# A biophysically-based neuromorphic model of spike rate- and timing-dependent plasticity

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## AUTHOR SUMMARY

Learning and memory are emergent animal behaviors governed by modifications in neural activity in response to changing environments. Modification of neural activity is driven partly by changing the connection strength between neurons in a process called synaptic plasticity—the degree to which a presynaptic neuron can trigger a postsynaptic one to produce a nerve impulse—following the paired activation of the pre- and postsynaptic neurons. Two classic paradigms for inducing Hebbian synaptic plasticity (1) in the mammalian hippocampus (the region of the brain associated with memory formation) and the neocortex (the gray matter) are spike rate-dependent plasticity (SRDP), in which synaptic plasticity are determined by presynaptic firing rate; and spike-timing-dependent plasticity (STDP), in which the precise timing of pre- and postsynaptic activities determines the direction and strength of synaptic plasticity.

The two protocols differ in their information transfer capabilities, but mechanistically, the induction protocols of SRDP and STDP activate similar calcium-dependent processes that lead to (i) the induction of synaptic long-term potentiation (LTP) (the long-term enhancement of synaptic excitatory strength) or (ii) long-term depression (LTD). This common mechanistic link suggests a possible underlying interrelationship between these two seemingly distinct forms of Hebbian synaptic plasticity (2).

Previous modeling studies of SRDP and STDP were mostly based on numerical simulations of model equations on digital computers. Compared to digital computers, neuromorphic (or neuro-inspired) electronic circuits have an extremely small size and low power requirements for modeling the neural system at a large scale and performing simulations at a high speed. Here, we propose an analog very-large-scale-integrated (VLSI) circuit implementation of “learning synapse” that includes circuit model of an excitatory postsynaptic compartment in a hippocampal neuron, and produces both the SRDP and STDP rules for the induction of LTP and LTD.

The chip contains CMOS (complementary metal-oxide-semiconductor) building-block circuits biased in the subthreshold regime for modeling ionic signaling (iono-neuromorphic) as described previously (3). The circuits allow tremendous flexibility in emulating synapses from various brain structures by simply tuning a small (1–4) set of parameters. The learning-rule implementation underlying on-chip synaptic plasticity is an adaptation of a model proposed by Shouval et al. (4) that relies on calcium dynamics in the cell to determine synaptic plasticity. The iono-neuromorphic synapse design is biologically intuitive and allows the application of experimental manipulations to observe emergent behaviors. All simulations were in real biological time.

We tested the learning synapse circuit by using several well known induction protocols to draw direct comparisons with biological preparations. We showed that SRDP induction protocols reproduce the classical calcium-dependent plasticity. When we subjected the learning synapse to an STDP stimulation protocol, our results reproduced the LTD portion of the STDP window.

For LTD, the situation is much more complicated than for LTP. For the artificial synapse circuit with only the NMDA channel as a calcium source, STDP protocols did not display an abrupt transition in the calcium level around $\Delta t \sim 0$ (4). We therefore hypothesized a second coincidence detector may lie beyond the NMDA channel, as discussed in several recent papers. A second biological coincidence detector that accounts for postsynaptic LTD may be endogenous cannabinoid (endocannabinoid) molecules (5) (Fig. P1A). To account for possible coincident detection via retrograde signaling, we performed research; G.R. and C.-S.P. designed research; G.R. and C.-S.P. performed research; G.R. and C.-S.P. analyzed data; and G.R., H.Z.S., and C.-S.P. wrote the paper.

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designed a new artificial synapse model and included circuit models of cannabinoid receptor type 1, such that the coincident activation of cannabinoid receptors type 1 and presynaptic NMDA autoreceptors results in long-term reduction of neurotransmitter release. Fig. P1B shows several runs of the postpre STDP protocol and the resultant postsynaptic calcium signal.

The present work has important implications in understanding the mechanisms of STDP from the perspective of computational neuroscience. Our results support the notion that a second coincidence detector involving cannabinoid receptor type 1 may be involved in the full expression of the canonical STDP curve, as suggested in several brain systems.

Our results demonstrate successful implementation and testing of an iono-neuromorphic circuit model of both SRDP and STDP Hebbian learning algorithms on a miniature, low-power CMOS chip. Our combined use of analog iono-neuromorphic modeling of NMDAR-dependent synaptic and calcium dynamics in the cell and retrograde endocannabinoid signaling allows robust on-chip simulations of bidirectional LTP and LTD induction based on either the STDP or SRDP learning-rule. The proposed neurally inspired digital storage of synaptic weights for long-term maintenance of LTP and LTD emulating the insertion and removal of AMPA receptor channels in biologic neurons provides an optimal mixed-signal hardware environment for reliable real-time simulation of Hebbian synaptic plasticity using power-efficient and compact analog VLSI circuit technology. Such neurotechnological advances provide a new dimension for understanding how the brain works and for transitioning this knowledge to practical applications, such as brain-machine interface, machine learning, and neural-inspired adaptive control problems.

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