

POSTER PRESENTATION

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# An improved translational switch for long term maintenance of synaptic plasticity

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Memory lasts a lifetime, yet the physiological substrate of memory, synaptic contacts, are composed of proteins that have much shorter lifetimes. A physiological analog of memory formation, long-term potentiation (LTP), has a late protein synthesis dependent phase (L-LTP) that can last for many hours in slices, or even days in vivo [1,2]. Our previous studies show that maintenance of L-LTP and memory can be accounted by persistent regulation of on-site synthesis of plasticity-related proteins by a self-sustaining regulation of translation. It has been shown that a  $\alpha$ CaMKII-CPEB1 molecular pair can act as a bistable switch with different total amounts of  $\alpha$ CaMKII in potentiated and non-potentiated synapses [3].

The molecular interaction model in our previous study comprised  $\alpha$ CaMKII which could be in an inactive, active and active and phosphorylated forms together with a translation regulating molecule CPEB1, which can be in an active or inactive form. The model included both degradation and new protein synthesis of  $\alpha$ CaMKII. We have shown that this model is bistable [3]. The bistability was caused by interaction of  $\text{Ca}^{2+}$ -Calmodulin dependent and auto-phosphorylation activation, spontaneous degradation and synthesis loops of  $\alpha$ CaMKII. This model could successfully account for maintenance of L-LTP over a long period of time and also proposes an explanation for why application of protein synthesis and  $\alpha$ CaMKII inhibitors at induction and maintenance phases of L-LTP result in very different outcomes [3-5]

However, the protein synthesis loop in our previous model was very simplistic. Here, we suggest a more detailed model of translation with explicit implementation of mRNA and poly-ribosome concentration in the

pre-synaptic spine. We assume that activated CPEB1 activates mRNA which then binds preferentially to poly-ribosome, as compared to a non-active mRNA, for  $\alpha$ CaMKII synthesis. We show that this system can act as a bistable switch. We also look at the behavior of this system at low poly-ribosome and mRNA concentration levels using stochastic simulations with Gillespie algorithm.

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