INTRODUCTORY REMARKS TO SYMPOSIUM VIII:

CONCEPTS OF NEURONAL COOPERATIVITY IN THE CORTEX

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It is now generally accepted that internal correlations in neuronal activity admit no simple interpretation in terms of fixed synaptic wiring diagrams. Rather, it is very likely that the correlation dynamics apparent from time-resolved multiple-channel measurements reflect variable and context-dependent coalitions among neurons and groups of neurons. A systematic relation with animal behavior can frequently be established. The spatio-temporal scales which are considered as potentially relevant for neuronal cooperativity range from millisecond-precise spike patterns [Prut et al. 1998; Riehle et al. 1997] and transient states of coherent activity [Vaadia et al. 1995a,b] in multiple single-unit spike trains, over fast oscillatory synchronization in multi-unit activity [Singer et al. 1997], non-coherent rate covariation in sequentially recorded spike trains [Schwartz 1994] to spatially coherent activation of large brain areas [Arieli et al. 1996; Ohl et al. 1998]. Accordingly, Hebb's theoretical concept of neuronal assemblies [Hebb 1949] has experienced extensions in several directions, attempting to incorporate new experimental facts.

The notion of neuronal cooperativity employed by a researcher depends on the type of measurements to be explained. Based on single-electrode recordings, the classical view of sensory processing invokes a feed-forward hierarchy of processing steps. It is assumed that the signals from sensory epithelia eventually converge to cortical detectors for compound stimulus features [Hubel & Wiesel 1962]. From this perspective, highly specific percepts would be represented by the elevated firing of a small group of neurons or even of a single nerve cell [Barlow 1972; Gallant & Van Essen 1993; Perret et al. 1987]. It has been seriously questioned, however, whether such a scheme qualifies as a universal method for representation in the brain, due to a number of conceptual shortcomings. First of all, the number of objects, which must have fixed and distinct representations, is most likely to exceed the number of neurons available for that purpose. In addition, a coding scheme, where each individual representation depends on the secure function of a small number of nodes, is vulnerable and bound to fail. Finally, it remains unclear how behaviorally relevant information can be extracted from such specific and localized representations, and which circuits would be necessary for an organized recall.

Recent experiments involving stimulation of sensory neurons outside their classical receptive fields lead to the conclusion that the tuning properties of neurons are much more subtle and complex than previously thought, and that they are not fixed but subject to stimulus-dependent modulations [Aertsen & Johannesma 1981; Buonomano & Merzenich 1998; Fregnac et al. 1996a; Gilbert 1998; Roelfsema et al. 1998]. Researchers stressed the importance of long-range connections and recurrent interactions for these properties [Braitenberg & Schüz 1998; Fregnac et al. 1996b; Gilbert 1992]. Experiments probing the global interactions between different areas of the visual system also indicate that the network operates in a parallel and distributed manner, with feed-back playing an essential role [Sillito et al. 1994; Van Essen et al. 1992; Hupe et al. 1998; Nowak & Bullier 1997; Fabre-Thorpe et al. 1998].

The generation of overt behavior typically involves the simultaneous and coordinated action of many effectors. Current thinking about the representation of movements in the motor cortex involves the activation of large distributed populations of neurons which act as a whole by means of the population vector [Georgopoulos et al.]. The read-out of such a population code must be based on convergent connections, whereas planning and initiation of motor action involves a divergence of signal flow. The degree of functional specialization and the degree of functional redundancy in the distributed networks of the motor system, however, is still under debate [Newsome et al. 1989; 1993; Schwartz 1994; Donchin et al. 1998].

Beyond the physiological and anatomical evidence in favor of the distributed network hypothesis, brain theoreticians and artificial intelligence engineers have long been exploring the scope of connectionist networks as models for brain function. This is due to the fact that these artificial systems share a number of distinctive properties with higher functions of the brain. The list of features covered by connectionist models includes content-addressable associative memory, the ability of pattern completion and error correction, the possibility of competition among simultaneous inputs, and the ability of the network to aquire suitable structure through adjustments of synaptic strengths [Anderson & Rosenfeld 1988, 1990]. Most models constructed in this context treat groups of neurons, rather than single nerve cells, as the functional building blocks for representation and processing of information. The desired properties emerge due to the use of overlapping and redundant representations, rather than simple labeled lines. In this broad sense, they may be considered as instantiations of Hebb's concept of neuronal assemblies.

