Focus Review

Protein homeostasis and synaptic plasticity

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It is clear that de novo protein synthesis has an important function in synaptic transmission and plasticity. A substantial amount of work has shown that mRNA translation in the hippocampus is spatially controlled and that dendritic protein synthesis is required for different forms of long-term synaptic plasticity. More recently, several studies have highlighted a function for protein degradation by the ubiquitin proteasome system in synaptic plasticity. These observations suggest that changes in synaptic transmission involve extensive regulation of the synaptic proteome. Here, we review experimental data supporting the idea that protein homeostasis is a regulatory motif for synaptic plasticity.

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Introduction

The brain generates representations of environmental inputs received from sensory systems and must constantly update these representations to effectively interact with a changing environment. The process of learning and memory relies on the plastic properties of brain circuits. The ability of the nervous system to respond adaptively relies on modifications to existing proteins as well as changes in gene transcription, protein synthesis and protein degradation. Most neurons possess three distinct compartments—the cell body, the axon and dendrites. The axon of one cell (presynaptic neuron) comes into contact with the dendrite of another cell (postsynaptic neuron) to form a synapse. Each cell possesses from 1000 to 10 000 synapses, which arise, in some cases, from unique presynaptic neurons. Given this network architecture, the question of specificity poses a problem. How can the products of gene expression be differentially targeted to alter synaptic strength at some synapses?

The neuron doctrine based on the work of Santiago Ramón y Cajal and Camilo Golgi proposed the cell body as the metabolic centre of the nerve cell. However, numerous studies have shown that many cell biological processes can function autonomously in isolated dendrites, axons or synaptoneurosomes (subcellular preparation enriched in presynaptic structures with attached postsynaptic densities). This capacity for local control can provide, in principle, a means to modify synapses independently from their neighbours. The benefits for local control mechanisms include the following: (i) the initiation of rapid responses at stimulated synapses distant from the cell body, (ii) the confinement of different biochemical processes to different neuronal compartments and (iii) the creation of microenvironments that may enable input-specific modulation of synapses.

Protein synthesis is required for flexibility in the nervous system

It is now clear that protein synthesis is required for animals to establish long-term memories. Over 40 years ago, it was shown that injections of the protein synthesis inhibitor puromycin into the brain of the mouse from 1 to 3 days after learning blocked the animal’s ability to remember the location of a shocked arm in a Y-maze (Flexner et al, 1963). Injections that were made later than 3 days after training did not result in any consistent memory deficit. In addition, later studies showed the selective incorporation of radioactive amino acids into brain proteins when mice and goldfish learned a new task (Hershkowitz et al, 1975; Shashoua, 1976). Newly synthesized proteins may serve to replenish or upregulate levels of pre-existing proteins or provide isoforms that will ultimately stabilize or consolidate animal memory.

The above behavioural studies are paralleled by in vitro studies of long-lasting synaptic plasticity. Two prominent forms of plasticity, promoting either a long-lasting enhancement of synaptic transmission (long-term potentiation, LTP) or a long-lasting depression of synaptic transmission (long-term depression, LTD), require new protein synthesis for the plasticity to endure. The application of protein synthesis inhibitors, around the time of the inducing stimulus, results in LTP (or LTD) that slowly decays back to baseline (Krug et al, 1984; Stanton and Sarvey, 1984; Linden, 1996). In addition, the concept of synaptic tagging (Frey and Morris, 1997) posits that newly synthesized proteins are delivered to synapses that have been tagged during the induction of plasticity. One result of this idea is that synapses that generate tags with stimuli sub-threshold for plasticity can capture plasticity proteins (Frey and Morris, 1997). This notion has been advanced for studies of LTP and LTD. In addition, one provocative study suggested ‘cross-capture’, the notion that proteins generated during LTP induction can be used at other synapses to express LTD and vice versa (Sajikumar et al, 2005). If this idea is correct, then the pool of...
proteins important for different forms of plasticity (e.g., LTP or LTD) is to some extent interchangeable. This would indicate that the identity of the protein does not determine the sign of the plasticity, but perhaps rather the stoichiometry is important. More recently, genetic approaches have provided further support for the function of protein synthesis in memory formation (Kelleher et al., 2004; Costa-Mattioli et al., 2005; Banko et al., 2006).

