Summary

• We present experimental evidence for **three** cholinergically-induced oscillatory regimes in the hippocampal slice. Frequencies are within the 'delta' **(.5-2Hz)**, 'theta' **(5-10Hz)** and 'gamma' **(40-70Hz)** bands, and depend on the concentration of the neuromodulator (carbachol) applied.

• CCH-theta and CCH-delta are initiated in CA3 and depend essentially on AMPA receptor activation.

• CCH-theta involves the synchronous firing of CA3 pyramidal cells, at most once per cycle, while the majority of CA3 interneurons fire tonically (at theta) in a non-synchronized manner.

Summary

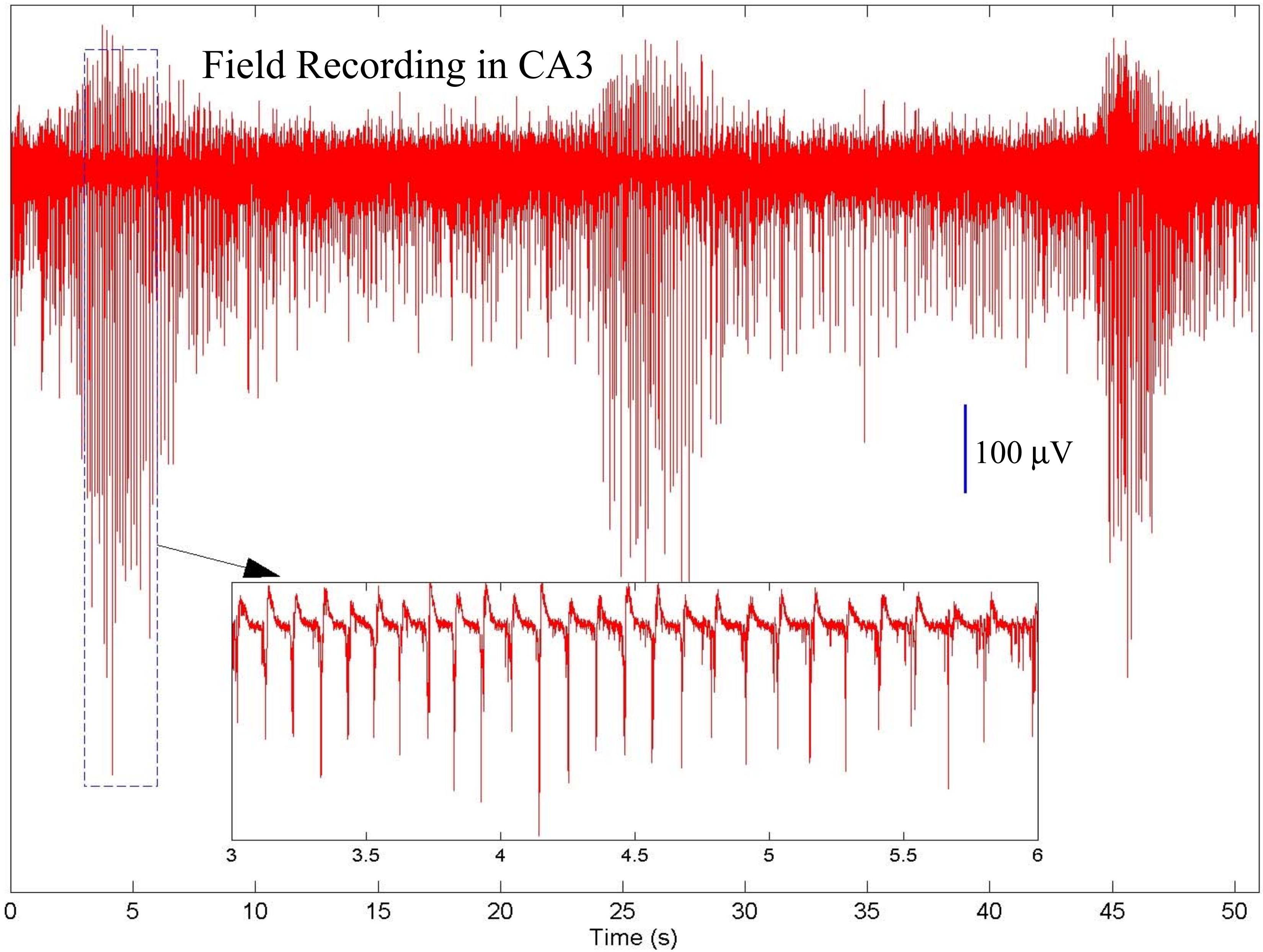
- Low concentrations of neuromodulator result in CCH-delta; large CA3 regular population discharges that entrain CA1.

- APV (10 µM) reversibly turns the CA1 CCH-theta rhythm into CCH-delta.

- At medium concentrations, repeated stimulation of the Schaeffer collaterals result in CCH-gamma ripples in CA1. Spontaneous CCH-gamma epochs may occur in isolation, or combined with CCH-theta and CCH-delta rhythms.

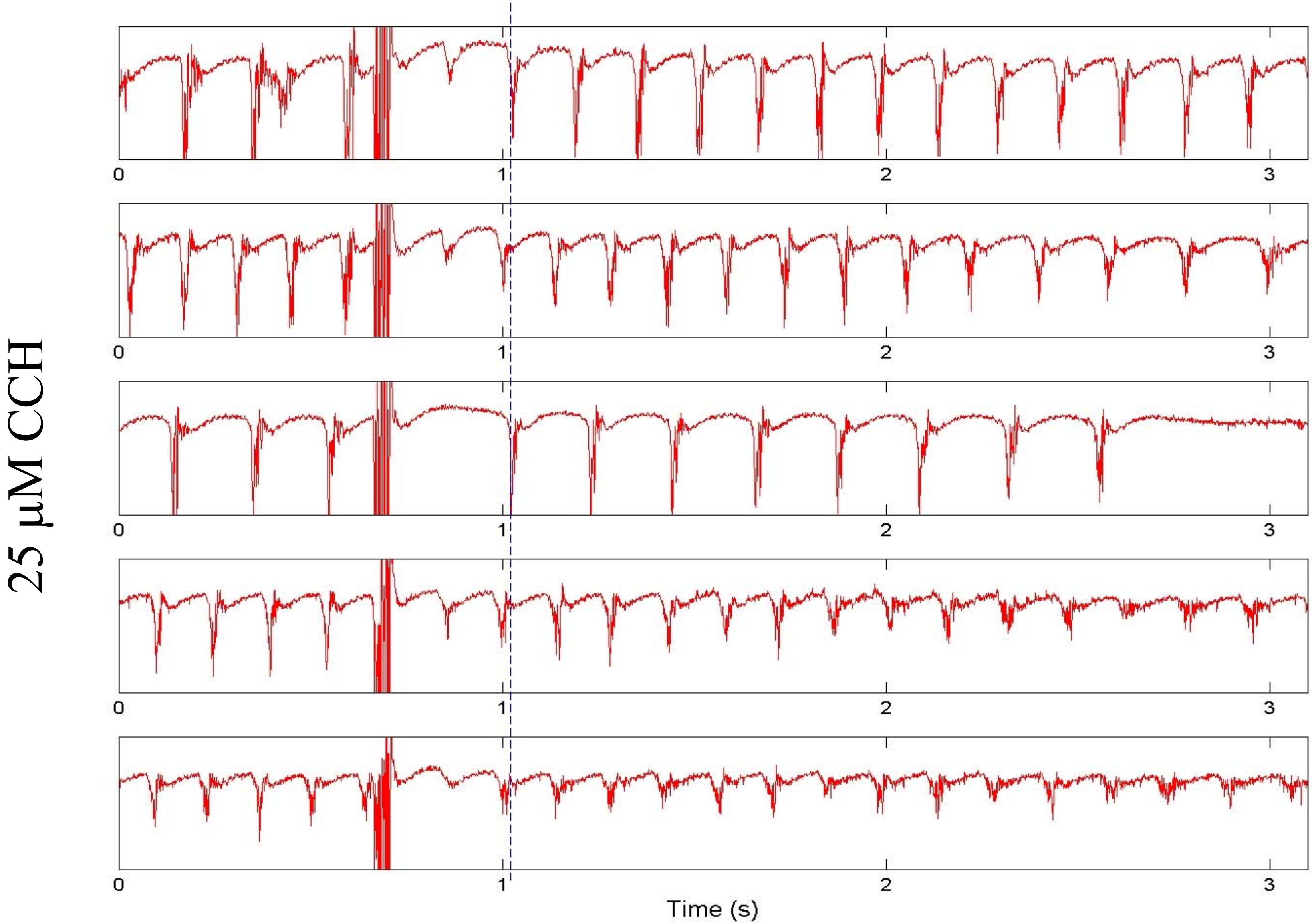
- CCH-theta and CCH-delta are present simultaneously in the longitudinal CA3 slice.

