Chapter 2

Basic approaches in computational neuroscience

2.1 Computer simulations

Computer simulations in neurobiological research have brought neuroscience to a new level in understanding of the functioning of complex neurobiological systems. Let us briefly consider the main stages of neurobiological research and the tasks of computer simulations.

Typically, the investigation starts with a series of experiments that result in the accumulation of experimental information about the system. In some cases the experimental equipment is able to provide the information necessary for the defined task and the behavior of the investigated system can be associated with problems of a similar nature. In such a case experimental research alone can supply the required information.

However, often the experimental information alone is not enough to explain the functioning of particular components and the system as a whole. In this case a computer simulation of the investigated system can be used. First of all, the experimentalist has to choose a conceptual model which can be applied. One has to decide which features of the system are essential and what can be left out from consideration. On this stage one decides which level of abstraction is suitable to fully describe the system functioning. The lack of some information can be covered by making assumptions about the structure of the model, the connections between neurons, the presence of activated channels and the mechanisms of neuron excitation. The computer simulation will help to understand the role of particular elements on the basis of theoretical models. Thereby, it can be able to provide information that is difficult to obtain from experimental tests.

The next step of investigation is the computational modelling. During this step one decides which level of modelling will be used in the simulation process. The choice of the particular level of abstraction is defined by the amount of available information and the defined task. The researcher decides how faithfully the model structure should be described to reproduce the behavior observed in the experimental tests. The level of abstraction should be chosen in such a way that the modelling tests show the essential features of the studied phenomenon, which have been observed in the experiments.

After the model definition, the building of the computer programs and the simulation itself is the central task. The realization of the program needs the exact mathematical description of the defined model, which could require some model simplifications.

The computer simulations have an important advantage compared to the real experiments in being flexible to change the structure and the properties of the investigated model. Thereby elements can be added or excluded from the model. Different hypotheses, which are impossible to confirm during experiments, can be checked. One can perform a series of modelling experiments to find which features have an influence on the behavior of the model.

The simulation efforts lead to the verification of the suggested hypothesis. At this stage the modelling inquiry consists of modelling tests performed at different levels of abstraction until a suitable level of description of the neuron system is achieved. Basing on the results of the developed simulation some ideas about the structure and main features of the investigated system can be suggested or retracted. The choice of model parameters can be also corrected. One needs to repeat the simulation process again with corrected assumptions about the essential system properties. It is important to carefully test the model behavior on each of these levels.

One decides to end the simulation activity when the computer modelling either shows good agreement with experimental results or establishes further possible directions in experimental studies.

To conclude, it is clear that neurobiological research is developing as a combination of computational modelling and experimental studies.

2.2 Directions of development of computational neuroscience

Nowadays, two main directions in the development of computational neuroscience could be pointed out. First, artificial networks are developed as an attempt to describe brain activity at a high level of abstraction and as an effective computational paradigm allowing the realization of systems with "artificial intelligence" features. The second direction is the computational modelling of real neurobiological systems, which takes place at different levels, depending on the purpose and available data. These models include the characteristics of real neurons, which are chosen according to the information collected from neurobiological experiments.

2.2.1 Artificial neural networks

Living organisms reveal a very complex behavior. Such behavior requires the recognizing of sensory inputs and the decision making about appropriate action response. The neural networks are responsible for making these decisions. These are well-organized systems consisting of a huge amount of single neurons organized in common networks. The amazing functionality of these real neural network systems has inspired researchers to create artificial neural networks copying the main features of the real neural systems.

The computational properties of artificial neural networks are realized on the basis of computational units incorporating the basic functions of real neurons. The main principle of creation of artificial neural network is the use of simple threshold units (neurons) and simple connections (synapses), which are described by only one parameter - connection strength.

The most important feature of artificial neural networks is that they are organized in a hierarchical structure which can be related to the anatomy of the brain. Neurons are considered as simple processing elements that can perform parallel computational operations [27, 37, 61]. Such artificial neural networks demonstrate functionalities similar to the brain's activity. They can learn from experience and generalize from a set of examples to a new one.