Until recently, most neuroscientists assumed that all of the proteins required for all neuronal function were made in the cell body (with the exception of mitochondria). Bodian (1965) published his observations of ribosome particles in proximal dendrites adjacent to synaptic ‘knobs’ in monkey spinal cord motoneurons, speculating that the ‘…selective establishment of synaptic contacts may be determined by specific proteins synthesized at the synaptic membrane’ and that local synthesis might also participate in ‘…the adaptive adjustments of synapses’. Steward and Levy (1982) detected polyribosomes in the distal dendrites of dentate granule cell neurons in electron micrographs, pointing out that the synthesis of proteins at synapses could allow for the specific modification of synapses. In 1996, the first function for local protein synthesis was discovered: local protein synthesis is required for the rapid enhancement of synaptic transmission induced by exposure to the growth factor BDNF (Kang and Schuman, 1996). These findings have been furthered by subsequent studies in different model organisms showing that local protein synthesis has an important function in inducing different forms of plasticity (Martin et al., 1997; Huber et al., 2000; Miller et al., 2002; Cracco et al., 2005; Huang and Kandel, 2005; Vickers et al., 2005). Miller et al. used a gene-targeting approach to generate a transgenic animal expressing a form of CaMKIIz that is mainly expressed in the cell body. Mutant mice display a significant reduction of CaMKIIz in postsynaptic densities, altered LTP, defects in spatial memory, associative fear conditioning and object recognition memory.

**Homeostatic synaptic plasticity and protein synthesis**

Homeostasis is the property of a system to regulate its internal environment and the tendency to maintain a stable condition (Cannon, 1932). Homeostatic synaptic plasticity refers to the ability of neurons to adjust their own excitability relative to network activity. For example, when postsynaptic neurons experience a long-term reduction in action potential activity, a compensatory increase in glutamate receptor currents or presynaptic release probability gradually develops. This synaptic scaling serves to maintain the strengths of synapses relative to each other. In addition to the release of neurotransmitter caused by action potentials, there exists the spontaneous release of neurotransmitter (a.k.a. miniature synaptic responses or minis) from presynaptic nerve terminals (Fatt and Katz, 1952). Schuman and co-workers showed that the spontaneous release of transmitter serves as signal for the integrity of the synapse. When minis are prevented in a local segment of dendrite, local protein synthesis is engaged to enhance the responsiveness of the postsynaptic cell to the perceived decrease in input (Sutton et al., 2004, 2006). This scaling response increases synaptic glutamate receptor population by local synthesis and synaptic insertion of homomeric GluR1 receptors (Sutton et al., 2006).

**mRNA trafficking**

Local protein synthesis provides a potential solution for the specificity problem, as it not only provides the opportunity to stimulate ribosomes near to activated synapses, but it also implies that mRNAs need to be selectively localized. As a typical pyramidal neuron of the CA1 region of the hippocampus has dendrites that extend to distances up to 300 μm. How are mRNAs transported to distal synapses? If mRNAs are required to be transported to specific distant places in the cell, there should be mechanisms to actively transport them. Selective mRNA transport has been shown to be a means to spatially and temporally restrict gene expression in different cell types (Martin and Ephrussi, 2009). One of the best-characterized mechanisms of mRNA localization is the transport of the ASH1 mRNA to the bud tip of growing yeast cells (Bertrand et al., 1998). ASH1 mRNA is targeted and locally translated to control mating-type switching (Long et al., 1997). In Drosophila, the bicoid, oskar, nanos and gurken mRNAs are some of the transcripts that display spatial localization and local translation. They are targeted to the anterior and posterior poles of the embryo to establish a gradient that underlie the proper spatial patterning (Johnstone and Lasko, 2001). It is thought that mRNAs are recognized through cis-acting RNA elements (zip codes), which are mainly found in the untranslated regions (UTRs), primarily in the 3'-UTR (Andreassi and Riccio, 2009). These elements are variable in length and sequence (Bramham and Wells, 2007), and are believed to fold into distinct secondary structures that work as recognition platforms for trans-acting factors (RNA-binding proteins). As these elements have the capability of creating complex structures, the identification of motifs using computational predictions is very challenging. Neurons share similar mRNA localization mechanisms. Previous studies have shown the presence of axonal- and dendritic-targeting elements (DTEs) in neuronal mRNAs. A well-characterized example for a neuronal mRNA localization motif is the DTEs of the CaMKIIa mRNA. Although it has been shown that this mRNA is transported to dendrites and minimal sequences for targeting have been identified, the evidence from various groups is contradictory and it is still not clear what is the precise mechanism for localization (Mori et al., 2000; Blichenberg et al., 2001; Miller et al., 2002). Among the neuronal trans-acting factors, the protein ZBP1 is one of the best-known factors. ZBP1 binds the 3'-UTR of the β-actin mRNA (Zhang et al., 2001) and drives its localization to growth cones and dendrites (Eom et al., 2003; Lin and Holt, 2007). In addition, ZBP1 has been involved in activity-dependent trafficking to dendritic spines (Tiruchinapalli et al., 2003), in repressing the translation of mRNAs while they are transported and in activating local translation (Huttelmaier et al., 2005). Additional RNA-binding proteins that might have functions similar to ZBP1 are Staufen, fragile X mental retardation protein (FMRP) and hnRNP A2.

