Summary

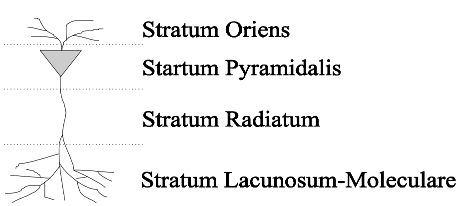
• We present preliminary experimental evidence for <u>three</u> cholinergically-induced oscillatory regimes in the hippocampal slice observed using field recordings in CA1. Frequencies are within the delta (.5-2Hz), theta (5-10Hz) and gamma (50-90Hz) bands, and depend on the concentration of the neuromodulator (carbachol). We show that these oscillations can occur in a superimposed manner. Moreover, theta can be initiated terminated and phase-reset by afferent stimulations.

• We also show that these oscillations occur with markedly different patterns in the longitudinal slice, in CA3.

• We suggest that the hippocampal circuitry is capable of 'resonating' at three frequencies, in the same neuromodulatory conditions. This system offers a framework for the computational modeling of the neuromodulation of a single circuit yielding multiple oscillatory modes.

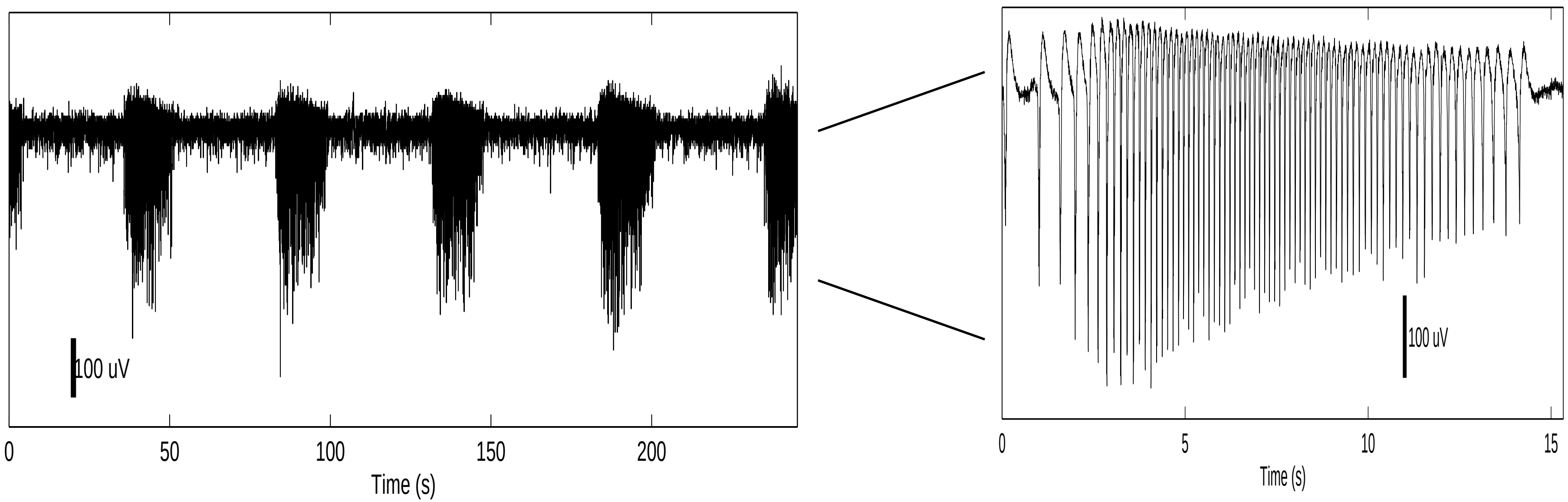
Method

We use young (20-30 days) Long-Evans rats from which 400μm thick slices are obtained. Slices are submerged in ACSF (mM: NACl, 124; NaH2CO3, 26; D-glucose, 10; KCl, 5; CaCl2, 2; MgSO4, 2; NaH2PO4, 1.2) at 31-32 oC and perfused at constant flow (2ml/min). Electrophysiological recordings in CA1 are achieved using extra-cellular recording microelectrodes (ACSF filled, 300-400 KΩ). All drugs are freshly prepared in ACSF and bath applied. Stimulation are administred through a unipolar glass electrode, filled with ACSF, and placed in the Stratum Radiatum. Stimulation and recording are monitored by oscilloscope and computer, and saved on disk for off-line analysis. Data analyses are performed by programs written in C, and using the Matlab software in a Windows95 environment.



