Emergence of Reliable Spike Patterns in Models of CA1 Cells Contacted by Unreliable Synapses

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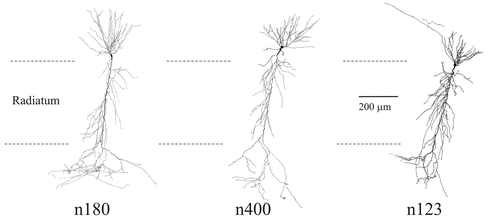
INTRODUCTION

- The firing of CA1 neurons during place field traversal is elicited at specific phases of EEG theta cycle with a high degree of precision.
- Excitatory synapses onto CA1 pyramidal cells are unreliable and may fail about 80% of the time. How can a CA1 cell fire precisely with such unreliable synapses?
- We hypothesize that the precision of postsynaptic firing depends on various characteristics of the presynaptic trains, such as their Gaussian profile, their theta modulation and the presence of bursts.

METHODS

Simulations were performed using NEURON in 3 multi-compartmental reconstructed CA1 cells with passive dendritic trees.



A use-dependent model of stochastic synaptic transmission is implemented.

The probability of release of a single synapse was given by:

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

Where F and D were time dependent variables representing facilitation and depression:

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

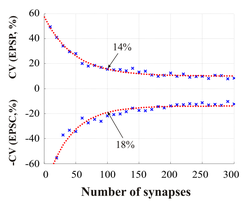
$$D(t) = D0 + \sum_{t_i<t,\, t_i\in S} d(t-t_i) \qquad d(s) = \beta e^{-s/\tau'}$$

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

- τ = 120 ms τ'= 2.5 s to match experimental data (Dobrunz et. al., 1997; Dobrunz and Stevens 1997). The values for α and β were adjusted on the basis of PPF data (Dobrunz and Stevens 1997).

- For each arriving spike, a probability of release $P_r(t)$ was calculated based on the presynaptic spike history. A random number (uniform distribution) was drawn. If the random number was smaller than $P_r(t)$, an EPSC was generated. Facilitation occurred regardless of release, depression only occurred if there was release.

The model reproduces the variability of somatic EPSP and EPSC amplitudes.

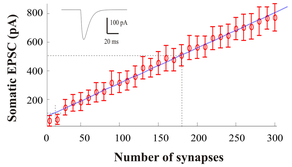


For about 100 synapses, the modeled cells showed an average CV of about 18% for ESPCs and 14% for EPSPs, close to experimental data {EPSCs 15.8% ±3.4, EPSPs 13.7% ± 3 (Otmakhov et. al. 1993)}.

RESULTS

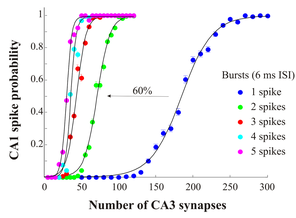
The model predicts the number of synapses recruited in vitro.

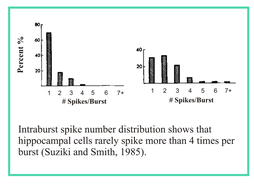
All 3 cells required at least 25 and up to 180 synapses to yield a 100-500 pA somatic EPSC amplitude.



More than 3 spikes per burst in CA3 inputs are unnecessary to elicit postsynaptic CA1 spiking.

In all cells, CA3 bursts of 2-3 spikes required about 60% less synapses than single spikes to elicit the same CA1 spiking probability. There was relatively little gained by having more than 4 spikes per burst.

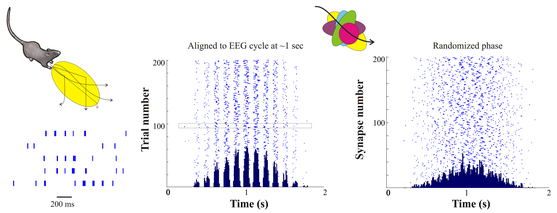




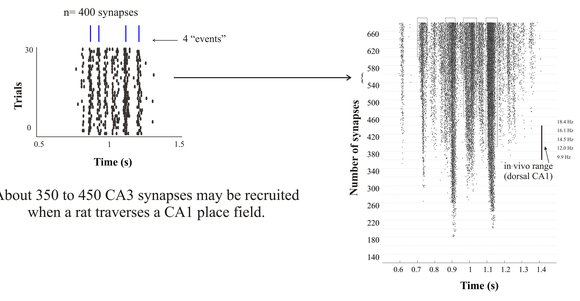
Intraburst spike number distribution shows that hippocampal cells rarely spike more than 4 times per burst (Suziki and Smith, 1985).

Reconstructed CA1 cells generate reliable spike patterns in response to simulated CA3 presynaptic trains.

- Inputs to CA1 cells were simulated by generating theta modulated presynaptic CA3 spike trains that contained bursts of 1-4 spikes. The phase of EEG theta was randomized to simulate the activity of simultaneously recorded CA3 cells with overlapping place fields.



- CA3 spike trains yielded reliable CA1 firing.