If local protein synthesis provides a source for the demand of AMPA receptors during synaptic plasticity, then the mRNAs for the different subunits must be localized to dendrites. Indeed, studies using high-resolution in situ hybridizations have shown that the mRNAs for GluR1 and...
GluR2 have been localized to dendrites and their localization is regulated by neuronal activity (Grooms et al., 2006). Supporting the idea that these mRNAs are locally translated into functional receptors, it has been shown that dendritically synthesized GluR1 and GluR2 can be inserted into synaptic sites in response to neuronal stimulation (Kacharmina et al., 2000), and the insertion is accompanied by an increase in the frequency or amplitude of minis (Smith et al., 2005; Sutton et al., 2006).

One question that arises from the studies showing that dendritic protein synthesis has an important function in decoding the different forms of synaptic plasticity is whether local translation responds in a stimulus and transcript-specific manner. It should be expected that under conditions that promote potentiation of synapses, the locally translated mRNAs will code for proteins related to enhancing NMDA and/or AMPA receptors function at the postsynaptic membrane. On the other hand, protocols that induce depression and/or AMPA receptors function at the postsynaptic membrane. On the other hand, protocols that induce depression will more probably lead to activation of the translation of mRNAs related to receptor internalization or negative regulation of receptor function. Martin and co-workers have recently shown that translation at synapses during long-term facilitation (LTF) in Aplysia is indeed transcript and stimulus specific (Wang et al., 2009). LTF is activated by the repeated application of the neurotransmitter serotonin to the cell body of a sensory neuron. In a sensory neuron–motor neuron culture system, a photoconvertible protein synthesis reporter harbouring the 5′- and 3′-UTR regions of the sensorin mRNA is locally translated when five pulses of serotonin (LTP inducer) were applied. The reporter’s local translation was dependent on the sensorin 5′-UTR and was activated when five pulses of serotonin are locally perfused, suggesting that local protein synthesis is input specific. The effects were stimulus specific in nature as local delivery of FMRFamide (LTD inducer) did not trigger local protein synthesis of the reporter. In addition, local translation was dependent on the sensorin 5′-UTR, as a mutant reporter that lacks that region is not competent for local translation. This study did not show, however, that the reporter harbouring both UTRs is localized through an active transport mechanism. It is possible that the sensorin 5′-UTR increases the stability of the reporter mRNA and stable transcripts reach synapses by simple diffusion. It remains to be determined which elements in the sensorin 5′-UTR bring specificity for LTF. Altogether, these findings support the idea that different patterns of activity stimulate discrete patterns of local protein synthesis that facilitate the induction of the suitable plasticity mechanisms.

Protein degradation

Remodelling of the synaptic proteome can also be accomplished by regulated protein degradation. For example, in the case that negative regulators of transmission are present at synapses during the induction of plasticity, selective protein degradation provides a mechanism to relieve inhibition and promote synaptic strengthening. Recent experiments have highlighted a function for the ubiquitin proteasome system (UPS) in synaptic plasticity (Ehlers, 2003; Patrick et al., 2003; Bingol and Schuman, 2006; Fonseca et al., 2006; Dong et al., 2008). The UPS comprises a group of enzymes that activate and then attach ubiquitin to lysine residues of specific substrates, a modification that triggers the subsequent degradation of the ubiquitylated protein by the 26S proteasome.