Theta (5-10 Hz) Oscillations

When carbachol is added to the perfusion medium, background activity increases and spontaneous theta episodes emerge as “waxing and waning” patterns of synchronized populations bursts.

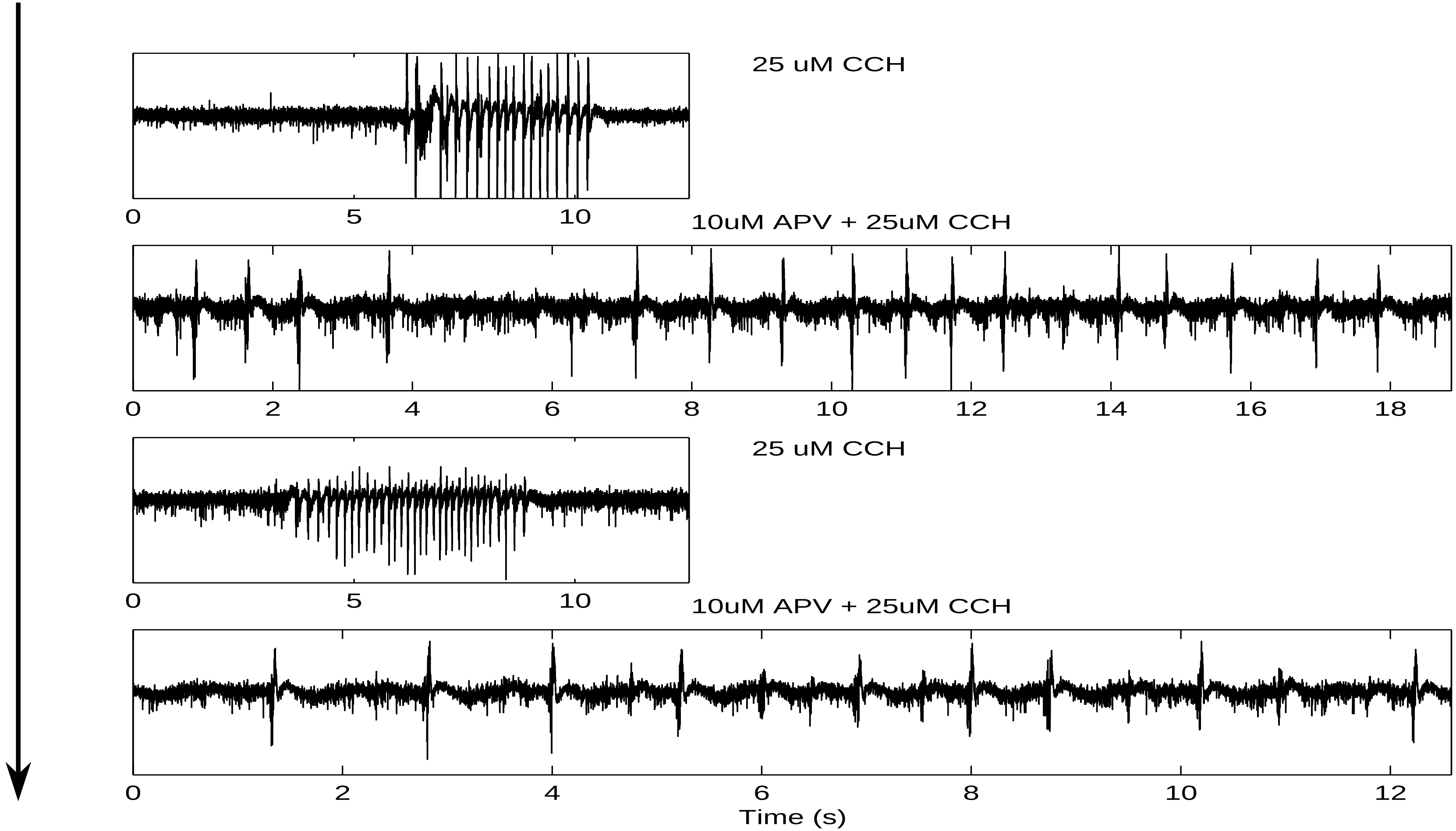


Excitatory Transmission

CNQX reversibly blocks CCH-induced theta.