25 µM: CCH-Theta

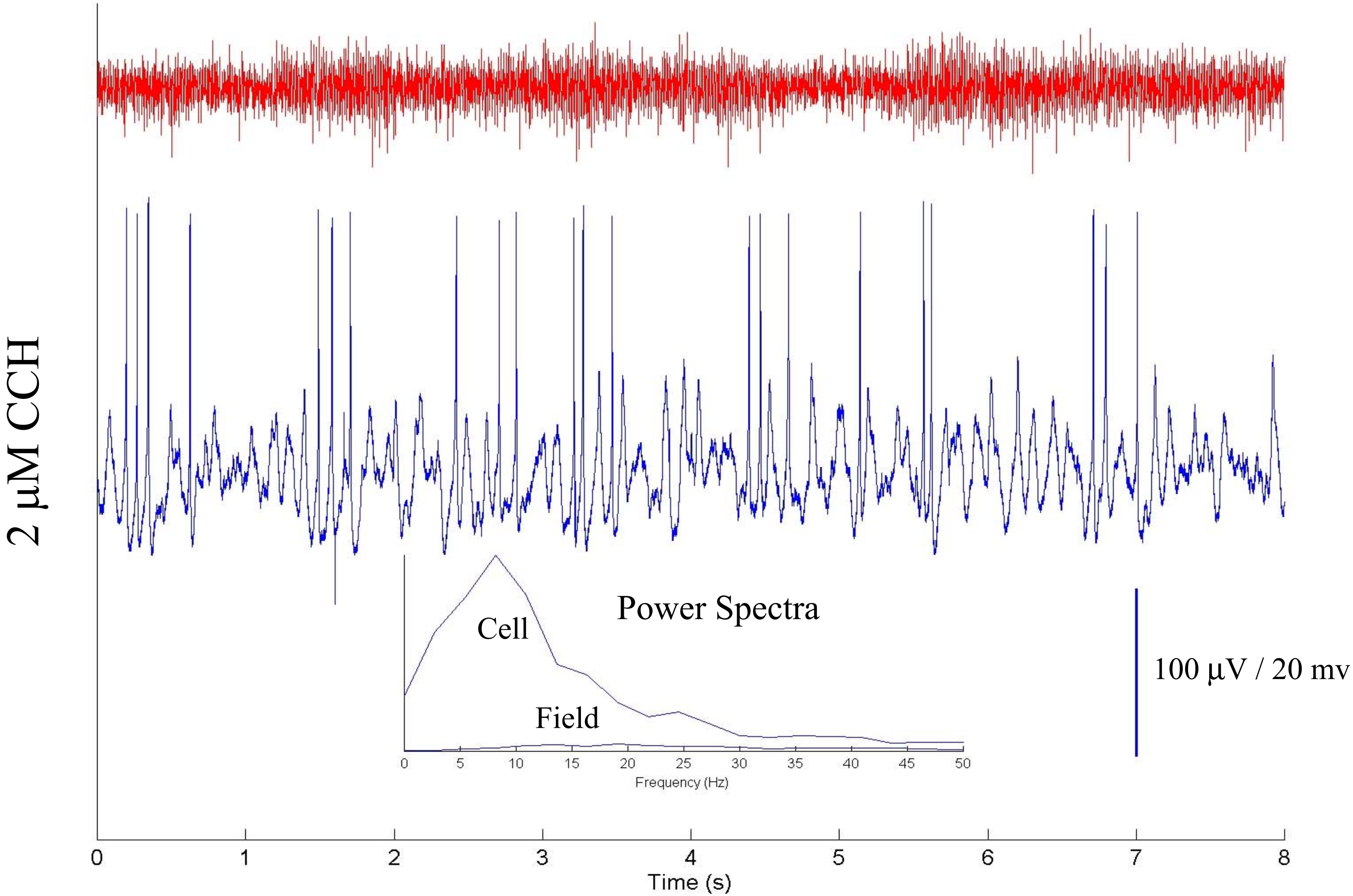


Theta Reset

Schaeffer stimulation resets ongoing theta episodes.