A link between the UPS and synaptic plasticity was initially described in LTP observed in Aplysia (Hegde et al., 1993). During LTF, activated PKA is translocated to the nucleus where it phosphorylates the transcription factor cAMP-response-element-binding (CREB) protein to promote the transcription of immediate early genes. One of the genes activated by CREB encodes a deubiquitylating enzyme that binds the proteasome and facilitates the degradation of more PKA regulatory subunits, thus promoting a boost in PKA activity and generating a regulatory loop between mRNA transcription, protein synthesis and protein degradation that ultimately leads to synaptic strengthening.

The UPS also modulates plasticity in the CNS. Early studies showed that bilateral infusion of lactacystin, a selective proteasome inhibitor, to the CA1 region of the rat hippocampus causes full retrograde amnesia for one-trial inhibitory avoidance learning when added 1–7 h after training (Lopez-Salon et al., 2001). Avoidance training also results in an increase in ubiquitination and proteasome proteolytic activity. It has been also shown that proteasome inhibitors affect LTP in the Schaeffer collateral-CA1 synapses (Lopez-Salon et al., 2001; Fonseca et al., 2006; Karpova et al., 2006; Dong et al., 2008).

The presence of the translation machinery in synapses implies that the UPS might locally monitor proper protein levels (Figure 1). Indeed, it has been shown that protein degradation through the UPS control proper synaptic balance by maintaining optimal protein levels, thus promoting functional equilibrium (Ehlers, 2003; Bingol and Schuman, 2006).

Evidence favouring the idea of synaptic proteasome activity comes from studies from different laboratories showing that components of the UPS are localized near synapses (Ehlers, 2003; Patrick et al., 2003). Both ubiquitin and the proteasome subunits are present in synapses and in postsynaptic density fractions (Ehlers, 2003; Patrick et al., 2003). In addition, blocking either polyubiquitination or proteasome activity prevents the agonist-induced internalization of glutamate receptors (Colledge et al., 2003), suggesting that the acute activation of GluRs leads to the regulation of ubiquitin conjugation system and the degradation of proteins required for receptor internalization. Another study showed the same manipulations that result in homeostatic synaptic plasticity that give rise to global changes in postsynaptic density protein content and signalling through the UPS (Ehlers, 2003). More recently, using GFP-based proteasome activity reporters, Patrick and co-workers found that proteasome activity is bidirectionally modulated by either blockade or increase of action potentials using TTX and bicuculline, respectively (Djakovic et al., 2009).

The dynamic recruitment of the proteasome to dendritic spines of hippocampal neurons has been also shown (Bingol and Schuman, 2006; Bingol et al., 2010). Depolarization of neurons or treatment with NMDA receptor agonist NMDA causes rapid redistribution of a GFP-tagged proteasome subunit (Rpt1) as well as the endogenous proteasome from dendritic shafts to synapses in an NMDA receptor-dependent manner. Moreover, a GFP-based proteasomal degradation reporter is locally degraded when NMDA is perfused to a dendritic segment, suggesting that synaptic stimulation leads to activation of the proteasome. These findings are comple-
mented by recent studies showing that CaMKIIα mediates the activity-dependent recruitment of proteasomes to dendritic spines (Bingol et al., 2010). The artificial tethering of CaMKIIα to the postsynaptic density leads to recruitment of the proteasome to dendritic spines in the absence of stimulation. Taken together, the above experiments suggest that protein synthesis together with degradation provide a general mechanism to fine-tune protein availability and receptor function in synapses and that extensive regulation of the neuronal proteome is critical for the long-lasting storage of information (Figure 1).

Several studies have suggested functions for both protein synthesis and degradation in plasticity. For example, treatment of cultured hippocampal neurons and hippocampal slices with (S)-3,5-dihydroxyphenylglycine (DHPG) results in increased levels of the activity-regulated cytoskeleton-associated protein (Arc/Arg3.1) (Park et al., 2008; Waung et al., 2008). Arc/Arg3.1 is a protein encoded by an immediate early gene, which has been shown to be involved in AMPA receptor trafficking (Chowdhury et al., 2006). Together with the endocytosis-related proteins dynamin and endophilin3, Arc/Arg3.1 accelerates endocytosis and reduces surface expression of GluR1. In support of a function for the Arc/Arg3.1–endophilin–dynamin complex in synaptic plasticity, ectopic expression of Arc/Arg3.1 in pyramidal neurons of area CA1 of organotypic hippocampal slice cultures results in a selective downregulation of AMPA receptors that mimics LTD (Rial Verde et al., 2006). In general, DHPG treatment triggers the synthesis of Arc/Arg3.1, MAP1B and STEP, which are proteins involved in AMPA receptor internalization to reduce the number of functional receptors in the postsynaptic membrane, thus, leading to synapse depression. On the other hand, Greenberg and co-workers recently showed that neuronal activity induces transcription of the ubiquitin ligase Ube3A and that Ube3A then regulates excitatory synapse development by controlling the degradation of Arc (Greer et al., 2010).

