

Role of corticothalamic feedback in generating hypersynchronized 3Hz discharges by intact thalamic networks: a mechanism for absence seizures?

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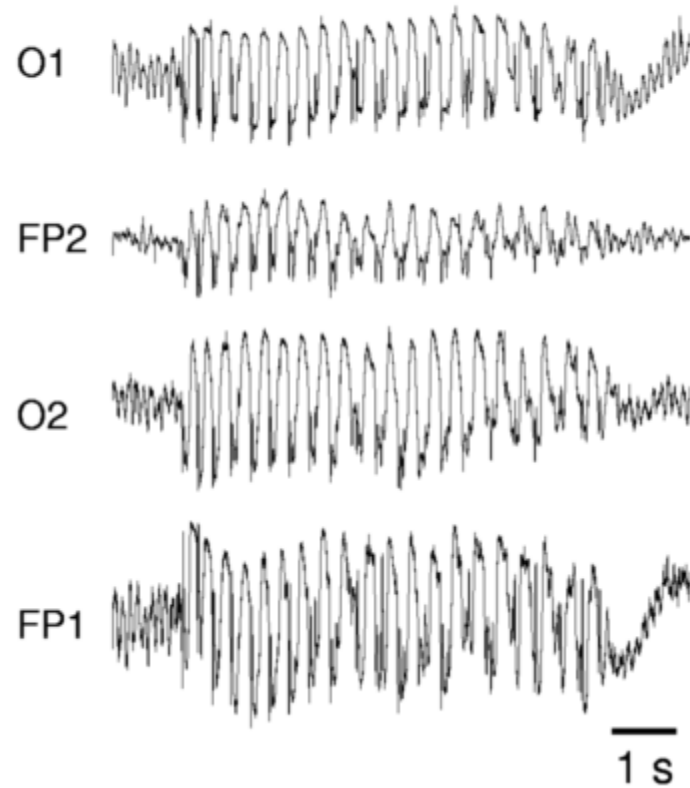
CNRS
Gif-sur-Yvette, France

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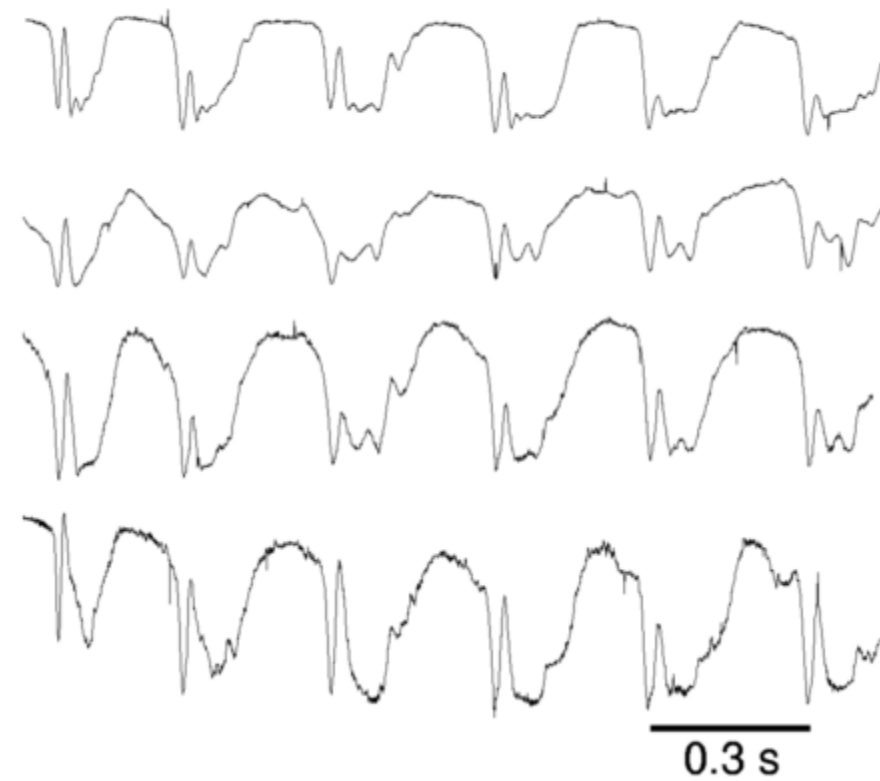
Collaborators: Thierry Bal (UNIC),
Diego Contreras (University of Pennsylvania, USA)

(Courtesy of Alex Thomson,
University of London, UK)

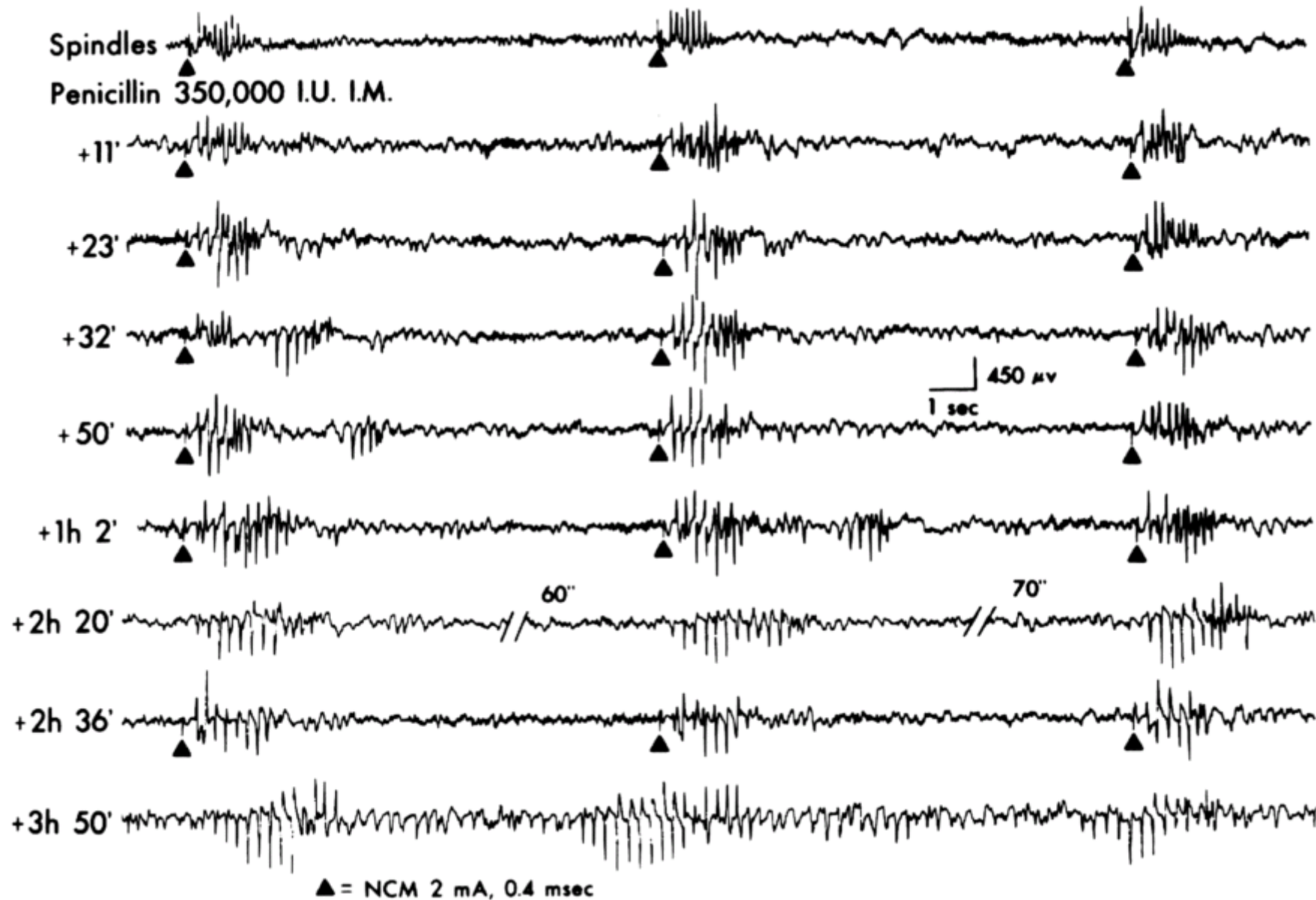
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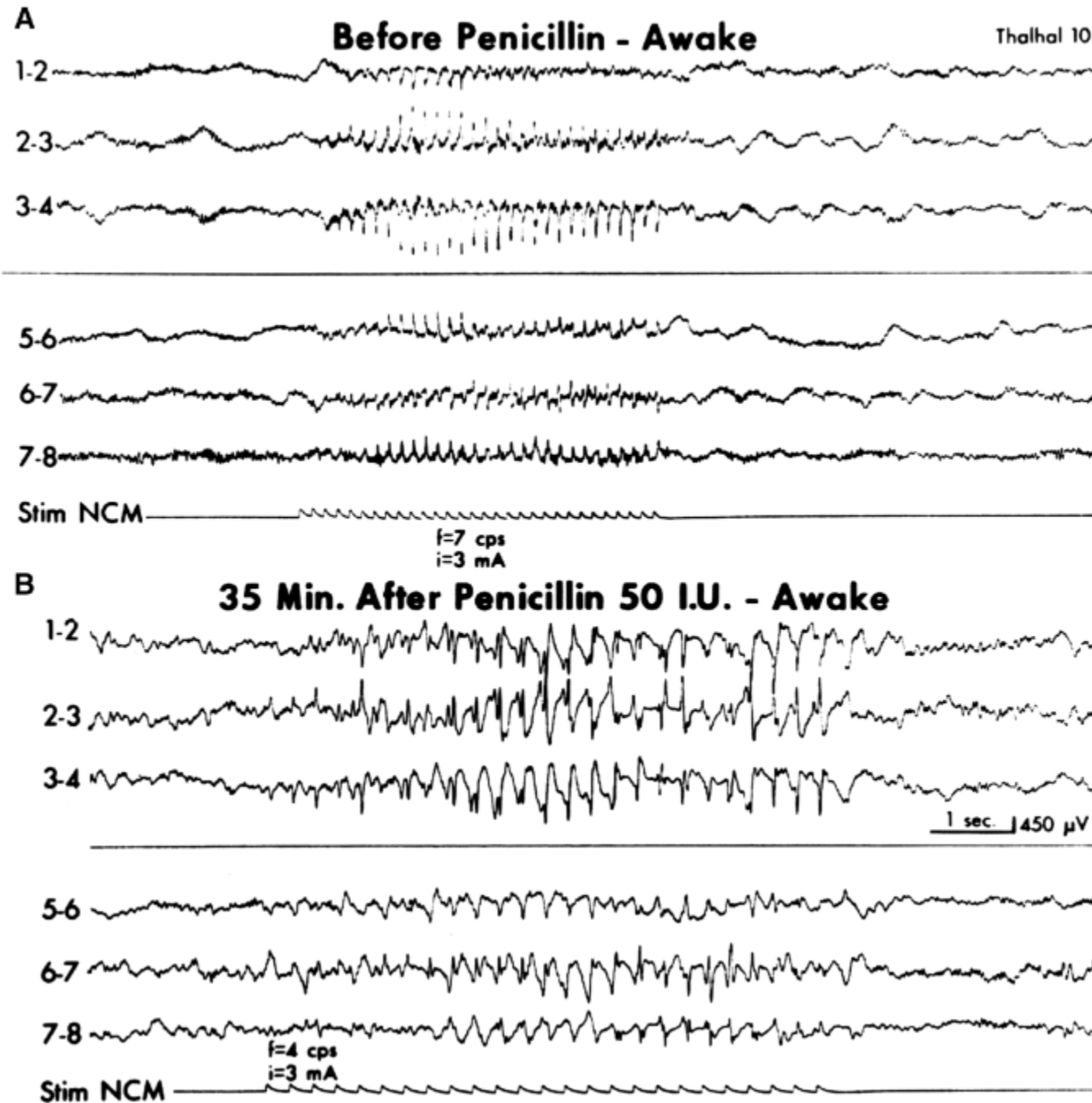
B