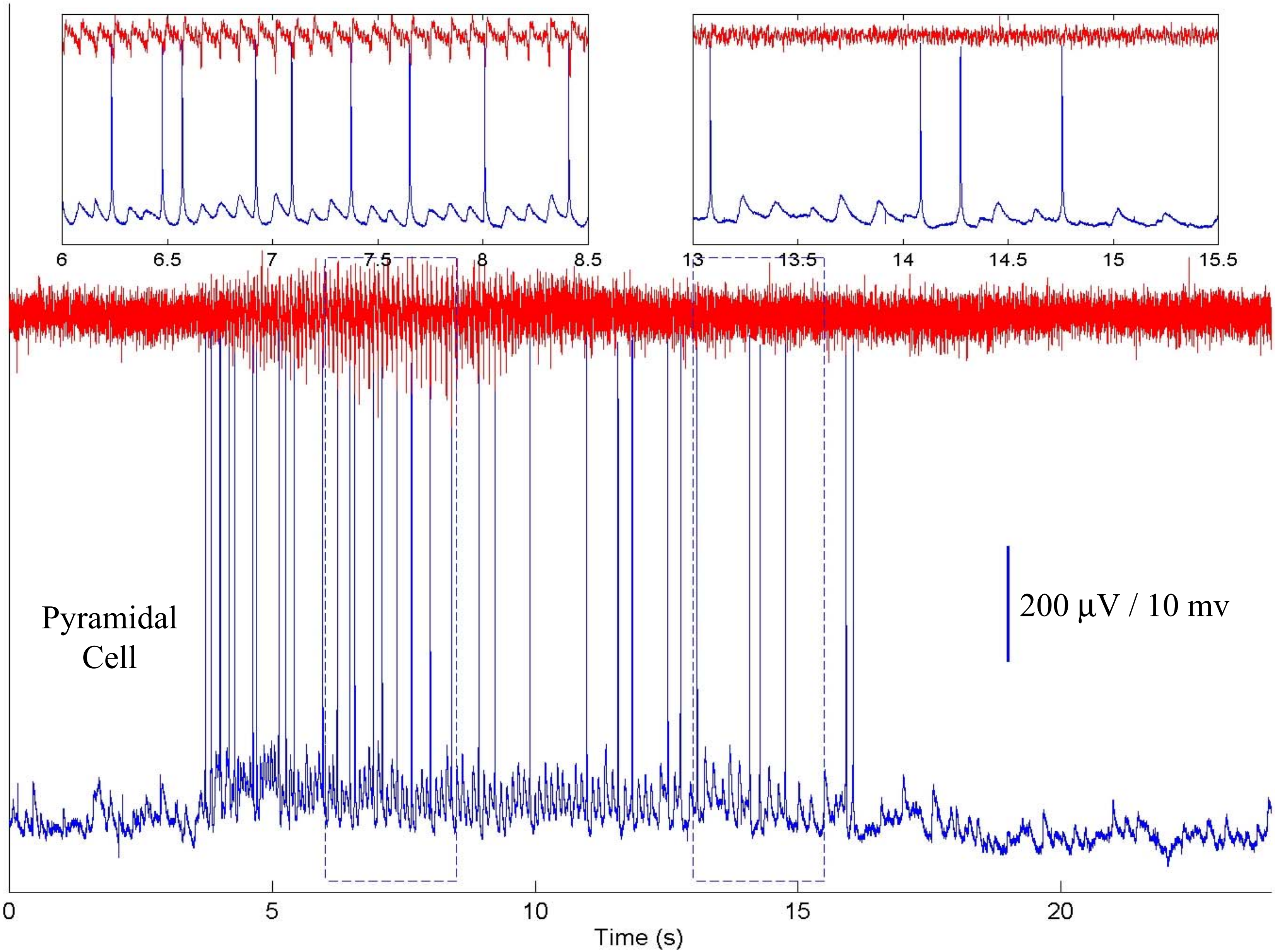


Subthreshold CCH-theta in CA3 at low CCH



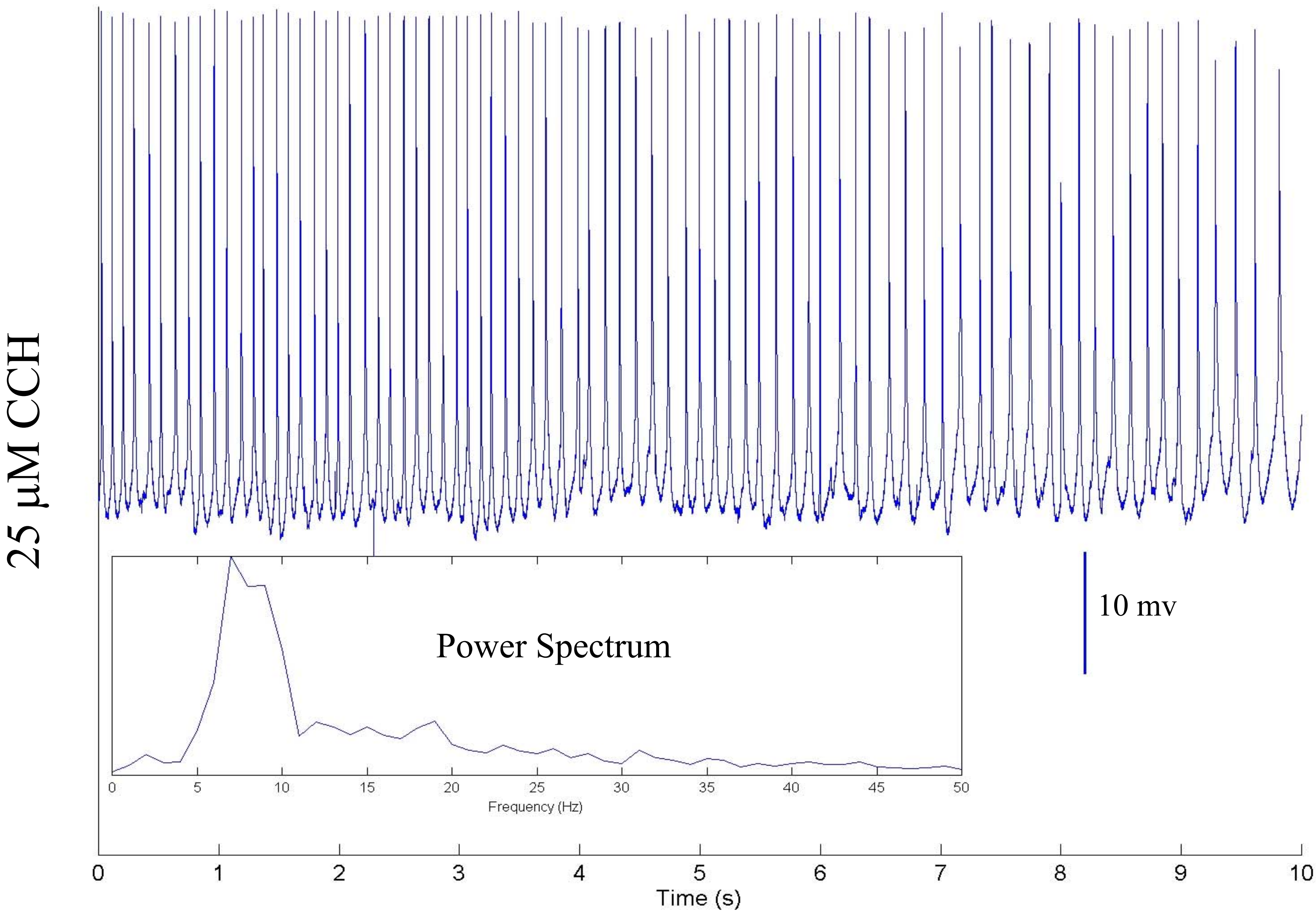
Synchronous CA3 discharges at high CCH

25 μM CCH



