# Computational studies of the role of stochastic synaptic transmission in hippocampus (and cortex)

A. Buntaine[1], V. Hoang[1], N. Bhanpuri[1], J-M Fellous[1,2]

*1. Biomedical Engineering, Duke Univ., Durham, NC, 2. Psychology, Univ. of Arizona, Tucson, AZ.*

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## 1. Introduction

- Synaptic transmission at excitatory synapses in hippocampus and cortex is unreliable with as much as 4 failures to transmit for every 5 presynaptic action potentials.

- CA1 pyramidal cells fire however with a very high signal to noise ratio when a rat traverses its place field.

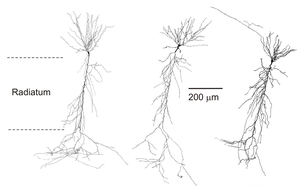
- We hypothesize that, given the nature of entorhinal and CA3 inputs, the stochastic properties of synaptic transmission to CA1 are tuned to facilitate reliable CA1 firing.

- We derive and tightly tune a model of stochastic transmission and test its behavior during simulated place field traversal.

## 2. Methods

All simulations performed with NEURON (dt=0.1 ms)

### Cells




Active Currents (soma)

$I_{Na^+}$, $I_{Kdr}$, $I_m$

Passive properties (dendrites)

$$R_m(d) = R_{end} + \frac{R_{soma} - R_{end}}{1 - e^{\frac{400-d}{50}}}$$

### Synapses

$$P_r(t) = 1 - e^{-F(t)/D(t)}$$

$$F(t) = F0 + \sum_{t_i<t} f(t - t_i) \qquad f(s) = \alpha e^{-s/\tau}$$

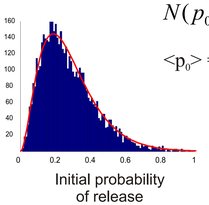
$$D(t) = D0 + \sum_{t_i<t, t_i \in S} d(t - t_i) \qquad d(s) = \beta e^{-s/\tau'}$$

{t}= presynaptic spike times, S= {t} when release occured.

The initial release probability $p_0$ is not uniform across hippocampal synapses, in the same cell, or across many cells (Huang and Stevens, 1997; Gandhi and Stevens, 2003; Murthy et al., 1997)

$$N(p_0) = {p_0}^2 e^{-\lambda p_0}$$

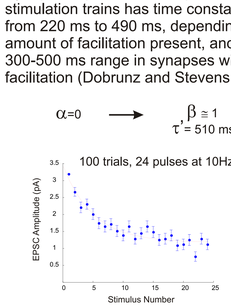
$$\langle p_0 \rangle = 0.28$$

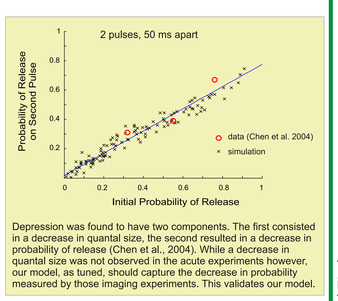



## 3. Constraining the model

### A. Depression.

Synaptic depression in response to 10Hz stimulation trains has time constants varying from 220 ms to 490 ms, depending on the amount of facilitation present, and is in the 300-500 ms range in synapses with no facilitation (Dobrunz and Stevens, 1997).



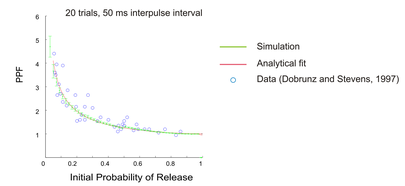




Depression was found to have two components. The first consisted in a decrease in quantal size, the second resulted in a decrease in probability of release (Chen et al., 2004). While a decrease in quantal size was not observed in the acute experiments however, our model, as tuned, should capture the decrease in probability measured by those imaging experiments. This validates our model.

### B. Facilitation.

Minimal stimulation (Dobrunz and Stevens, 1997) and imaging experiments (Murthy et al., 1997) demonstrated that the amount of paired pulse facilitation was inversely related to the initial release probability of a synapse. For both a 40 ms and a 50 ms interpulse interval, the probability of release on the second pulse $p_2$ is well described by:

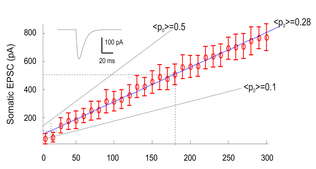
$$p_2 = 1 - (1 - p_0)^{\frac{1}{\sqrt{p_0}}}$$ → Solve analytically for α, τ is given by experimental data (120 ms)




### C. Synaptic Conductances.

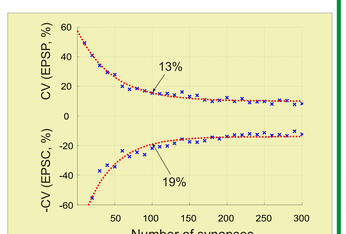
The EPSC amplitude when putative single synapses are stimulated was about 14 pA measured at the soma under voltage clamp at -60mV when inhibitory neurotransmission was blocked (Dobrunz et al., 1997; Dobrunz and Stevens, 1997) and is compatible with recordings from isolated synaptic boutton stimulation (Chen et al., 2004). A unitary synaptic conductance of **3 nS** yielded an average somatic EPSC size of 14.4 pA.