Cat penicillin model of spike-and-wave

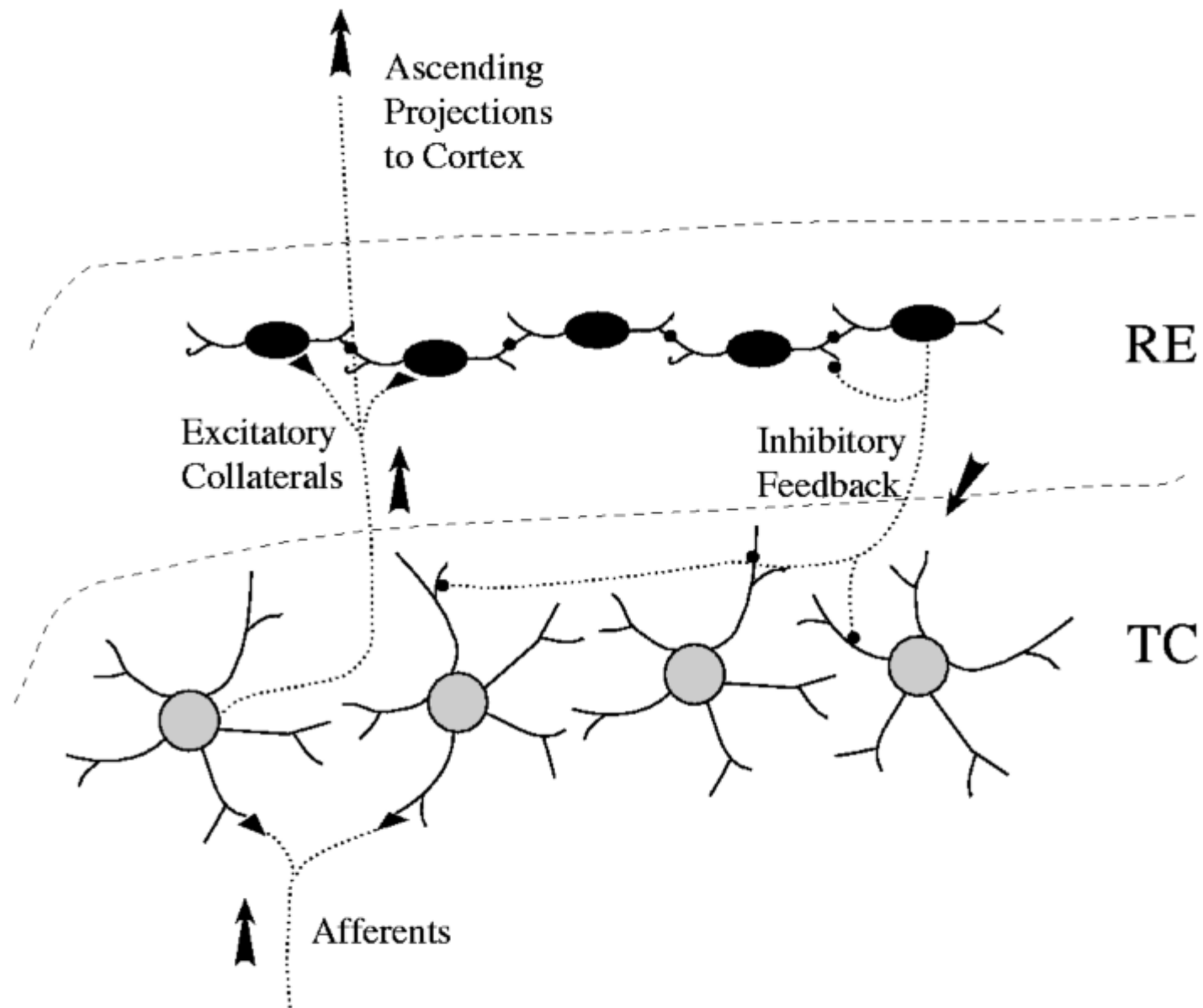


Kostopoulos et al.,
Exp. Neurol. 1981

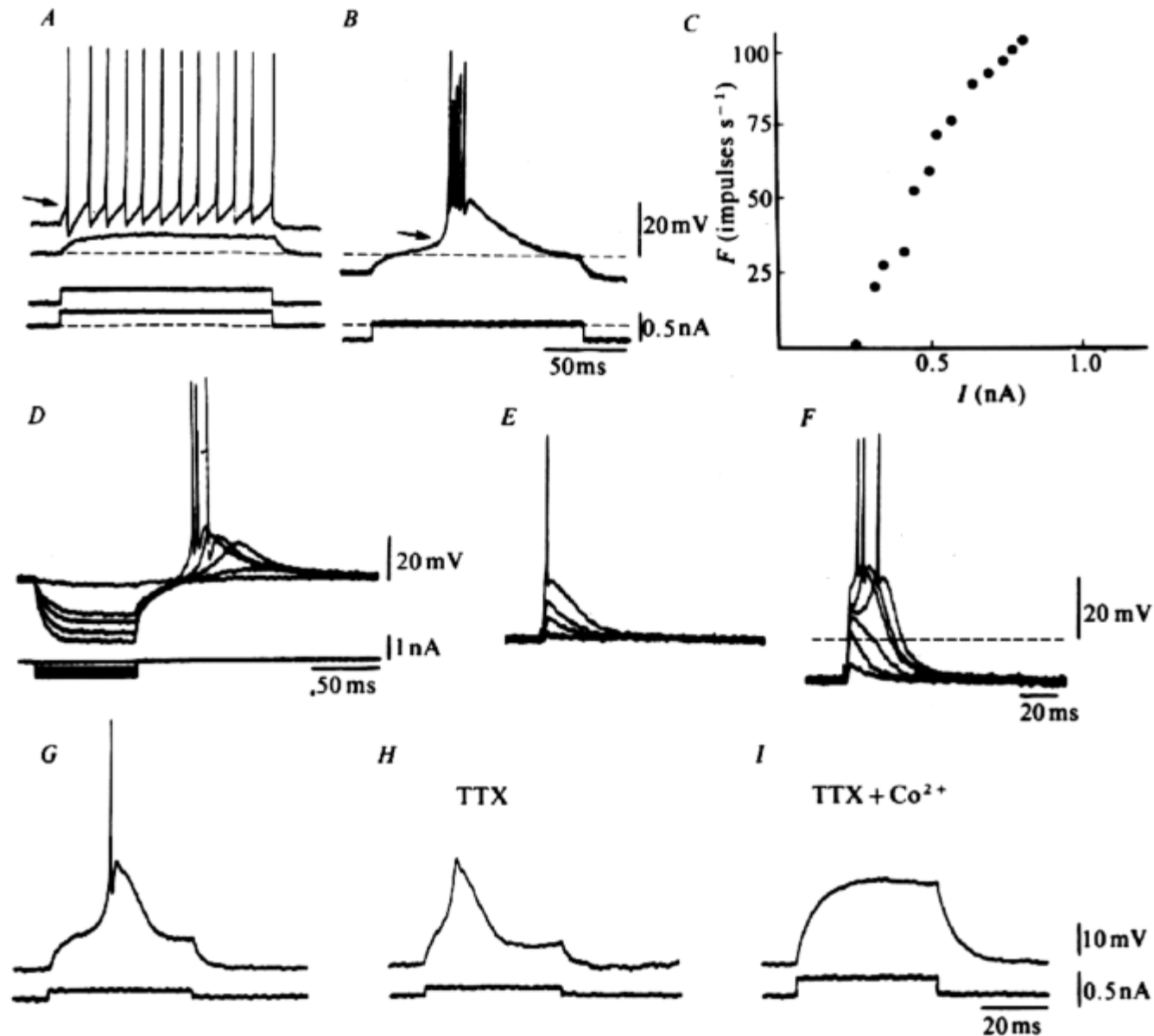


- 1. Intra-thalamic loops
- 2. Intra-cortical loops
- 3. Thalamo-cortical loops

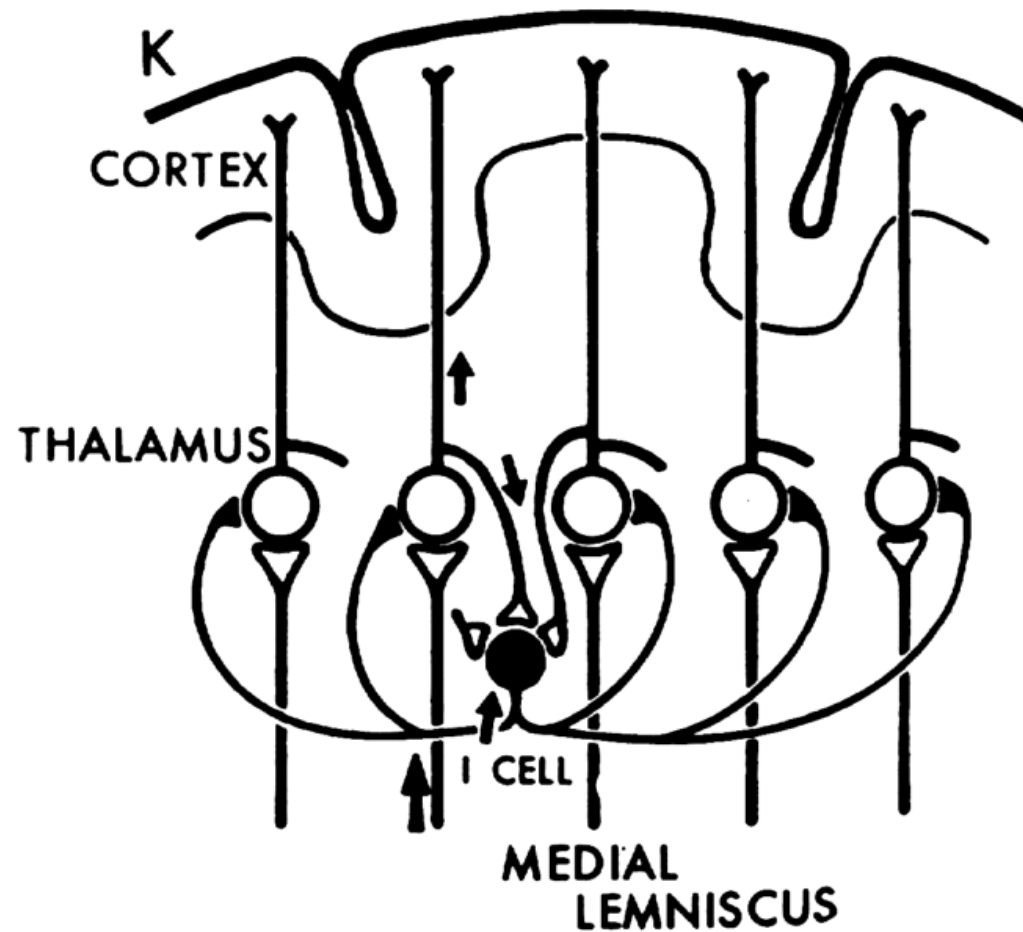
Connectivity of thalamic cell types



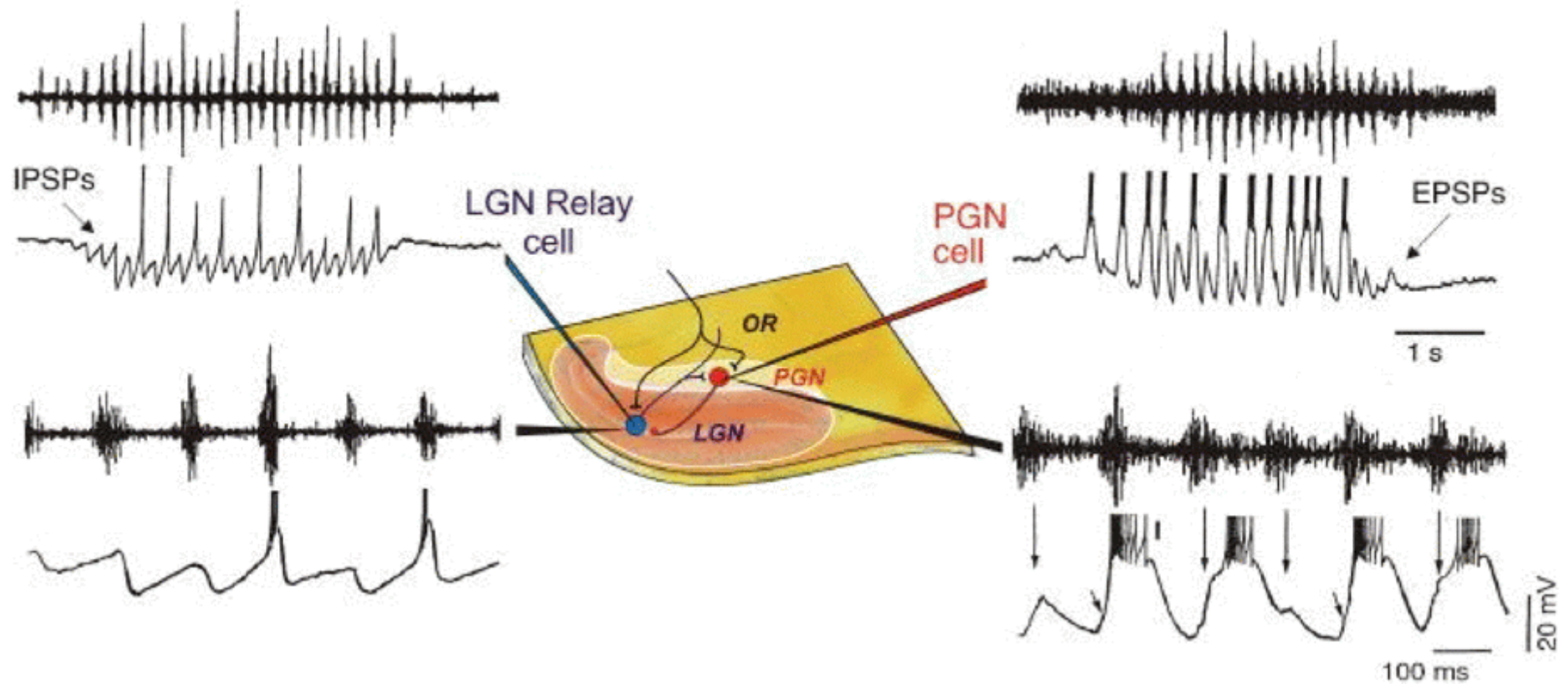
Intrinsic properties of thalamic neurons



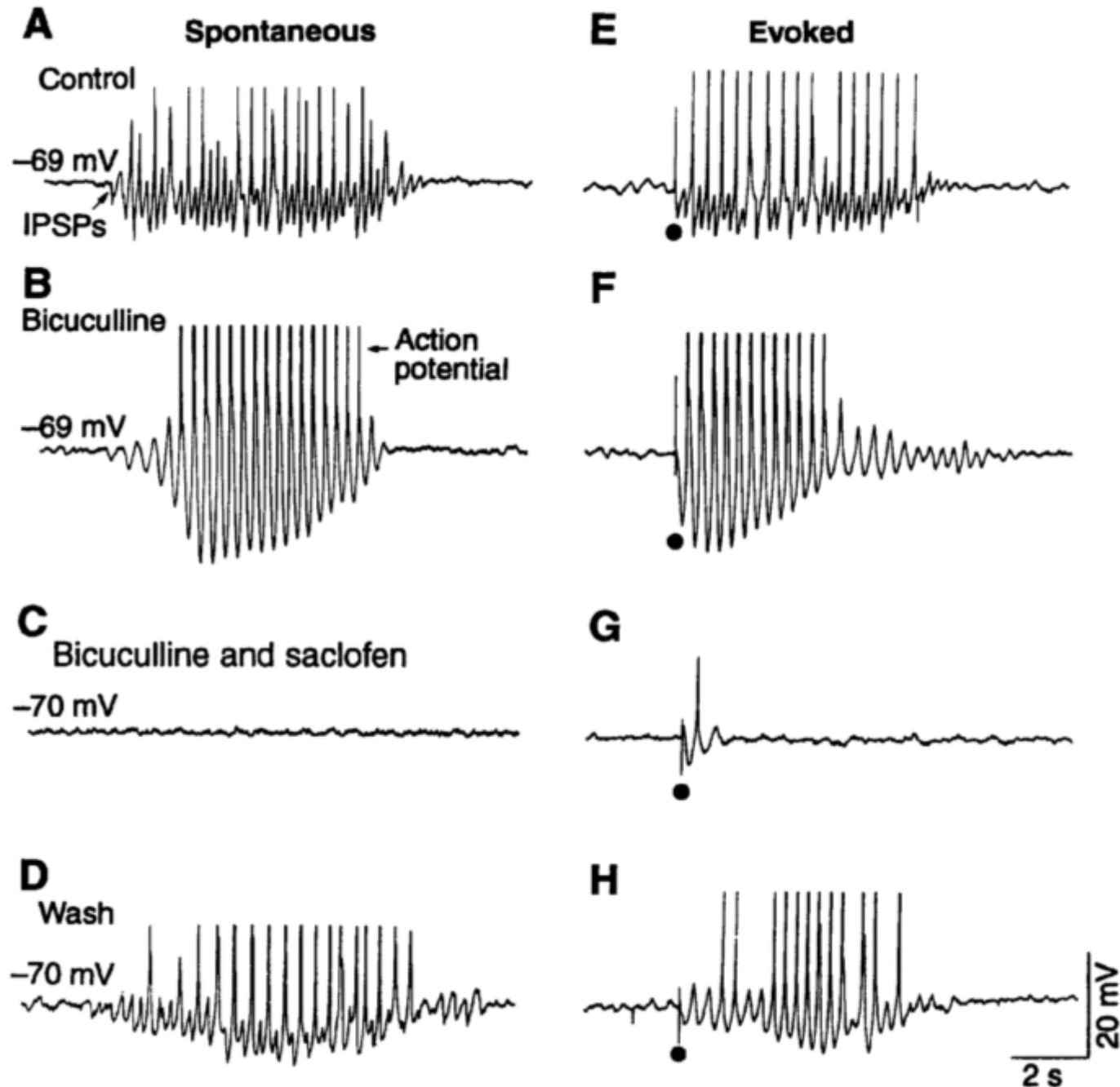
Thalamic oscillations from inhibitory-rebound interactions



Spindle waves in thalamic slices

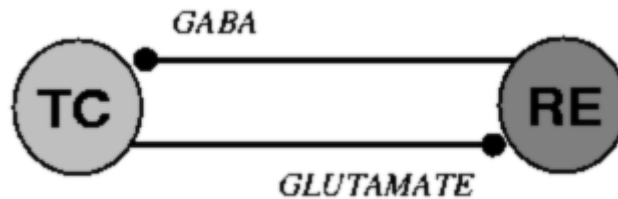


Slow (~3Hz) oscillations following application of bicuculline



Model of thalamic oscillations

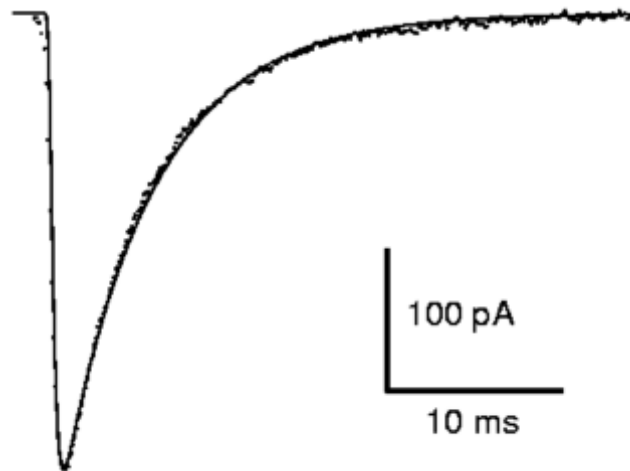
TC cells: IT, I_h,
Calcium regulation



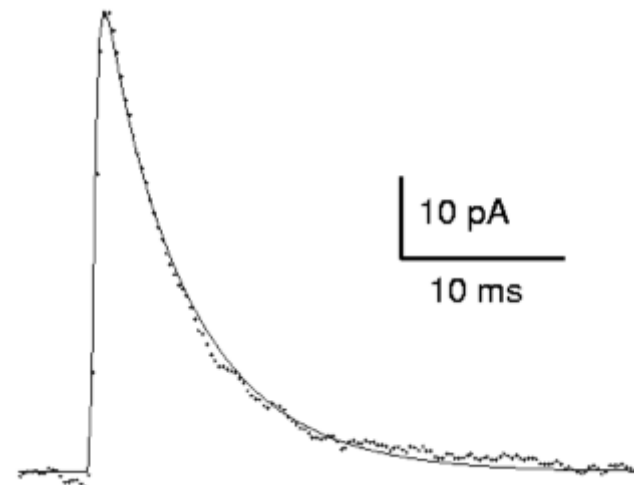
RE cells: IT, I_K[Ca],
ICAN, Calcium

Synaptic interactions:

