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Simulation of Spike Timing Dependent Plasticity Induced By Spike Triplets with Stochastic Transmitter Release

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Abstract

Experimental results indicate that synaptic plasticity produced by multi spike protocols cannot be accounted for by linear superposition of synaptic plasticity produced by spike pairs (Froemke and Dan, 2002; Wang et al., 2005). We have postulated that our previously published (Shouval et. al., 2002) plasticity model, together with realistic assumptions about cellular and synaptic dynamics such as paired pulse depression can account for these multi spike induction protocols. When applied to plasticity of layer 4 to layer 2/3 neurons of visual cortex the model preforms well, except for the post-pre-pre region in which the model predicts potentiation while the experimental results predict depression. Moreover, this qualified sucsess may not generalize well to synaptic pathways that exhibit paired pulse facilitation (e.g. hippocampal neurons).

Models previously applied for multi spike plasticity, while taking into account detailed properties of synaptic and cellular dynamics, do not take into account the stochastic nature of synaptic transmission. In the present work, we implemented stochastic transmitter release in the presynaptic neuron as well as the depletion of readily available neurotransmitter responsible for paired pulse depression. This stochastic model has average synaptic dynamics that are identical to the deterministic model. However, the stochastic model, by adandoning the simplified deterministic approximation, is able to replicate experimental data in all regions. We are currently applying thesed ideas to synapses that exhibit paired pulse facilitation as well.

Unified model for spike timing dependent plasticity

(Shouval et al., 2002)

1. The Ca control hypothesis

$$\dot{W} = \eta([Ca])\,(\Omega([Ca]) - \lambda W)$$

Low level, sustained increase in Ca results in depression; high level Ca results in potentiation.

2. The NMDA receptors are primary source of calcium.

3. The back propagating action potential (BPAP) which has a slow tail contributes to Ca current flow.

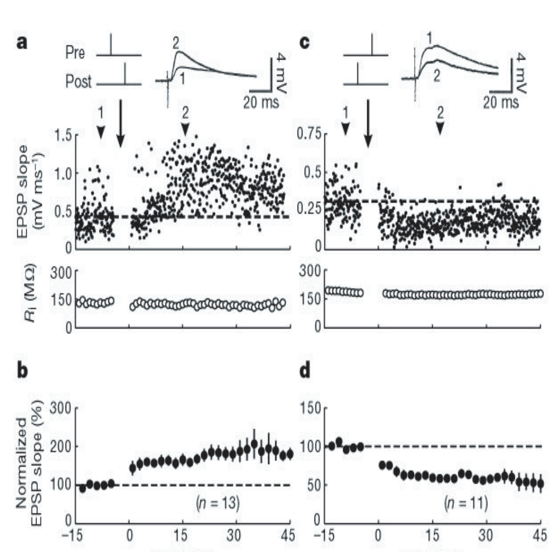


Fig. 1 Pre-post pair leads to potentiation, and post-pre pair leads to depression (Froemke and Dan, 2002.).