A closer look on recent concepts of neuronal cooperativity, however, reveals some important differences among them. Aiding the structured analysis of experimental observations and the design of new and pioneering experimental paradigms, the biggest differences between competing theories refer to the role of time. Distinct hypotheses are held on the temporal organization of neuronal activity, as well as on the nature and time scale of cooperativity. Covariation of firing rates [Georgopoulos et al. 1993; Schwartz 1994], local field potentials [Ohl 1997; Schulze et al. 1997; Ohl et al. 1998; Wetzel et al. 1998], or optically measured activity distributions [Arieli et al.

1995; Arieli et al. 1996] on a time scale of tens of milliseconds and above is, as a concept, put into contrast to spike synchronization on different time scales [Abeles 1991; Abeles et al. 1993; Prut et al. 1998; Riehle et al. 1997; Vaadia et al. 1995a,b] and the formation of neuronal groups by locking to the phase of fast oscillations [Eckhorn et al. 1988; Gray et al. 1989; Singer et al. 1997].

The model in the mind of the experimenter determines the spatial and temporal scale of the expected phenomena. The choice of the recording method is again a consequence of this. The aim to observe coordinated activity makes it obligatory to simultaneously record from multiple single cells, local groups or patches of cells, or from large and scattered populations of many cells. The temporal scale of interest recommends specific recording techniques, and, equally important, different algorithms for data analysis. The average event-locked spiking response in the form of a PST-histogram, for instance, depends strongly on the precision of the locking to the trigger event. Therefore, this method is typically not able to reveal millisecond precise repetitive spike patterns like the ones reported by Abeles and coworkers [Abeles 1991; Abeles et al. 1993; Prut et al. 1998] and other groups [Riehle et al. 1997]. Specialized pattern search algorithms must be employed for this purpose. Once the patterns are found by these methods, their (loose) correlation with behavior is readily established. Recent theoretical work [Abeles 1991; Aertsen et al. 1996] demonstrated that the occurrence of such patterns could be explained by synchronized activity, which propagates through converging/diverging chains of neurons acting as coincidence detectors (the synfire-chain model).

In contrast, the model proposed by Singer [Singer et al. 1997; Singer (in press)] assumes less specific anatomy. Rather, it is the neuronal response synchronization *per se*, which defines the common membership in an assembly. In particular, correlated oscillatory activity of several local groups of neurons may subserve the binding of distinct stimulus features into a coherent percept. In accordance with the presumed columnar organization of cortex, the local signal is carried by the combined activity of many neighboring neurons, measured as multi-unit activity (MUA).

Related concepts of cooperative neuronal activity have been employed to understand the dynamic organization of the motor system. In contrast to the classical view of motor control, Vaadia and his coworkers could show that the directional tuning of neurons in primary motor areas to movements of the contralateral arm may be modulated by simultaneous movements of the ipsilateral arm [Donchin et al. 1998]. Earlier work demonstrated that not only the activity transients but also the dynamics of rate correlations as computed from multiple single unit recordings are specific for the behavior [Vaadia et al. 1995a,b]. Such effects call for an explanation in terms of distributed cooperative networks. The concept of dynamic population vectors, as employed by Schwartz [Schwartz 1994; Lin et al. 1997] in extension to the original (static) population vector [Georgopoulos et al. 1993], assumes that single arm movement parameters are coded in the dynamic activity of neuronal populations. On the basis of the tuning curves for movement directions, the trajectory of a movement can be faithfully reconstructed from the sequential observation of a large number of differentially tuned single-units.

Large scale activity distributions of whole cortical areas cannot be gathered with localized recordings. Surface electrodes [Ohl 1997; Schulze et al. 1997; Ohl et al. 1998; Wetzel et al. 1998] or optical methods based on the usage of voltage-sensitive dyes [Arieli et al. 1995; Arieli et al. 1996] may be used instead. Important information about the nature of neuronal cooperativity can be expected from simultaneous measurements of group activity on both coarse and fine spatio-temporal scales. The approach of Arieli [Arieli et al. 1995] is to record population activity with optical methods and, at the same time, extracellular spike trains and even the intracellular membrane potential of single neurons from this population. This is currently the most direct assessment of the coupling of single neurons to the fields generated by the ongoing activity in neuronal populations.