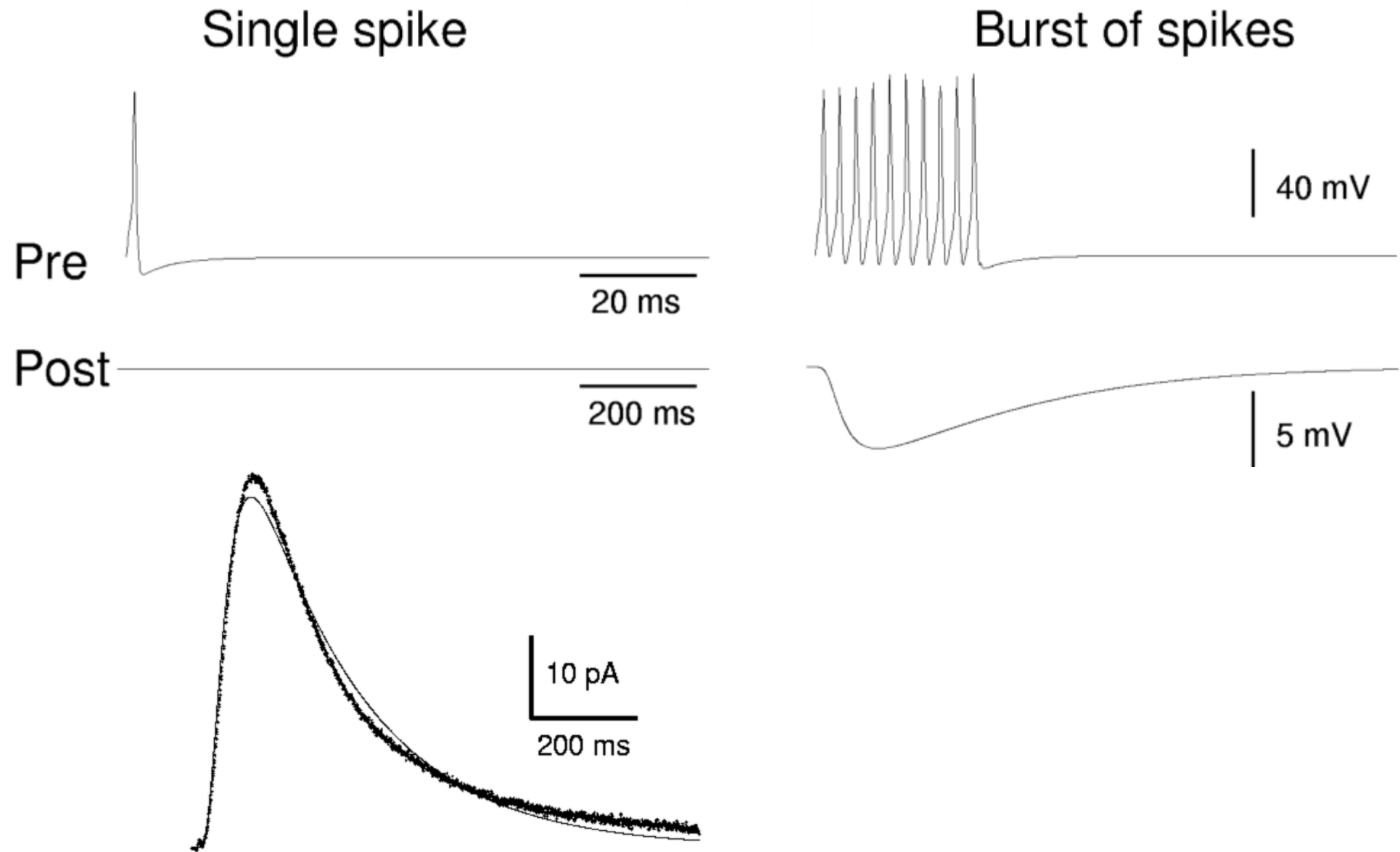
Glutamate AMPA receptors



GABA(A) receptors

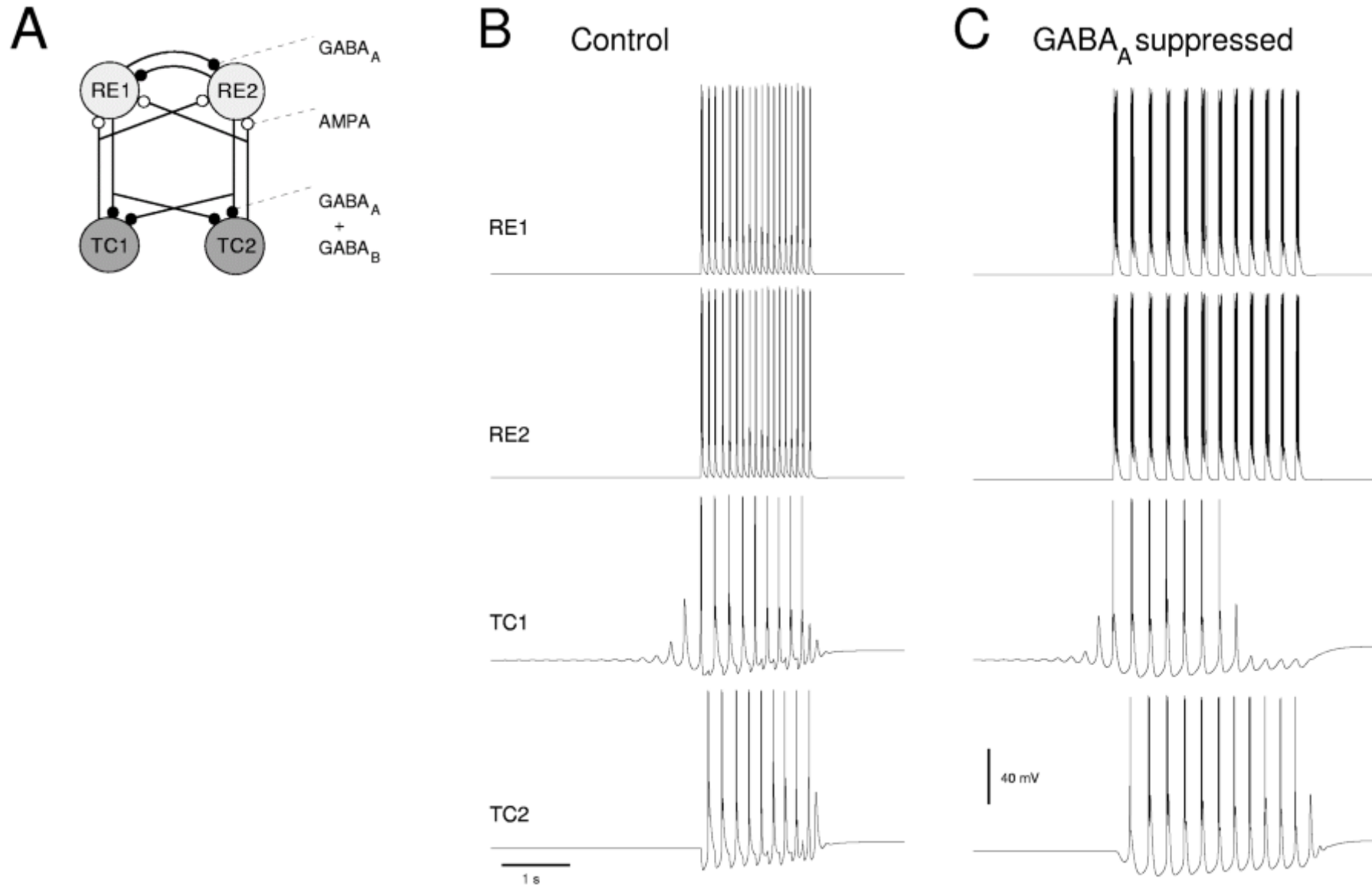


Model of GABA(B) receptors



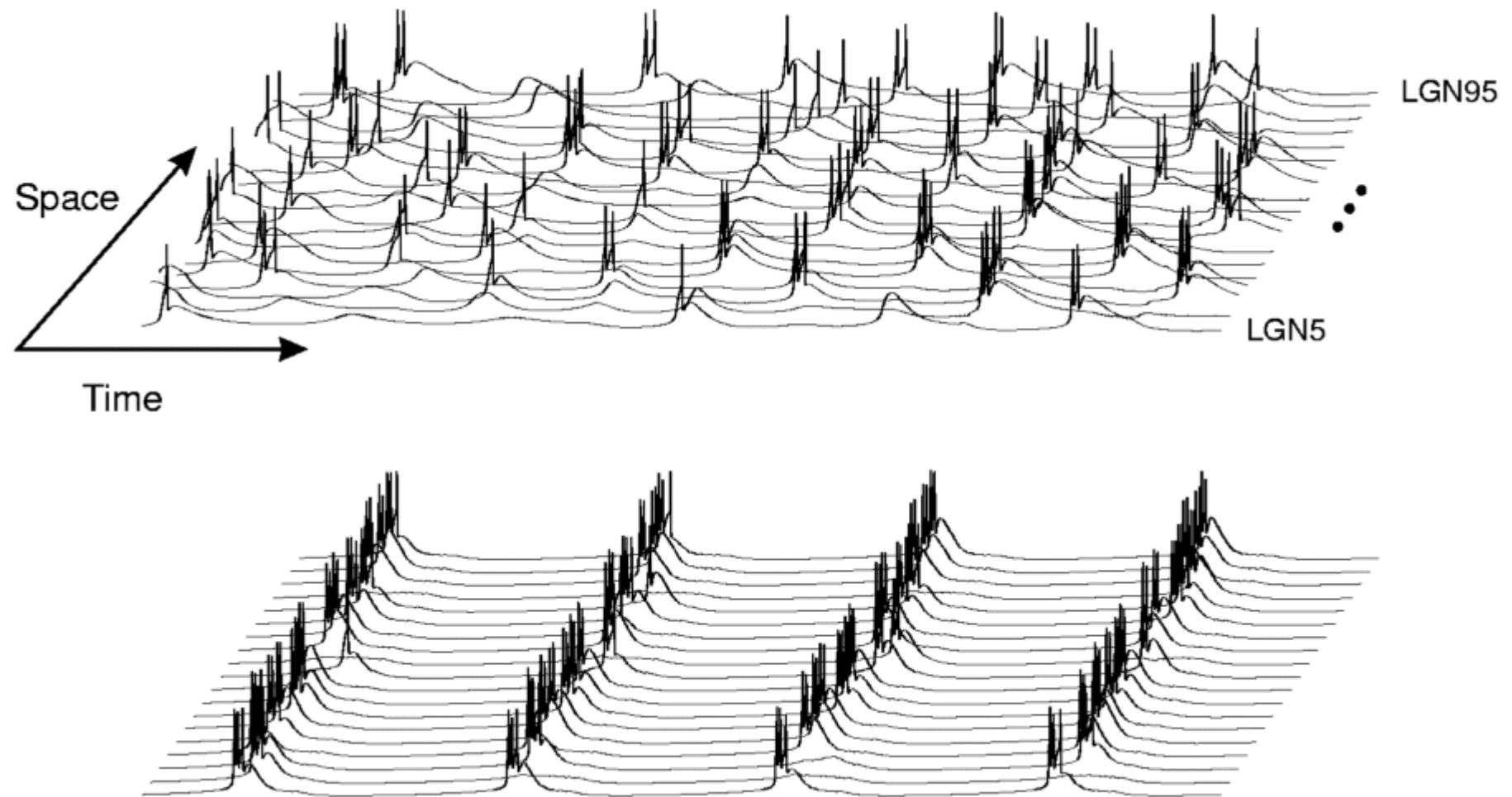
Destexhe & Sejnowski,
PNAS, 1995

Model of spindle waves and 3Hz oscillations



Destexhe et al.,
J. Neurophysiol., 1996

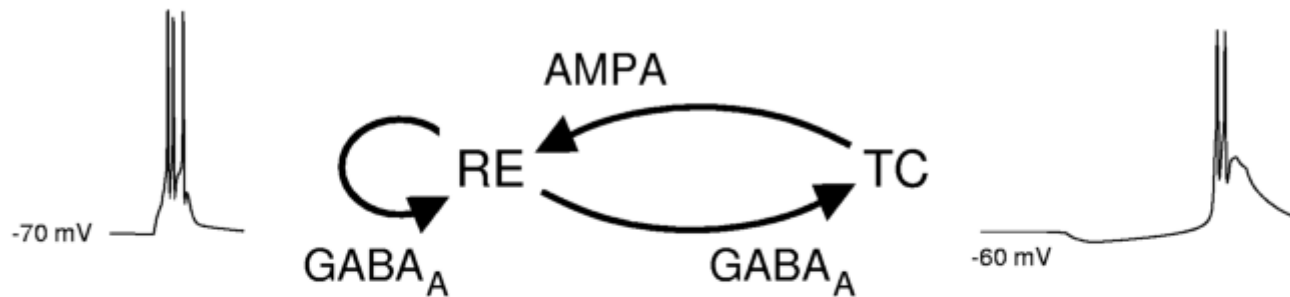
Model of spindle waves and 3Hz oscillations



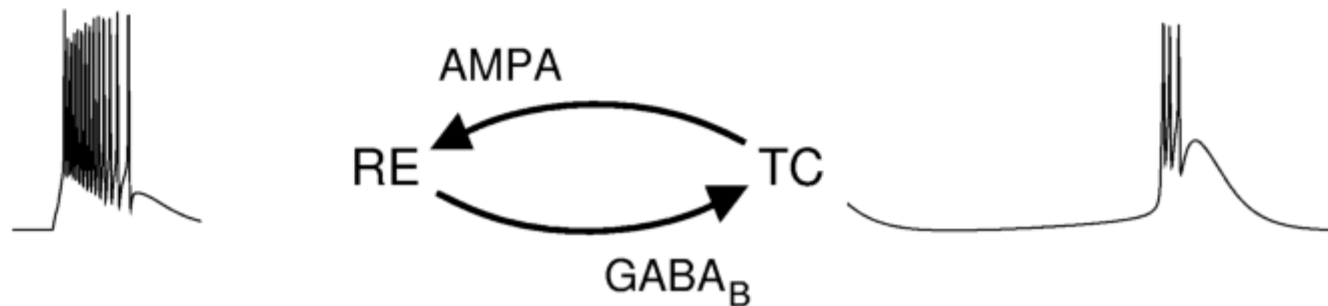
Destexhe et al.,
J. Neurophysiol., 1996

Model of spindle waves and 3Hz oscillations

Thalamic spindle oscillations

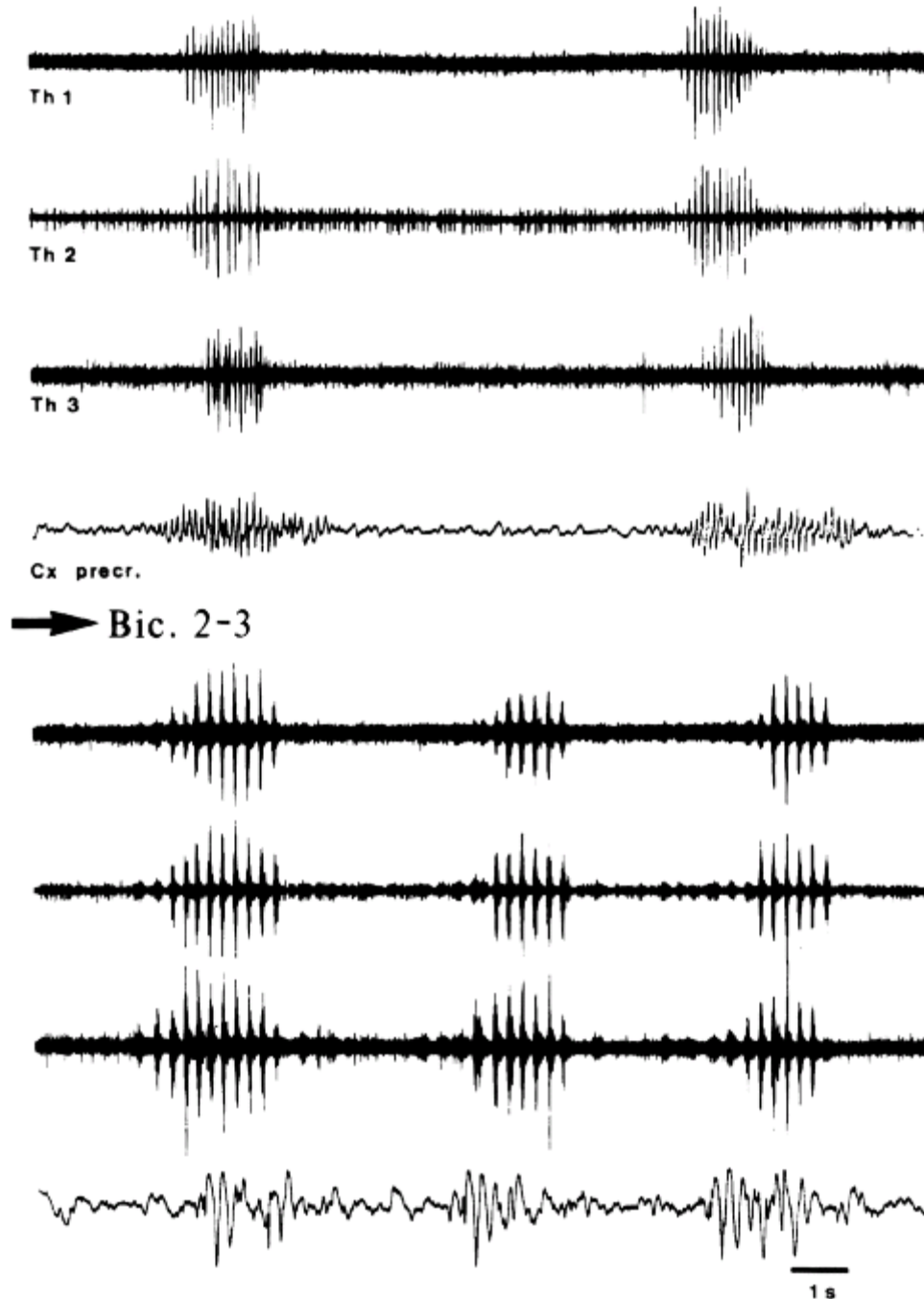


Thalamic 3 Hz oscillations



Destexhe et al.,
J. Neurophysiol., 1996

Slow bicuculline-induced oscillations in vivo

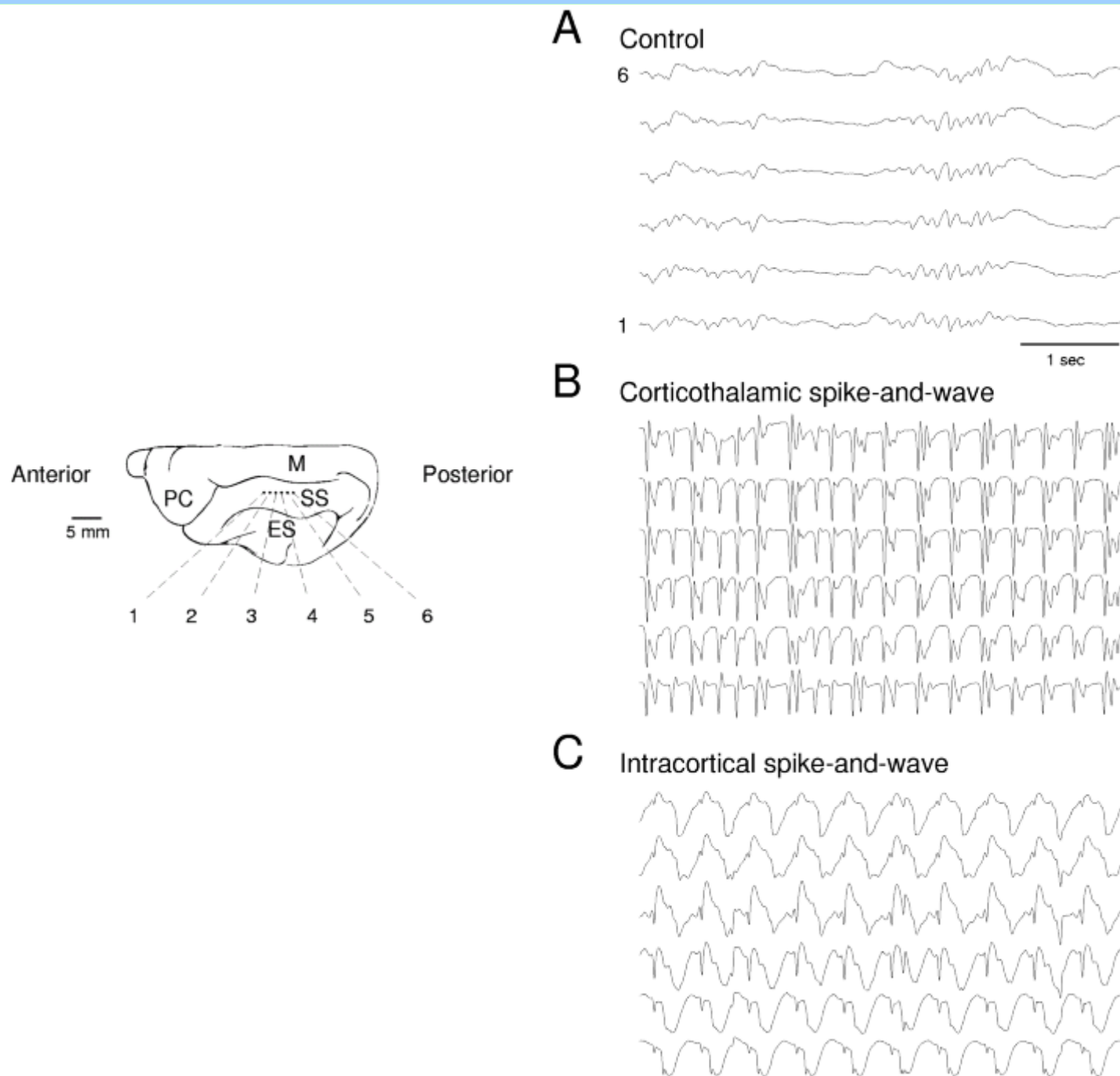


Contreras and Steriade,
J. Neurophysiol., 1999

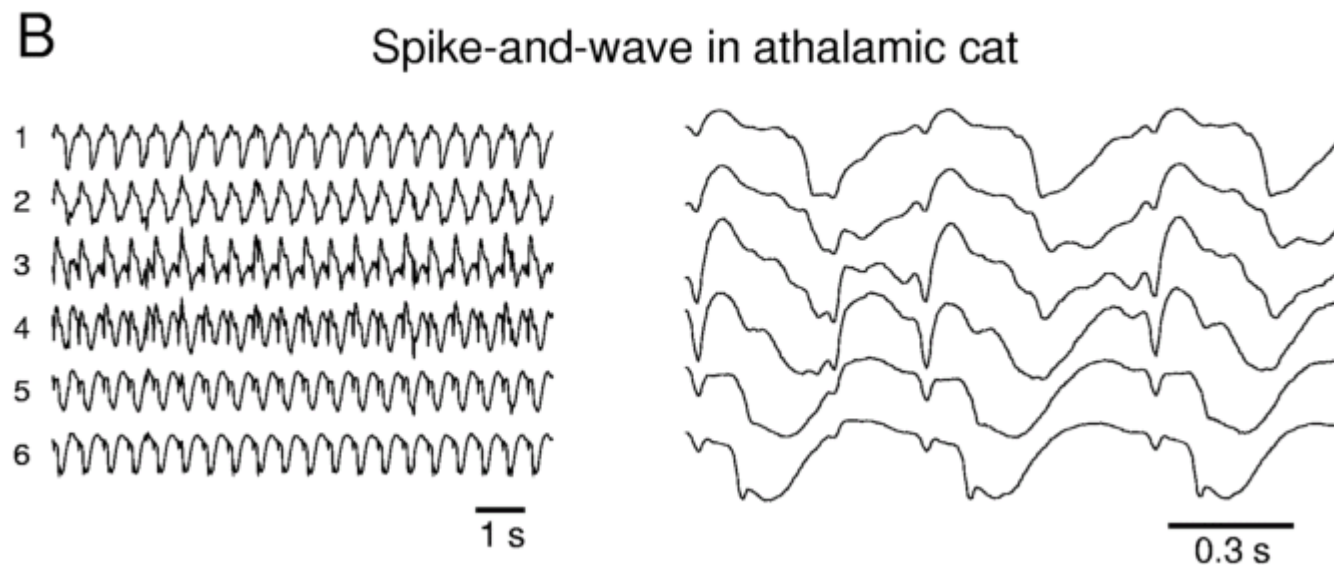
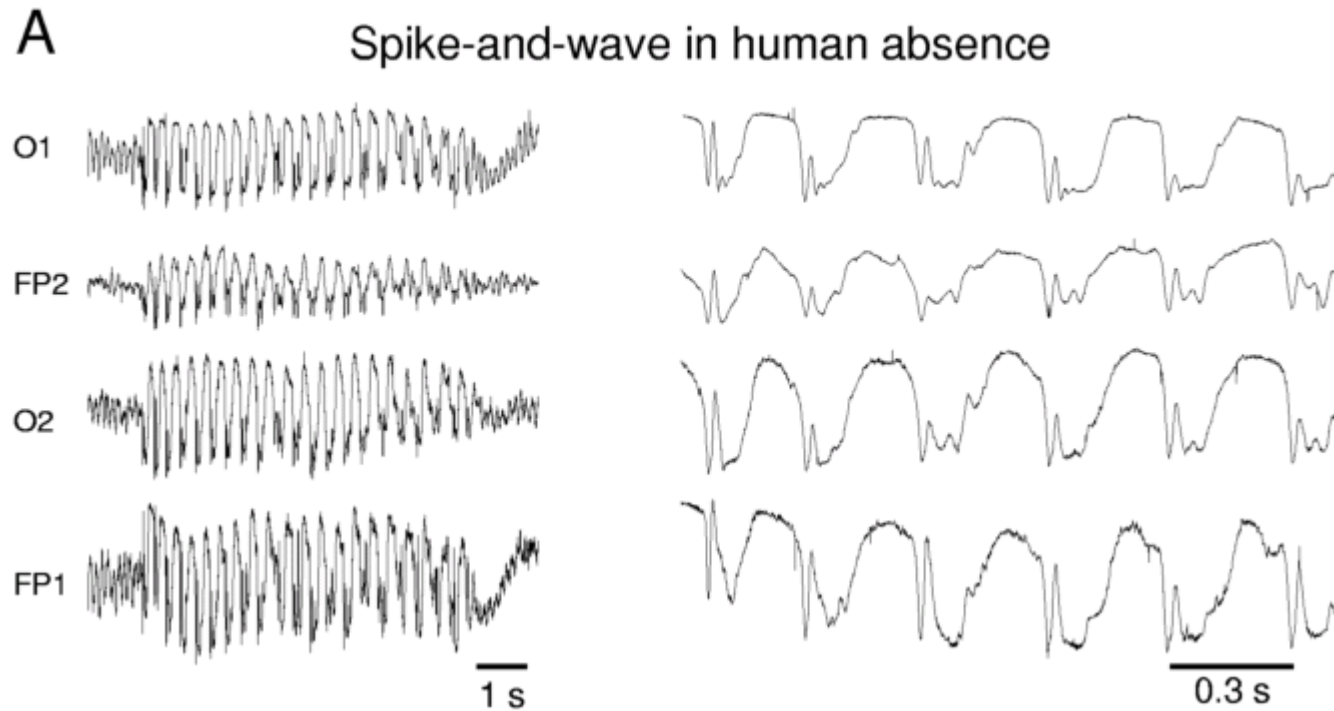
- Thalamic circuits can generate hyper-synchronized 3 Hz oscillations following application of convulsants, such as bicuculline
- These slow oscillations are distinct from the spike-and-wave discharges of the EEG

