Progress in neural plasticity

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One of the properties of the nervous system is the use-dependent plasticity of neural circuits. The structure and function of neural circuits are susceptible to changes induced by prior neuronal activity, as reflected by short- and long-term modifications of synaptic efficacy and neuronal excitability. Regarded as the most attractive cellular mechanism underlying higher cognitive functions such as learning and memory, activity-dependent synaptic plasticity has been in the spotlight of modern neuroscience since 1973 when activity-induced long-term potentiation (LTP) of hippocampal synapses was first discovered. Over the last 10 years, Chinese neuroscientists have made notable contributions to the study of the cellular and molecular mechanisms of synaptic plasticity, as well as of the plasticity beyond synapses, including activity-dependent changes in intrinsic neuronal excitability, dendritic integration functions, neuron-glial signaling, and neural network activity. This work highlights some of these significant findings.

long-term plasticity, synaptic transmission, intrinsic excitability, dendritic integration, neuron-glial signaling, neurological disease


One of the primary qualities of the brain is its ability to learn and to memorize. Learning is the modification of behavior by experience, and memory is the retention of that modification over time [1]. For more than a century, use-dependent modification of the synapse – the cellular structure responsible for communication between neurons – has been postulated to be the primary cellular mechanism underlying learning and memory. The discovery of activity-induced synaptic modulation was first made by Feng Te-Pei in the 1940s. He found that a brief period of high frequency stimulation of motor nerves resulted in the potentiation of neuromuscular transmission for a few minutes [2,3], a phenomenon now known as post-tetanic potentiation. Thirty years later, Bliss and Lømo [4] reported that a train of high-frequency stimulation of presynaptic inputs induces long-lasting potentiation of synaptic transmission (LTP) in the hippocampus of the rabbit brain, and this potentiation lasts for hours to days [5]. Later studies also demonstrated that prolonged low-frequency activity leads to long-term depression (LTD) at many synapses [6]. Synaptic modifications associated with LTP/LTD have generally been regarded as a cellular basis for learning and memory [7,8] and for the experience-dependent developmental refinement of neural circuits [9,10]. It is increasingly evident that learning- or experience-induced persistent modification also exists for many other neuronal functions, including intrinsic neuronal excitability, dendritic integration, and neuron-glial signaling. All of these different forms of plasticity act together to shape the neural circuit properties which underlie information processing and memory storage.

1 LTP of excitatory synapses

The principal neuron in many brain regions is the pyramidal cell that uses excitatory neurotransmitter glutamate. Exten-
sive studies of the excitatory synapses between pyramidal cells have led to the emergence of two models for describing how patterned neuronal activity induces synaptic plasticity: the spike frequency-dependent Bienenstock-Cooper-Munro (BCM) model and the spike timing-dependent model. In the former model, the level of synaptic activity and/or subsequent postsynaptic depolarization is vital for controlling the polarity of synaptic plasticity-high frequency stimulation (HFS) induced LTP and low frequency stimulation (LFS) induced LTD [11,12]. The spike-timing dependent model emphasizes the necessity of the precise timing and the temporal order of pre- and postsynaptic spiking (at a low frequency) in determining the polarity of synaptic modifications—i.e. presynaptic spiking before postsynaptic spiking within a narrow timing window induces LTP, whereas spiking of the reverse order induces LTD [13,14]. Such spike timing-dependent plasticity (STDP) functionally allows neurons to detect and enhance causal associations between their inputs [14,15], a feature essential for associative learning and memory in the brain. Together, spike frequency- and/or timing-dependent synaptic plasticity has provided a cellular basis for most models of learning/memory and circuit development, although very few experiments were able to directly connect the synaptic plasticity to particular behaviors.