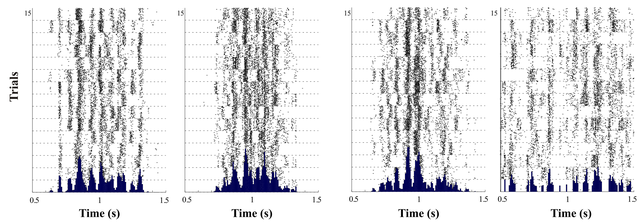


About 350 to 450 CA3 synapses may be recruited when a rat traverses a CA1 place field.

The emergence of reliable spike patterns depends on the Gaussian profile of the CA3 inputs, their theta modulation, and their bursts.

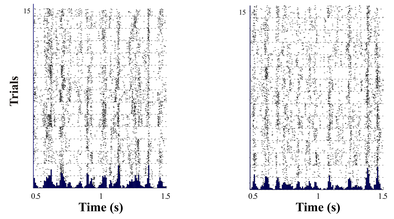
Removing the Gaussian profile, theta modulation or bursts individually had little effect on the emergence of spike patterns.

	Control	No bursts	No theta	No Gaussian
Average firing rate:	17. 55 Hz	16.10 Hz	15.41 Hz	21.18 Hz
Number of synapses:	260	440	260	480



However there are was a substantial decrease in alignments if combinations of presynaptic train characteristics were removed.

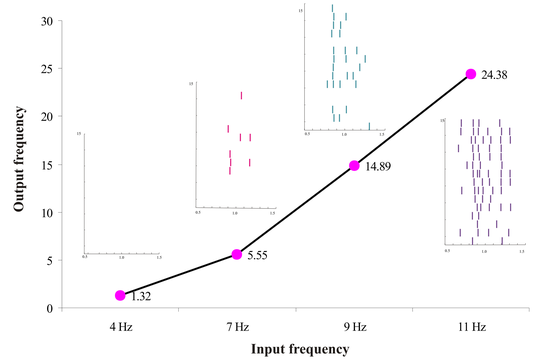
	No Gaussian, no theta	No Gaussian, no theta, no bursts
Average firing rate:	19.01 Hz	16.05 Hz
Number of synapses:	500	520



Different input frequencies yield different spike patterns.

Changes in CA3 input frequency generated drastic changes in output frequency.

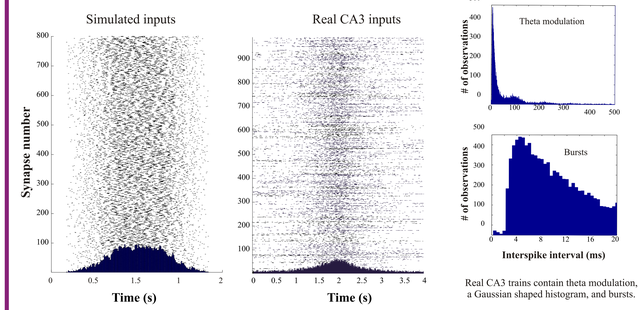
Changes in CA3 input frequency also yielded different number of events.



Leutgeb et. al. (2005) have shown that if selective cues are changed in the rat's environment there is a change in the firing frequencies but not in the spatial locations of place fields in both CA3 and Ca1. This phenomenon is termed 'rate remapping'.

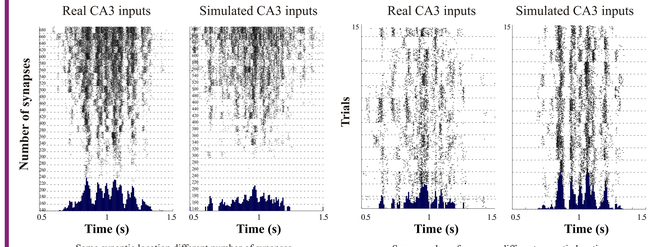
Reconstructed CA1 cells also generate spike patterns in response to real CA3 inputs.

Real CA3 spike trains were obtained from 26 different CA3 cells recorded simultaneously in a freely moving rat (Leutgeb et. al., 2005). The place fields for all the cells were aligned in order to simulate overlapping place fields.



Real CA3 trains contain theta modulation, a Gaussian shaped histogram, and bursts.

The outputs generated by the simulated CA3 inputs resemble those obtained form the real CA3 data.



Same synaptic location different number of synapses

Same number of synapses different synaptic location

CONCLUSIONS

- We use a stochastic model of excitatory synaptic transmission between CA3 and CA1 to show that bursts of more than 3 spikes are unnecessary for reliable postsynaptic firing.
- Actual or simulated CA3 presynaptic spike trains yield reliable CA1 postsynaptic spike patterns with theta frequency content.
- The number and temporal structure of the patterns depend on the presence of bursts, theta modulation and on the Gaussian profile of the CA3 presynaptic spike trains.
- Changes in the presynaptic input frequency yield changes in both the postsynaptic firing rates and the number of reliable events. This phenomenon could be at play during "rate remapping" (Leutgeb et. al., 2005).

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ACKNOWLEDGMENTS

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