- 1. Intra-thalamic loops
- 2. Intra-cortical loops
- 3. Thalamo-cortical loops

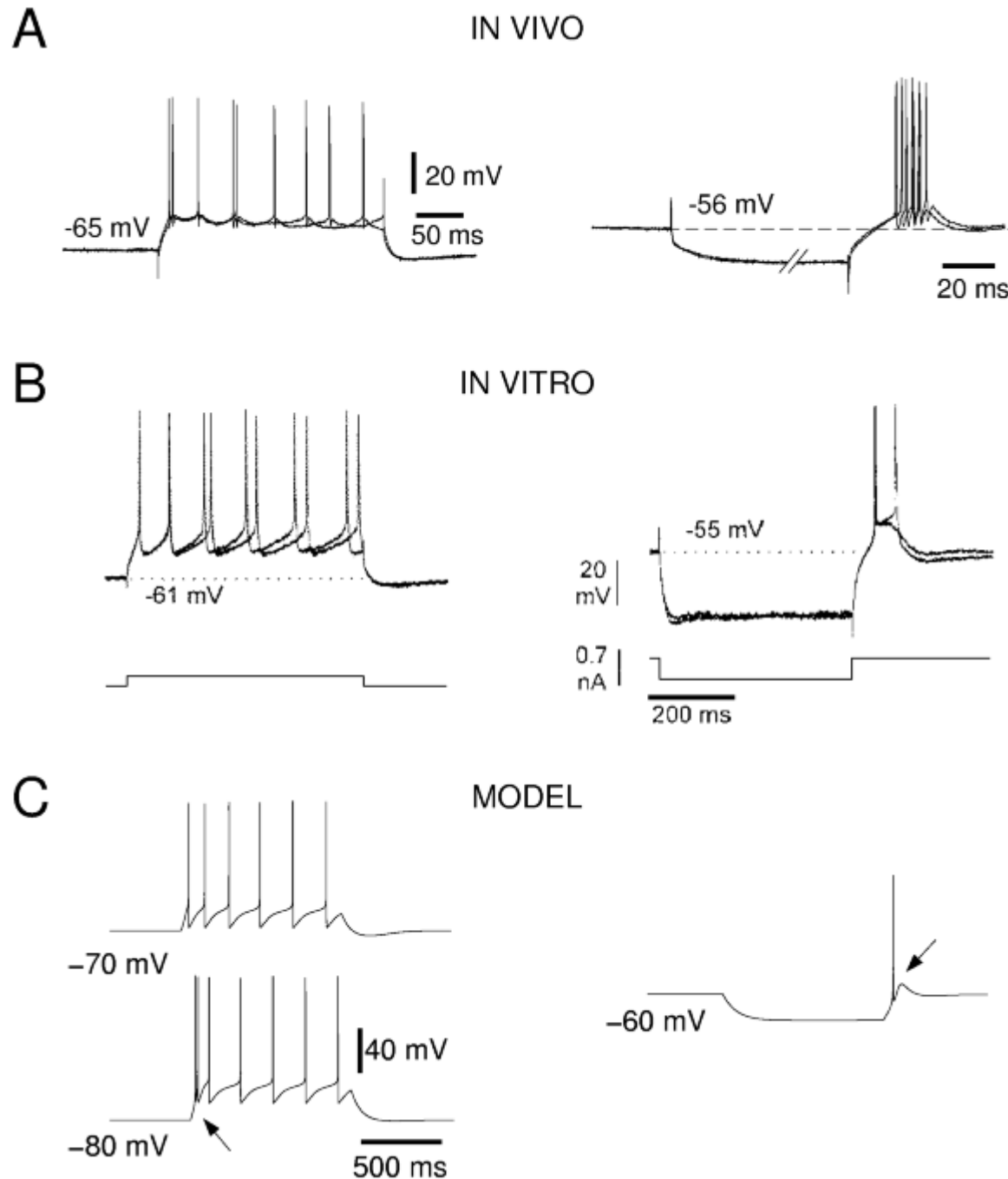
Intracortical spike-and-wave oscillations



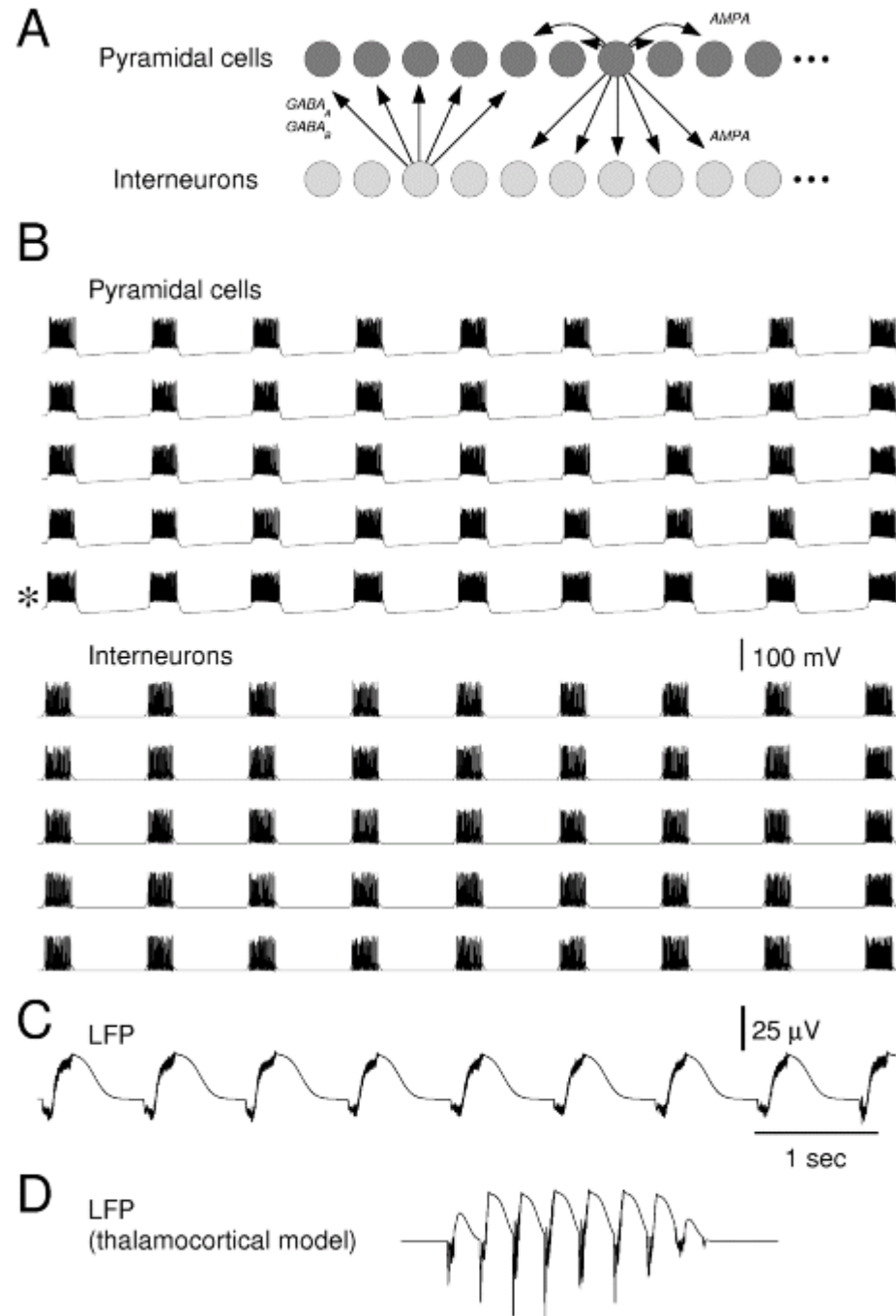
Intracortical spike-and-wave oscillations



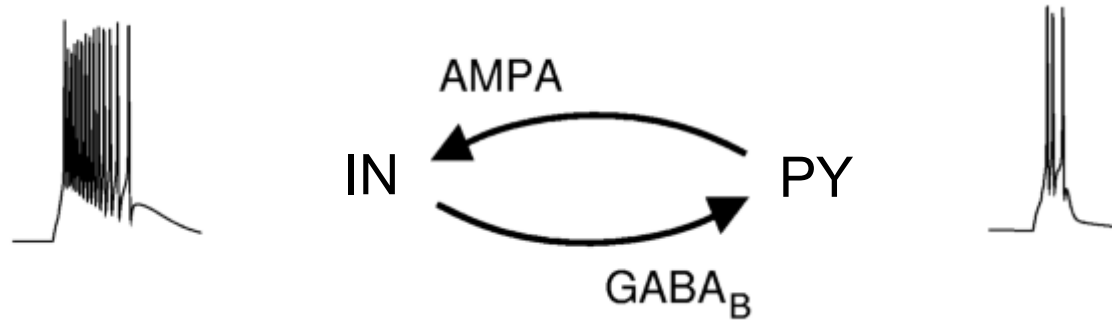
LTS neurons in cerebral cortex



Model of intracortical spike-and-wave

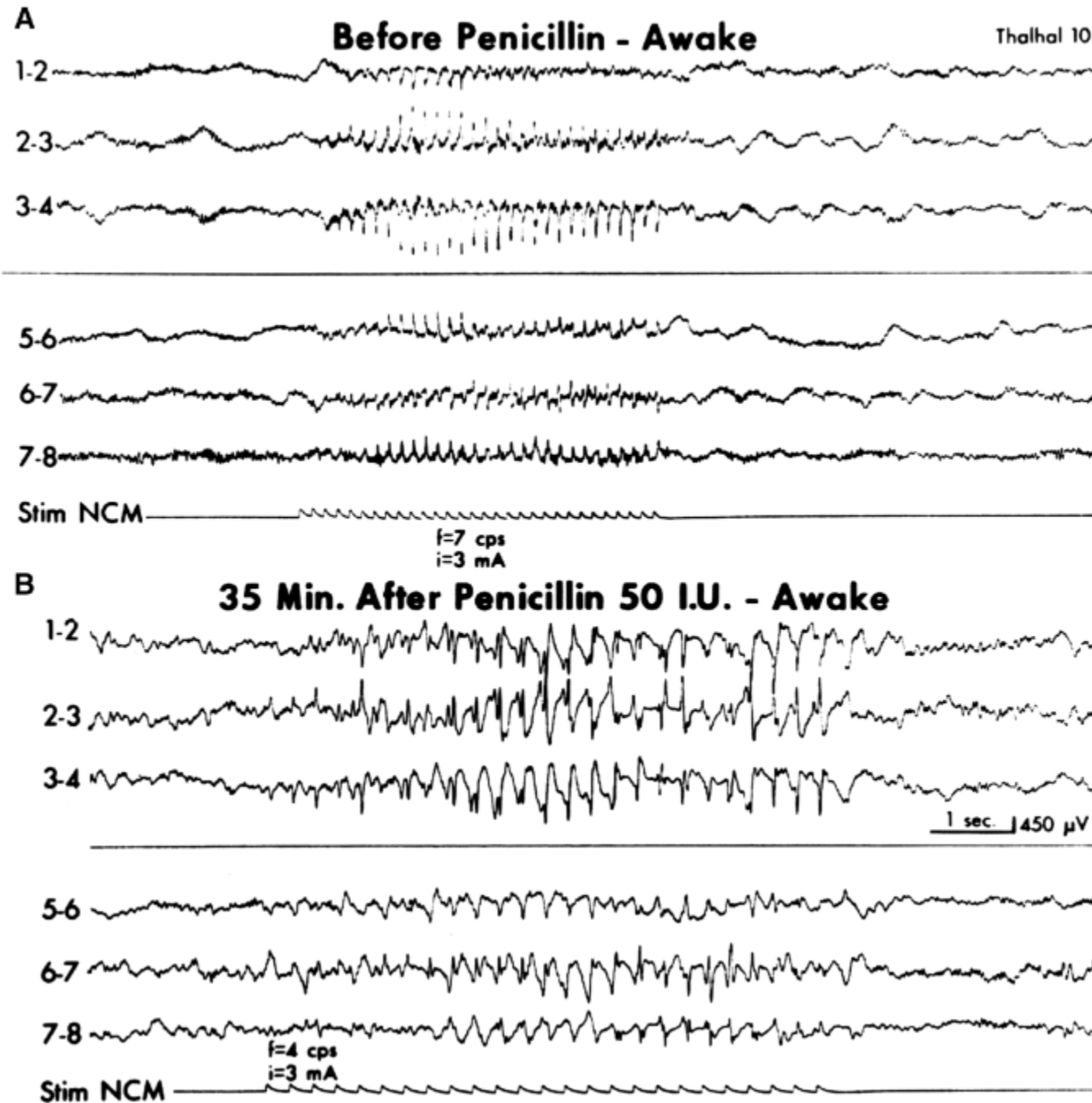


Model of intracortical spike-and-wave



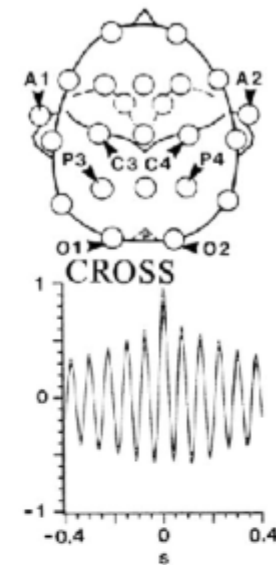
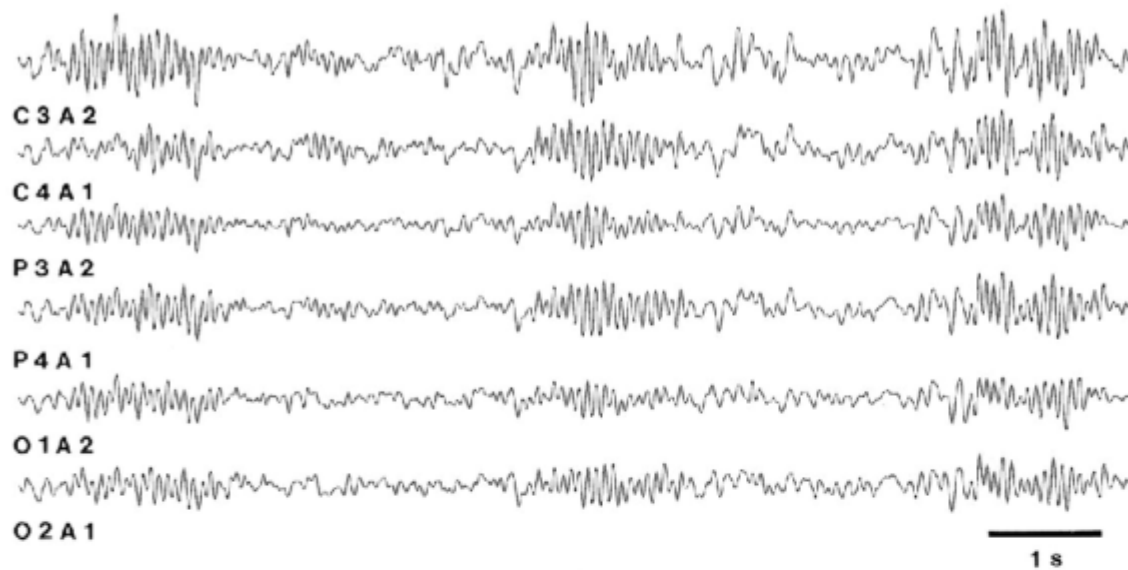
- Cortical circuits can generate a form of slow spike-and-wave oscillation based on inhibitory-rebound mechanisms intrinsic to cortex
- These oscillations are however slower and have an atypical morphology

- 1. Intra-thalamic loops
- 2. Intra-cortical loops
- 3. Thalamo-cortical loops

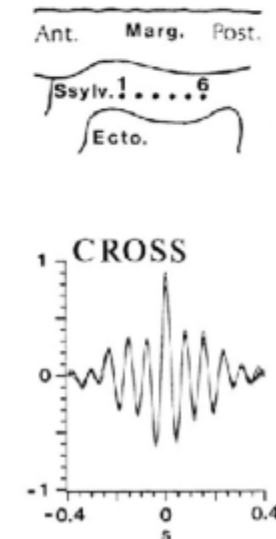
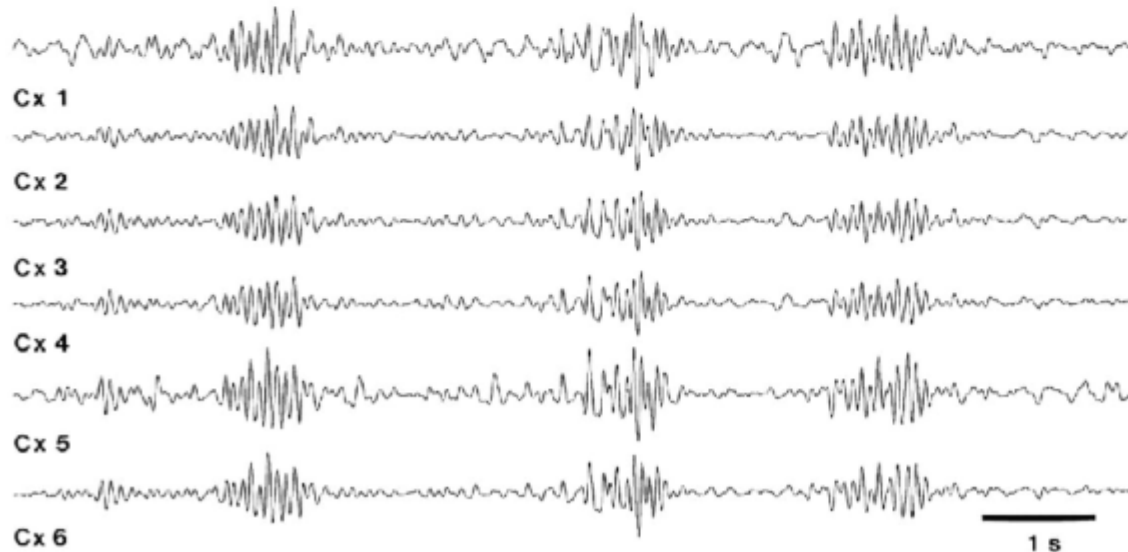


