delta t < t - t_i^{(f)} \end{cases} \tag{1.5}$$

with parameters $\eta_0, \tau, \Delta t > 0$. In the limit of $\Delta t \to 0$ the square pulse approaches a Dirac δ function; see Fig. 1.4.

The positive pulse marks the moment of spike firing. For the purpose of the model, it has no real significance, since the spikes are recorded explicitly in the set of firing times $t_i^{(1)}, t_i^{(2)}, \ldots$. The negative spike-afterpotential, however, has an important implication. It leads after the pulse to a "reset" of the membrane potential to a value below threshold. The idea of a simple reset of the variable u_i after each spike is one of the essential components of the integrate-and-fire model that will be discussed in detail in Chapter 4.

If $\eta_0 \gg \vartheta$ then the membrane potential after the pulse is significantly lower than the resting potential. The emission of a second pulse immediately after the first one is therefore more difficult, since many input spikes are needed to reach the threshold. The negative spike-afterpotential in Eq. (1.5) is thus a simple model of neuronal refractoriness.

Example: formal spike trains

Throughout this book, we will refer to the moment when a given neuron emits an action potential as the firing time of that neuron. In models, the firing time is usually defined as the moment of threshold crossing. Similarly, in experiments firing times are recorded when the membrane potential reaches some threshold value ϑ from below. We denote firing times of neuron i by $t_i^{(f)}$ where $f = 1, 2, \ldots$ is the label of the spike. Formally, we may denote the spike train of a neuron i as the sequence of firing times

$$S_i(t) = \sum_f \delta(t - t_i^{(f)}), \tag{1.6}$$

where $\delta(x)$ is the Dirac δ function with $\delta(x) = 0$ for $x \neq 0$ and $\int_{-\infty}^{\infty} \delta(x)\, dx = 1$. Spikes are thus reduced to points in time.

1.3.2 Limitations of the model

The model presented in Section 1.3.1 is highly simplified and neglects many aspects of neuronal dynamics. In particular, all postsynaptic potentials are assumed to have the same shape, independently of the state of the neuron. Furthermore, the dynamics of neuron i depends only on its most recent firing time $\hat{t}_i$. Let us list the major limitations of this approach.

(i) Adaptation, bursting, and inhibitory rebound

To study neuronal dynamics experimentally, neurons can be isolated and stimulated by current injection through an intracellular electrode. In a standard experimental protocol we could, for example, impose a stimulating current that is switched at time t_0 from a value I_1 to a new value I_2. Let us suppose that $I_1 = 0$ so that the neuron is quiescent for $t < t_0$. If the current I_2 is sufficiently large, it will evoke spikes for $t > t_0$. Most neurons will respond to the current step with a spike train where intervals between spikes increase successively until a steady state of periodic firing is reached; cf. Fig. 1.5A. Neurons that show this type of adaptation are called regularly firing neurons (Connors and Gutnick, 1990). Adaptation is a slow process that builds up over several spikes. Since the model SRM_0 takes only the most recent spike into account, it cannot capture adaptation. Detailed neuron models which will be discussed in Chapter 2 describe the slow processes that lead to adaptation explicitly. To mimic adaptation with formal spiking neuron models we would have to add up the contributions to refractoriness of several spikes back in the past; cf. Chapter 4.

Fast-spiking neurons form a second class of neurons. These neurons show no adaptation and can therefore be well approximated by the model SRM_0 introduced

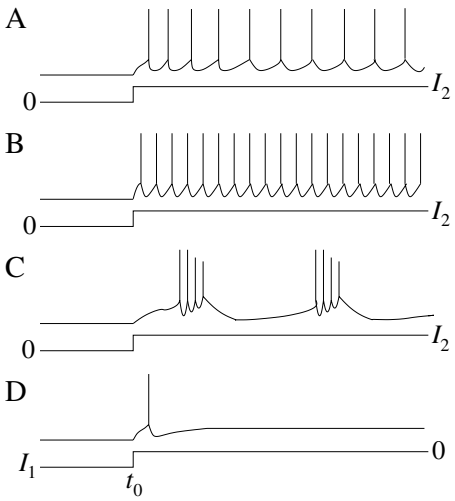

Fig. 1.5. Response to a current step. In **A**–**C**, the current is switched on at $t = t_0$ to a value $I_2 > 0$. Regular-spiking neurons (**A**) exhibit adaptation of the interspike intervals whereas fast-spiking neurons (**B**) show no adaptation. An example of a bursting neuron is shown in **C**. Many neurons emit an inhibitory rebound spike (**D**) after an inhibitory current $I_1 < 0$ is switched off. Schematic figure.

in Section 1.3.1. Many inhibitory neurons are fast-spiking neurons. Apart from regular-spiking and fast-spiking neurons, there are also bursting neurons which form a separate group (Connors and Gutnick, 1990). These neurons respond to constant stimulation by a sequence of spikes that is periodically interrupted by rather long intervals; cf. Fig. 1.5C. Again, a neuron model that takes only the most recent spike into account cannot describe bursting. For a review of bursting neuron models, the reader is referred to Izhikevich (2000).

Another frequently observed behavior is postinhibitory rebound. Consider a step current with $I_1 < 0$ and $I_2 = 0$, i.e., an inhibitory input that is switched off at time t_0; cf. Fig. 1.5D. Many neurons respond to such a change with one or more "rebound spikes": even the release of inhibition can trigger action potentials. We will return to inhibitory rebound in Chapter 2.

(ii) Saturating excitation and shunting inhibition

In the model SRM_0 introduced in Section 1.3.1, the form of a postsynaptic potential generated by a presynaptic spike at time $t_j^{(f)}$ does not depend on the state of the postsynaptic neuron i. This is of course a simplification and reality is somewhat more complicated. In Chapter 2 we will discuss detailed neuron models that describe synaptic input as a change of the membrane conductance. Here we simply summarize the major phenomena.