

Preface

Synapses are sites of a specialized cell-cell contact between neuronal cells and represent the major structure involved in chemical neurotransmission in the nervous system. It is widely believed that glutamatergic synapses are important loci for modifying the functional properties of CNS networks, possibly providing the basis for phenomena collectively referred to as “learning and memory”. Given their importance, it is not surprising that enormous efforts are being made to understand the formation, structure, function and regulation of glutamatergic synapses. To date, significant progress has been made in our understanding of their ultrastructure, molecular composition, and physiological properties, as well as the principles of how these synapses are initially assembled and “plastically” modified.

The term synaptic plasticity covers many different aspects of use-dependent synaptic modifications and is commonly used in a broader sense describing aspects of synaptic signal transmission as well as structural alterations in the molecular make-up of the synapse related to synaptic signaling events. The capacity of the nervous system to modify its own organization is remarkable; plastic changes can occur as a consequence of many events, including the normal development and maturation of the organism, the acquisition of new skills (‘learning’) and after brain damage. This response specificity is not always intrinsic to neurons; rather, it can develop as a consequence of interaction with the environment and thus involves information processing and memory storage.

Disturbances of synaptic and neuronal plasticity ultimately result in diseases affecting cognitive functions and it has become increasingly clear during recent years that synaptopathies – disruptions in synaptic structure and function – in many cases are the major determinant of many brain disorders. These diseases and related animal models include Alzheimer’s, prion diseases, Down’s syndrome, Huntington’s or Parkinson’s diseases as well as schizophrenia and autism spectrum disorders that almost ultimately result in disturbed plasticity processes. In accord, it is becoming increasingly clear that studies of synaptic plasticity and memory formation are critical for understanding the initial stages of these disorders. At an early stage in most of these diseases no structural damage exists but rather an impairment

of synaptic function. Interventions aimed to preserve or even restore synaptic function will probably delay the onset or might even provide a cure for such disorders. A general strategy to treat these types of diseases can therefore be plausibly based on knowledge, how to maintain the plastic properties of neurons in the adult and aging brain.

Crucial technological advancements have recently accelerated progress in our understanding of synaptic processes, five of them are listed here: (1) Live-cell imaging has provided essential constraints regarding the kinetics (rate constants) and spatial organization of signaling pathways, (2) the development of next generation sequencing allows individual transcriptome profiling, (3) quantitative synaptic proteome profiling of normal and disease brain has established protein interaction networks databases for signaling pathway analysis, (4) optogenetic tools are available to study neuronal function *in vivo*, (5) and finally, progress in computer simulation and neuroinformatics has been crucial for improving the temporal and spatial scale of synaptic plasticity models, because simulating large spatial structures for long durations with high resolution requires trillions of calculations.

In higher mammals the majority of brain glutamatergic excitatory synapses is found on the principal neuron of the cortex and hippocampus, the pyramidal cell. Pyramidal cells are characterized by a complex dendritic cytoarchitecture harboring approximately 10^4 – 10^5 synaptic contact sites with other neurons. It is estimated less than 1% of all synaptic contacts of cortical pyramids is concerned with the wiring to subcortical areas, implying that the predominant synapse of the mammalian telencephalon is concerned with input from a closely related neuron in terms of cell lineage, morphology and functional characteristics. This fact is mainly emphasized because our knowledge about synaptic plasticity of this type of synaptic input is still very sparse.

We have focused our attention in this book mostly on postsynaptic molecular mechanisms because a lot more knowledge exists with respect to this side of the synapse especially with respect mechanisms underlining synaptic dysfunction and synaptopathies. The purpose of this book is to summarize this knowledge and to provide insights into the most recent developments in the field including the major technological advancements in recent years. The first part of the book concerns structural plasticity at the pre- and postsynaptic scaffold, the molecular dynamics of the synapse and synapto-dendritic plasticity in development and learning. In the second part the book includes chapters on synapse-to-nucleus communication and synaptic dysfunction and synaptopathies. Finally, we want to particularly thank the authors for their contribution. We are very happy that we could convince leading experts in this field to provide a detailed account of the most exciting recent developments.

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