Accurate Spike Synchronization in Cortex*

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In view of the enormous capacity and complexity of mammalian brains it is evident that a detailed account of their anatomy and physiology alone cannot lead to a complete understanding of their function. Computer simulation and mathematical analysis of abstract, yet biologically realistic models for neurons and networks yield additional and useful information about the interplay of the underlying anatomical structures, the physiological processes operating on the neuronal substrate, and the resulting brain functions during the performance of behavioral tasks. We discuss some contributions of such experiment-guided theory to the issue of accurate spike synchronization.

Introduction

The dynamic organization of neuronal activity is considered more and more important for an understanding of higher brain functions. The precise orchestration of all brain components is an essential prerequiste for a sensible interaction of perception and behavior with the environment. According to the classical view, firing rates play a central role in neuronal coding (Barlow, 1972; 1992). The firing rate approach indeed led to fundamental insights into the neuronal mechanisms of brain function (Georgopoulos *et al.*, 1993; Hubel and Wiesel, 1977; Newsome *et al.*, 1989).

In parallel, however, a different concept was developed, according to which the temporal organization of spike discharges within functional groups of neurons, the so-called neuronal assemblies (Hebb, 1949), also contribute to neural coding (Abeles, 1982a; 1991; Gerstein *et al.*, 1989; Palm, 1990; Singer 1993; von der Malsburg, 1981). It was argued that the biophysics of synaptic integration favors coincident presynaptic events over asynchronous events (Abeles, 1982b; Softky and

Koch, 1993). Accordingly, synchronized spikes are considered as a property of neuronal signals which can indeed be detected and propagated by other neurons. In addition, these spike correlations must be expected to be dynamic, reflecting varying affiliations of the neurons depending on the stimulus or behavioral context. Such dynamic modulations of spike correlation at various levels of precision have in fact been observed in different cortical areas, namely visual (Aertsen and Arndt, 1993; Eckhorn *et al.*, 1988; Gray and Singer, 1989; Roelfsema *et al.*, 1996; Singer and Gray, 1995), auditory (Ahissar *et al.*, 1992; de Charms and Merzenich, 1995; Eggermont, 1994; Sakurai, 1996), somatosensory (Nicolelis *et al.*, 1995), motor (Murthy and Fetz, 1992; Sanes and Donoghue, 1993), and frontal (Abeles *et al.*, 1993b; Vaadia *et al.*, 1995). Little is known, however, about the functional role of temporal organisation in such signals.

First important hints towards the importance of accurate spike patterns came from Abeles *et al.* (1993a; b). They could demonstrate that multiple single neuron recordings from the frontal cortex of awake behaving monkeys contain an abundance of precise spike patterns. These patterns had a total duration of up to several hundred milliseconds and were repeated with a precision of ±1 ms. Moreover, they occurred in systematic relation to sensory stimuli and behavioral events. Similarly, significant spike coincidences have been reported from recordings in the motor cortex of monkeys (Riehle *et al.*, 1997). The clear correlation of the

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spike coincidences with behavioral events again underlines their functional relevance (Fetz, 1997).

Pulse Packets and Synfire Chains

We attempted to link known properties of cortical architecture and physiology to emergent properties of activity dynamics, such as synchronization of action potentials. This can be achieved by a combination of computer simulation and mathematical analysis. In an ongoing modeling study we explored the mechanisms underlying the rapid synchronizations of cortical spiking activity, which have been observed in simultaneous multiple single-neuron recordings. Specifically, we focused on an explanation for the excessive occurrences of highly accurate spike patterns.

On the basis of the characteristic anatomy and physiology of the cortex, Abeles (1991) proposed that "synfire" activity propagating in volleys through diverging-converging chains of neurons could present a natural explanation for this phenomenon. We have investigated the conditions under which such synchronous volleys of action potentials can propagate reliably through the cortical network. We chose a theoretical approach combining extended network simulations and mathematical analysis (Diesmann et al., 1995).