High concentrations of APV (> 40μM) have no effects.

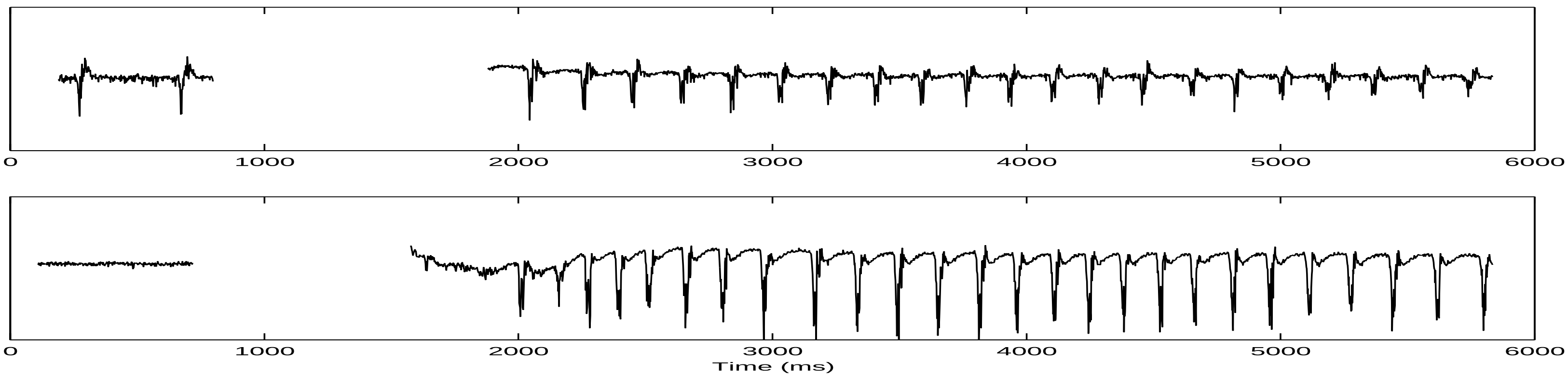
Low concentrations of APV (<10μM) turn theta into delta.