Artificial neural networks are based on a computational paradigm involving the simplification of neural activity to the single continuous variable x_N (see Fig.2.1a). The neurons are assumed to be active if the value of this variable exceeds the threshold value. The connection between neurons is described by the parameter w_N, the connection weight. The input signal is then given by the total input over all connections

$$u = \Sigma w_i x_i \tag{2.1}$$

The neuron excitation or the output is described by the function F, which is the threshold or sigmoid function in the simplest cases (see Fig.2.1b).

The specially developed mathematical techniques in the field of "artificial intelligence" can be applied to a large spectrum of real-world problems. Examples are the problems of speech and signal recognition, learning and classification. The techniques can be used for generalization and decision making based on incomplete data. Their principles are used for hardware development based on neuro chips.

The interest in development of artificial neural networks can be explained by two factors. First, they are powerful mathematical instruments for modelling of systems performing brain-like functions; second, neurobiologists expect that artificial neural networks will help to understand brain operations on the highest level of simplification when the information is stored as patterns without detailed knowledge about neuron structure.

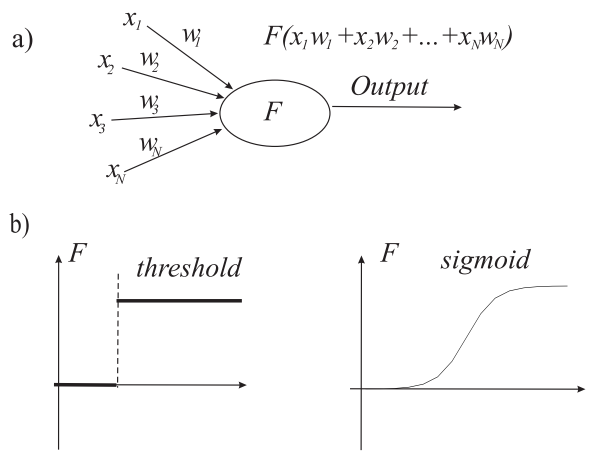

Figure 2.1: a) A schematic presentation of an artificial neuron. Inputs are represented by x_N, connection weights by w_N. b) Two standard forms of the function F: threshold and sigmoid.

2.2.2 Modelling of real neurobiological systems

Modelling of real neurobiological systems allows researchers to study the functionalities of groups of neurons and single neural elements [69]. One of the key points of this task is the development of models which realistically reproduce the behavior of real nervous system.

The choice of model depends on several factors. First of all, it depends on the purpose of the investigation. Then, it depends on the amount of available experimental information. Here one should keep in mind that more detailed models may be more difficult to analyze for extracting the required information, even if very detailed experimental information is available. Also, the implementation of highly complex models will require extended computational resources. Therefore, it is important to keep a balance between the complexity of the model and its transparency and tractability. One has to stop at the level that is sufficient for the defined task, yet simple enough to allow a clear interpretation of the results. A simpler model revealing experimentally observed behavior is also preferable compared to one including all available details, because it highlights the most important features of the real system.

In the following passage, I will briefly consider some of the common models of real neural networks using the following classification:

- Pulsed neural models
  - Firing-rate models
  - Threshold-and-fire models

- Compartmental models

The first level consists of so-called "pulsed neural networks", where the information is transferred between neurons by means of pulse sequences. This level includes firing-rate models, which provide ways of information coding based on the rate of firing, and the threshold-and-fire models, which use pulse timing to describe neural activities [73]. Compartmental modelling, modelling on the most detailed level, directly accounts a structure of neurons.

It is often difficult to find a border between the models of the mentioned groups. No classification will be unequivocal.

2.2.3 Pulsed neural models

The results of experimental research show that communication between neurons is based on the exchange of electrical signals referred to as spikes or pulses. A pulse sequence is usually referred to as a "spikes train". The experimental tests suggest that neurons use the timing of the spikes to encode and compute information. These observations have stimulated the growth of research activities in the field of pulsed neural networks, which capture the spiking nature of neurons without taking into account their detailed biophysical properties [10, 72]. The models focus on the question how neurons code and process the information contained in the spike trains.