Existing approaches to synaptic transmission usually consider either of two extreme cases: full synchrony or random arrival of presynaptic spikes. The effect of intermediate temporal dispersion has hitherto not been systematically addressed. To quantify the degree of temporal synchrony in propagating volleys of spike activity we introduced the concept of "pulse packets" (Diesmann et al., 1996). A pulse packet is characterized by two parameters, its strength (the total number of spikes belonging to the volley) and its width (the standard deviation of the volley). A further important parameter is the background activity, which comprises spontaneous spikes impinging on the neuron apart from synchronous spike volleys.

Stable Propagation of Synchronous Spiking Activity

We studied the response of a single integrate-and-fire model neuron upon inputs with varying degrees of synchrony. To this end, we recorded the PST-histogram of responses to repeated presenta-

tion of pulse packets of given strength and width to the neuron. Assuming that all neurons in one particular group of the chain behave in a similar way, the appropriately normalized PSTH can again be interpreted as representing outgoing pulse packets, the strength and width of which can easily be determined. The resulting two-dimensional transfer function compactly describes the relation between incoming and outgoing pulse packets. In contrast to alternative approaches, where the neuron's firing probability is measured quasi-statically as a function of DC input, this new transmission function takes full account of the dynamic properties of the input distribution (Aertsen et al., 1996).

The fate of a pulse packet on its travel through the chain can be traced by iterating the transfer function. Keeping the width of the chain fixed at
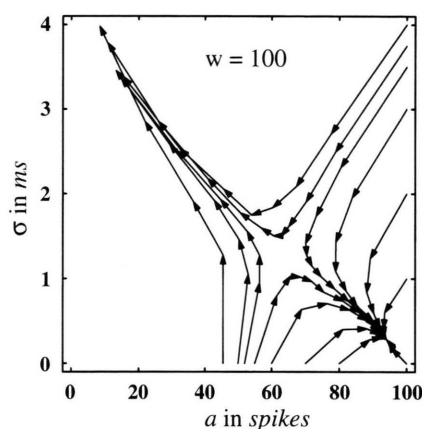

Fig. 1. Computer simulation of the synchronization dynamics in a "synfire chain". The figure displays the fates of various pulse packets on their way travelling through a diverging/converging feed-forward network of neurons. The pulse packets are parametrized by the number of spikes a contributing to the packet, and by the width σ of the packet. Each arrow corresponds to one processing step in the chain. Any pulse packet from the lower right segment of the state space evolves toward a very narrow pulse packet with invariant shape within a few processing steps. It is then stably propagated through the chain, in a self-repairing manner. Pulse packets from the other half of the state space will eventually die off. The width of the groups in the chain w is adapted to the amplitude of postsynaptic potentials and to the neurons' firing thresholds. If the chain width is too small, or if the EPSPs are too small relative to the firing threshold, the two fixed points of the corresponding iterative dynamics merge. In this case, no stable transmission is possible any more.

a value in the order of 100, the dynamics of the two-dimensional iterated system is characterized by one attractive fixed point and one saddle point (Fig. 1). Accordingly, the state space has two separate domains. Within one of these domains, there is stable propagation of pulse packets towards a very narrow packet of invariant shape. The parameters of this fixed point are independent of the initial pulse packet, if the latter is only taken from a certain range of parameters. For all other initial configurations, the result is eventual extinction of activity (Diesmann et al., 1997). By contrast, for a too small number of neurons per group, both fixed points dissappear and all trajectories lead to extinction. Synchronous spiking then is no longer a viable option for the chain. Important aspects of this synchronisation dynamics can be dissected and understood with the help of an analytical model (Gewaltig et al., 1997).

Assuming realistic values for the architectural and physiological parameters, our model predicts that the cortical network is able to sustain stable propagation of synchronous spike volleys consisting of spikes from 50–100 neurons with a temporal precision of about 1 ms. Preliminary evidence from additional computer simulations suggests that this synchronisation dynamics is strongly influenced by the activity climate in the surrounding network. In particular, the robustness and the propagation velocity of the synchronous spike volleys exhibited a non-monotonic dependence on the level of the background activity. This result has interesting consequences in view of recent findings regarding the relation between ongoing network activity and the variability of evoked responses, both in cortical activity and in behavioral responses (Arieli et al., 1996a; b).