Experimentally, the frequency- or timing-dependent LTP of excitatory synapses is temporally divided into two distinct phases: an early phase (E-LTP) which lasts for up to 1–2 h and involves modification of existing transmission machinery and a late phase (L-LTP) which persists for many hours to days and requires synthesis of new RNAs and proteins [16]. The L-LTP is particularly significant as a substrate for long-term memory in the brain. Genetic and behavioral studies have suggested that the transcription factor cAMP response element-binding protein (CREB)-target gene expression is essential for L-LTP maintenance and memory formation [17,18]. However, the mechanism that mediates the transfer of repetitive synaptic signals to the nucleus for the initiation of CREB-target gene expression remains elusive. Xiong and colleagues of the Institute of Neuroscience (ION), CAS, in Shanghai recently reported that the CREB coactivator TORC1 (transducer of regulated CREB activity 1) may act as one of such mediators which sense cytoplasmic Ca$^{2+}$ and cAMP changes in postsynaptic neurons during LTP induction. It is translocated from the cytoplasm to the nucleus to drive persistent transcription of CREB target genes and to maintain LTP [19,20]. These authors demonstrated that suppression of TORC1 activity, by the over-expression of a dominant negative TORC1 or of a down-regulating TORC1 expression, prevented activity-induced transcription of CREB target genes and the maintenance of spaced HFS-induced L-LTP in the hippocampus, whereas elevating TORC1 activity facilitated both the transcription of CREB target genes and the induction of hippocampal L-LTP. In parallel, Li and colleagues [21] at Fudan University in Shanghai found that in the medial prefrontal cortex (mPFC), another signaling pathway of phosphatidylinositol 3-kinase (PI3K)/Akt-mTOR (mammalian target of rapamycin) was activated by HFS, and the infusion of the inhibitor of either PI3K or mTOR into the mPFC in vivo suppressed HFS-induced LTP as well as the long-term retention of trace fear memory. These results suggest that activation of the PI3K/Akt-mTOR signaling pathway is essential for mPFC synaptic plasticity and the associated high cognitive functions.

The development of a neural circuit requires activity-dependent formation and refinement of synaptic connections [9,10]. One of the synaptic mechanisms involved in the latter process is to “switch-on” silent synapses, which are found at a high frequency in the nascent synaptic networks. Silent synapses are often defined as the glutamatergic synapses which contain N-methyl-D-aspartate (NMDA) receptors but no AMPA receptors. Because NMDA receptors are mostly closed at resting membrane potential, such synapses are typically “mute”. However, LTP-inducing activity is known to rapidly convert those “mute” synapses into functional ones exhibiting both AMPA receptor-mediated responses [22]. However, whether the conversion of silent synapses occurs through pre- or postsynaptic mechanism is still a matter of debate in the field. Recent evidence from Duan and colleagues [23] at ION in Shanghai strongly suggest that a brief burst of action potentials rapidly awakens silent synapses between cultured hippocampal neurons by increasing the availability of synaptic vesicles for transmitter release, through BDNF triggered presynaptic actin remodeling that is mediated by the small GTPase Cdc42. This extensive study involved the use of electrophysiology, optical imaging, electronic microscopy, and gene manipulation uncovered a presynaptic mechanism which enables rapid un-silencing of nonfunctional synapses by neuronal activity. The mechanism involving actin polymerization-dependent maturation/regulation of presynaptic transmitter secretion shown in this study appears very significant for activity-dependent synaptogenesis and the plasticity of the synaptic network during development.

2 Metaplasticity of excitatory synapses

The extent of LTP and LTD is regulated by neuromodulation and the recent history of neural activity. The latter form of plasticity regulation has been termed metaplasticity, i.e. the plasticity of synaptic plasticity [24]. Basically, metaplasticity entails an alteration in the physiological or biochemical state of neurons or synapses which change their ability to undergo synaptic plasticity. A common paradigm for experimentally inducing metaplasticity involves the change of NMDA receptor function resulting from priming synaptic activity (or inactivity) or pharmacological agents. This causes a change in the polarity or the magnitude of
LTP or LTD. Lu and colleagues [25] at Nanjing Medical University demonstrated that hippocampal Schaffer collateral (SC)-CA1 synapses exhibited a novel form metastability which the polarity of activity-induced synaptic modifications was reverted via lateral diffusion of NMDA receptors into activated synapses. They detected an activity-dependent lateral trafficking of extrasynaptic NMDA receptors (mainly NR1/NR2B receptors) into the synaptic site over time after wash-out of the bath-applied irreversible NMDA receptor open-channel blocker MK-801, resulting in a nearly full recovery of NMDA receptor-mediated synaptic response at the SC-CA1 synapse. Following this recovery, LTP-inducing activity resulted in LTD, an effect which was attributed to changes of the number and subunit composition of synaptic NMDA receptors during the recovery period [25]. In addition, these results also suggest that the subunit composition of synaptic NMDA receptors may alter the rule of synaptic modification, consistent with the model of sliding synaptic plasticity, in which activity-dependent changes in the NR2A/NR2B ratio alter the threshold of LTP/LTD induction \( \theta_{\text{LTP/LTD}} \) in the BCM model [24,26]. In a follow-up study, they systematically examined how the activity-dependent subunit changes of synaptic NMDA receptors regulate \( \theta_{\text{LTP/LTD}} \). They found that the same number of prior priming stimuli (PS) at low frequency (1–5 Hz, LPS) and high frequency (50–10 Hz, HPS) respectively caused a decrease and an increase of NR2A/ NR2B ratio, which correlated with the LPS-induced leftward shift (decrease) of \( \theta_{\text{LTP/LTD}} \) and the HPS-induced rightward shift (increase) of \( \theta_{\text{LTP/LTD}} \) of the subsequent synaptic plasticity [27]. These results underscore the notion that activity-dependent regulation of NMDA receptor subunit composition is a critical factor in the metastable regulation of the LTP/LTD threshold and is a possible molecular basis for the sliding synaptic modification model. As a result, this NMDA receptor-dependent metastable regulation of LTP and LTD may contribute to the maintenance of synaptic efficacy within a dynamic range and of an appropriate network state for learning and memory.