Spike trains The sequences of repeated events presenting neuron activity can be observed by measuring the membrane potential in the neuron body (soma) (see Fig. 2.2). Short pulses, having an amplitude of about 100 mV and a duration of 1-2 ms, are usually initiated in the neuron body and propagated to the next neuron without changes in the form. Since the form of the spikes generated by a neuron is similar, it means that the information should be contained in the number and the timing of the spike generation. Therefore, one can record just a time of action potential generation without taking into account the structure of pulses. The spike trains are the resulting record of such neurobiological experiments.

Pulsed neural networks describe the neural activity using the information contained in spike trains [71, 22, 74]. The form of the spikes is ignored to make the computational models more transparent.

There are two important groups of pulsed neural networks according to the levels of available information. The first group, firing-rate models, captures the schemes of information coding, suggesting that information contained in the neural code is based on the " mean firing rate ". The so-called threshold-and-fire models describe computational properties of biological neurons and are based on the assumption that the firing occurs if the neuron state exceeds the threshold value.

Firing-rate models Firing-rate models describe the neuron activity using the "firing rate" as a characteristic of the neuron activity. The traditional way to

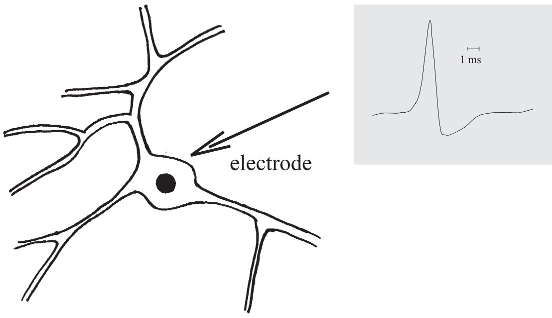

Figure 2.2: Schematic representation of the recording of neural activity using a microelectrode.

define the firing rate is the temporal averaging (see Fig. 2.3a)) that is performed by dividing the spike number $n_{sp}(T)$, that is observed during the time interval T, by the length of that time interval:

$$\nu = \frac{n_{sp}(T)}{T} \tag{2.2}$$

This definition together with the concept of the rate coding was introduced by Adrian [2, 3] and successfully used in experiments on sensory neurons and later in other applications of the neural computational field [22, 67].

This definition of the firing rate can not be used to describe the fast reaction of real neurobiological systems on a changing stimulus; however, it can be used in models of slowly-changing stimuli [63]. Despite these shortcomings, this definition is actively used. The concept of mean firing rate has led to the idea that neurons encode information by regular spike trains, while the irregularities can be considered as noise.

In the case of time dependent stimulation, other averaging techniques should be used. If it would be possible to record the spike trains resulting from the repetition of the same stimulation sequences, one would be able to average over the number of repetitions. Here the activity of a neuron between $[t, t + \Delta t]$ is obtained by dividing the spike number $n(t; t + \Delta t)$ by the number of repetitions K. Dividing by the time interval length, one obtains the spike density

$$\rho(t) = \frac{1}{\Delta t} \frac{n(t; t + \Delta t)}{K}. \tag{2.3}$$

Fig. 2.3b) illustrates this definition.

Such averaging allows one to describe fast variation in neural activity by relating the firing rate to the short time intervals. Spike density defined in this way is often referred to as time-dependent rate. However, it is obvious that such a definition should be applied rather in laboratory experiments than as a description of the functioning of real neural systems. In the real world the

