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DISSERTATION SUMMARY

Experimental analysis of input summation in neocortical neurons

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Neurons receive and integrate signals from thousands of synapses arriving to the surface of their membrane. Understanding the arithmetic used by dendrites in combining afferent signals is a fundamental problem in neuroscience. The rules of input summation are crucial in determining neuronal output properties: linear summation would preserve the importance of individual inputs. Non-linear integration, i.e. when the algebraic sum of single postsynaptic responses differs from the neuronal response to simultaneous activation, would significantly increase the computational power of both single nerve cells and neural networks. Theoretical studies also predict that the modes of integration of coincident inputs depend on their subcellular location and timing. However, due to the lack of direct experimental analysis, the rules of neural input interactions are not clear.

To test these models experimentally, we simultaneously recorded from three or four neocortical neurons *in vitro* and investigated the effect of the subcellular position of two convergent inputs on response summation in the common postsynaptic cell. When scattered over the somatodendritic surface, combination of two coincident excitatory or inhibitory synaptic potentials summed linearly in layer 2/3 pyramidal cells as well as in GABAergic interneurons. Slightly sublinear summation with connection specific kinetics was observed when convergent inputs targeted closely placed sites on the postsynaptic cell. The degree of linearity of summation also depended on the type of connection and the relative timing of inputs (Tamás et al. 2002). Simultaneous activation of many co-aligned inputs might lead to more significant nonlinear interactions especially in compartments of relatively small diameter. The axon initial segment of pyramidal cells has a limited volume and it receives inputs only from a moderate number of axo-axonic interneurons yet the summation of unitary axo-axonic inputs was only slightly sublinear (9.4%; Tamás and Szabadics 2004).

These results suggest that the majority of afferent permutations undergo linear integration, maintaining the importance of individual inputs. However, compartment and connection specific nonlinear interactions between synapses located close to each other could increase the computational power of individual neurons in a cell type and connection specific manner.

We then tested how subthreshold rules of summation would be translated to suprathreshold firing behaviour of postsynaptic neurons. We recorded two simultaneous EPSPs arriving on the same interneuron and detected their effects on postsynaptic firing. The number of postsynaptic spikes in response to simultaneously arriving EPSPs was similar to the summed number of spikes triggered by individual EPSPs. However, simultaneous presynaptic activation caused significant nonlinearities by shifting the temporal distribution of postsynaptic spikes towards the presynaptic spike and by narrowing the time window for postsynaptic activity. Furthermore, asynchronous (<10 ms) presynaptic activation was nonlinearly translated to single postsynaptic action potentials. When triggering postsynaptic spikes, preceding inputs eliminated the spike triggering effectiveness of follower EPSPs. In turn, EPSPs arriving after subthreshold preceding inputs triggered spikes with shortened latency.

Our results provide evidence that the rules of summation can be switched by the operational state of postsynaptic neurons. Close to linear subthreshold input summation rules can turn to highly nonlinear interactions enhancing temporal precision of network processes and altering spike-triggering effectiveness of individual inputs.

References

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