3 Plasticity of inhibitory GABAergic circuits

Inhibitory GABAergic neurons constitute 10%-20% of all neurons in the hippocampus and the cortex, but are crucial for establishing the functional balance, complexity, and computational architecture of hippocampal or cortical networks [28,29]. Given the significance of the inhibition, it seems most likely that inhibitory synapses are also an essential locus of persistent change during learning and experience-dependent plasticity. Reports of activity-dependent plasticity of the GABAergic synapse, although far fewer than that of excitatory synapses, have also shown the frequency- or timing-dependent plasticity at inhibitory synapses, with a few properties distinct from that of excitatory synapses [30]. For example, the GABAergic synapse on hippocampal pyramidal neurons exhibits a different form of STDP, requiring nearly correlated pre- and postsynaptic spiking, but independent of the temporal order of this correlated activity [31]. Zhang, Poo and colleagues [32] at ION recently reported that at the developing hippocampal GABAergic synapse on CA1 pyramidal cells, LTD and LTP were respectively induced by repetitive coincident pre- and postsynaptic spiking at low (5 Hz) and high (20–50 Hz) frequencies. Furthermore, activation of extrasynaptic GABA\(_{\beta} \) receptors was found to be required for LTD induction by high-frequency activity and converted LTD induced by low-frequency activity to a slight LTP, suggesting that GABA\(_{\beta} \) receptor activation mediates the frequency-dependent LTD of GABAergic synapses. This study further elucidated the cellular mechanism underlying LTD induction at these GABAergic synapses: it requires postsynaptic Ca\(^{2+}\)/CaMKII signaling and a local increase of membrane Na\(^+\)/K\(^+\)/2Cl\(^-\) (NKCC1) transporter activity at or nearby activated GABAergic synapses. Such plasticity of GABAergic synapses is restricted at the very early stage of postnatal development when GABA exerts a depolarizing action. This provides a potential mechanism for self-refinement of GABAergic connections during early postnatal development [32]. This study has uncovered a mechanism for the induction of the LTD/LTD at developing GABAergic synapses by patterned synaptic activities, and suggests a novel function of GABA\(_{\beta} \) receptors in regulating the long-term plasticity of developing GABAergic synapses in the hippocampus.

A prominent feature of interneurons is the high heterogeneity of their morphology, physiological properties, cellular constituents and wiring patterns [28,29]. Such heterogeneity suggests that different plasticity rules may exist for synapses made by and onto interneurons. A recent report by Zhang XiaoHui, Poo Mu-ming and colleagues at ION has provided direct support for this notion [33]. They showed that divergent excitatory synapses made by a pyramidal cell on different types of inhibitory GABAergic interneurons in the layer II/III of the rat somatosensory cortex, spike timing-dependent LTD/LTD exhibits a strong dependence on the target cell: both the induction and expression of STDP depend on the type of postsynaptic GABAergic interneurons [33]. Thus, the same pattern of repetitive activity is likely to lead to distinct synaptic modifications at divergent excitatory synapses on different types of cortical GABAergic interneurons, providing a potential circuit mechanism for the differential processing and storage of neuronal information through connections mediated by distinct subpopulations of inhibitory interneurons in cortical circuits.