The goal of the symposium is to collect and jointly discuss physiological results demonstrating the existence and specific properties of neuronal groups and their dynamics, to evaluate the scope of the methods used for the detection of both, and to explore the biophysical basis and the functional implications of cooperative activity in the context of appropriate neuronal theories. In particular, it is attempted to incorporate insights from different levels of spatio-temporal resolution into a unified conceptual framework of cortical function. It is assumed that the biophysical properties of neurons and the architecture of networks present important constraints for brain function. A thorough understanding of these constraints may greatly support the better understanding of the nature and the role of neuronal cooperativity.

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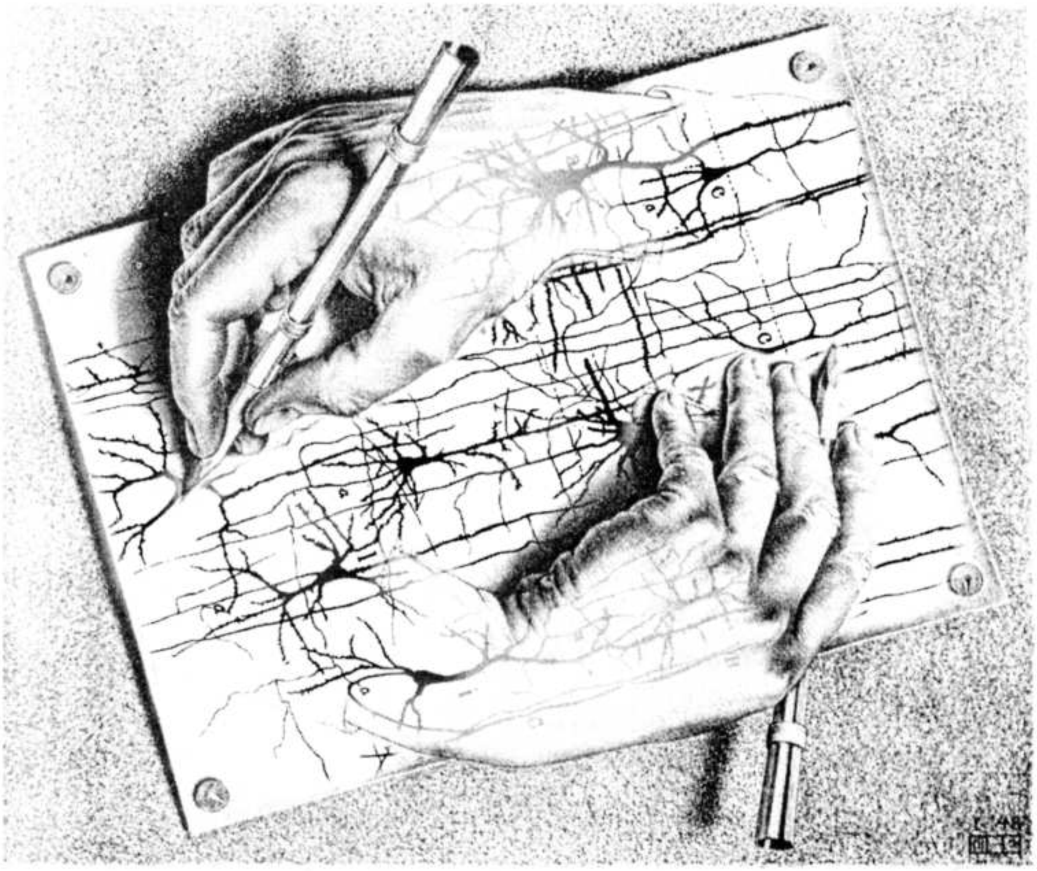

Concepts of Neuronal Cooperativity in the Cortex

Adapted from M.C. Escher (De werelden van M.C. Escher, Meulenhoff, Amsterdam, 1971) and S. Ramón y Cajal (Revista Trimestral Micrográfica 4:1-63,1899)