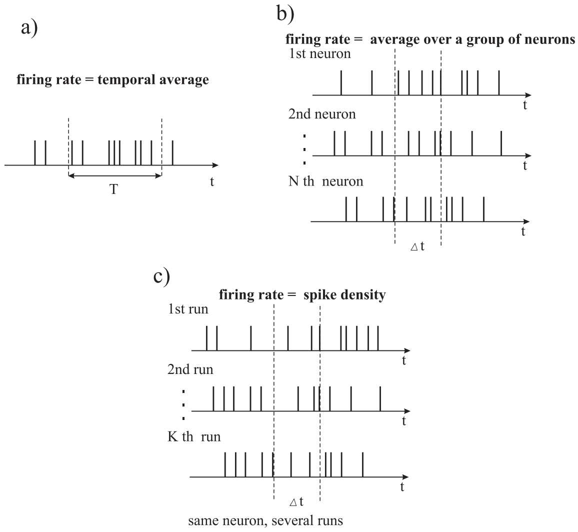

Figure 2.3: Different definitions of firing rates used in pulsed neural networks models.

repetition of stimulus would rather be an artifact and response action should be made on a single stimulus.

The previous scheme can be adopted to describe the response to stimulus in terms of a time-dependent firing rate if the number of similar neurons which experienced the same stimulation is large. In this case averaging can be done over the number of firing neurons (see Fig. 2.3c)) and referred to as "population activity of neurons". The activity of a group of neurons is defined as

$$\nu(t) = \frac{1}{\Delta t}\frac{n(t; t + \Delta t)}{N} \tag{2.4}$$

where N is the number of firing neurons and $n(t; t+\Delta t)$ is the number of spikes occurring during $[t, t+\Delta t]$ of a neural population. This scheme can account for the fast changing stimuli, but assumes a large number of neurons [50, 26].

During the last years it has been observed that the decoded information based on the firing rate can not present all of the information contained in the spike trains. It was found that the timing of the spikes is important for the processing of information in the neural systems. Therefore, techniques explicitly treating the timing of the spikes have attracted interest among neurobiologists. Techniques using temporal, phase and correlation coding are among them [63, 48, 70].

The temporal coding approach, also called time-to-first-spike coding, uses the information about the first incoming spike time after the refractory period. The importance of this information can be explained by the fact that during this period the trigger zone is depolarized and can not generate the second action potential.

The concept of coding by phases assumes that the information is encoded by the phase of a pulse with respect to the background oscillation. It requires the presence of an "internal clock" in the system which can be described by oscillations of some variable.

The idea of the correlation/synchronization coding technique is that the information is coded by the degree of synchronization of the neuron firing.

Threshold-and-fire models In contrast to the firing-rate models, threshold-and-fire models do not perform averaging of the spike trains, although they explicitly treat the spike events. They belong to the pulsed neural models, since the pulse structure is neglected. The neuron activity is approximated by two possible states: first, the neuron is not active; second, a spike is generated (the neuron is active). Using threshold-and-fire models, one can receive realistically-looking results of neural activity represented by a single variable (the activity of a neuron).

Let us consider the implementation of threshold-and-fire models on the example of the *Spike Response Model*. Mathematically, the state of the neuron i is described by the variable u_i. The neuron is assumed to fire if the state variable u_i reaches the threshold ϑ. The variable u_i is analogous to the membrane potential. All the firing times t_i (when the activity exceeds the threshold) arrange the set F_i. The value of the variable u_i is determined by two factors: the input signals from the presynaptic neurons and the contribution of refractoriness after the firing.