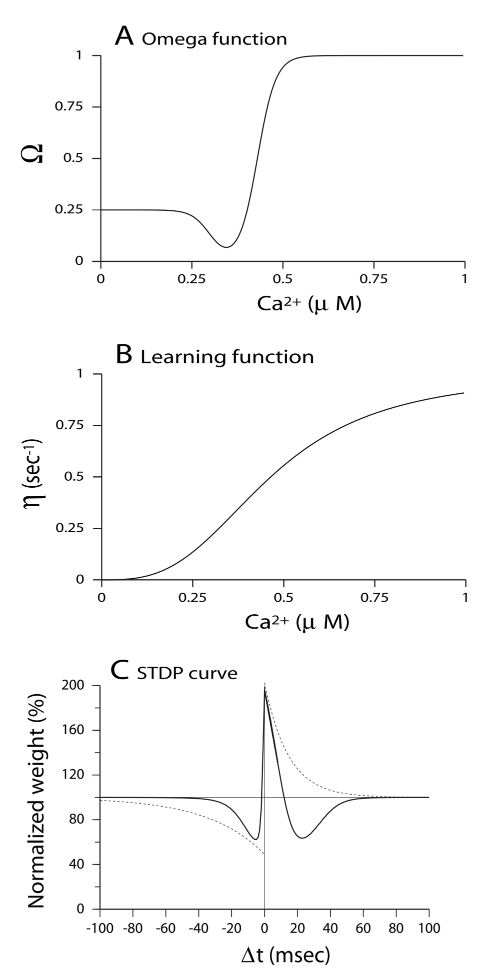


Fig. 2 The omega function (A) and learning function (B) implements the Ca control hypothesis. C. The resulting STDP curve, with dashed line indicating fit to Froemke and Dan (2002) data.

Plasticity induced by complex spike patterns

Pre-post or post-pre pairs are not interesting enough, as natural spike trains in cortical neurons are much more complex. Triplets and quadruplets mimic natural spike trains better.

However, both experimental data and computer simulation suggest that the response to spike triplets are not simple summations of reponses to spike pairs!

Two additional assumptions based on physiological data:

1. Depression and recovery of presynaptic vesicle release
2. Depression and recovery of back propagating action potential (BPAP)

Response to triplets: deterministic vs. stochastic

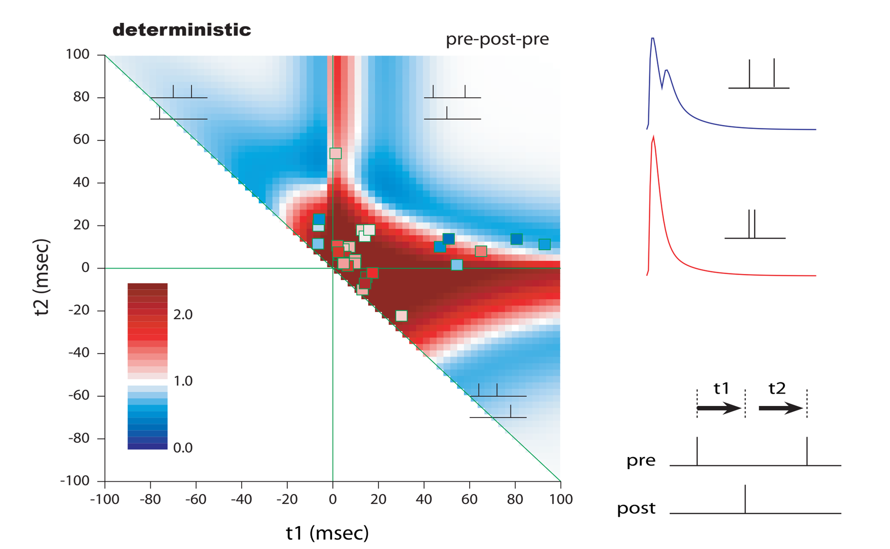
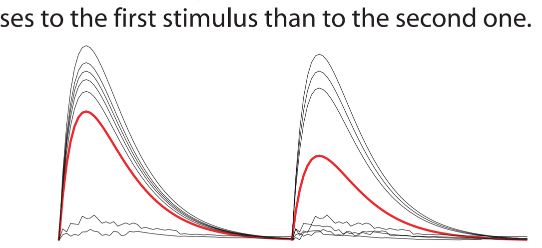


Fig.3 Responses of the deterministic version of the model. It does not fit experimental data for the post-pre-pre region. Insert at upper right shows the Ca transients at (-6, 12) and (-6, 90).

Why the deterministic model fails in the post-pre-pre region?

The deterministic model simulates the average behavior instead of what is actually happening. Take the example of paired pulse depression, the average EPSP size in response to the first stimulus is bigger than that to the second (Fig. 4, red) . However, what is really happening is that there are more successes to the first stimulus than to the second one.

Fig.4 Schematics demonstrating paired pulse depression.