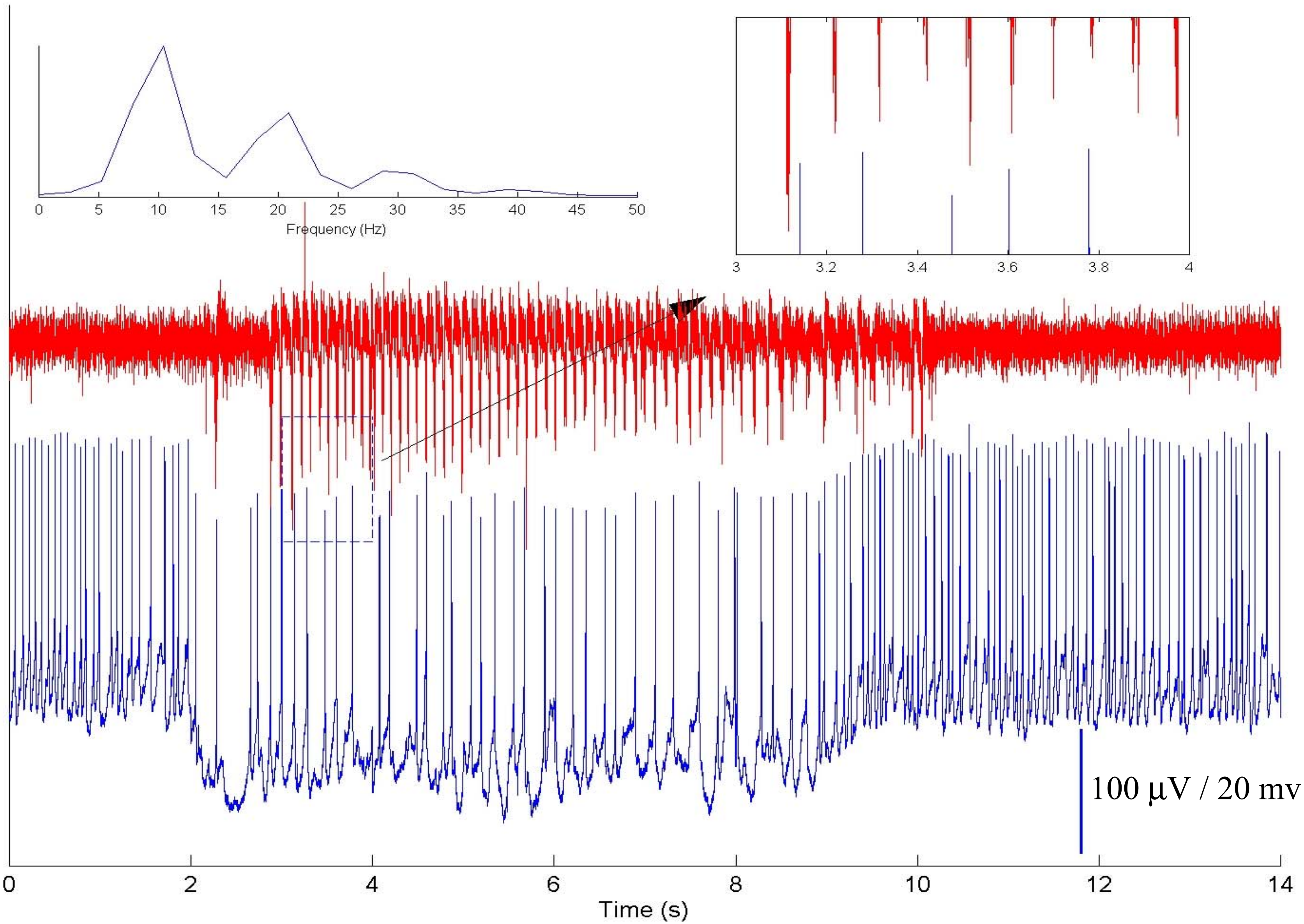
(MacVicar and Tse, 1989)

Some CA3 interneurons are tonically active



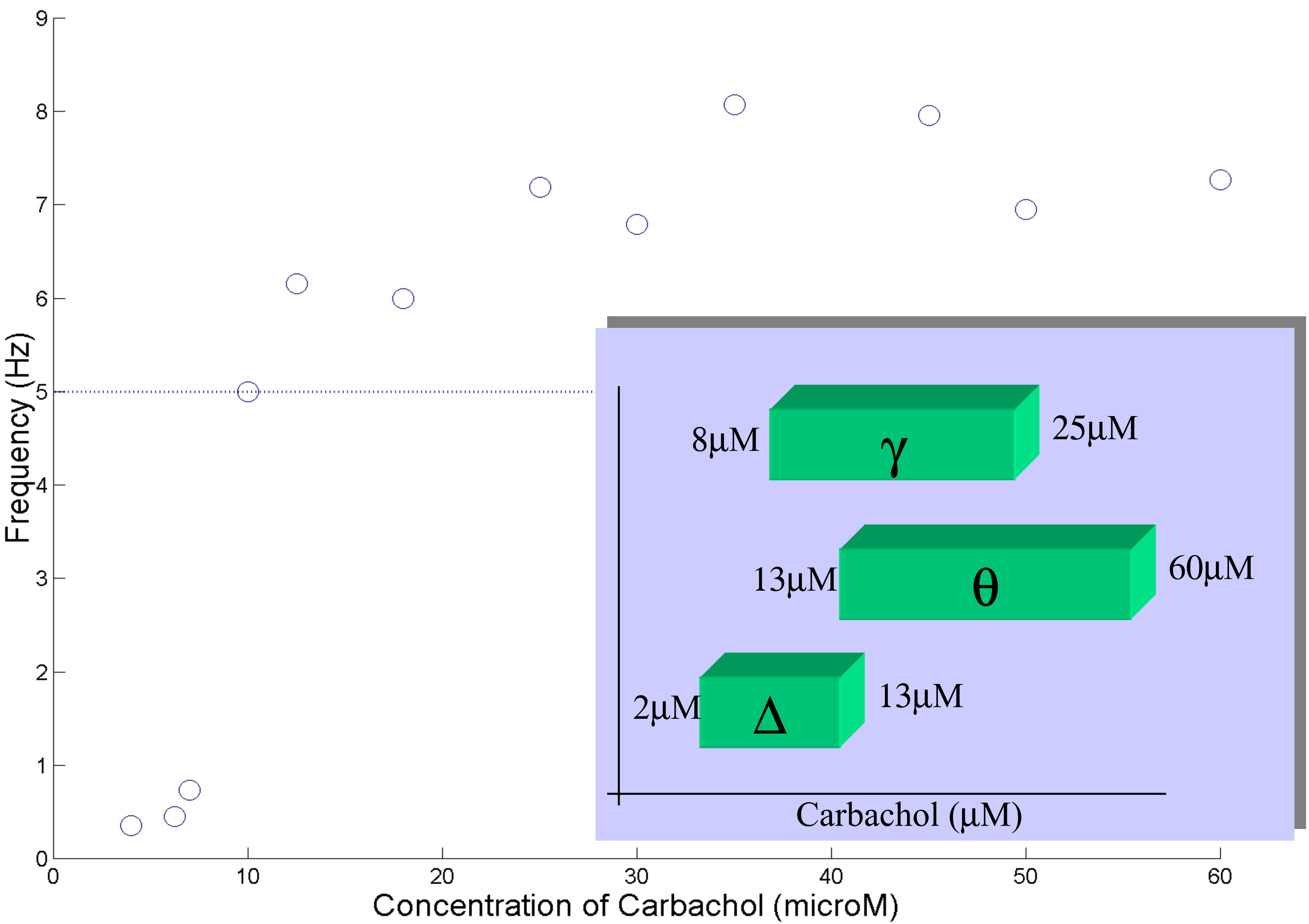
But are not synchronous with field events