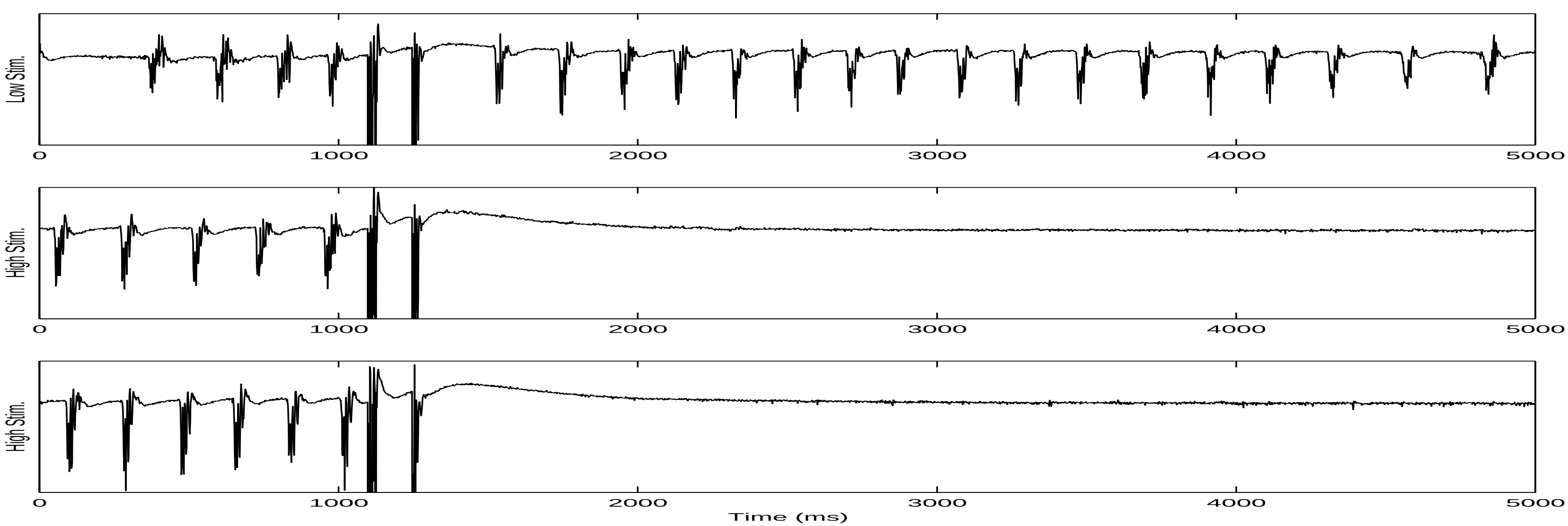
Theta Initiation and Termination

8 μM CCH

Repeated stimulations can initiate a theta episode

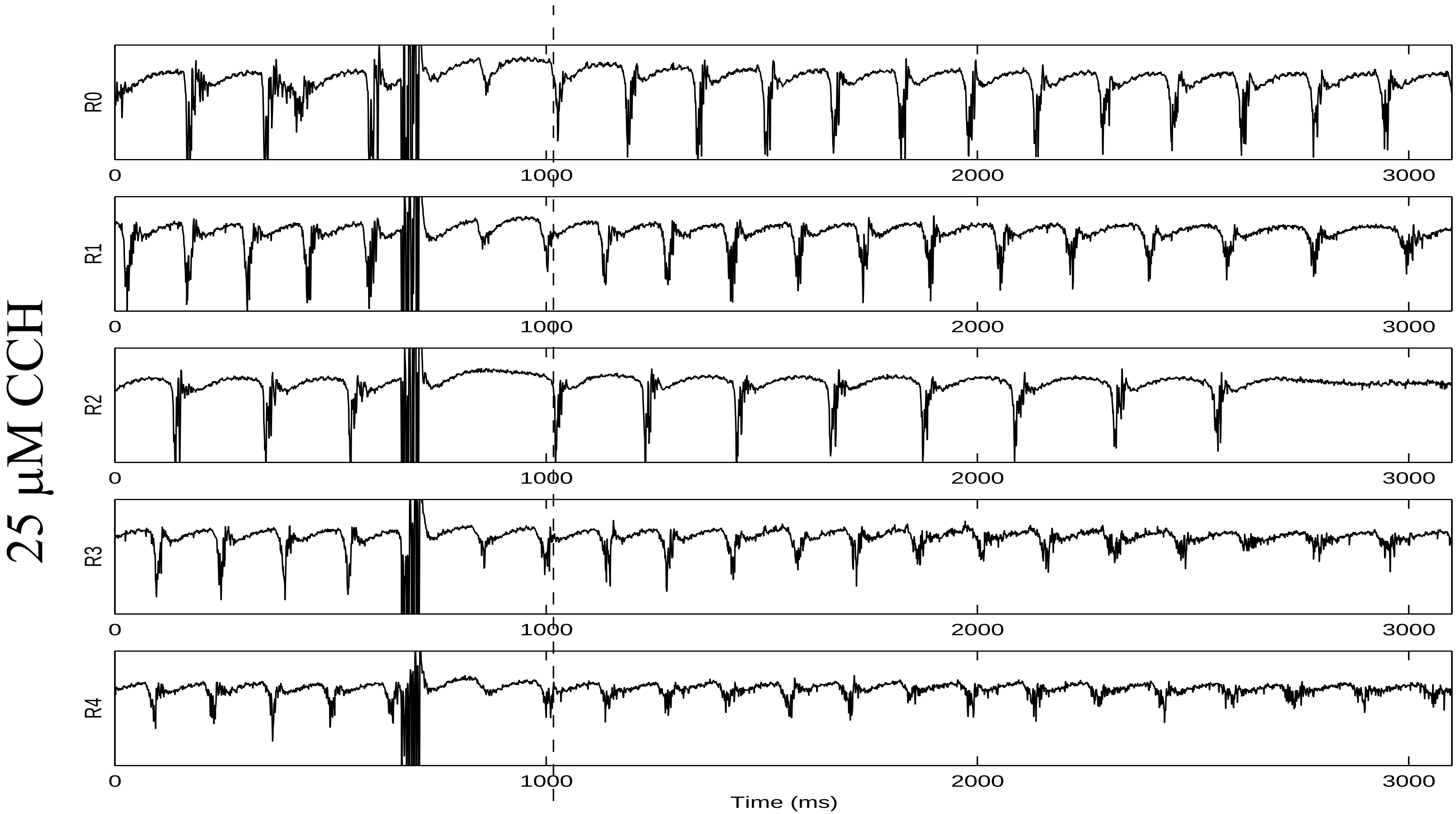


Strong Schaeffer Collaterals stimulations terminate theta.