Model with stochastic transmitter release fixes the post-pre-pre region

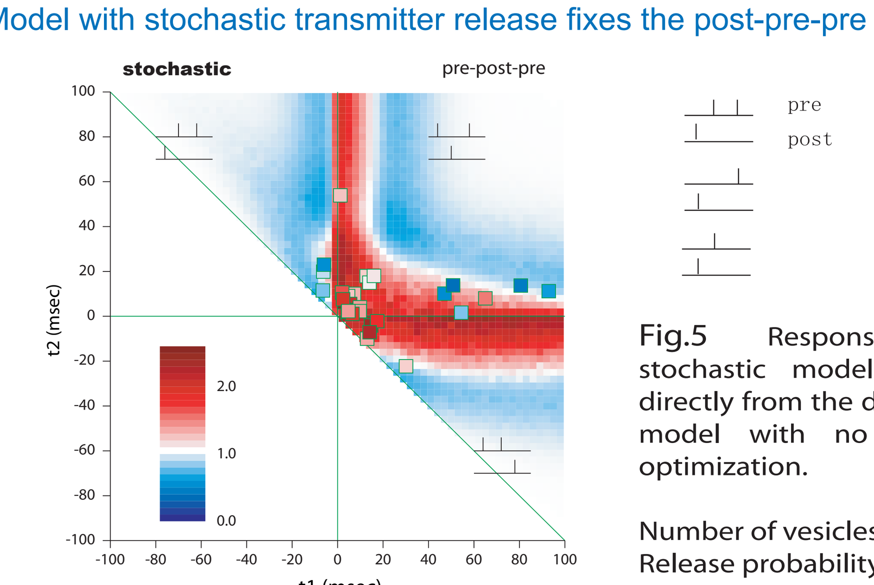


Fig.5 Responses of the stochastic model converted directly from the deterministic model with no parameter optimization.

Number of vesicles: 4

Release probability: 0.25

Comparison of Ca and weight changes in deterministic and stochastic models

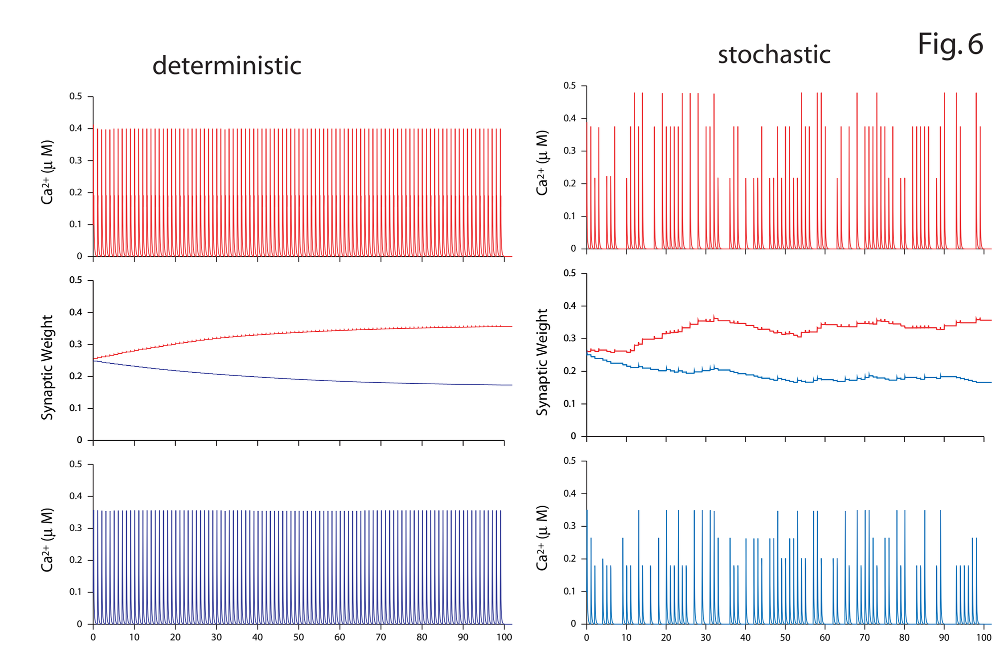


Fig.6

Summary of responses of stochastic model to triplets

We implemented stochastic synaptic release:

- Number of vesicles: 2
- Release probability for each vesicle: 0.3
- Probability of failure (no release): 0.49
- Stimulus frequency: 1 Hz

A single persynaptic vesicle release saturates postsynaptic NMDA receptors.