Proteins involved in regulating mRNA translation are also synthesized in response to agonists that can cause synaptic depression. For example, the elongation factor 1A (EF1A) and the ribosomal S6 protein are rapidly accumulated when hippocampal slices are treated with DHPG (Antion et al., 2008). As LTD is a protein synthesis-dependent form of synaptic plasticity, synthesis of proteins related to the translation machinery might help in enhancing the translation capacity of neurons to maintain a long-lasting response. Interestingly, Arc/Arg3.1, MAP1B and EF1A mRNAs are targets of the FMRP, an RNA-binding protein that is synthesized during mGLuR-LTD (Hou et al., 2006). The latter is surprising as FMRP has been shown to bind mRNAs to repress their translation (Laggerbauer et al., 2001; Li et al., 2001). Thus, it implies that upon mGLuR-LTD activation FMRP represses the translation of its bound mRNAs.

Interestingly, Klann and co-workers showed that the increase in FMRP is very transient and that its levels return to basal after 10 min of DHPG treatment. The UPS mediates the decrease in excess FMRP, supporting the idea that similar to LTP, mGluR-LTD is dependent not only on protein synthesis, but also on protein degradation. Indeed, perfusion of hippocampal slices with MG132 or lactacystin prevents the induction of mGluR-LTD in the Schaeffer collateral pathway. A simple explanation for this FMRP regulatory loop is that FMRP levels are regulated by activity to repress or relieve the translation of mRNAs important for mGluR-LTD. These findings further support the notion that the neuronal proteome is dynamically regulated to induce different forms of synaptic plasticity.

**Figure 1** Local protein synthesis and degradation in a hippocampal neuron. Protein concentration is given by the rate of synthesis and degradation in the different cellular compartments. (A) Cell body and (B, C) distal dendrites. Under steady state (B), the ribosomes and the proteasomes are mainly localized to the dendritic shaft. Activation of synapses leads to the recruitment of ribosomes and proteasomes to dendritic spines (C), where they cooperate to modulate the local proteome.
Recently, Kosik and colleagues found that MOV10, a homologue of the Drosophila DExD/H-box RNA helicase Armitage, is present at synapses and is rapidly degraded by the proteasome in an NMDAR-mediated activity-dependent manner (Banerjee et al., 2009). Interestingly, MOV10 has been shown to bind the proteins Ago1 and Ago2, two important catalytic components of the RNA-induced silencing complex (RISC), to mediate microRNA-guided RNA cleavage and gene silencing (Meister et al., 2005). The results from this study suggest that activity-induced changes in the structure of the RISC might cause the dissociation of MOV10 from the RISC, and these changes will lead to MOV10 degradation. The latter implies that MOV10 degradation will promote release of the RISC complex from localized mRNAs and will relieve miRNA-mediated translational repression. This study has major implications as it suggests that there exist multiple interrelated levels of local gene expression regulation that will ultimately lead to fine tuning of the synaptic proteome.

Coordination of local protein synthesis and degradation in non-neuronal systems
The tight level of regulation of gene products at synapses implies local interplay between the protein synthesis and the proteasome degradation machineries. That connection has been best studied in non-neuronal systems that exhibit temporal dynamics such as the cell cycle, circadian rhythm and the major histocompatibility complex (MHC) class I system (Johnson et al., 1984; Minshull et al., 1989; Princicotta et al., 2003). In the immune system, T cells have a critical function in protecting against intracellular pathogens by either killing infected cells or releasing cytokines that interfere with pathogen replication. This immunosurveillance is based on the recognition of MHC class I molecules harbouring oligopeptides derived from pathogen proteins. The source of these peptides is a cytosolic pool of proteins that are degraded by proteasomes (Rock and Goldberg, 1999). Interestingly, a subset of these peptides is generated shortly after protein synthesis (most likely as a result of the inability of proteins to achieve a functional state) (Schubert et al., 2000), suggesting that the ribosome and the proteasome might communicate during immunity to achieve efficient immunosurveillance.