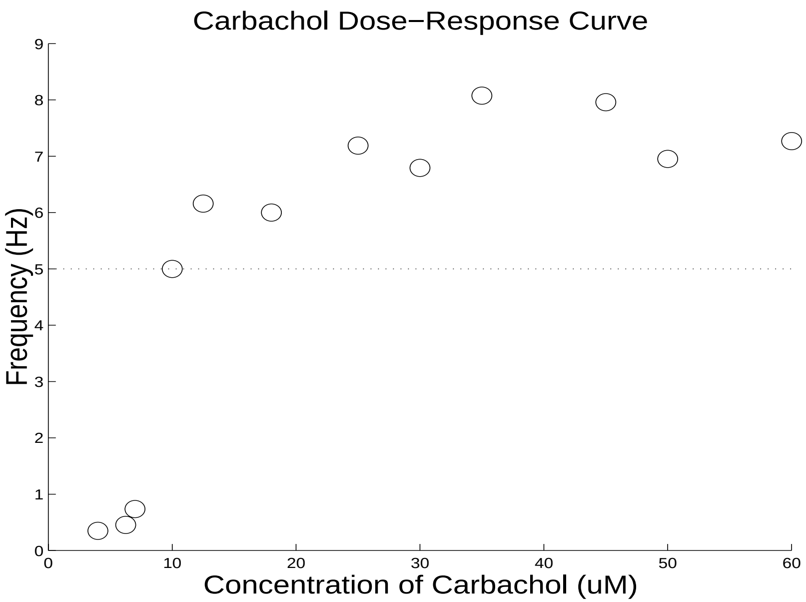


Theta Reset

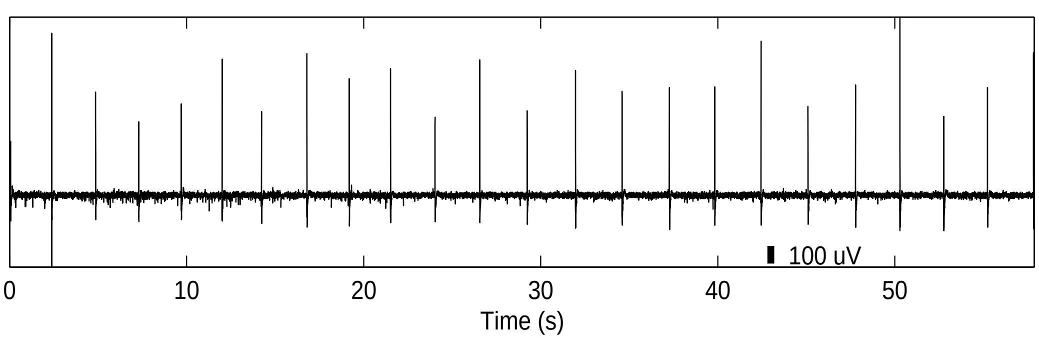
Medium stimulus strengths reset an ongoing theta episode.