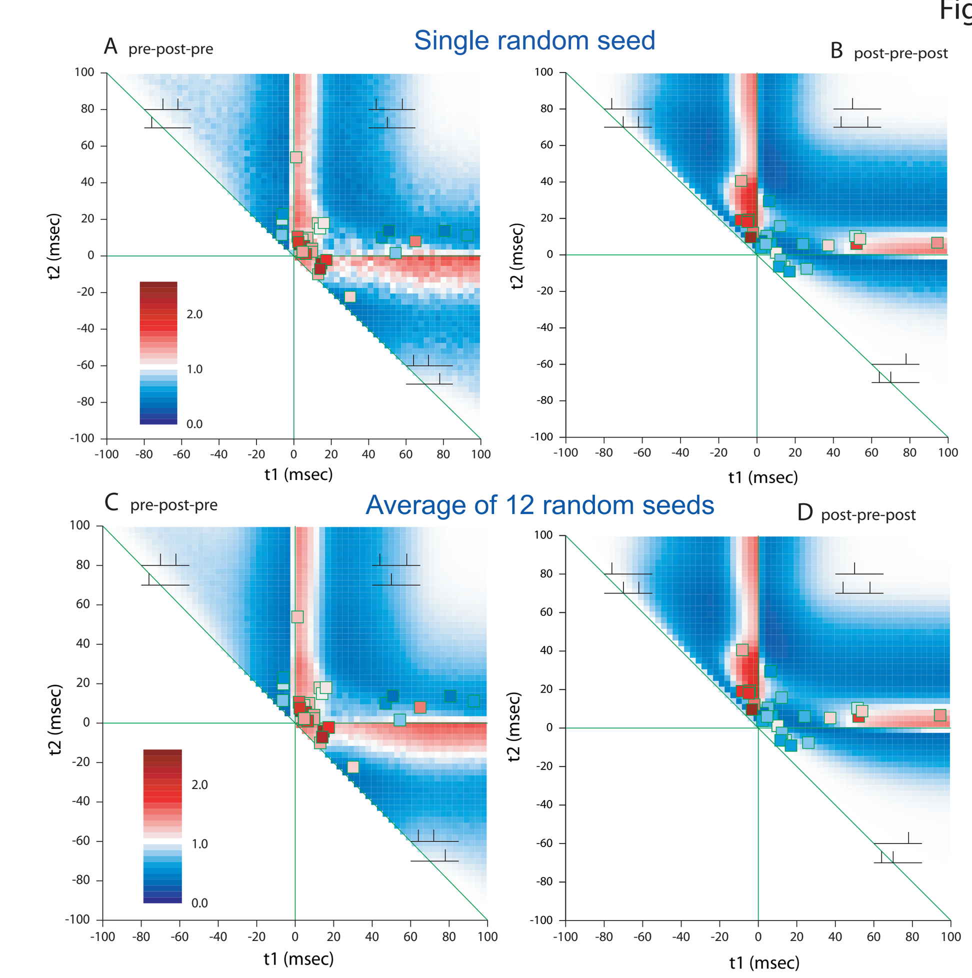
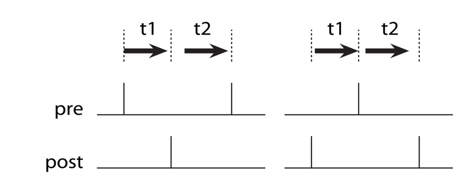
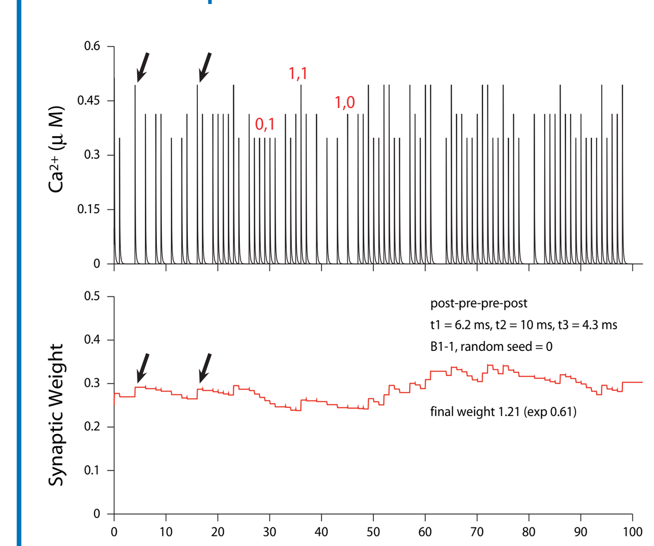