4 Plasticity of global or local excitability

Although most studies of neural plasticity are focused on
synaptic plasticity, other neuronal functions beyond the synapse are also susceptible to modification by neuronal activity. There is strong evidence that, in addition to persistent changes in synaptic efficacy, correlated pre- and postsynaptic activity also results in persistent changes of the intrinsic excitability of pre- and postsynaptic neurons. In cultured hippocampal neurons, induction of LTP by correlated pre- and postsynaptic activation is accompanied by an immediate and persistent enhancement of the intrinsic neuronal excitability of the presynaptic neuron, a modification caused by the enhanced activation kinetics of Na⁺ channels [34]. Poo, Duan and colleagues at ION also showed that there is a reduction of intrinsic neuronal excitability following the induction of LTD by correlated pre- and postsynaptic activation in hippocampal cultures and in somatosensory cortical slices [35]. This presynaptic effect is attributed to an enhanced activation of voltage-dependent slow-inactivating K⁺ channels, a process that requires postsynaptic Ca²⁺ elevation and presynaptic protein kinase A (PKA) and PKC activities. Together, these results suggest an immediate retrograde signaling associated with the induction of LTP/LTD and a rapid spread of cytosolic signals throughout the presynaptic neuron, leading to global modifications of ion channels.

In addition to global changes of the intrinsic excitability in the presynaptic neuron, local morphological changes of dendrites and alteration in the properties or the distribution of ion channels are also likely to modify the dendritic summation of synaptic potentials in postsynaptic neurons. Poo, Duan and colleagues at ION found that in the CA1 pyramidal neuron of the hippocampus, the induction of LTP/LTD is accompanied by corresponding bi-directional changes in the linearity of the spatial summation of synchronous EPSPs from independent inputs [36]. Similar increases in the linearity were also observed in the summation of asynchronous EPSPs (temporal summation) following LTP induction in a study by Zhang, Poo and colleagues [37]. Local modifications of dendritic Iₒ channels (hyperpolarization activated cation channels) and the NMDA receptors may account for the observed changes in the dendritic integration [36,37]. The correlated activity-induced increase in EPSP summation linearity strongly depends on the dendritic location and the timing of the arrival of synaptic inputs in a pyramidal cell. As a result, such spatiotemporally specific plasticity of dendritic summation differentially enhanced the respective coincidence detection and temporal integration at the distal and proximal dendrites [37]. Thus, correlated pre- and postsynaptic activities also induce persistent modification of dendritic integration, providing an additional dimension of activity-dependent plasticity beyond synaptic potentiation or depression. These new findings are likely to be highly relevant to the function of neural circuits in information processing and storage.

5 Plasticity of neuron-glia signaling

Glia make up most of the cells in the brain, and they are regulatory factors in neurogenesis, synaptogenesis, and synaptic function and plasticity, in addition to functioning as the “glue” or as a supporting constituent of the brain [38]. Dynamic bidirectional communication does occur between the neuron and the astrocyte, a distinct subpopulation of glia which is structurally tied with neuronal synapses. The best-known “transmitters” released by astrocytes are glutamate, ATP and D-serine. A series of recent studies from the laboratories of Duan and Xu at ION have shown that these glial transmitters exert both short- and long-term modulations of neuronal synaptic transmission (refs [39]–[41], see a review by Duan in this issue).

Recent work from Duan’s laboratory further shows that the efficacy of neuron-glia signaling is also dynamically regulated by neuronal activity and undergoes modification similar to the LTP of neuronal synapses [42]. In this study of hippocampal slices, tetanic stimulation of SC fibers in the CA1 area, which is normally capable of inducing LTP in neurons, was found to cause an LTP-like persistent elevation of SC-evoked slow depolarization in perisynaptic astrocytes. The increased slow depolarization in astrocytes after the tetanic stimulation was abolished by an NMDA receptor antagonist and potassium channel inhibitors, suggesting the involvement of an increased extracellular K⁺ accumulation accompanying neuronal LTP. All of these changes in astrocytes and the synaptic cleft may reduce the efficiency of the glial glutamate transporter, which is a primary factor in clearing glutamate in the synaptic cleft and controlling the strength and kinetics of synaptic activity. This work suggests the existence of a novel functional plasticity in the feedback regulation of neuronal activity by astrocytes, in parallel with the known structural plasticity of glial processes accompanying neuronal LTP [43].

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In summary, Chinese neuroscientists have significantly
helped to elucidate the plasticity of neuron-glial communication. In addition to glial-mediated modulation of the synaptic function and plasticity, the newly discovered plasticity of neuron-glial signaling points to another dimension of brain plasticity beyond classical synaptic plasticity. It is necessary to determine whether or not and how the LTP-like increase of glia signaling contributes to the induction and expression of neural circuit plasticity and to the learning and memory functions of neural circuits.