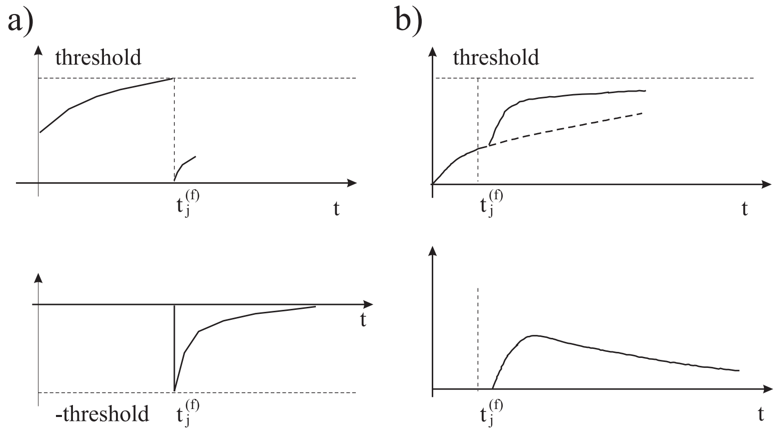

Figure 2.4: The response of the neuron i to the presynaptic spike and the change of its activity after its own spike. a) The form of the function $u_i(t)$ and $\eta_i(t)$ at the moment of the spike initiation and immediately after that. b) The form of the function $u_i(t)$ and ϵ_{ij} at the moment when the presynaptic spike reaches neuron i. Adapted from [71].

The input from the presynaptic neuron $j \in \Gamma_i$ is equal to the product of the connection weight ω_{ij} and the postsynaptic response $\epsilon_{ij}(t - t_i^{(f)})$. The function ϵ is usually modelled as the kernel function:

$$\epsilon_{ij}(t - t_i^{(f)}) = \Big[\exp\Big(- \frac{t - t_i^{(f)}}{\tau_m} \Big) - \exp\Big(- \frac{t - t_i^{(f)}}{\tau_s} \Big) \Big] H(t - t_i^{(f)}), \tag{2.5}$$

where $H(t - t_i^{(f)})$ is the Heaviside step function, and τ_m and τ_s are time constants.

The second factor, the refractoriness contribution, represents the function that sets the state of a neuron to a low value after each firing of the neuron. This factor is responsible for no-initiation of spikes during the absolute refractory period, the minimal time between two spikes. The refractoriness factor is usually defined by the kernel function

$$\eta_i(t - t_i^{(f)}) = -\vartheta \exp\big(- \frac{t - t_i^{(f)}}{\tau} \big) H(t - t_i^{(f)}), \tag{2.6}$$

Fig. 2.4 shows how these two contributions change the form of the neural activity u_i.

The total activity of a neuron i is given by the formula

$$u_i(t) = \sum_{t_i^{(f)} \in F_i} \eta_i(t - t_i^{(f)}) + \sum_{j \in \Gamma_i} \sum_{t_i^{(f)} \in F_i} \omega_{ij} \epsilon_{ij}(t - t_i^{(f)}) \tag{2.7}$$

Summing up, the neuron activity in the Spike Response Model depends on the timing of the spikes and do not take into account the exact mechanisms of spike generation (dynamics of ionic channels or spatial structure of the dendritic tree).

The next best-known example in the class of threshold-and-fire models is the *Integrate-And-Fire Model* [7, 10]. These models take into account the biophysical properties of the neuron in an explicit description of the electrical properties of the membrane. The most important assumption of these models is that the spike is generated if the membrane is depolarized above the threshold value.

The basic electrical circuit of the Integrate-And-Fire Model is shown in Fig. 2.5. The circuit consists of a capacitor C_m which results from the insulation property of the membrane, connected in parallel with the resistance R_m presenting all passive channels. The resistance R_m is associated with the resting potential of the neuron, i.e. the potential of the cell when no ions are moved through the channels. In this scheme the neuron's activity is described by the membrane potential V_m. The injected current is represented by the symbol I_{inject}. E_{rest} is the resting potential of the neuron, typically about -70 mV. Thus, if no current is injected ($I_{inject} = 0$) and the system comes to an equilibrium, the membrane potential V_m will be equal the resting potential E_{rest}. This electrical circuit of a neural cell is described by the following equation

$$I_{inject} = C_m \frac{dV_m}{dt} + \frac{V_m - E_{rest}}{R_m} \tag{2.8}$$

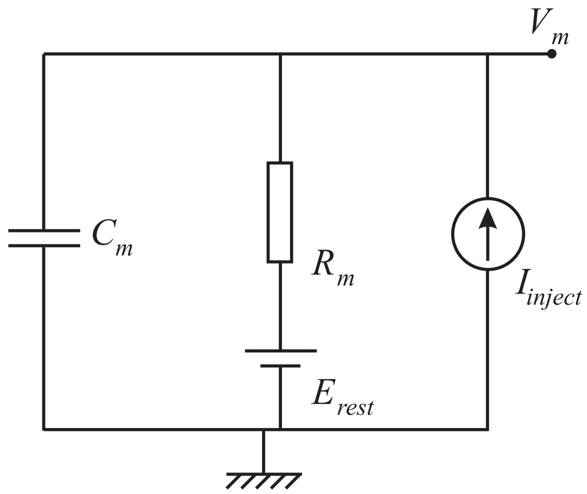

Figure 2.5: The basic circuit of an *Integrate-And-Fire Model*.