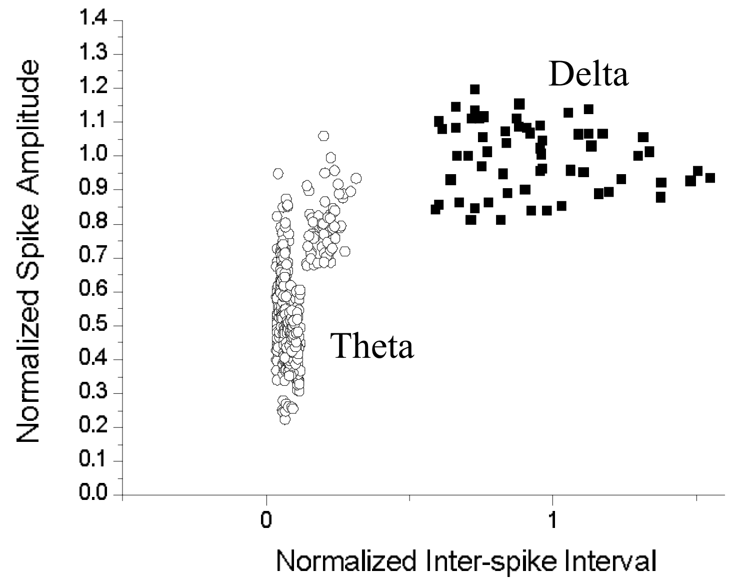
Delta (.5 - 2 Hz)



8μM CCH



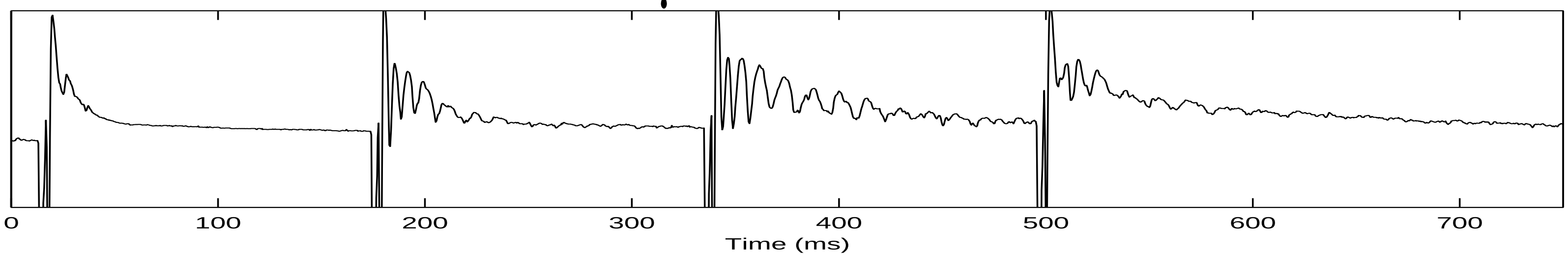
Delta and theta might involve different population sizes.