25 μM CCH



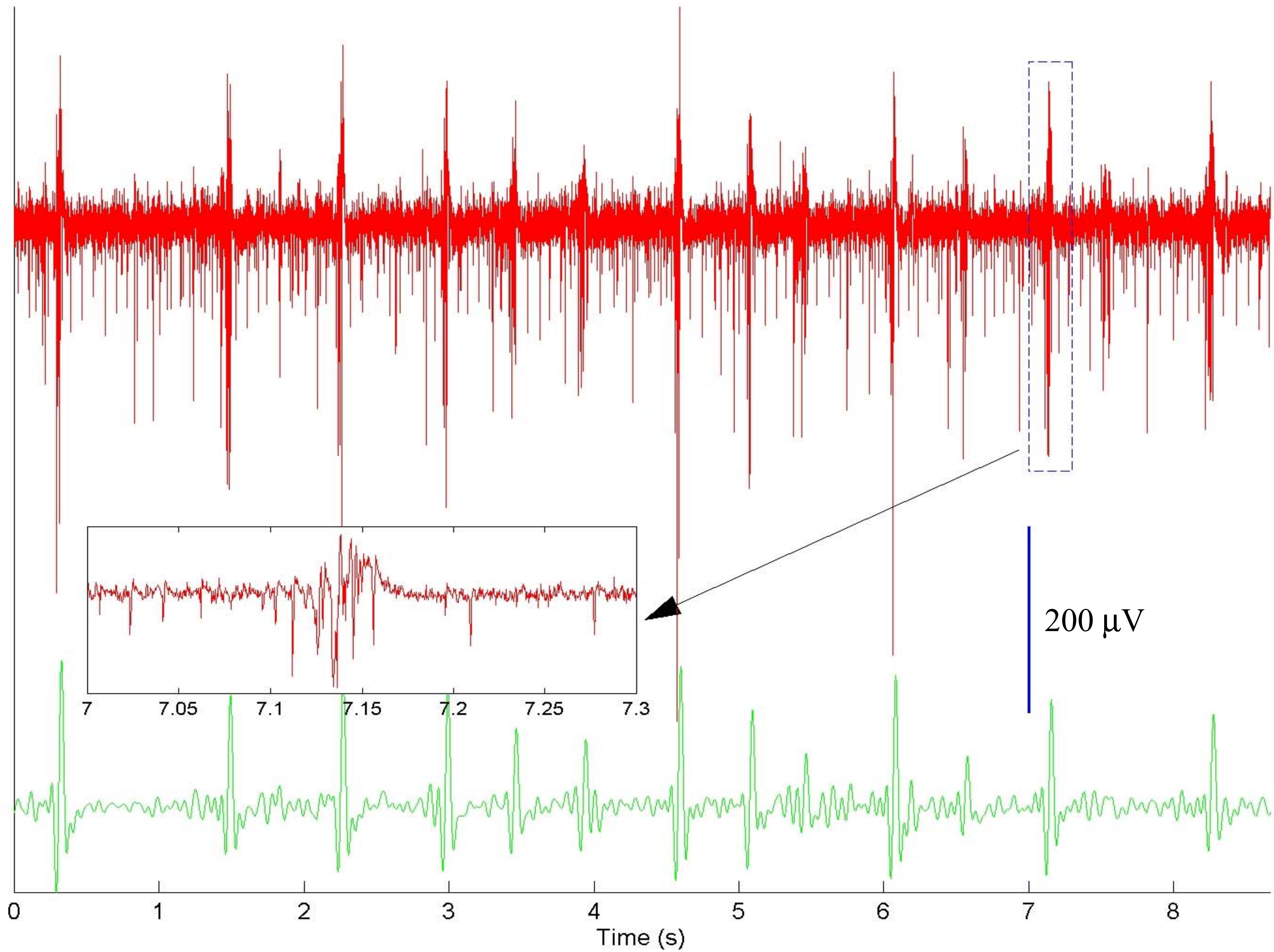
Mixed Class II/Class III (McMahon et al. 1998)