The solution of the differential equation (2.8) $V_m(t)$ can be found numerically. As was mentioned above, in the Integrate-And-Fire Model after reaching the threshold, the neuron's activity will be reset to the value E_{rest}. To take into account the contribution of refractoriness, the resting value of the membrane potential is maintained for an absolute refractory period Δt:

$$V_m(t; t+\Delta t) = \begin{cases} E_{rest}, V_m > threshold \\ V_m(t), \text{otherwise.} \end{cases} \tag{2.9}$$

Summing up the properties of the Integrate-And-Fire Model, most of the biophysical properties of the neuron are included, along with the simplification about the threshold structure of the spike generation.

2.2.4 Compartmental modelling

Taking into account the biophysical properties of the neural membranes is possible in the frame of the compartmental modelling approach. The electrical action potentials generated by neurons result from the ion flow through the ionic channels of the cell membrane. The detailed modelling aims to describe the processes going on at the subcellular level. It includes studying of the anatomical properties of the neurons, the biophysics of ionic channels, as well as the synaptic interactions between the cells. This computational approach can be applied to the neural systems whose anatomical and biophysical properties are well studied experimentally [35, 33].

The first important breakthrough in this field was made by Hodgkin and Huxley in 1952 [1] and was based on experiments with the giant squid axon.

Hodgkin and Huxley considered the functioning of a single cell on the basics of the differential equations following from the biophysics of the membrane. They succeeded in building a model that describes the mechanisms of the processes responsible for action potential generation. The description of the spike generation and the propagation mechanism was considered on the basis of studies of the currents through the ionic channels of the neuron membrane. The model includes detailed information about the biophysics of the ionic mechanisms underlying the neural spike dynamics. Despite the numerous discoveries of other types of ionic channels, the work of Hodgkin and Huxley remains one of the basic works in this field.

Detailed descriptions of the neuron morphology can be included in the models using the compartmental approach. Since it takes into account the processes flowing on the microscopic level, it describes the mechanisms of the opening/closing of the ionic channels that are embedded in the cell membrane. The activation of the ionic channels is usually voltage- and time-dependent, and can also depend on the presence or absence of various chemical messenger molecules [28].

One divides the neuron into a definite number of segments, called "compartments", each of which is presented by a capacitance-resistance circuit (similar to the one presented in Fig. 2.5). In addition, the current from the ionic and synaptic channels as well as the current from neighboring compartments are taken into account. A system of differential equations based on the presentation of the neuron as an electrical circuit and including the description of the channel dynamics can be constructed.

The advantage of compartmental modelling is that the microscopic structure of the cell and the description of the ionic channels are directly included in the model. It uses anatomical and biophysical data provided by experiments.

2.3 Summary

In this chapter, I have shortly considered the main directions of the development in computational neuroscience. First, the main aspects of artificial neural networks were discussed. After that, I described the principles of modelling real neurobiological systems using examples of different models. I started with rate models, ignoring the time structure of spike trains. Then, the pulsed neural network directly treating the structure of spike trains was presented. Finally, compartmental models based on the morphological and anatomical structure of neurons, which are used for detailed modelling, were shortly introduced.

In the next chapter, I will give a more extensive description of detailed modelling. The reader will find an introduction into the physiology of the real cell, which helps to understand the functioning of cells. The mathematical description of conductance-based models, starting from the Hodgkin-Huxley model and developing into detailed compartmental models, will be given.