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An improved translational switch for long term maintenance of synaptic plasticity

Animesh Agarwal[1,2], Naveed Aslam[1], Harel Z Shouval[1,2*]

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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 αCaMKII-CPEB1 molecular pair can act as a bistable switch with different total amounts of αCaMKII in potentiated and non-potentiated synapses [3].

The molecular interaction model in our previous study comprised αCaMKII 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 αCaMKII. We have showen that this model is bistable [3]. The bistability was caused by interaction of Ca^{2+}-Calmodulin dependent and auto-phosphorylation activation, spontaneous degradation and synthesis loops of αCaMKII. 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 αCaMKII 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 CBEB1activates mRNA which then binds preferentially to poly-ribosome, as compared to a non-active mRNA, for αCaMKII 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.

Author details
[1]Department of Neurobiology & Anatomy, University of Texas Medical School, Houston, TX 77030, USA . [2]Department of Biomedical Engineering the University of Texas, Austin, TX 78712, USA.

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References

1. Bliss TV, Collingridge GL: **A synaptic model of memory: longterm potentiation in the hippocampus.** *Nature* 1993, **361**:31-39.
2. Feng TP: **The involvement of PKC and multifunctional CaM kinase II of the postsynaptic neuron in induction and maintenance of long-term potentiation.** *Prog Brain Res* 1995, **105**:55-63.
3. Naveed Aslam, Yoshi Kubota, David Wells, Shouval ZHarel: **Translational switch for long-term maintenance of synaptic plasticity.** *Molecular Systems Biology* 2009, **5**:284.
4. Otmakhov N, Griffith LC, Lisman JE: **Postsynaptic inhibitors of calcium/calmodulin-dependent protein kinase type II block induction but not maintenance of pairing-induced long-term potentiation.** *J Neurosci* 1997, **17**:5357-5365.
5. Sanhueza M, McIntyre CC, Lisman JE: **Reversal of synaptic memory by Ca2+/calmodulin-dependent protein kinase II inhibitor.** *J Neurosci* 2007, **27**:5190-5199.

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* Correspondence: harel.shouval@uth.tmc.edu
[1]Department of Neurobiology & Anatomy, University of Texas Medical School, Houston, TX 77030, USA