Gamma (50-90 Hz) Oscillations

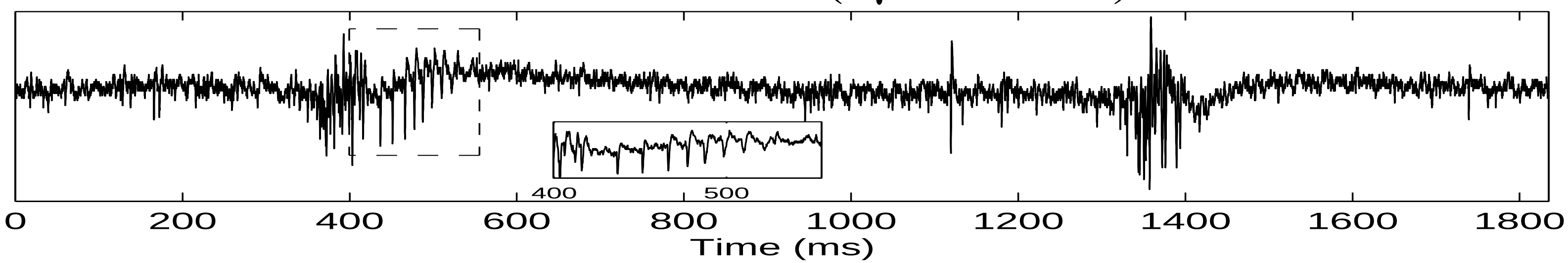
Evoked

8μM CCH

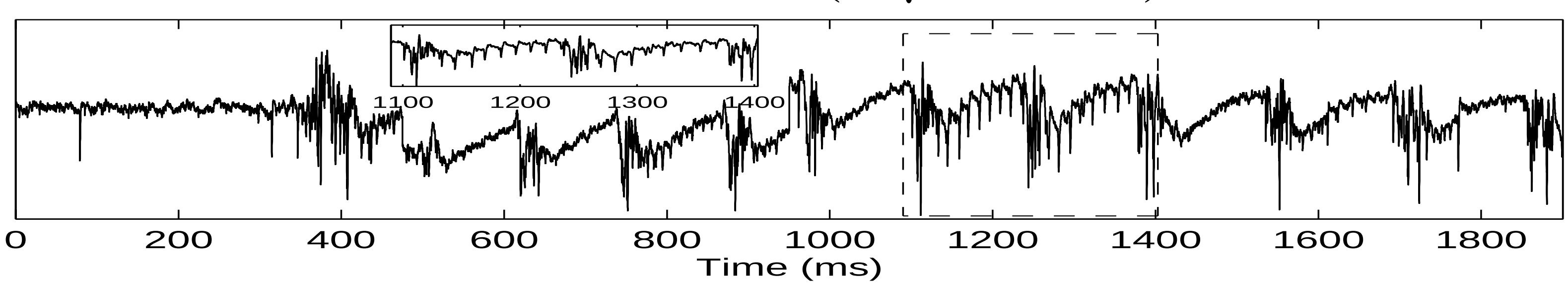


Spontaneous

Delta-Gamma (8μM CCH)

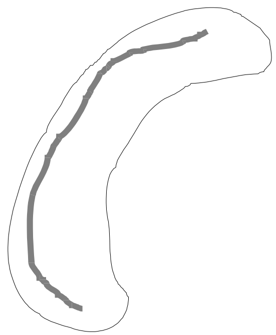


Theta-Gamma (25μM CCH)



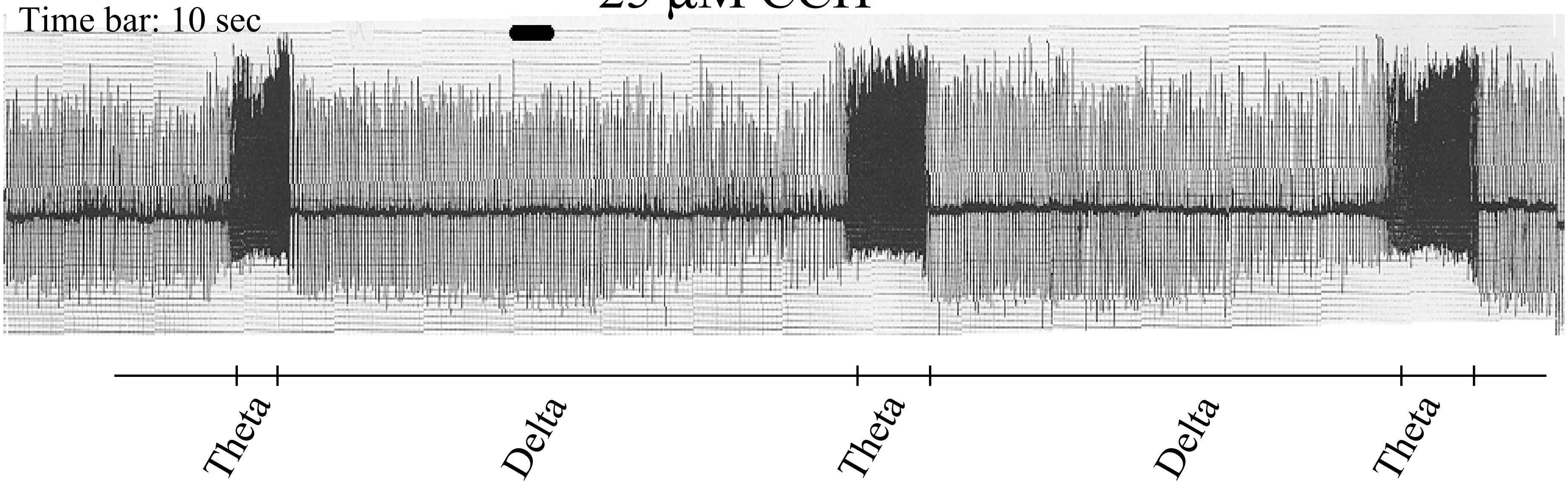
Longitudinal Slice

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



Theta oscillations are longer-lasting and more pronounced in longitudinal slices.