Large-scale coherence of oscillations in vivo

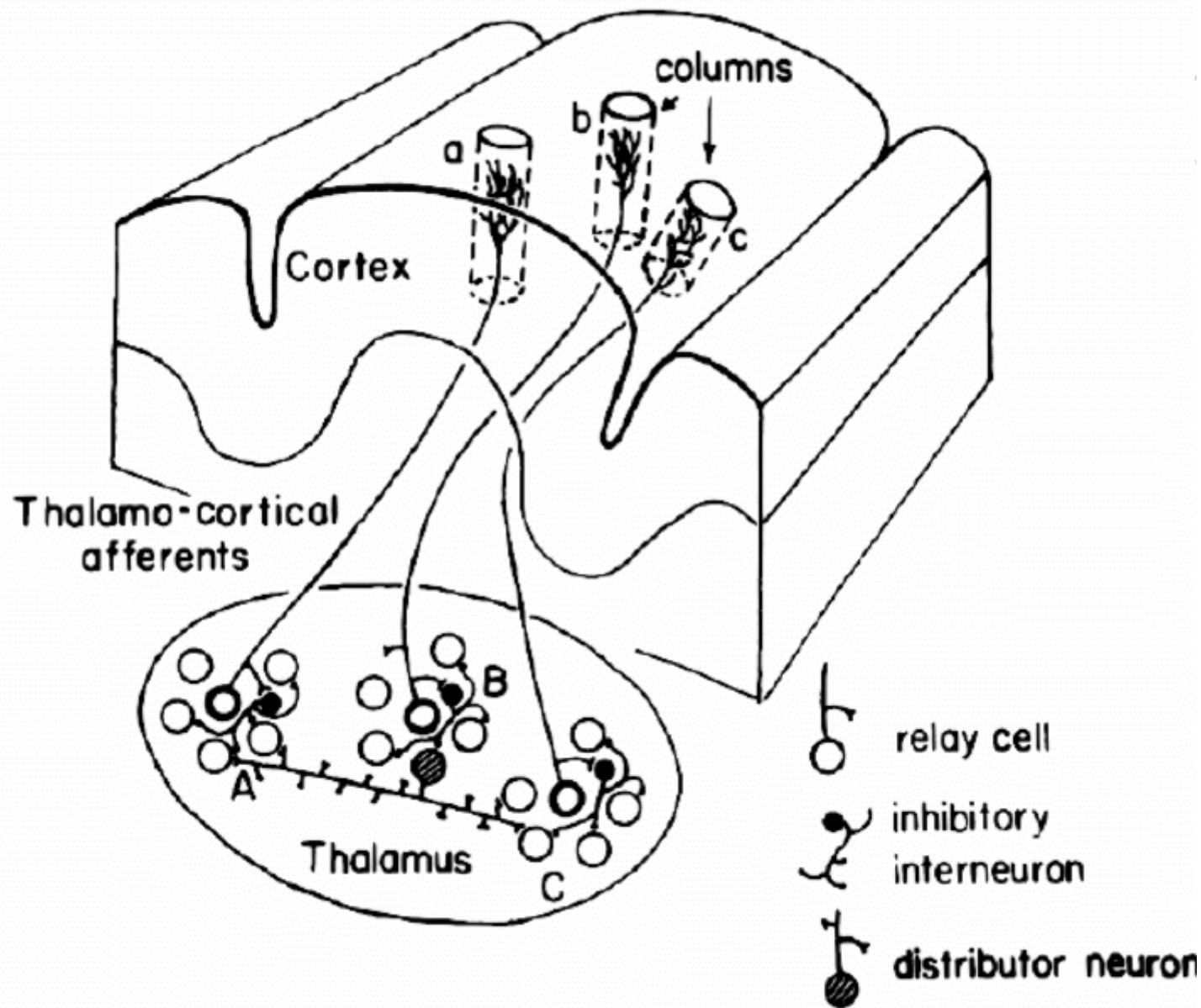
HUMAN



CAT

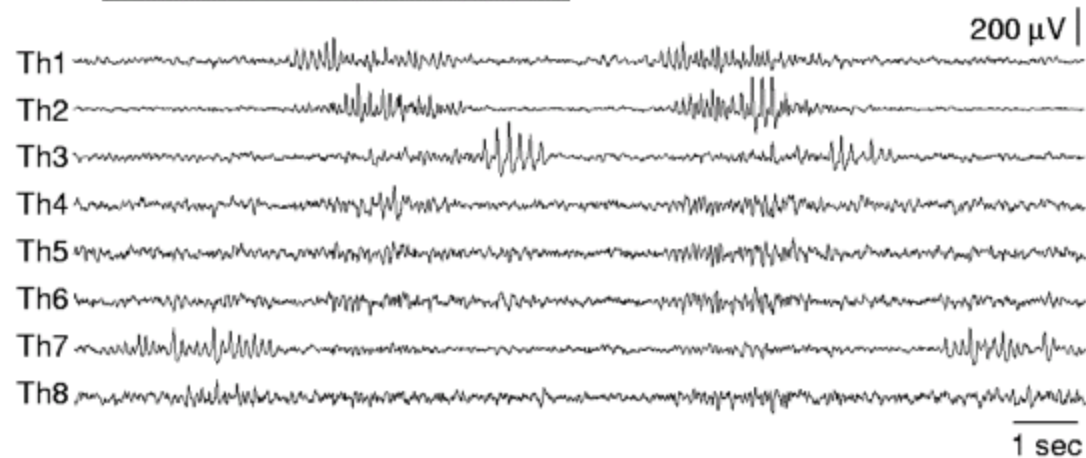
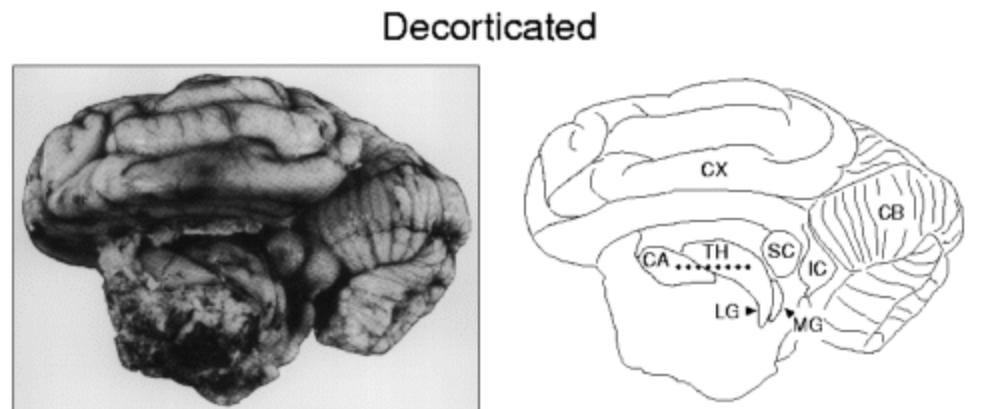
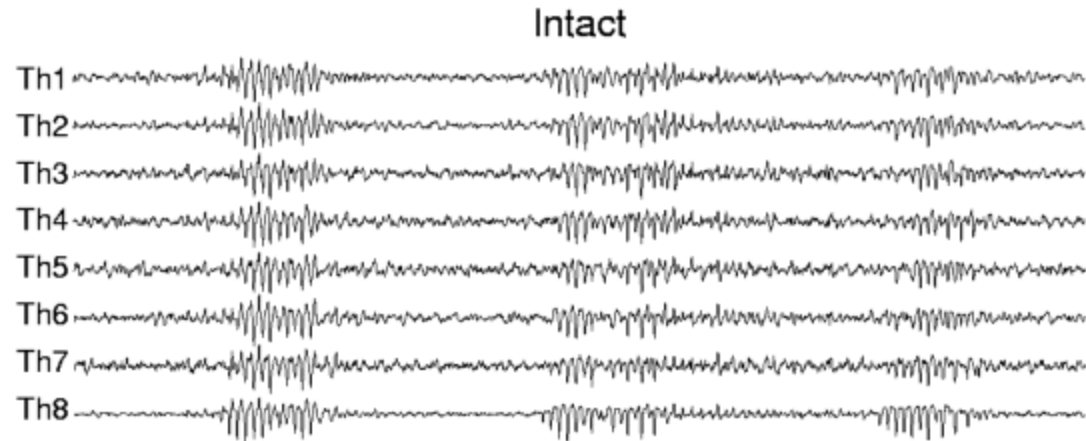


How cortical synchrony is achieved ?

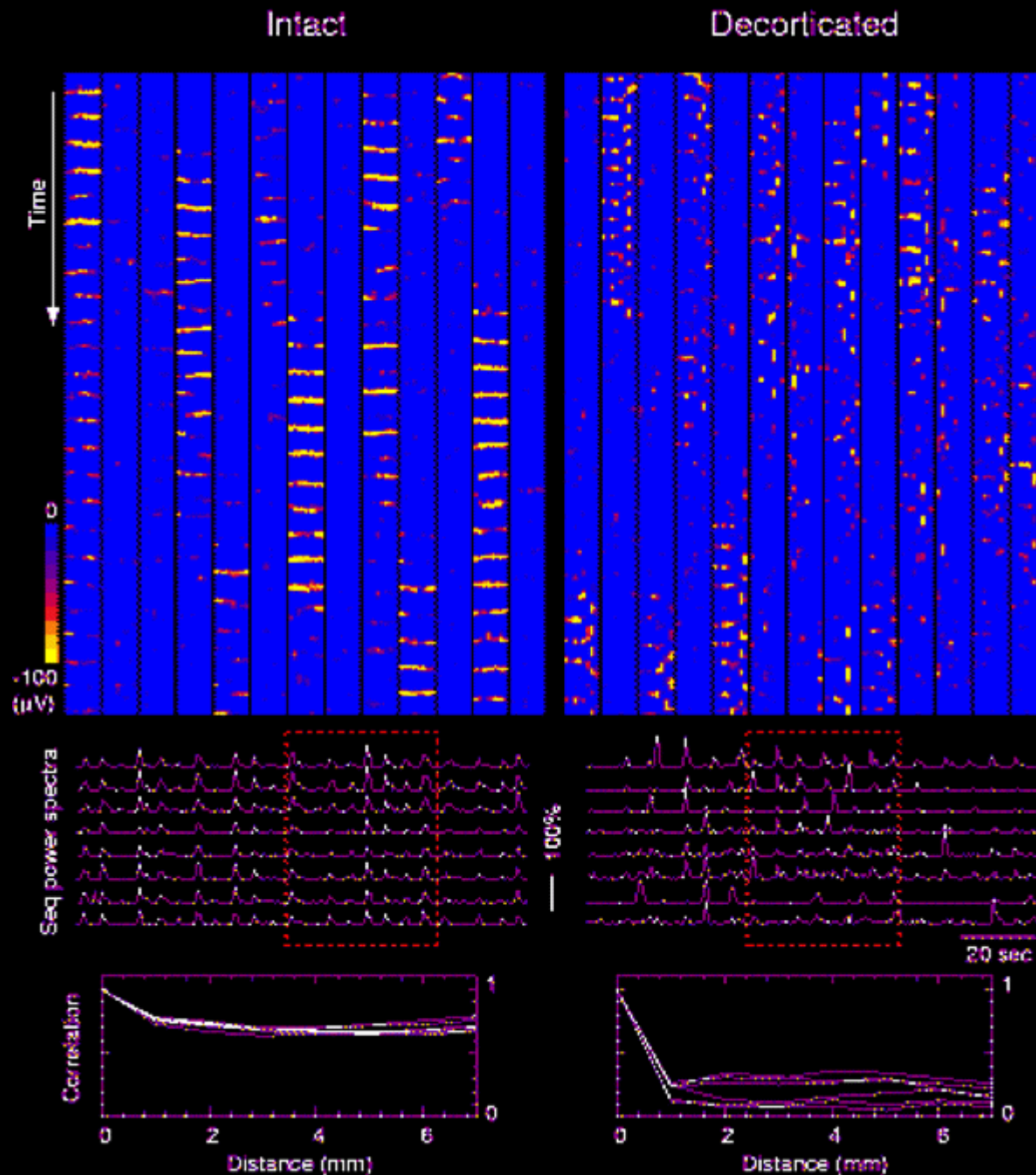


Andersen & Andersson, 1968

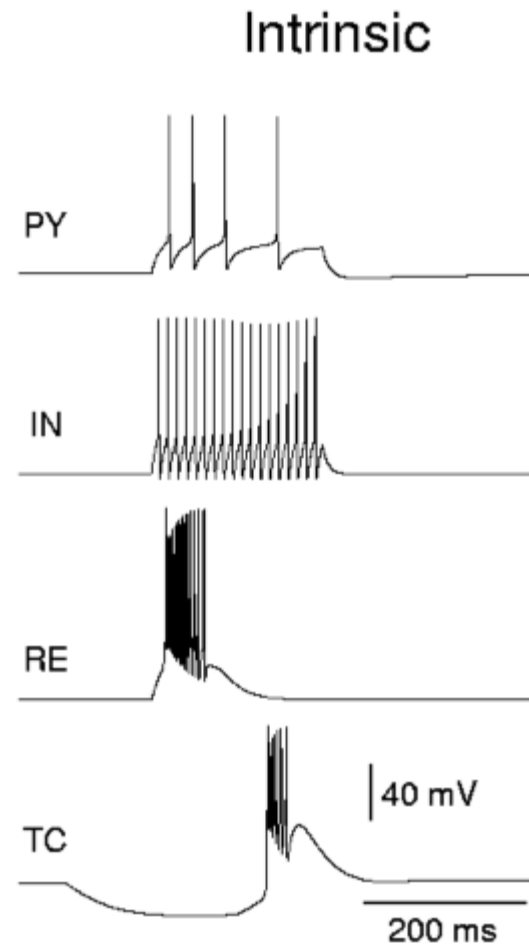
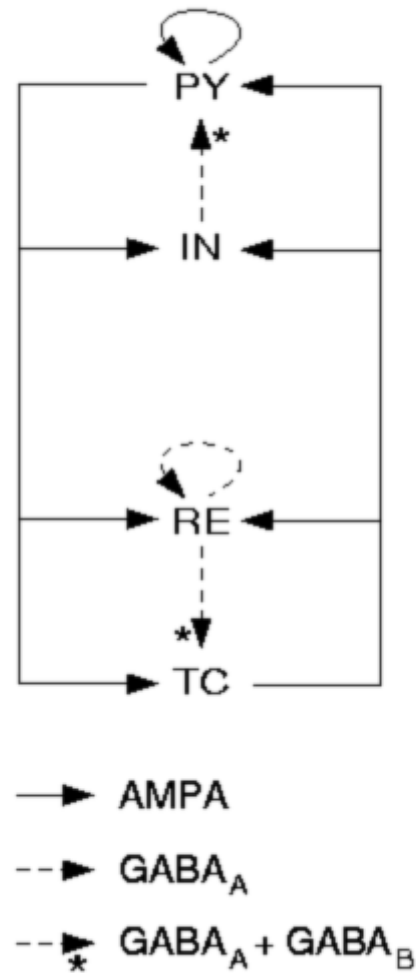
Large-scale coherence is lost after decortication



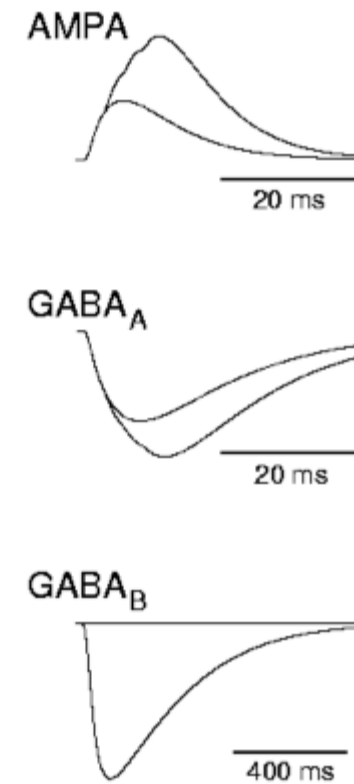
Large-scale coherence is lost after decortication



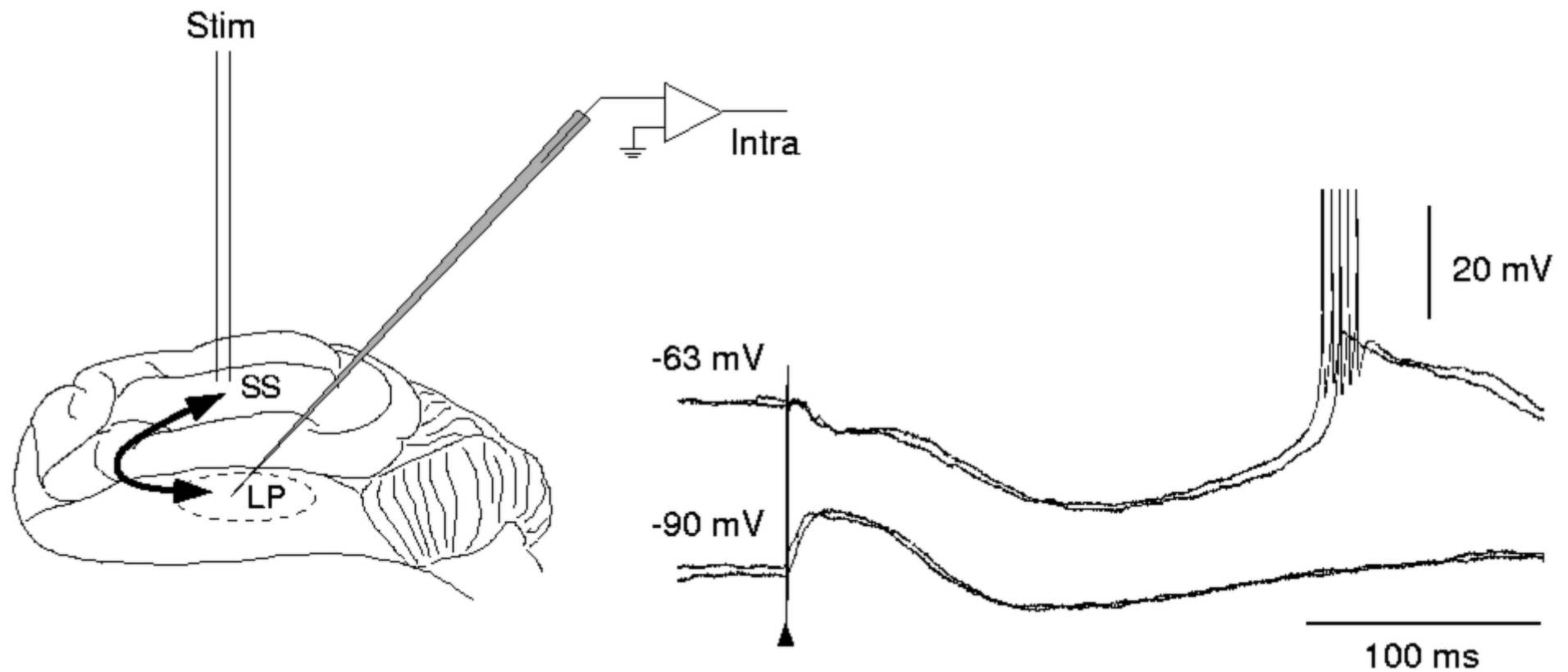
Model thalamocortical networks



Synaptic

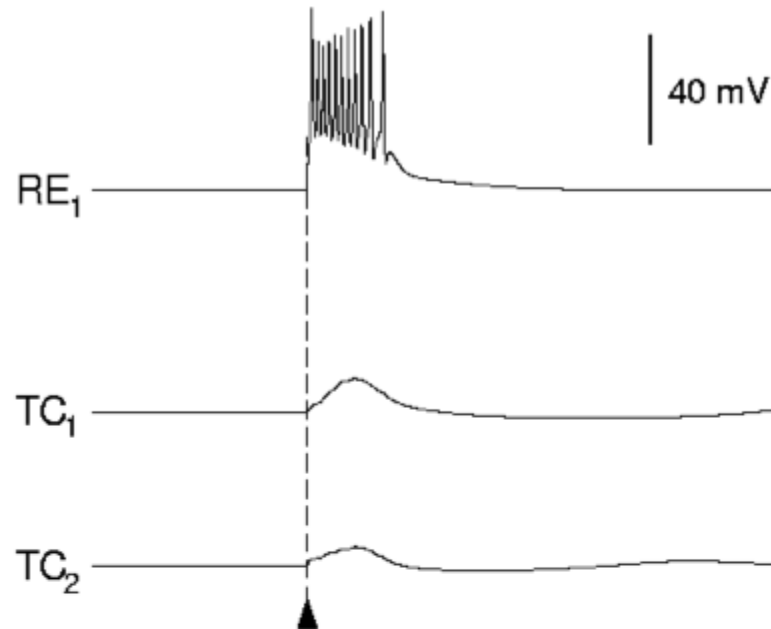
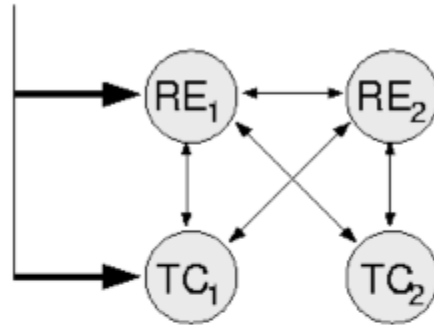