The cyclins, proteins synthesized after fertilization of sea urchin eggs and degraded at specific points of the cell cycle, represent another excellent example of coordinated regulation by translation and degradation (Evans et al., 1983). The original discovery of cyclins was based on the observation that activation of eggs from different species of sea urchins led to qualitative differences in global protein synthesis. Although the general trend was an increase in protein synthesis, several proteins showed distinct characteristics, as they were degraded every time the embryo divided. It is now known that cyclins are important regulators of the cell cycle and that periodic patterns of protein synthesis and degradation control cell division.

The circadian rhythm in the dinoflagellate alga Gonyaulax polyedra also controls changes in the turnover (synthesis and degradation) of enzymes critical for rhythmic activity (Johnson et al., 1984). Specifically, luciferase enzyme expression and activity in cells maintained in a 12 h light:12 h dark cycle showed rhythmicity, suggesting that luciferase functionality was controlled by patterns of protein synthesis and degradation triggered by the circadian rhythm. Thus, the pathways controlling protein metabolism in the cell coexist as counterbalancing mechanisms to keep tight regulation of the proteome and proper cell function.

Studies in neurons suggest a strong correlation between protein metabolic and catabolic processes; however, none has shown a direct link between the ribosome and the proteasome. Interestingly, a recent study showed that the eukaryotic translation initiation factor 3 (eIF3) assembles into a large supercomplex, which contains translation elongation factors, tRNA synthetases, proteins from the small and large ribosomal subunits, chaperones and the proteasome (Sha et al., 2009). This association supports the idea that factors involved in protein synthesis and degradation are physically linked to maintain optimal protein levels in cells. In addition, eIF3 complexes and the so-called COP9/signalosome, an evolutionary conserved macromolecular complex that regulates a specific class of ubiquitin ligases, share different subunits (Luke-Glaser et al., 2007), suggesting a link between the two macromolecular complexes. It is thus possible to posit that similar complexes and interactions may function to optimize protein composition at synapses. It is becoming increasingly clear that many neurological disorders are disorders of synaptic transmission (e.g. Alzheimer’s disease and Fragile X syndrome). It, therefore, seems quite likely that local control at synapses will be an important regulatory point for both normal and abnormal synaptic function. Interestingly, the COP9/signalosome has been localized to dendrites and has been involved in neurodegenerative diseases such as Smith–Magenis syndrome, Down’s syndrome, Alzheimer’s disease, Parkinson’s disease, Machado–Joseph disease and X-linked mental retardation syndrome (Elsea et al., 1999; Tarpey et al., 2007; Zou et al., 2007; Djagaeva and Doronkin, 2009).

Future perspectives
The results described here support the idea that protein homeostasis is a common regulatory motif for different forms of synaptic plasticity. It is also clear that mechanisms of local control have a paramount function in facilitating the implementation of changes in synaptic strength. However, as contemporary cell and molecular biology is mainly studied using reductionist approaches, there is lack of knowledge about the full complement of proteins that undergo regulation in response to the different plasticity paradigms. Systematic studies designed to identify ‘plasticity proteins’ that undergo synthesis and degradation during the different synaptic plasticity mechanisms will definitely aid in understanding how are the spatial and temporal dynamics of biochemical events controlling synapses.

There are several questions regarding mechanisms of local control that remain unanswered. For example, it is not known whether the machineries that mediate local protein synthesis (ribosomes) and degradation (proteasomes) harbour unique characteristics compared with the ones in the cell body. Is the efficiency of protein synthesis and protein degradation similar in the different neuronal compartments? It is also not known what is the code (if there is one) for dendritic mRNA localization. In addition, the possibility that locally synthesized proteins have distinct motifs compared with their counterparts in the cell body remains unexplored. Lastly,
even though it is well established that protein synthesis is required for many forms of synaptic plasticity, mRNA translation is not a straightforward process, in part because the intrinsic properties of RNA make it a very unstable molecule. That together with the fact that mRNAs travel relatively long distances in dendrites poses the question of whether stabilization of locally translated mRNAs is also a point of regulation during synaptic plasticity. The development of new technologies will definitely help to answer all of these questions.

Conflict of interest

The authors declare that they have no conflict of interest.