Three CCH levels, three rhythms

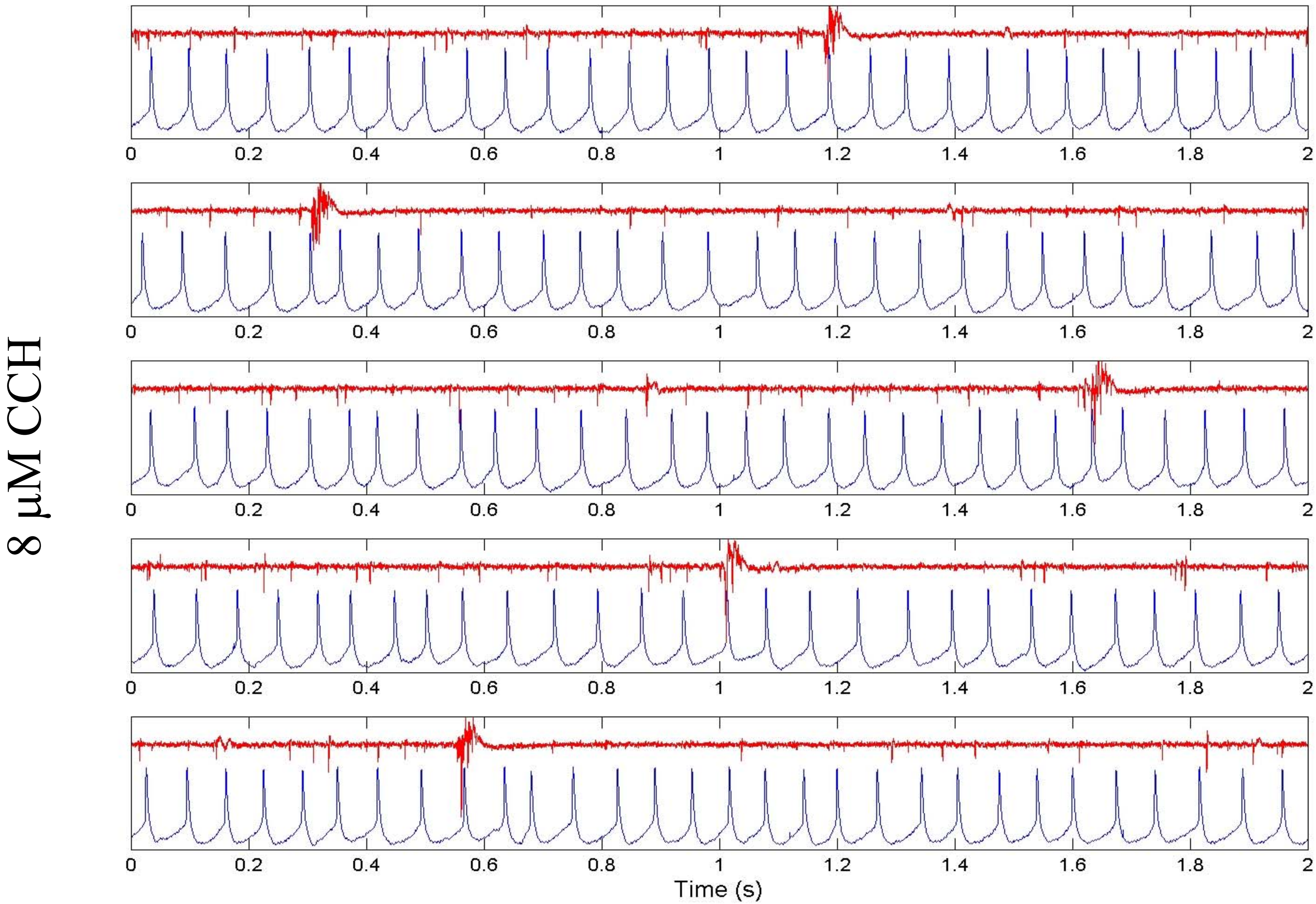


CCH-delta in CA1

8 μM CCH

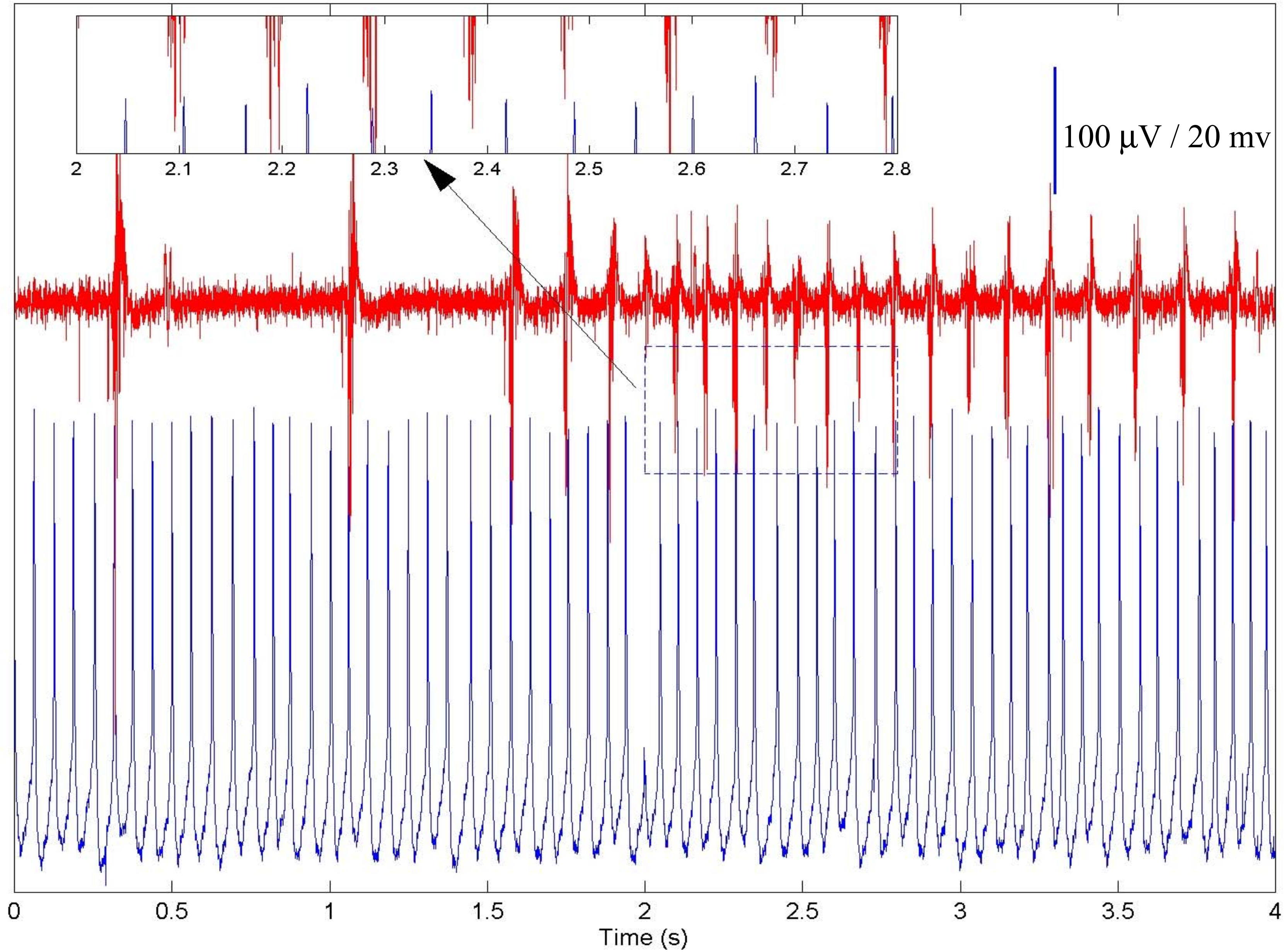


CA1 is preferentially recruited by CCH-delta



But not necessarily by CCH-theta

25 μM CCH

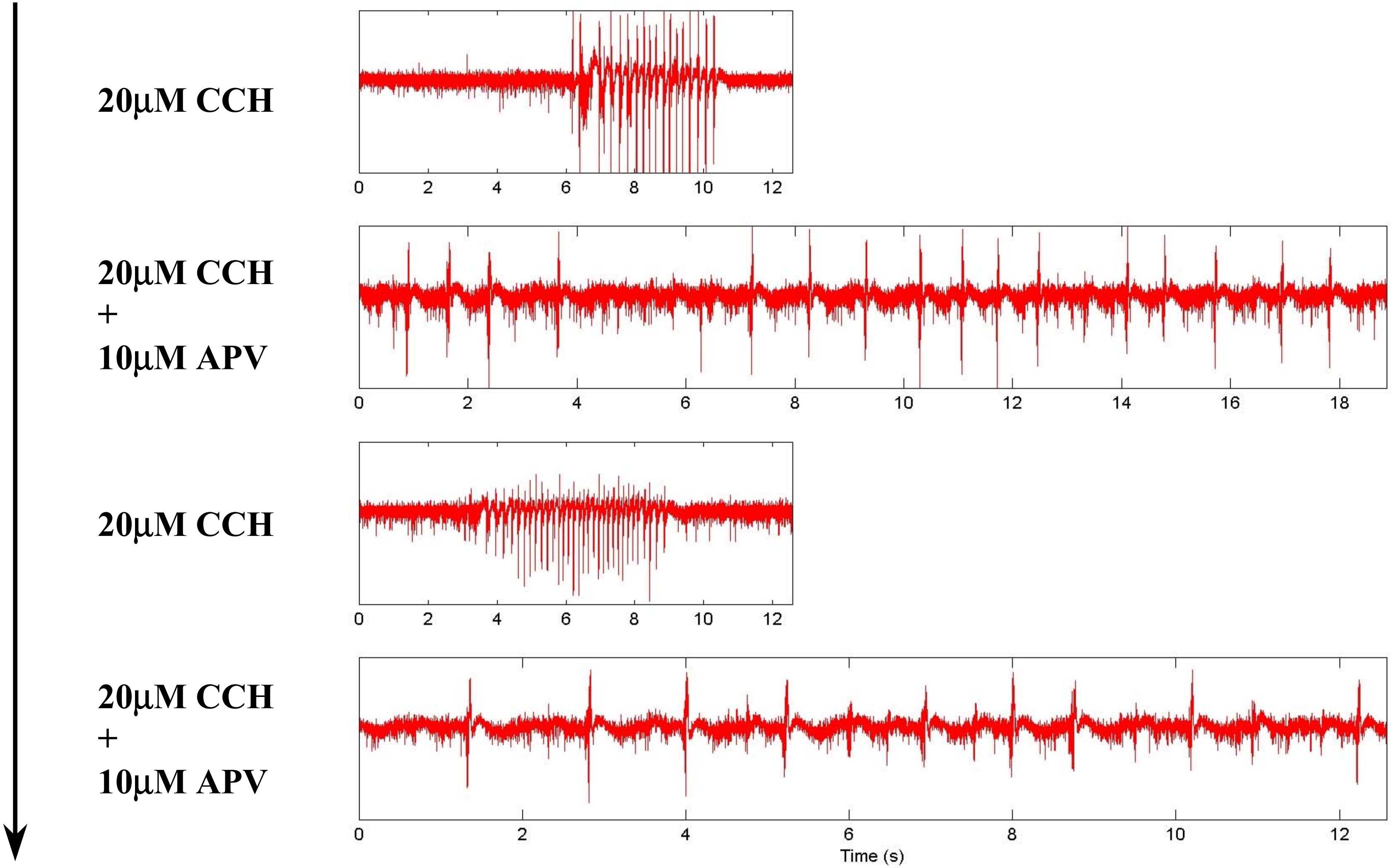


Class III (McMahon et al. 1998)