Fig. 7



Responses of stochastic model to quadruplets



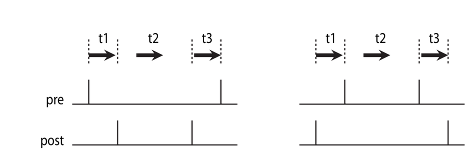


Fig. 8 When quadruplets were applied to the stochastic model optimized for triplets, the model generally showed potentiation for conditions that produced depression experimentally. That was because a few double releases (1,1 events, arrows) dominated. In the lower panel, we can see the corresponding jump in synaptic weight (arrows).

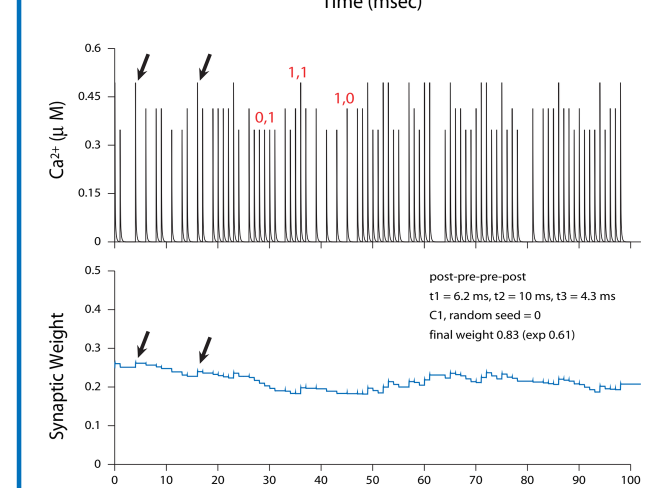


Fig. 9 After changes being made to the omega and learning functions to decrease the jump in synaptic weight and learning rate upon double releases, the model proformed well.

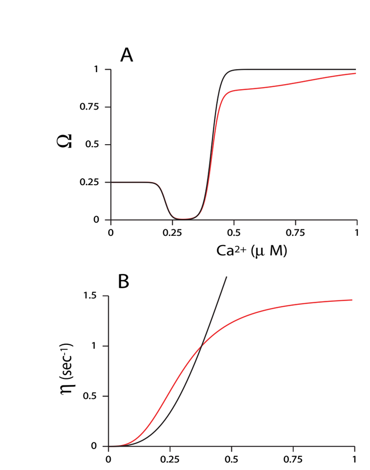


Fig. 10 Changes to the omega and learning functions (black: control).

Summary of quadruplet data

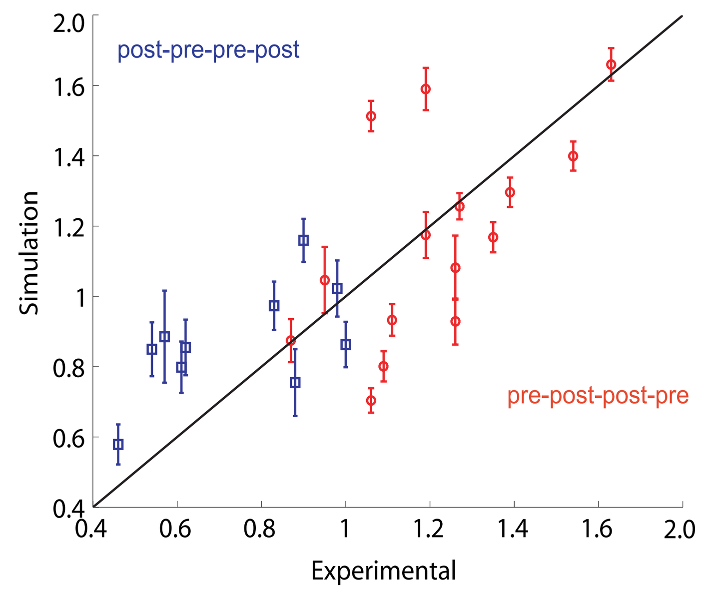
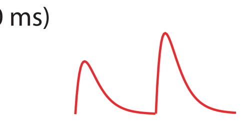


