Generic origins of irregular spiking in neocortical networks

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Abstract. We identify generic sources of complex and irregular spiking in biological neural networks. For the network description, we operate on a mathematically exact mesoscopic approach. Starting from experimental data, we determine exact properties of noise-driven, binary neuron interaction and extrapolate from there to properties of more complex types of interaction. Our approach fills a gap between approaches that start from detailed biophysically motivated simulations but fail to make mathematically exact predictions, and approaches that are able to make exact statements about only on levels of description that are remote from biology. As a consequence of the approach, a novel coding scheme emerges, shedding new light on local information processing in biological neural networks.

2. Strong input from next neighbors (i.e. from strongly connected neurons or from groups of synchronized neurons).
3. Medium-size interactions that may take account of changing neighborhood conditions on time scales typically of the order of an interspike interval.

Due to the enormous number of synaptic contacts, a large number of small-scale synaptic inputs arrive at a typical neuron (Abeles 1982; Koch 1999). Assuming a Gaussian central limit behavior of this input [other distributions that allow for a well-defined average are also suitable (Feller 1971)], an almost constant inflow of charge results that can be identified with a constant driving current. This point of view is also adopted in most simulation approaches (Hines 1989, 1994). To this driving current, simple pyramidal neurons respond with regular spiking. Mathematically, this behavior is described by a limit-cycle. Limit cycles are objects by mathematical abstraction, like fixed-points, defined in terms of characteristic stability properties of their response to perturbations. Abstract models of pyramidal neurons fulfill these criteria. The proof that also biological pyramidal neurons are limit cycles has been given in detail in (Stoop et al. 2000a). Substantial input by strongly connected neurons or by strongly synchronized groups of neurons lead to considerable perturbations of these limit-cycles. This is our concept of noise-driven neocortical interaction. In our opinion, part of the complicated geometrical structure of the neuronal dendrites may only serve to establish reliable stable driving currents, where it is perfectly possible that different functional driving currents could be generated on the same neuron. This aspect of our approach is similar to the recent observation that, on the microscopic level, thermal noise can be converted into directed activity (by so-called Brownian motors (Chillemi and Barbi 1999)). In our investigation, effects generated by strong waves of neural excitability will be excluded. Under these quasistatic network conditions, spike-time coded information transmission is naturally prevalent.

1 Noise-driven neurons

In our study, we focus on the properties of pyramidal neurons that make up about 70% of all cortical neurons. From physiological observations, these cells are expected to be of special importance for the integrative tasks in biological neural networks. The vast majority of the pyramidal neurons outside of layer V consist of intrinsically regularly spiking neurons (Abeles 1982; Koch 1999). Our approach to studying generic biological neuron interaction is based upon the distinction of different levels of synaptic input to these cells. Although synaptic transmitter release is quantal, different orders of magnitude of input are received:

1. Small-scale input (e.g. from remote synapses) drives the neuron towards regular spiking with well-defined spiking frequency. This small-scale input will be referred to as noisy input. It is able to reflect local gradients of excitation in the network.
2 Interaction of noise-driven neurons

The response of a regular spiking neuron upon a strong synaptic perturbation is the main biological ingredient in our approach. This characteristic of a neuron can be captured in the phase-response function \( g(\phi) \), which measures the lengthening/shortening effect to the unperturbed interspike interval, as a function of the phase \( \phi \) at which a strong synaptic perturbation of strength \( K \) arrives. If \( i \) denotes the perturbed and \( u \) the unperturbed interval length, we have \( g(\phi) = i(\phi)/u \), which is equally easily calculated in simulations and in experiments. We start our presentation by focusing on fixed values of \( K \), until we include the dependence on the perturbation strength in a straightforward way.

In our experiments with real neurons, slices of rat neocortex were prepared for in vitro recording. Following standard techniques, simple pyramidal neurons of the barrel cortex were intracellularly recorded with sharp electrodes. To induce regular firing, a constant current was injected into the neurons (Abeles 1982; Reyes and Fetz 1993; Koch 1999). Regularly firing neurons were periodically perturbed by strong extracellular stimulations of synaptic inputs to the neurons. Excitatory perturbations were generated by the stimulation of adjacent white or gray matter by means of bipolar electrodes. Inhibitory perturbations were generated when fast excitatory transmission was pharmacologically blocked by application of DNQX and AP5, while regular current pulses were applied to fibers making a synaptic contact with the regularly firing neuron. Typical results of our experiments are shown in Fig. 1, for inhibitory and for excitatory perturbations. In the context of in vivo neural networks, these perturbation paradigms can be regarded as the representations of synaptic inputs from strong synaptic connections (Reyes and Fetz 1993). Our approach can be seen as an extension of related experiments described in detail by Reyes and Fetz. Our related theoretical development, however, leads in entirely new directions.

In our study, we are interested in the properties of networks of simple pyramidal neurons, into which both excitatory and inhibitory connections are incorporated. A simple case of such networks can be built up from intrinsically regularly firing neurons that are under continued perturbations by other neurons. Since the effects of perturbations decrease as a function of the topological neighboring order, in our model the perturbations are restricted to emerge from a number \( mn \) of next-neighbors, where we define as next-neighbors those neurons from which the strongest perturbations result. For all presented simulations, we choose the checkerboard (\( mn = 4 \)) topology of interaction, and the distribution between inhibitory and excitatory connections always reflects the generic situation in the neocortex (1 inhibitory: 4 excitatory connections). To represent the variability seen in biological networks, the remaining interaction characteristics (perturbation strengths \( K \), spiking frequencies, interaction types) are chosen at random, and then, unless stated otherwise, held fixed.

With the help of the experimentally measured perturbation response functions \( g(\phi) \) (cf. Fig. 1), the described concept can be implemented in a straightforward way.

In Fig. 2, the described network topology, the principles of the interaction, and a typical result are shown.

Figure 2 shows, for one typical neuron, the resulting spiking behavior. In the figure, the deviation at the \( n \)th spike event between average-based expected and actual spike time, \( \text{dev}(n) := n \delta t_{av} - \sum_i^n \delta t_i \), is displayed (where \( \delta t_i \) denotes \( i \)-th and \( \delta t_{av} \) denotes the over a sufficiently long time averaged mean interspike interval. For the plot, linear interpolation between spiking events has been used). The complexity of the spiking behavior is obvious, in spite of the simplicity of the network. Along