### D. How many synapses are recruited by Schaffer collaterals?




The EPSC typically measured at the soma after field stimulation of the Schaffer collaterals is about 100-500 pA in amplitude.

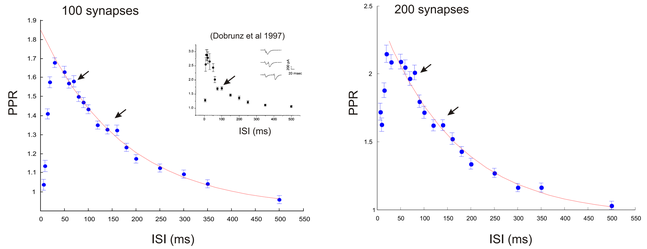
100-500 pA require **25-180 synapses**




Experimental data in vitro, with EPSCs measuring 204 ± 53 pA revealed EPSC variability of about 15.8% ± 3.4, and EPSP variability of about 13.7% ± 3 (Otmakhov et al., 1993). Using 100 synapses, the corresponding variability in our model was about 19%, and 13 % for EPSC and EPSPs respectively, compatible with the experimental findings. This validates our model.

## 4. Results

### A. Paired-pulse ratio: Preference for beta and theta frequencies.

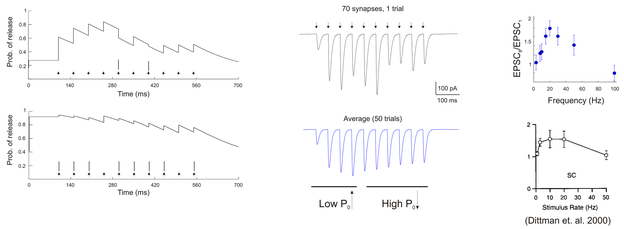




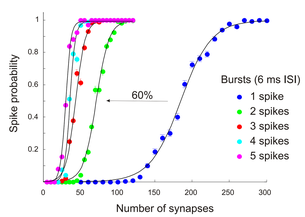


The model shows two 'shoulders' at 70-80 ms (beta range) and at 140-180 ms, ( theta range) inter-pulse intervals. The first is also apparent in the data (Sun et al., 2005; Dobrunz et al., 1997). This shoulder is due in part to a change in the balance between facilitation and depression.

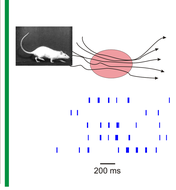
### B. During trains of field stimulation, facilitation is due to an increase in release probability of low $P_0$ synapses, and depression is due to a decrease of the release probability of high $P_0$ synapses.

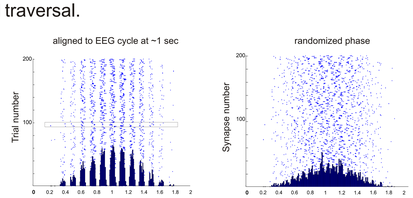



### C. Bursts reduce the need for the recruitment of synapses by at least 60%.




Simulation of place field traversal.



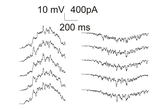





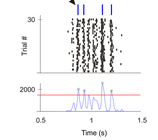


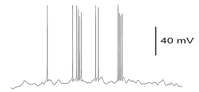
### D. Emergence of attractors

a. Different presynaptic patterns produce different postsynaptic attractors.

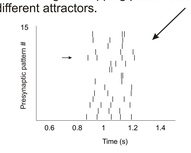


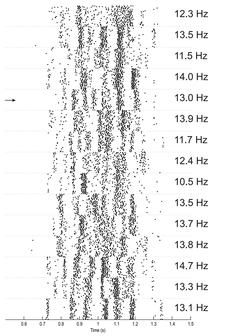

An attractor is defined as a reliable spike pattern.



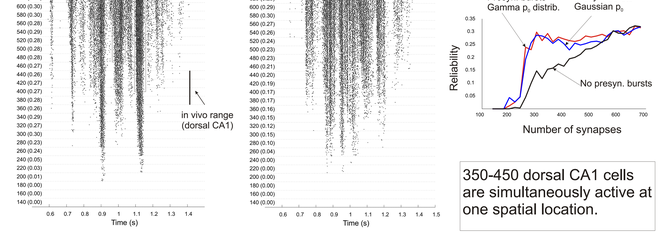




Different presynaptic patterns coming from the same distribution (i.e. from different cells having overlapping place fields) yield different attractors.




b. Desynchronized presynaptic bursts yield reliable postsynaptic bursts.




350-450 dorsal CA1 cells are simultaneously active at one spatial location.

## 5. Conclusions

- We proposed a new model of stochastic synaptic transmission. The model was constrained and validated using experimental data.

- The dynamics of synaptic transmission at a single synapse favored beta and theta presynaptic frequencies.

- High probability synapses carried the beginning of an afferent volley, while low probability carried the later stages.

- Presynaptic bursts allowed for sparse presynaptic patterns. There was no significant advantages for bursts longer than 3 spikes.

- Seemingly random presynaptic spike trains yielded stable postsynaptic attractors. The number and stability of the attractors depended on the dynamics of synaptic transmission and on the presence of presynaptic bursts.

## 6. References

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