Fig.11 Comparison of normalized synaptic weights from computer simulation and experiment data obtained in visual cortex in responses to quadruplets. Experimental data courtesy of Froemke, Raad and Dan. The unity line represents exact match between experimental data and computer simulation.

Simulation of hippocampal data

Difference from visual cortex

1. LTP dominates in hippocampus (due to different mechanisms?)
2. Synaptic facilitation
3. Slower recovery from depression (time constant 1-2 s vs. ~100 ms)



Implementation

1. The same basic model of synaptic plasticity as used in the simulation of visual cortex data
2. Synaptic facilitation ($r = 0.8$, $\tau = 100$ ms)
3. Longer recovery time constant
4. Number of vesicles = 2, p0 = 0.19

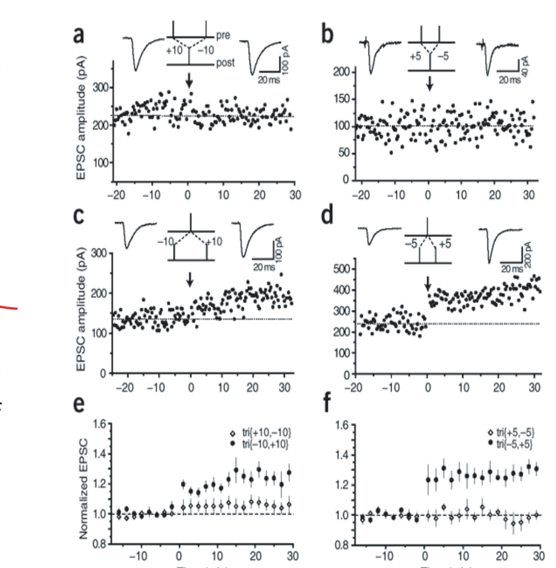


Fig. 12 Hippocampal data from Wang et. al, 2005

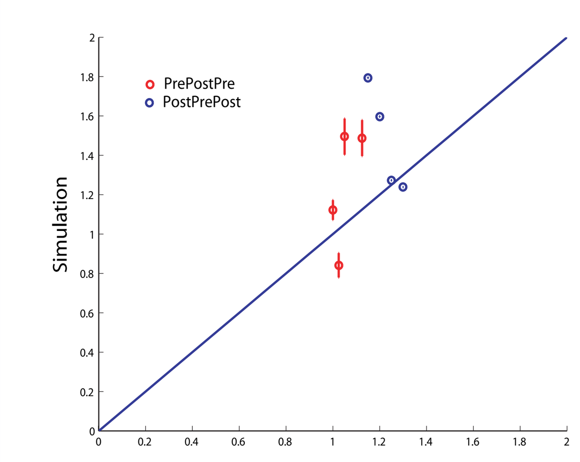


Fig. 13. Comparison of normalized synaptic weights from computer simulation and experiment data obtained in hippocampus in responses to spike triplets. Experimental data from Wang et. al (2005). The unity line represents exact match between experimental data and computer simulation.

Summary

1. Simulations for the triplet results are pretty robust with stochastic transmitter release.
2. Fine tuning of parameters is needed for quadruplets, suggesting that there may be elements that are not well understood played a role in the responses to quadruplets.
3. Difference in stochastic parameters may underlie the differences observed in visual cortex and hippocampus.

Acknowledgments

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