6 Hippocampal plasticity, opiate addiction and neurological diseases.

Opiate (or drug) addiction is thought to be an aberrant form of learning, mediated by adaptive changes in the brain's memory and reward systems [46]. For the hippocampus is a factor in the formation of episodic memory, and long-term activity-induced LTP and LTD in various regions of the hippocampus have been widely recognized as the cellular basis for hippocampus-related learning and memory. Pei Gang and colleagues at the Institute of Biochemistry and Cell Biology (IBCB) of CAS in Shanghai have examined the effect of chronic morphine or heroin treatment on LTP induction in the CA1 region of the rat hippocampus. They found that chronic exposure to opiates, which induced severe drug tolerance and dependence, markedly reduced the capacity for LTP induction in rat brain slices during the period of drug withdrawal [47]. The capacity for LTP was restored to the normal level by re-exposure of the animals to opiates, suggesting that the mechanism for synaptic plasticity is adapted to a state of dependence on opiates. Up-regulation of the cytoplasmic cAMP pathway may be responsible for the adaptive changes in hippocampal plasticity, as opiate-reduced LTP was restored by inhibitors of PKA. Further studies [48] showed that the expression of SNAP-25, a SNARE protein essential for synaptic vesicle exocytosis, was regulated in the hippocampus after chronic morphine treatment, with a reduction in the formation of a ternary complex of SNARE proteins in hippocampal synaptosomes.

More recently, Zhou and his colleagues [49] at the University of Science and Technology of China (USTC) in Hefei reported that prenatal morphine exposure resulted in the alteration of persistent potentiation of the population spike amplitude, but not in the LTP of perforant-dentate gyrus (DG) synapses in vivo, and such enhanced EPSP-spike potentiation was attributed to the decreased inhibition caused by a loss of GABAergic neurons in the DG region of juvenile rat offspring (postnatal day 22–31). This finding showed additional cellular mechanisms underlying the impaired spatial learning and memory in rat offspring prenatally exposed to morphine, in addition to the known mechanism associated with the reduction of hippocampal LTD and the depotentiation of LTP in the offspring [50].

One significant aspect of drug addiction is that the propensity of an individual for drug abuse, drug seeking and relapse is influenced by stress or glucocorticoids. There is evidence that stress may interact with drug addiction through a common mechanism of synaptic plasticity in the ventral tegmental area and hippocampus. Xu and colleagues [51] at the Kunming Institute of Zoology of CAS have made a concerted effort to examine the role of the hippocampus in the interaction between stress and drug addiction, based on the fact that the hippocampus is sensitive to stress and glucocorticoids and might be directly involved in learning and memory associated with drug addiction. They found that acute stress enables LTD induction by LFS, but acute morphine treatment causes synaptic potentiation. Exposure to an acute stressor reverses the effect of morphine from synaptic potentiation to depression, and precluded further LTD induction by LFS [52]. The synaptic depression caused by stress with morphine was abolished by blocking either glucocorticoid receptors or NMDA receptors. Application of corticosterone with morphine during the initial phase of drug use promoted later delayed-escape behavior (using the Morris water maze test), leading to persistent morphine seeking after withdrawal. These results support the notion that hippocampal synaptic plasticity may be a key factor in the effects of stress or glucocorticoids on opiate addiction. Further studies of the infusion of glucocorticoid receptor antagonists further suggest that glucocorticoid receptors in the hippocampus and nucleus accumbens are necessary for the formation of opiate-associated memory of place preference in rats [53]. These results have elucidated the relationship between stress, synaptic plasticity and drug addiction in specific neural circuits.