Spatio-Temporal Spike Patterns

We also studied the spatio-temporal dynamics of spiking activity in cortical networks with recurrent synaptic architecture. We used a network model, which is based on interacting stochastic point processes (Rotter 1994; 1995). Such systems can be formally described in terms of a Markov process, the dynamic state of which at a given point in time is the spatio-temporal pattern of previously generated spikes. The transition probabilities specify how the pattern gradually evolves in time. A

generalized type of integrate-and-fire dynamics thereby emerges as a mathematical consequence of the assumption that neurons communicate by action potentials. Assuming the existence of infinitesimal spike probabilities, which is in fact a very mild condition for physical systems, the corresponding dynamic equations are completely solved.

The solutions for special cases have been used to identify some important model parameters from electrophysiological recordings of real neurons. A simple parametric characterization of single neuron function is in fact achieved by fitting the model to the discharge behavior of various types of cortical pyramidal cells. Some fundamental properties of recurrent cortex-like networks assembled from such neurons can be readily predicted, most notably their ability to maintain stable low rates of activity without the help of inhibitory neurons (Rotter and Aertsen, 1997). Furthermore, computer simulations of random-topology, but otherwise realistic cortical networks indicate that high precision spatio-temporal patterns, embedded in periods of enhanced cooperative group activity, may play a role for coding and computation in such networks. This is true, even if neither the anatomy of the network nor the physiology of its neurons are in any sense specifically designed for that purpose. Plasticity of the temporal structure of such patterns is achieved by introducing Hebb-like synaptic plasticity into the network.

The Dynamic Repertory of Neuronal Processes

The "functional repertory" of a dynamic system can be understood as the set of non-equivalent, that is, functionally indistinguishable behaviors, which it is able generate and maintain. Generally, the two determinants for the dynamic repertory of a system of interacting point processes are its dictionary, that is, the set of reachable spatio-temporal patterns, and its syntax, that is, the collection of rules governing the evolution of patterns. Clearly, both a more voluminous dictionary and a more flexible syntax increase the number of words at the system's disposal.

Among the many properties of the cortical network, which contribute to its rich dynamic repertory, we emphasize the sheer number of neurons,

and the complexity of the network's organization as far as the processing of signals is concerned. The latter is reflected, among other things, by the degree of synaptic divergence and convergence, and by the degree of plasticity of the anatomical substrate during development. Another obvious source of dynamic diversity are cell-cell interactions, where extra complexity is added by postsynaptic currents with different temporal characteristics, as well as by spike-induced modulatory currents. Yet another aspect, which is truely at the heart of the stochastic model, is the precision in the control of timing as determined by the relationship between the strength of the inputs and the stochastic properties of their integration. It is likely that certain aspects of dendritic geometry and of the distribution of ion channels on the cell's soma and dendrite play a role in this context (Bernander *et al.,* 1993; Clay *et al.,* 1983). Finally, we mention the non-stationary aspects of interactions among cells, the local or non-local characteristics of synaptic plasticity, and the time constants of the cellular integration mechanisms (Markram and Tsodyks, 1996; Markram *et al.*, 1997). No doubt that all these parameters greatly affect the capacities of a neuronal network as an abstract language analyser and generator.

In principle, all factors which contribute to the dynamic repertoire of the neuronal process play a potential role for the evolution of cortical structure and function. One general evolutionary strategy could be to increase the number of distinguishable words in the dictionary to choose from, simply to provide for more powerful representations. This can be achieved by an increased number of independently operating mechanisms to elicit action potentials in single cells and mechanisms to synchronize spikes into spatial patterns which involve many cells. A related strategy could be to increase the flexibility and suitability of the syntax to represent relations among objects. This might involve, for instance, plasticity of the interactions between cells by means of synaptic learning rules, which evaluate correlations and similarities among the inputs (von der Malsburg, 1981).

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