Excitatory Transmission in CA1

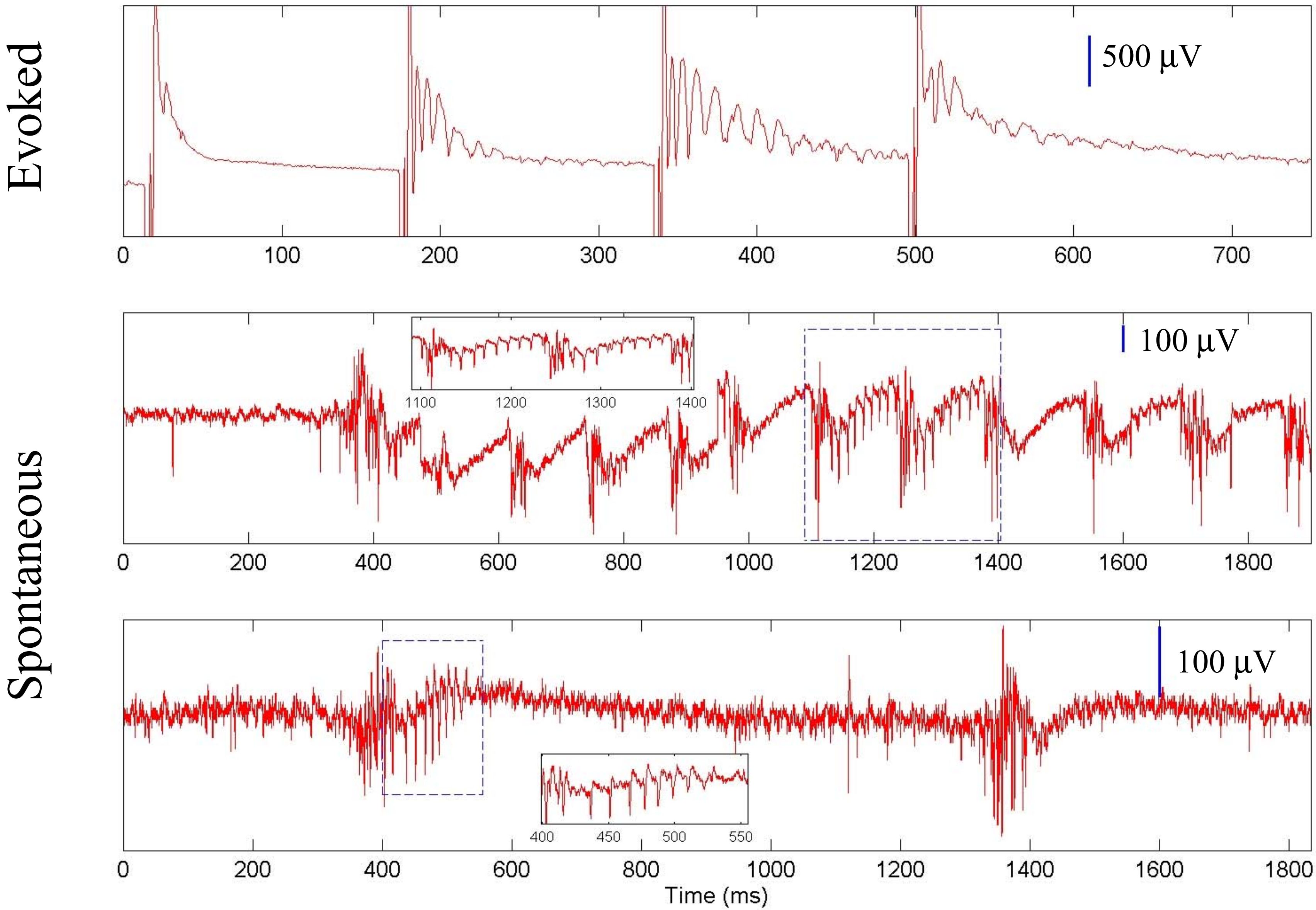
CNQX reversibly blocks CCH-induced theta.

Low concentrations of APV (<10µM) reversibly turns CCH-theta into CCH-delta.



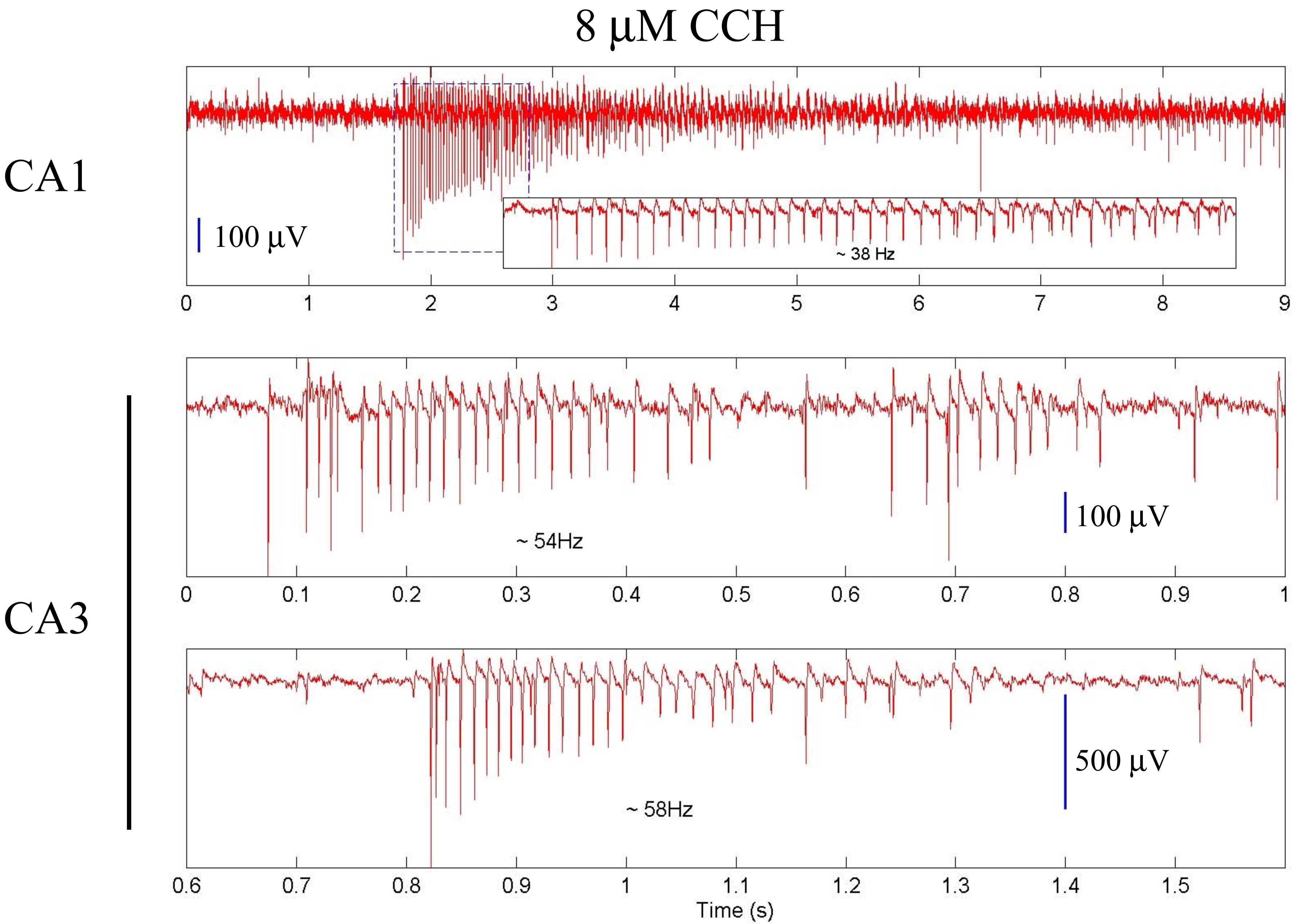
CCH-Gamma

8-25μM CCH



(Fisahn et al. 1998)