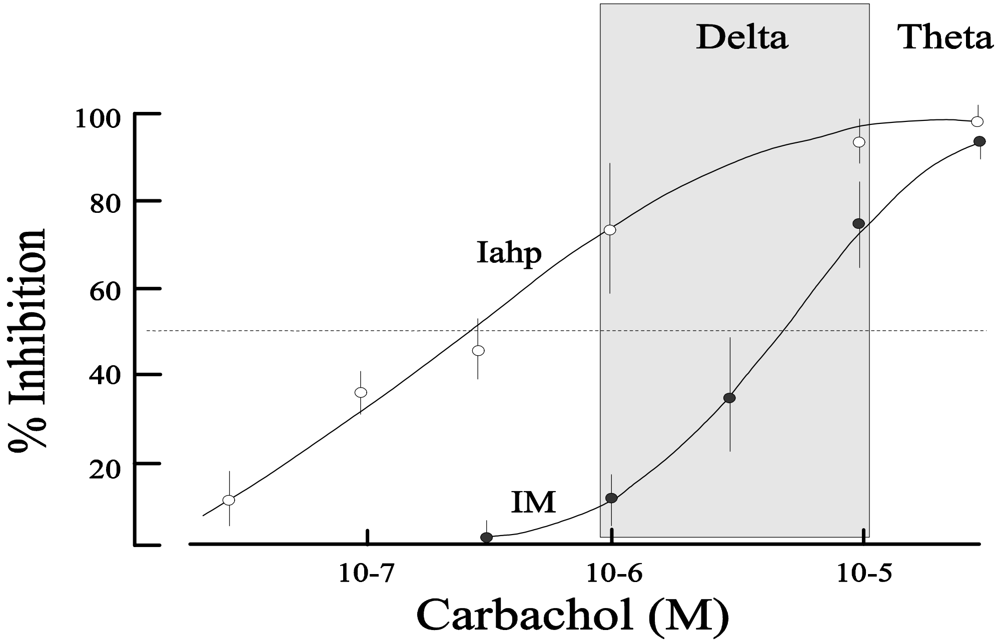
25 µM CCH



Cellular Effects of Carbachol

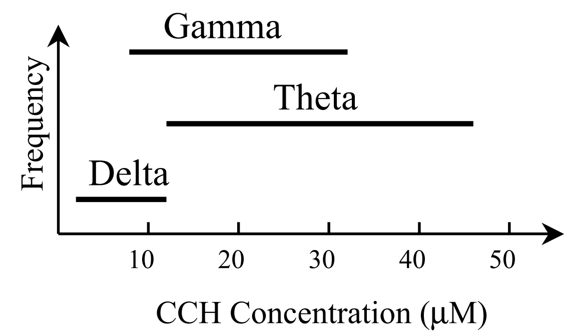
- Second messenger systems (IP3).
- Presynaptically depresses synaptic transmission.
- Directly depolarizes pyramidal cells and interneurons.

- IM - Iahp.



Adapted from (Madison et al. 1987)

Conclusions



- We presented experimental evidence for 3 cholinergically induced oscillations in the hippocampal slices: Delta (.5-2 Hz), Theta (5-10Hz) and Gamma (50-90Hz). These rhythms can coexist in pairs.

- **Relevance to in vivo EEG**. In vivo and in vitro delta, theta and gamma rhythms are possibly of different nature. However, the fact that a single neuromodulatory substance is capable of activating these 3 distinct rhythms in vitro is remarkable. We suggest that the hippocampus features a circuitry which is capable of 'resonating' at specific frequencies.

- **The computational roles** of these oscillatory modes are still largely unknown (but see Brad Wyble's workshop).
Theta has been involved in induction and reversal of LTP or LTD (Barr et al 1995; Huerta Lisman 1995). Theta can be used to synchronize pyramidal cells (Cobb et al, 1995), and may play a role in learning (Liljenstrom and Hasselmo 1995; Hasselmo et al 1996) and memory buffering (Jensen et al 1997).

- **Underlying circuit**: The only modeling study of CCH-induced rhythms has focussed on theta (Traub et al 1992) elicited in high CCH concentrations (40-50μM). The model only accounts for the 'waxing' phase of the oscillation. Further work is required to account for the waning phase, and to explain the other rhythms found at lower CCH concentrations.

Conclusions

Acknowledgments

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