Corticothalamic feedback is inhibitory dominant

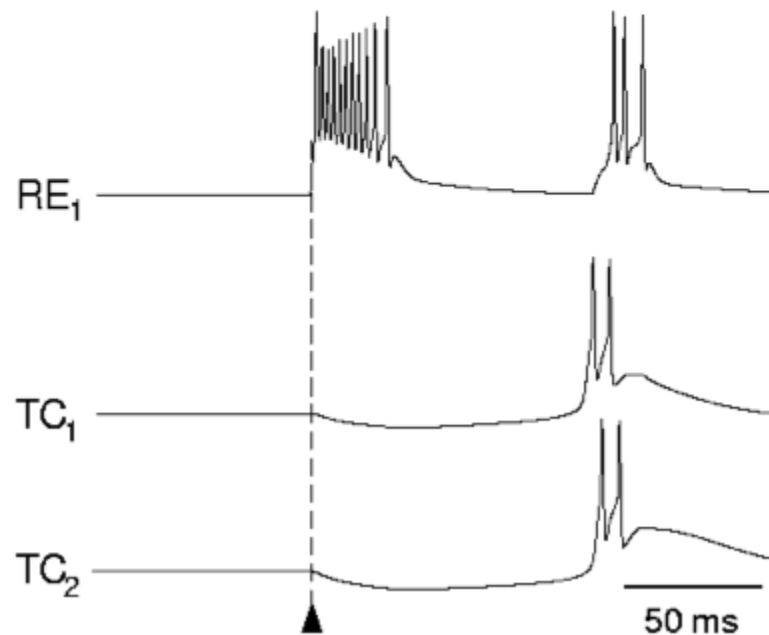
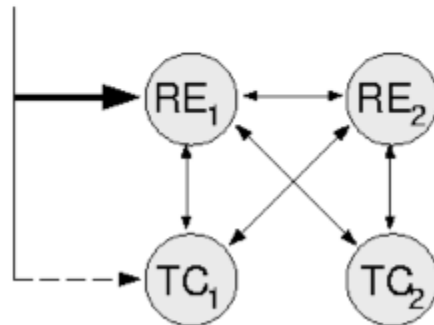


Model of inhibitory dominant corticothalamic feedback

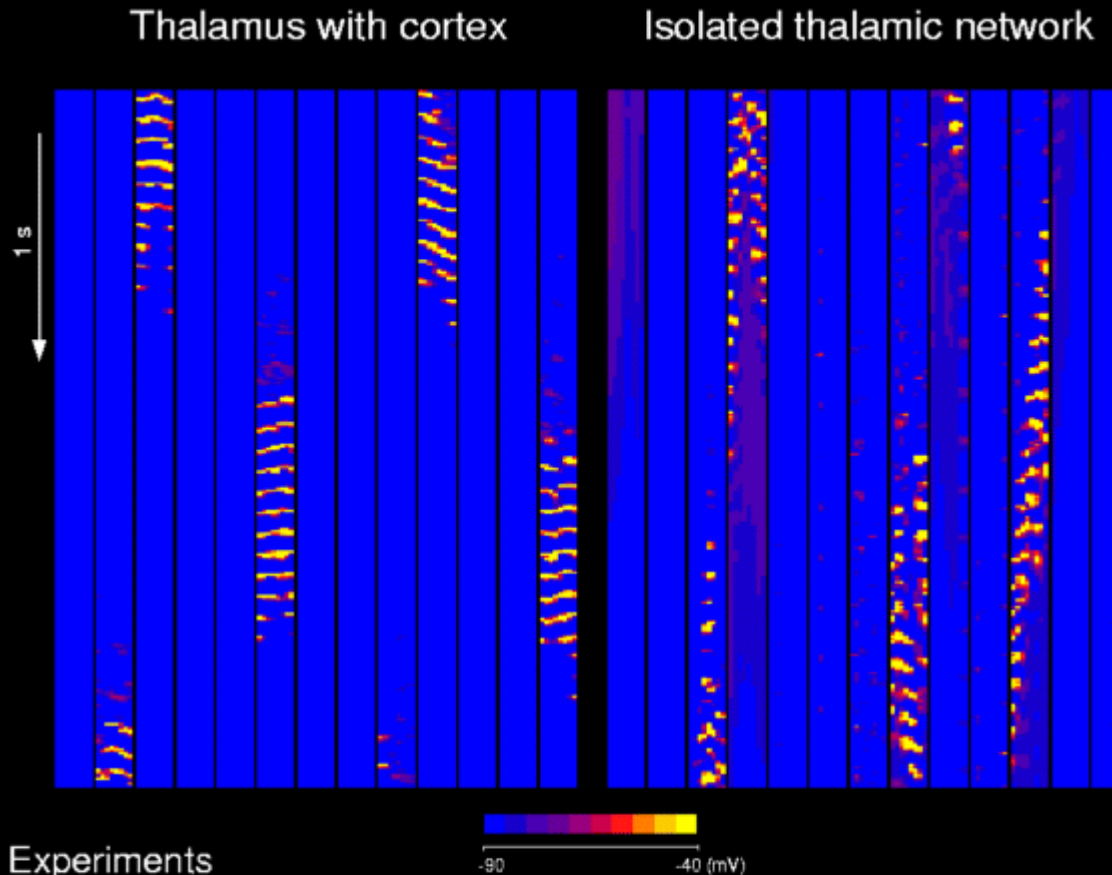
AMPA



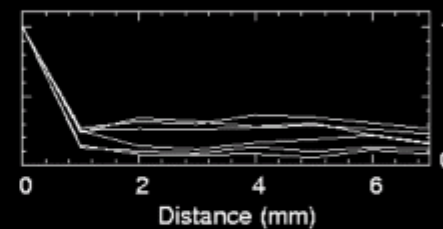
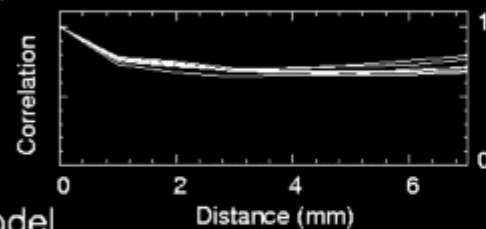
AMPA



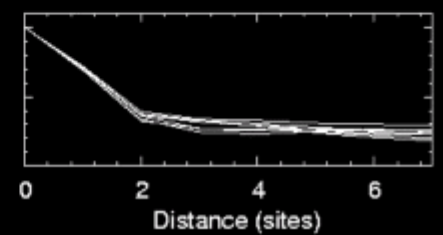
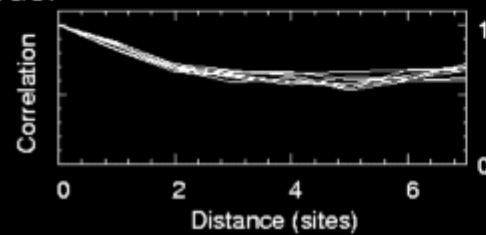
Model of large-scale coherence



Experiments

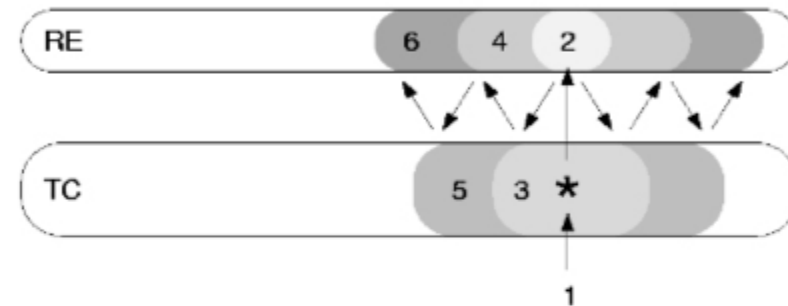
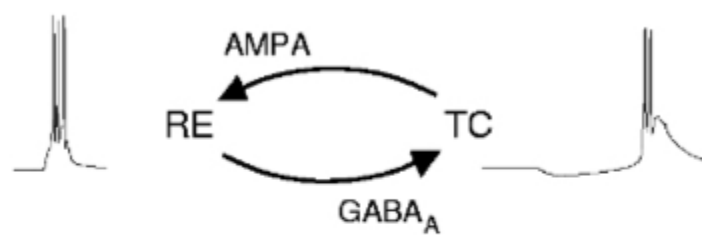


Model

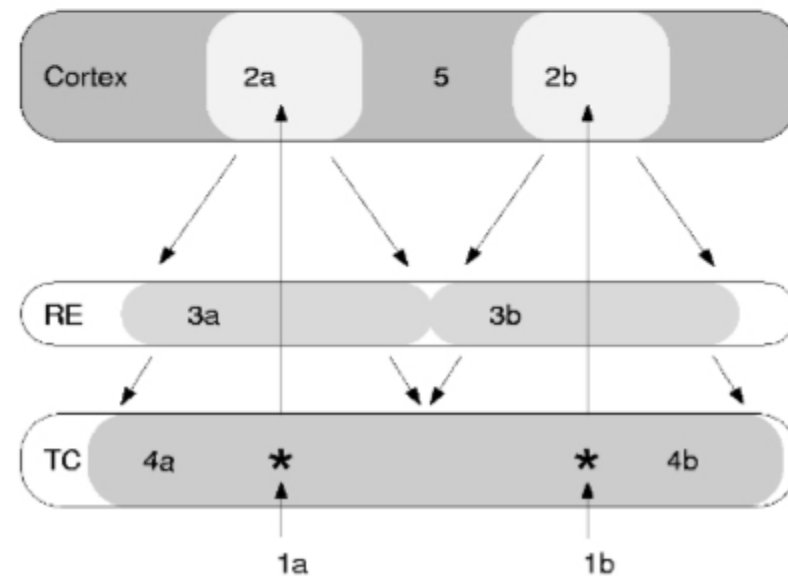
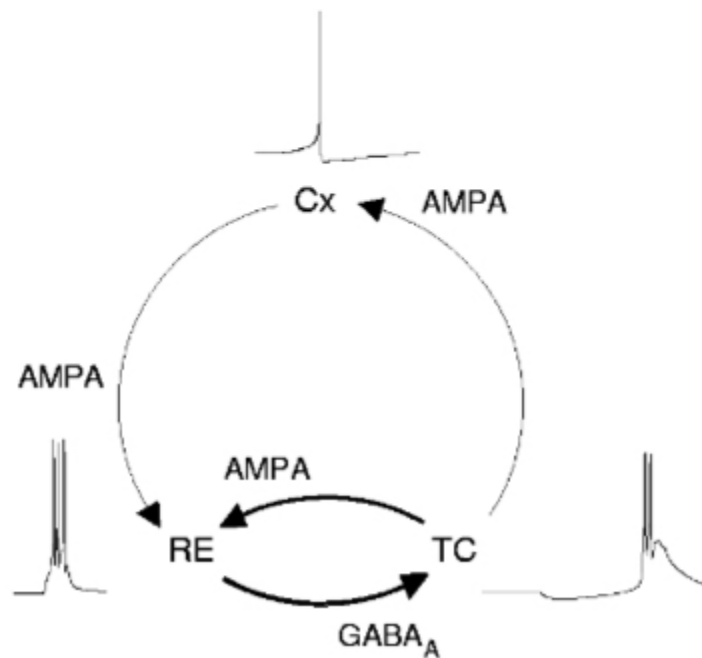


Synchronization mechanisms

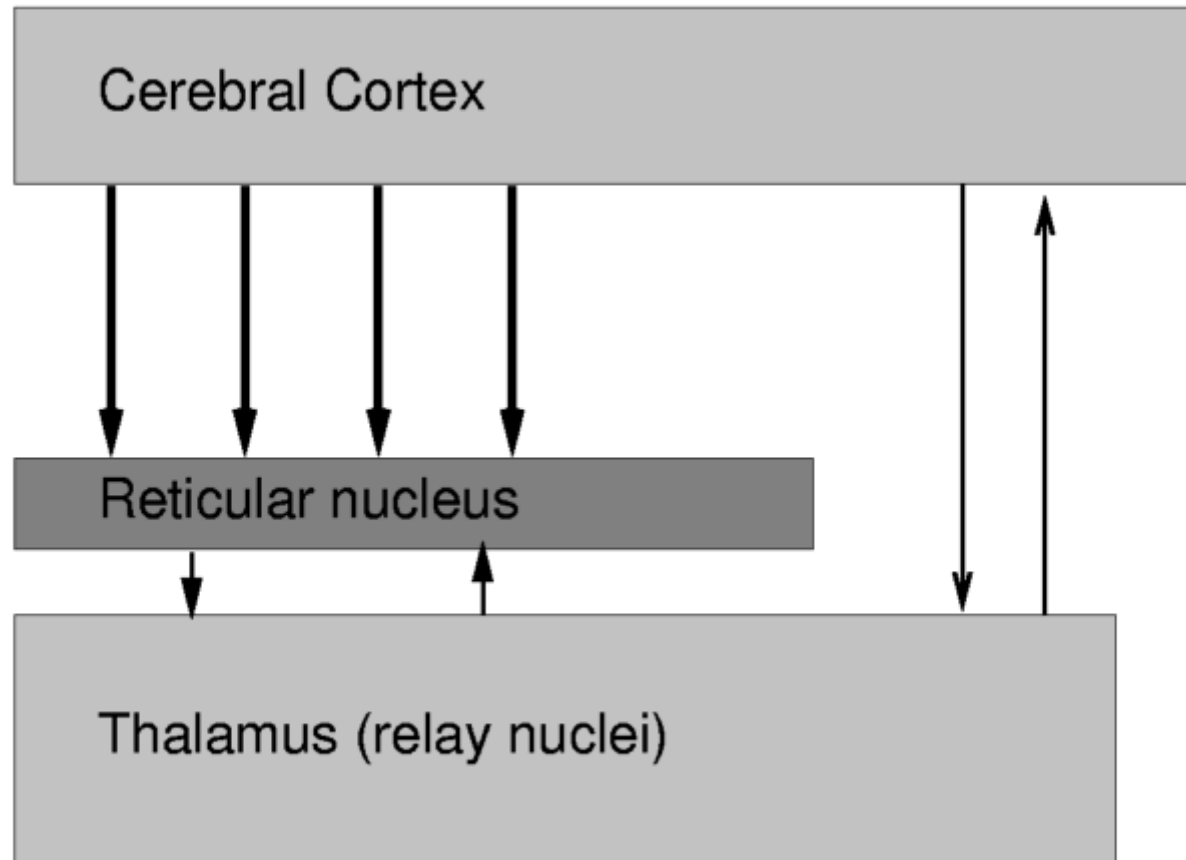
Isolated thalamus



Thalamocortical system

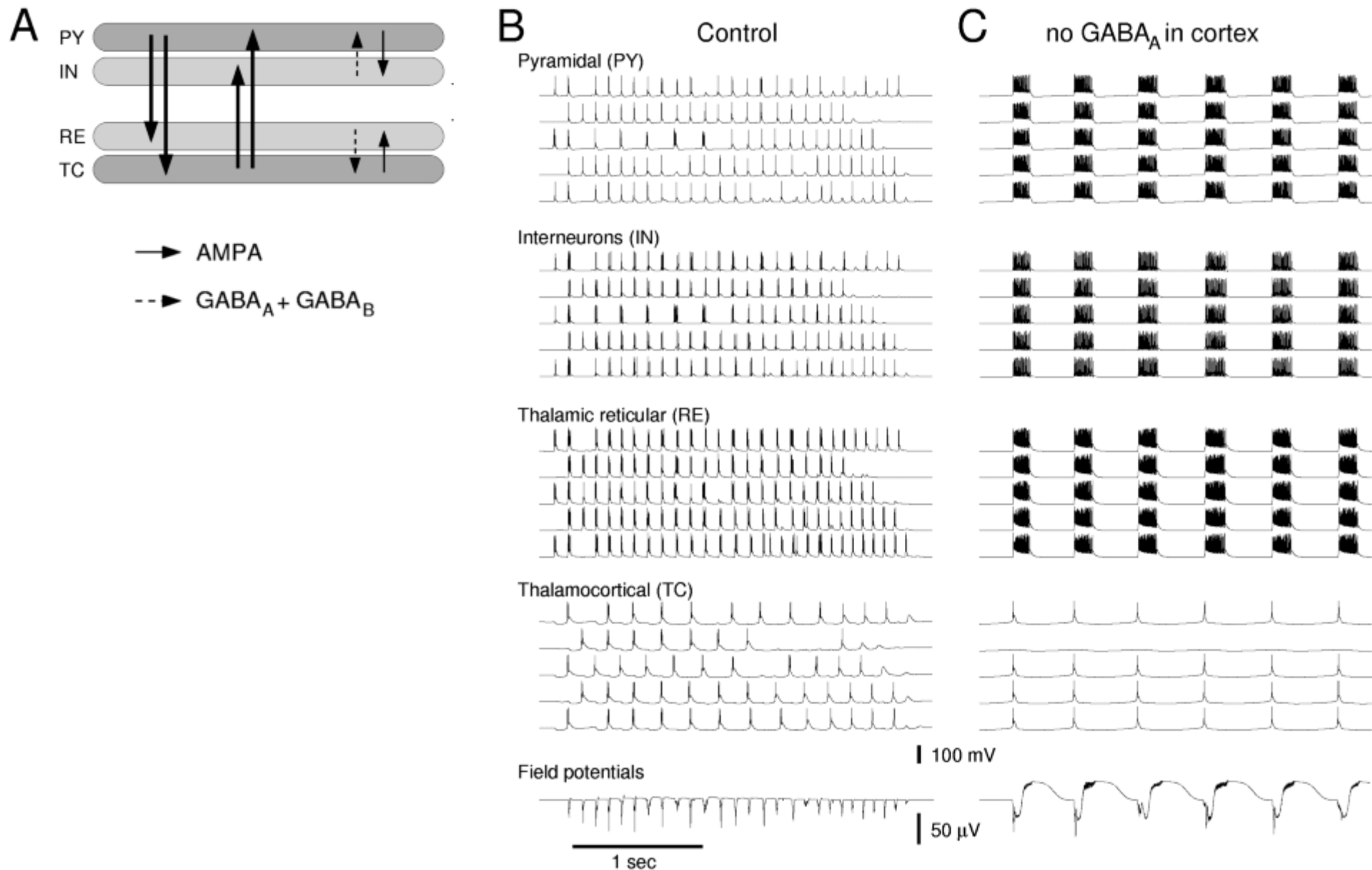


Mechanism of thalamocortical spike-and-wave

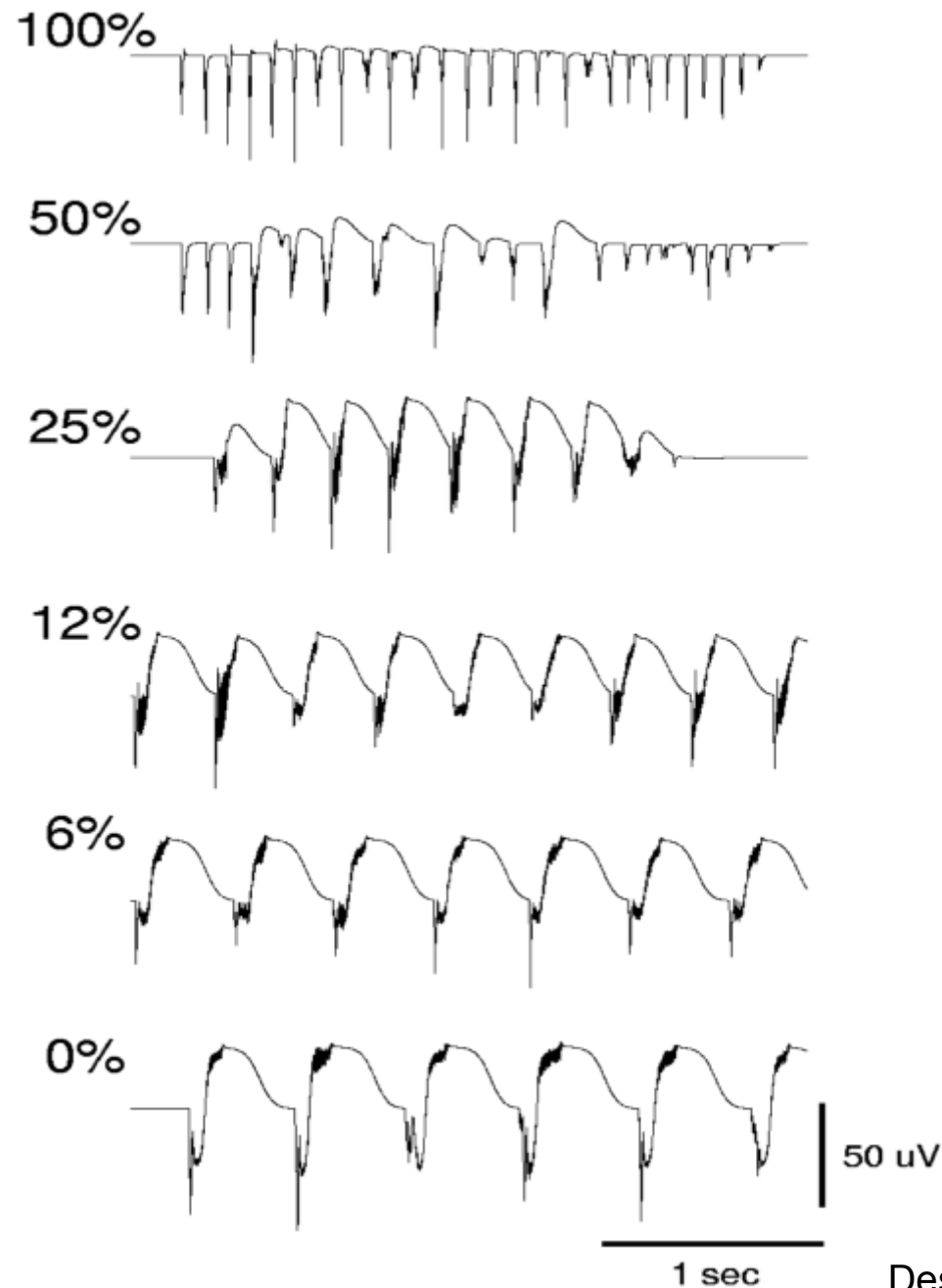


How to extrapolate this mechanism
to seizures ?