CCH-gamma in CA1 and CA3



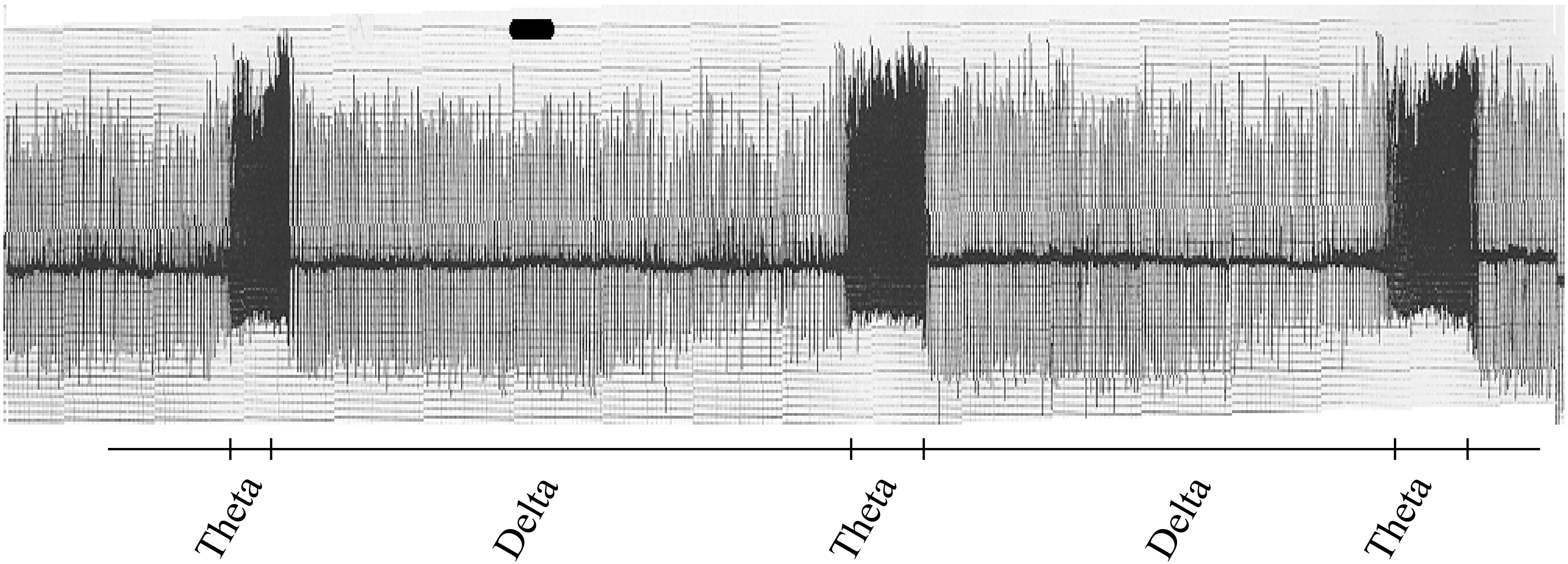
Longitudinal Slice

• In longitudinal slices, both CCH-theta and CCH-delta rhythms coexist, at CCH concentrations where they would not in transverse slices.

• CCH-theta oscillations are longer-lasting and more pronounced in longitudinal slices.

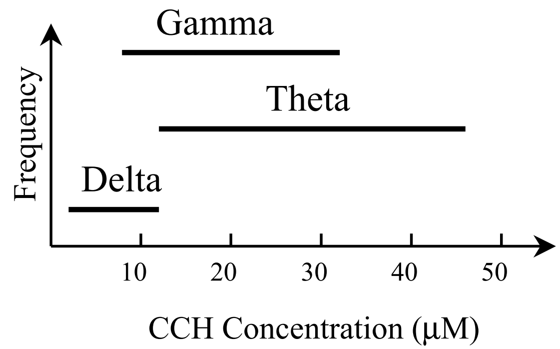
25 μM CCH

Time bar: 10 sec



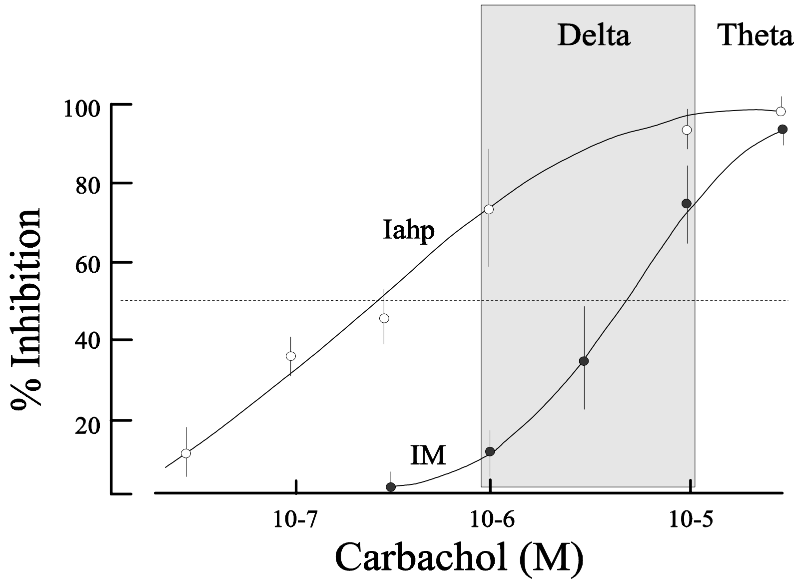
Conclusions

• 3 cholinergically induced oscillations in the hippocampal slices: **CCH-Delta** (.5-2 Hz), **CCH-Theta** (5-10Hz) and **CCH-Gamma** (40-70Hz).



• In vivo and in vitro delta, theta and gamma rhythms may be of different nature and involve the Septal inputs. Our results suggest that the hippocampus features a circuitry which is capable of 'resonating' at these three specific frequencies, depending on the level of cholinergic neuromodulation.

• The effect of various concentrations of carbachol on intrinsic and synaptic mechanisms has been studied (Madison et al. 1987). Computational modeling is possible to understand and explain how different concentrations of Carbachol may induce 3 *different* spontaneous oscillatory modes in the *same* neural circuitry.



Conclusions

• **Computational roles ?** Induction and reversal of LTP or LTD (Barr et al 1995; Huerta Lisman 1995)? Synchronization (Cobb et al, 1995) ? Learning (Liljenstrom and Hasselmo 1995; Hasselmo et al 1996)?

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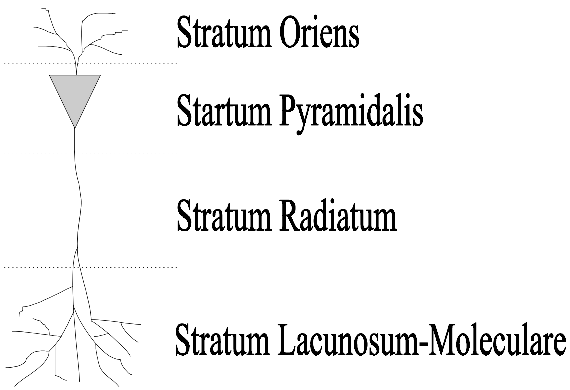
Methods

We use young (20-30 days) Sprague-Dawley rats from which 400µm thick slices are obtained. Slices are submerged in ACSF (mM: NaCl, 124; NaH_2CO_3, 26; D-glucose, 10; KCl, 5; $CaCl_2$, 2; $MgSO_4$, 2; NaH_2PO_4, 1.2) at 31-32 ^oC and perfused at constant flow (2ml/min). Field recordings are achieved using glass microelectrodes (ACSF filled, 300-400 KΩ). Whole cell patch clamp is achieved using glass electrodes containing (4-10 MΩ : mM: $KmeSO_4$, 140; Hepes, 10; NaCl, 4; EGTA, 0.1; Mg-ATP, 4; Mg-GTP, 0.3; Phosphocreatine 14). All drugs are freshly prepared in ACSF and bath applied. Stimulations are administred through a unipolar glass electrode, filled with ACSF, and placed in the Stratum Radiatum. Data are acquired with Labview, and analyzed with Matlab.



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