Several neurological disorders in humans are associated with impaired memory and other cognitive functions (to different extents). For example, Alzheimer’s disease (AD), the most common age-associated neurodegenerative disorder, exhibits progressively severer deficits of learning and memory. The patients or animal models of AD are characterized with two major neuropathological abnormalities in their brains: the extracellular deposition of β-amyloid peptides (known as plaques) and the intracellular neurofibrillary tangles composed of Tau, a hyperphosphorylated form of microtubule-associated protein. Most in vitro studies have suggested that the increased activity of glycogen synthase kinase-3β (GSK-3β) is one of the key factors mediating Tau hyperphosphorylation and the progressive formation of neurofibrillary tangles. Studies of rodent models have also suggested that enhanced GSK-3 activity induces the neurodegeneration and deficits in hippocampal memory formation related to AD, but the underlying mechanism remains uncertain. Wang and her research team at Tongji Medical College in Wuhan have performed a series of animal studies to elucidate molecular and synaptic mechanisms respectively underlying GSK-3 over-activation and AD-like pathologies in vivo [54,55]. They found that the inhibition of phosphoinositide-3 kinase (PI-3K) and PKC in vivo, by
injection of specific inhibitors of these two kinases into the left ventricle of the brain, resulted in the sequential events of the overactivation of GSK-3, tau hyperphosphorylation and impaired spatial memory in rats [54]. Further studies [55] showed that activation of GSK-3 by wortmannin (a general activator) or transient over-expression of wild-type GSK-3β suppressed the induction of HFS-elicited LTP in the murine hippocampal CA3 area, whereas simultaneous inhibition of GSK-3 by lithium (the seminal inhibitor) or SB216763 (a specific inhibitor), or transient expression of a dominant-negative GSK-3β mutant preserved the LTP. In presynaptic sites, up-regulation of GSK-3 led to the considerable decrease of presynaptic glutamate release probably due to its suppression of the expression/clustering of presynaptic vesicle protein synapsin I. Postsynaptically, GSK-3 over-activation also decreased the expression of the scaffolding protein PSD93 and NMDA receptor subunits NR2A/NR2B. Further electronic microscopy results indicated that less of the presynaptic active zone, thinner postsynaptic density, and a broader synaptic cleft at synapses were prominent in the hippocampal slices after HFS along with the activation of GSK-3, and these damages in the synaptic structure were attenuated when GSK-3 activity was inhibited [55]. Thus, this work provides direct evidence that upregulated GSK-3 activity impairs synaptic function and plasticity both functionally and structurally. All of the results of biochemistry, physiology, and EM together in this elegant study have yielded a potential cellular/synaptic mechanism underlying the GSK-3-involved AD-like deficit of memory impairment.

**7 Experience-dependent plasticity of neural network activity**

Neuronal oscillations at different frequency ranges manifest in many brain regions and reflect rhythmic alterations of neuronal ensemble activities between high and low excitability states [56,57]. It is increasingly evident that the oscillatory activities in defined frequency bands are associated with various cognitive functions. As most natural stimuli typically occur in rhythmic streams, it is probable that external rhythms may modulate the intrinsic rhythms of neuronal oscillations. Zhang, He and colleagues [58] at ION and Hong Kong Polytechnic University have reported that rhythmic sound stimuli with inter-stimulus intervals (ISIs) of several seconds effectively entrain slow oscillations (< 1 Hz) to the sound rhythm in the auditory thalamus when the animals are under anesthesia or during slow wave sleep. After termination of the sound stimulation, this entraining effect on thalamic slow oscillations persisted for tens of seconds. This work demonstrates a novel form of network plasticity which retains the information of stimulus interval in the order of seconds by modulating the intrinsic rhythmic slow oscillations in the brain. Similar rhythmic stimulation-induced entrainment of neuronal oscillations has been observed in the brain of low vertebrates [59] and high primates during behavioral tasks [57].

**8 Conclusion**

Neuroscience in China has expanded at an unprecedented rate over the past ten years. In the field of neural plasticity, Chinese researchers have reported significant findings concerning the diversity and complexity of brain plasticity. Use-dependent plasticity from synaptic to circuitry levels will remain the focus of neuroscientific research. What differential cellular mechanisms govern various forms of neural plasticity and how all of these different forms of plasticity within a functional circuit constitute the basis for the higher cognitive functions of the brain is of the highest significance.

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Research Interests

The brain is a network of neurons, constructed via the inter-neuronal synaptic connections. Among the cellular constituents of the brain, diverse types of interneurons, which releases inhibitory transmitter γ-aminobutyric acid (GABA), cause inhibition which establishes the functional balance, complexity, and computational architecture of neural circuits. We are interested in understanding the function and use-dependent plasticity of different classes of GABAergic interneurons, primarily by performing physiological studies in the acute brain slice in vitro and in the intact brain in vivo. Our ongoing studies have focused on: (i) Examining the action of spatiotemporally-specific GABA inhibition on the neuronal information processing of single pripyramidal cell; (ii) examining the inhibition mechanisms underlying the “critical period” plasticity of the primary visual cortex.