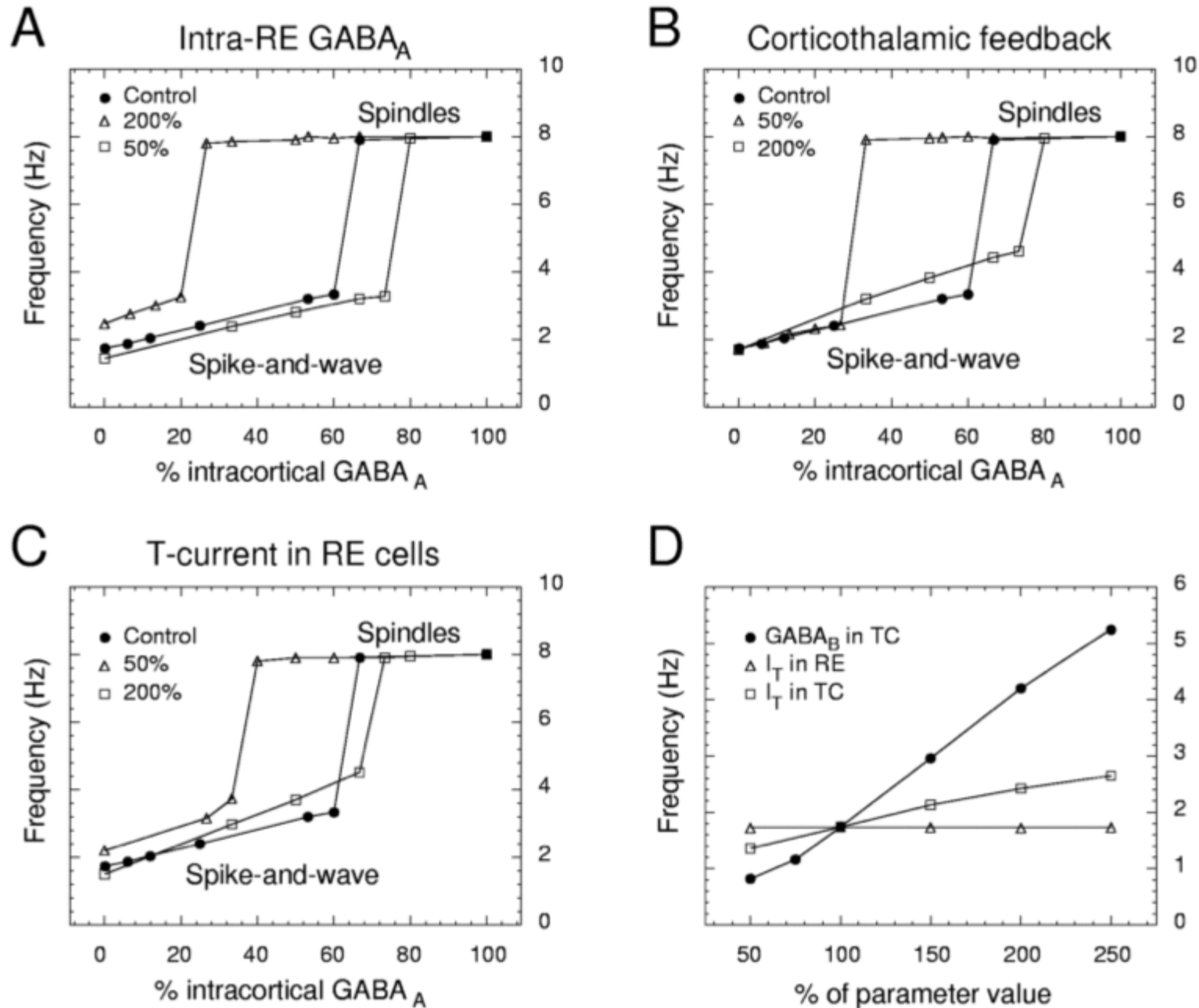
Thalamocortical spike-and-wave oscillations



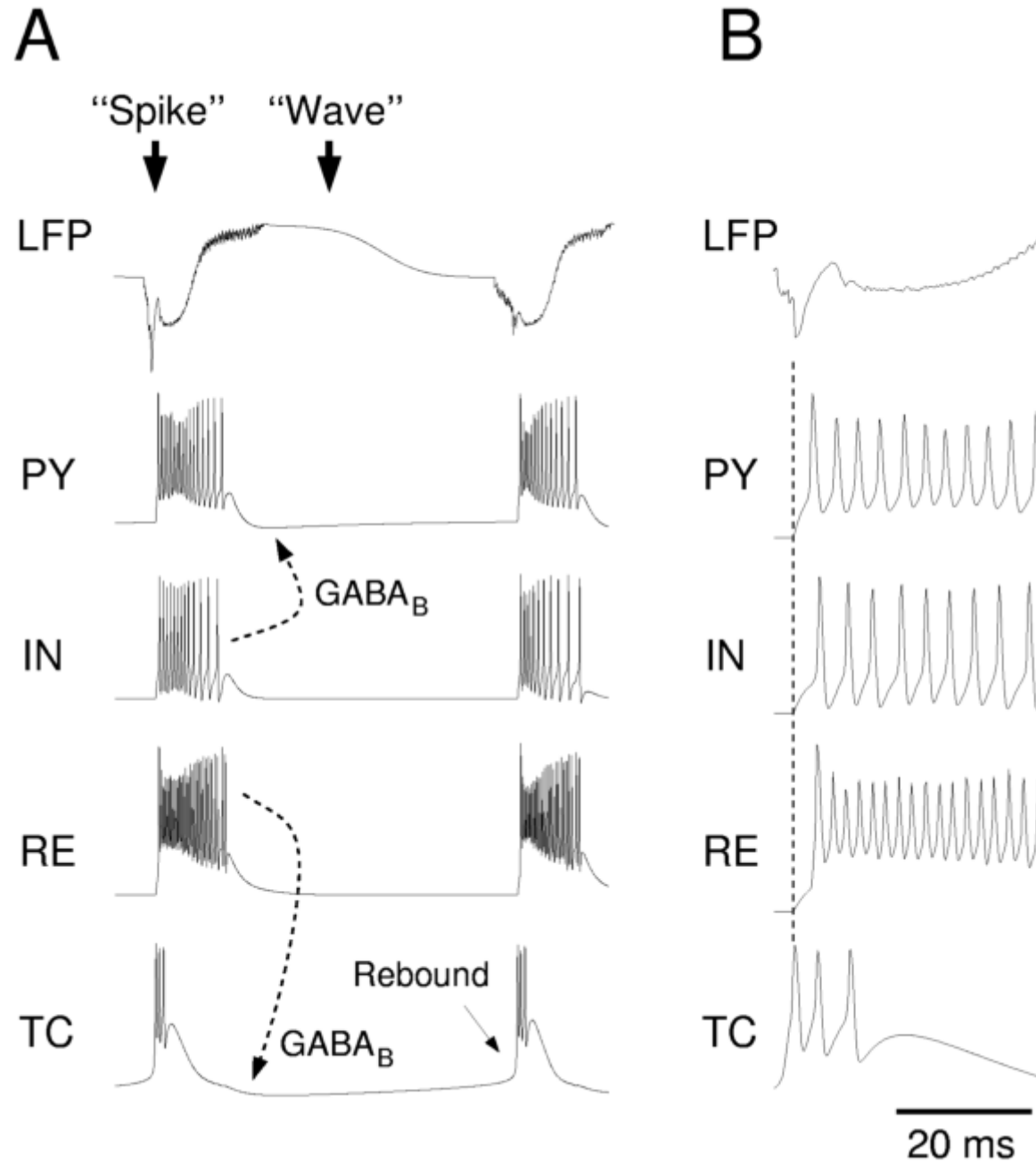
Spike-and-wave following alteration of cortical excitability



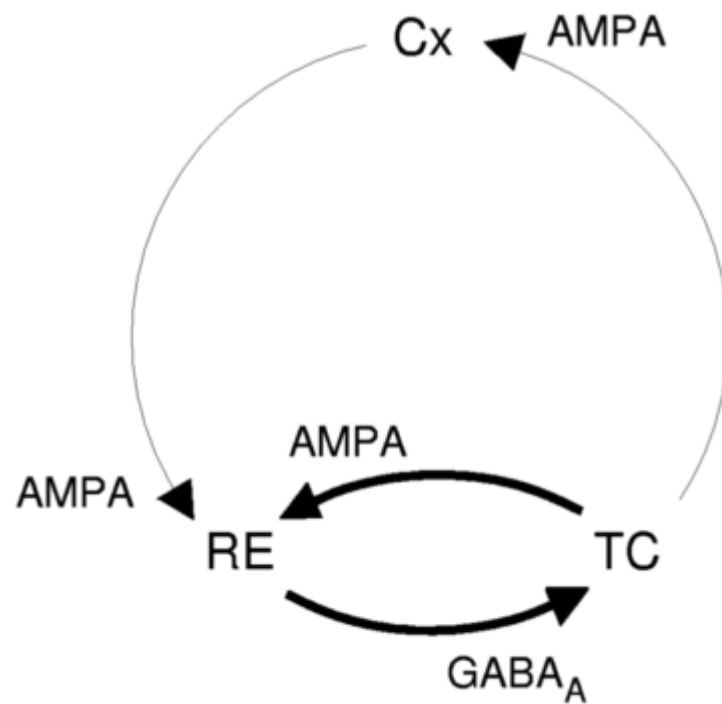
Properties of thalamocortical spike-and-wave



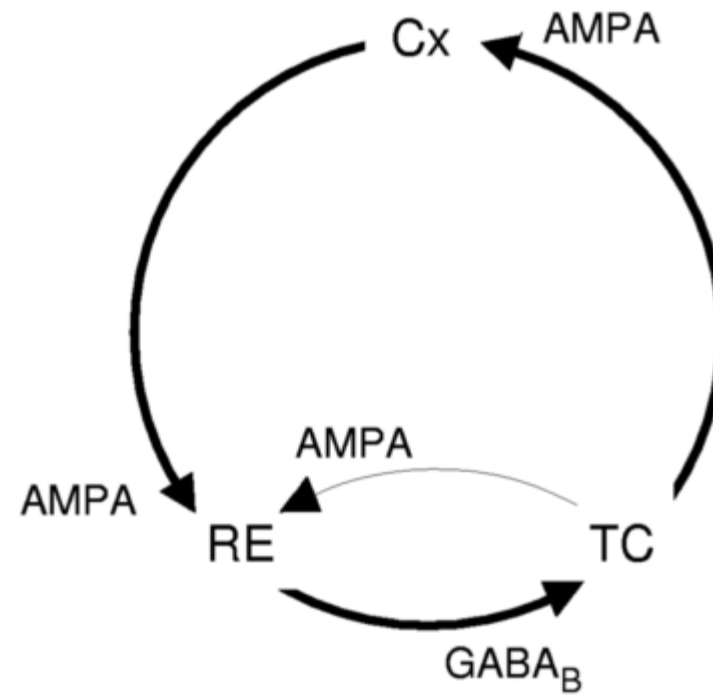
Thalamocortical spike-and-wave



10 Hz spindle



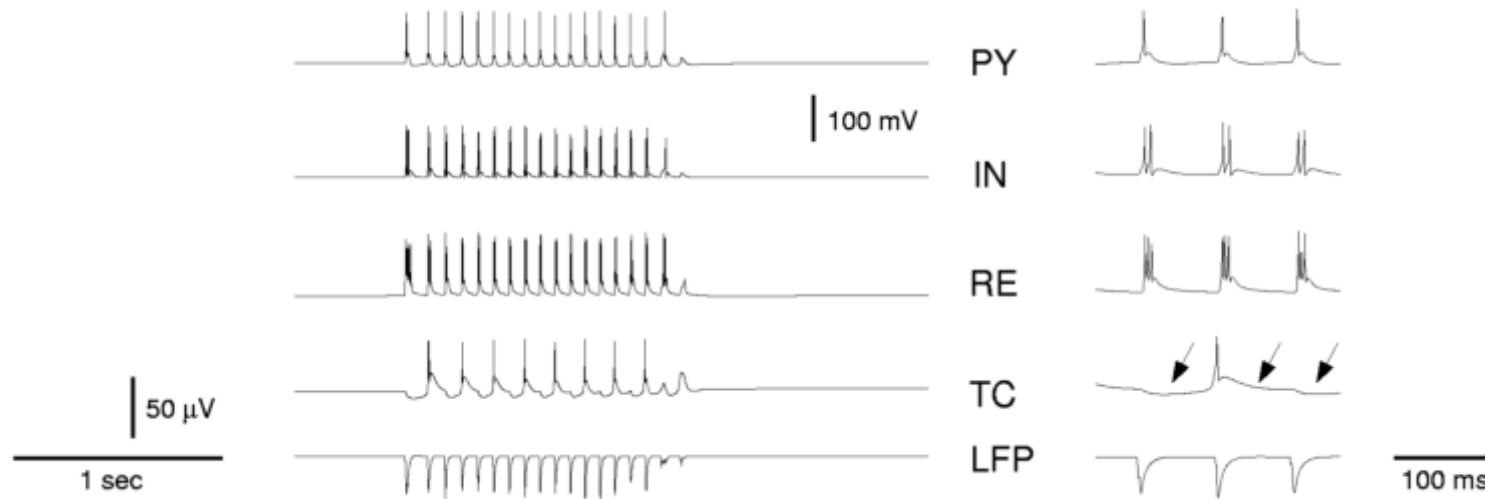
3 Hz spike-and-wave



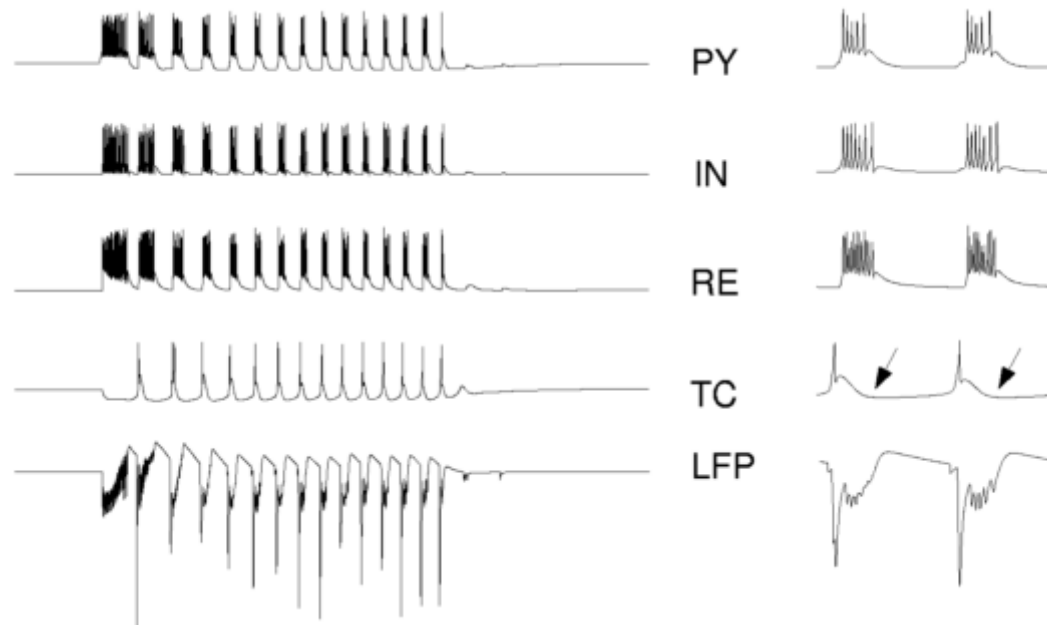
Can the same mechanism explain the “fast” oscillations during seizures in rodents ?

“Fast” (5-10 Hz) thalamocortical spike-and-wave

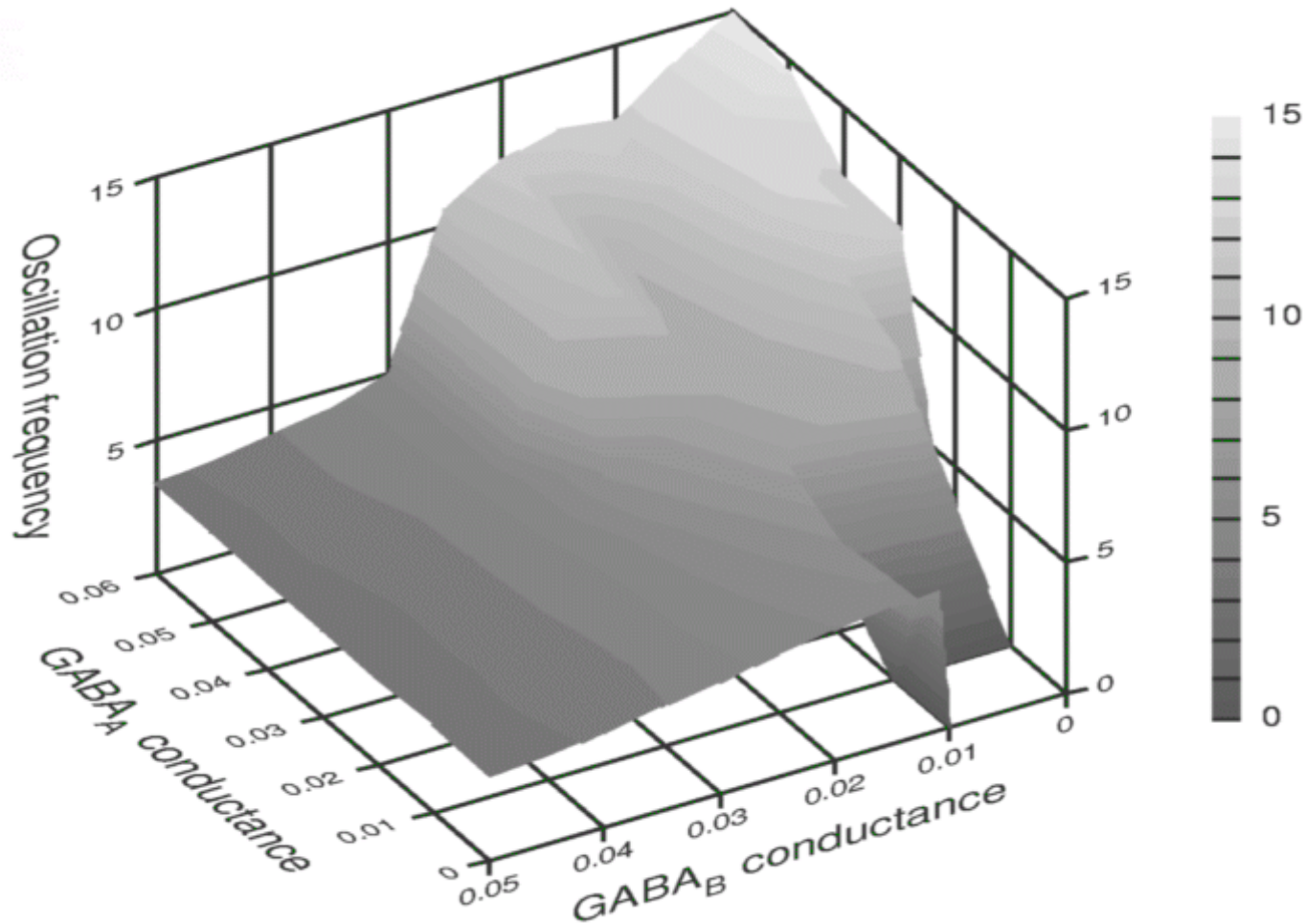
Spindles



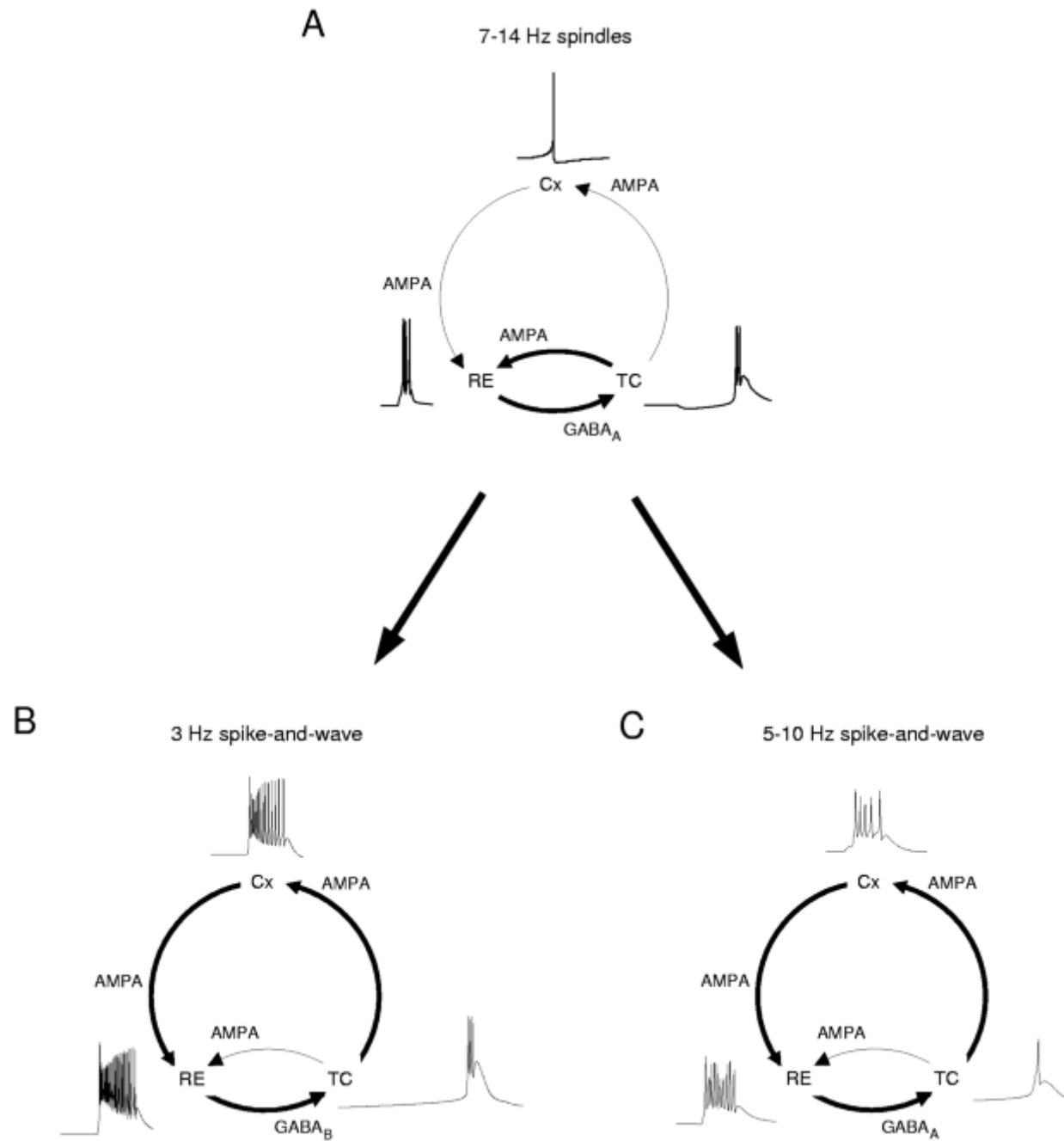
Spike-and-wave



A continuum of spike-and-wave oscillations ?



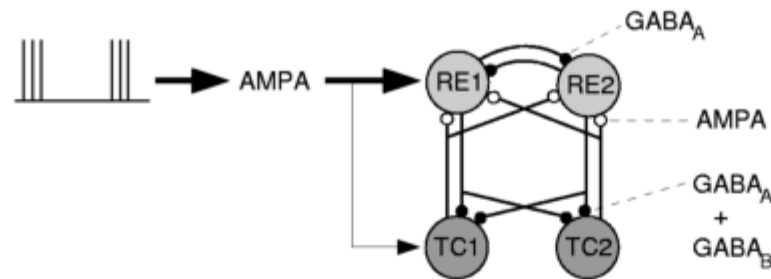
Thalamocortical loops



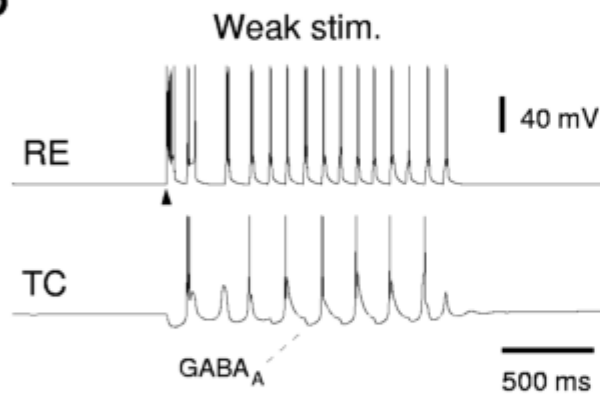
Can we test this mechanism
with appropriate experiments ?

Cortical input can force intact thalamic circuits at 3 Hz

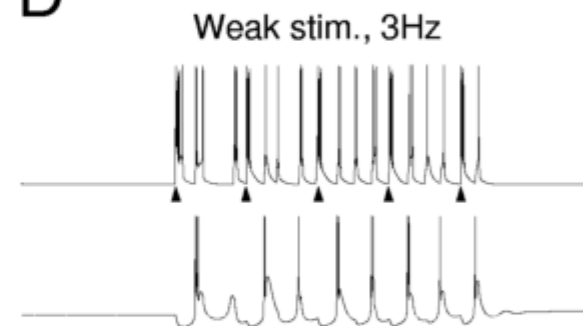
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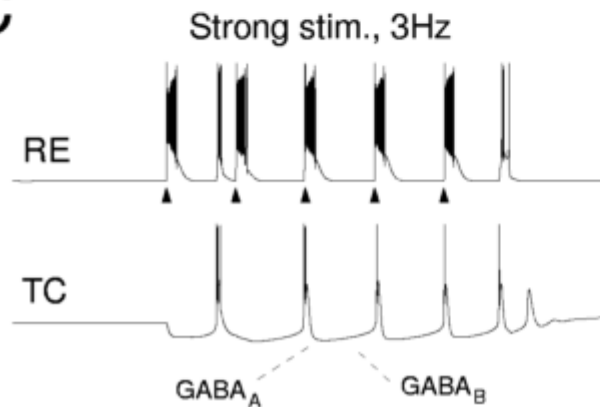
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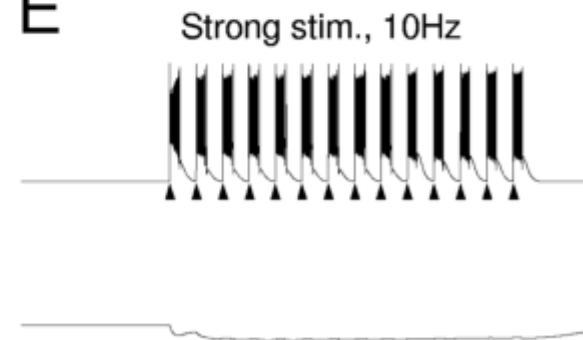
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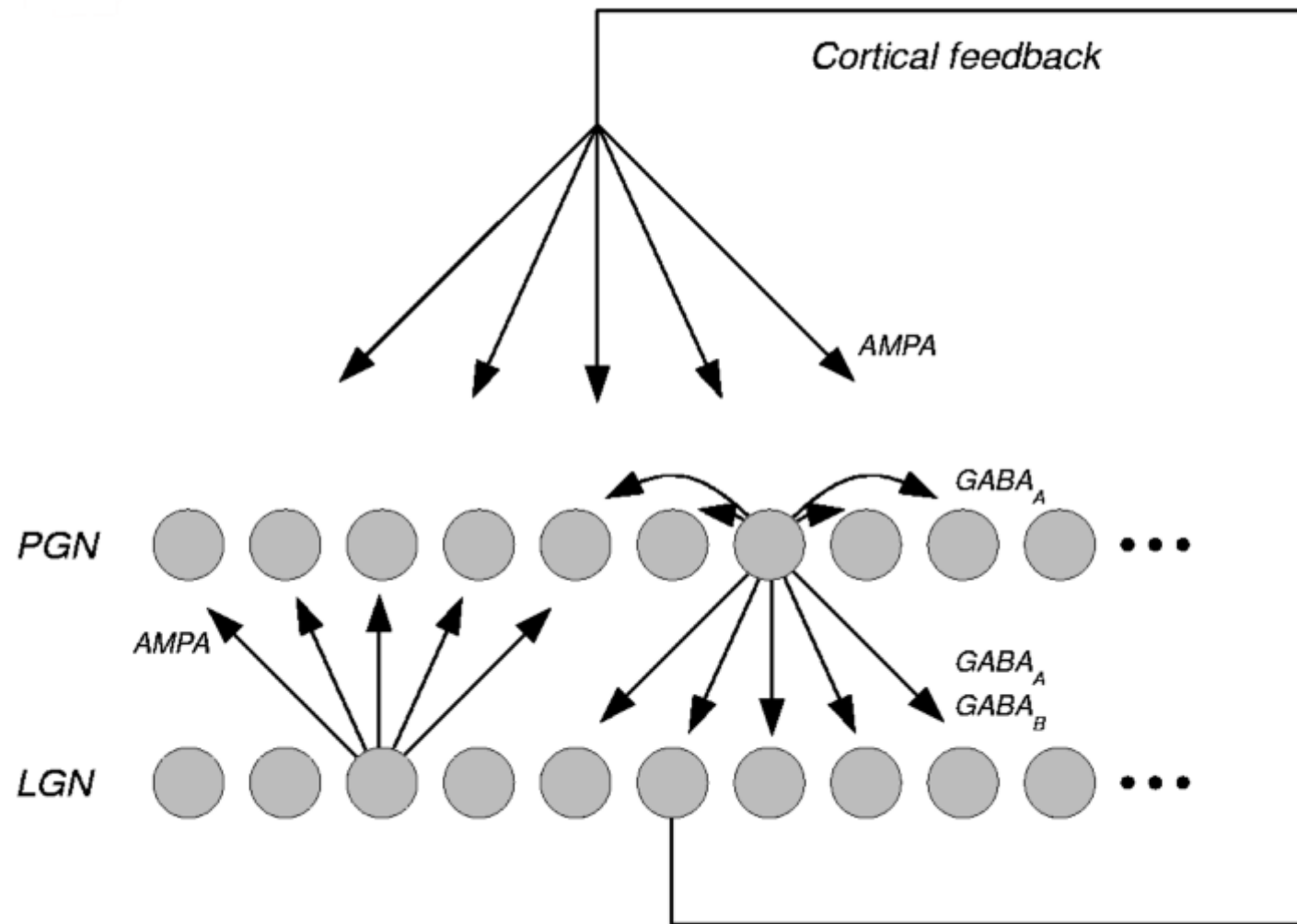
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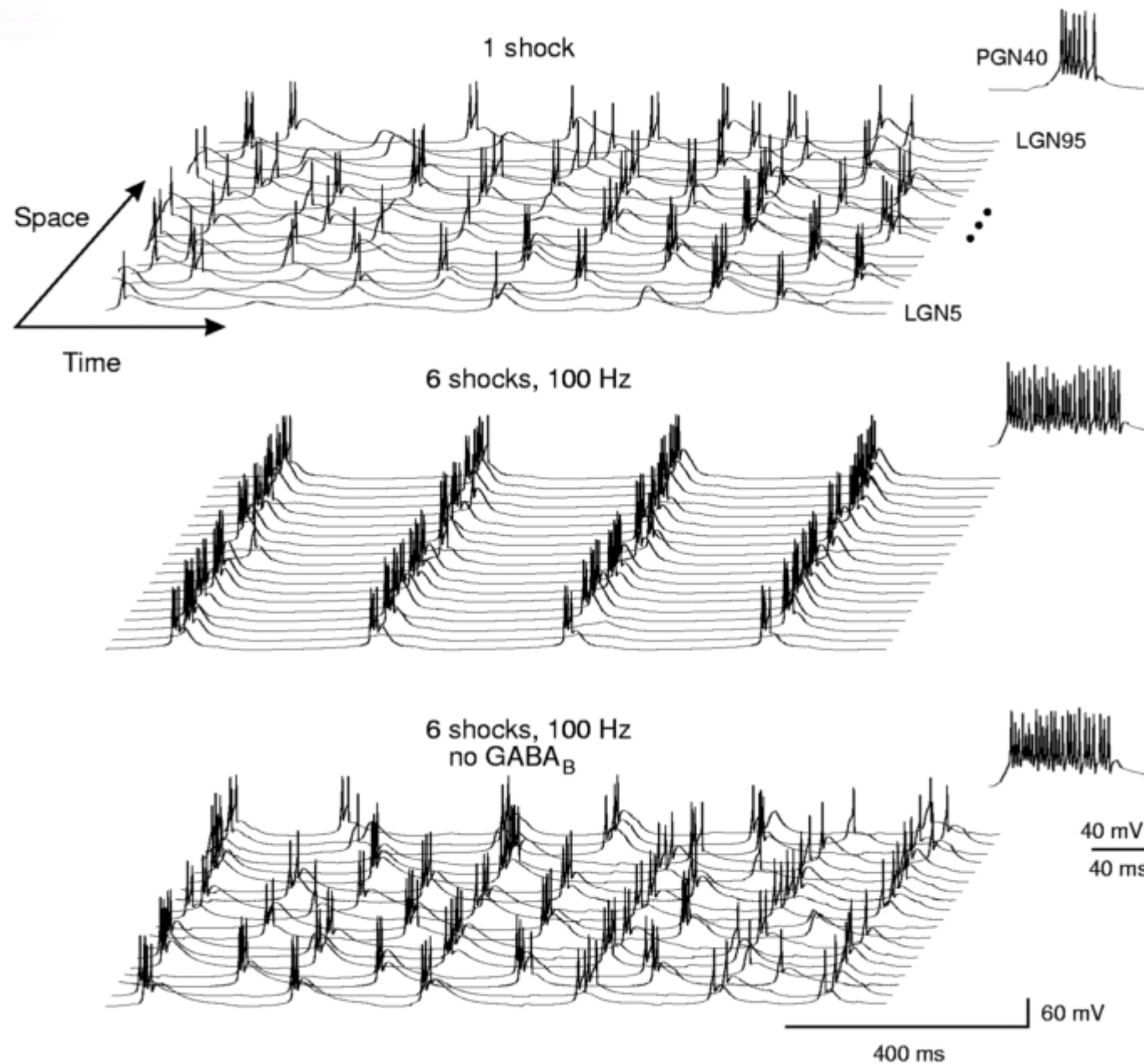
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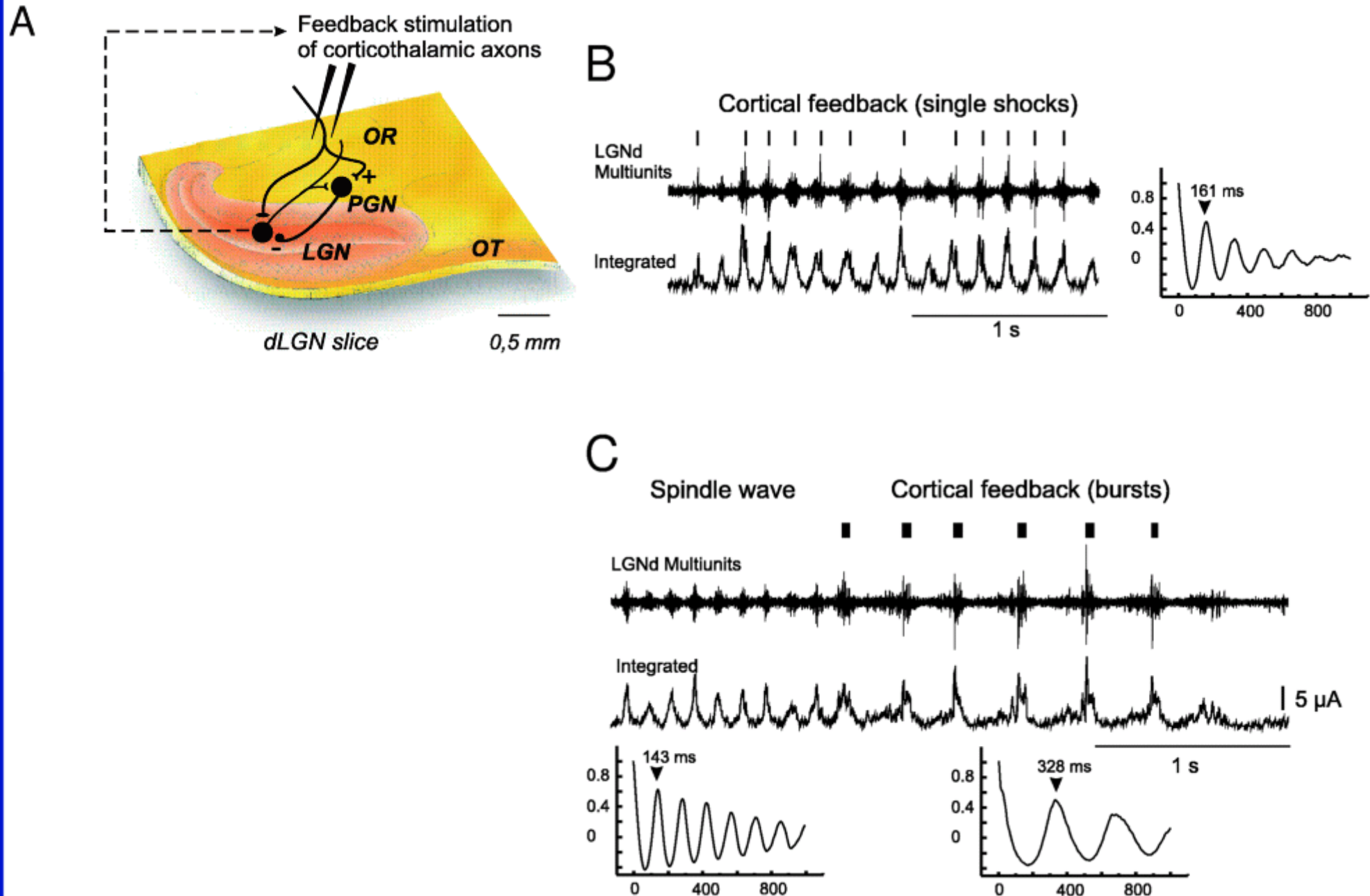
Feedback paradigm



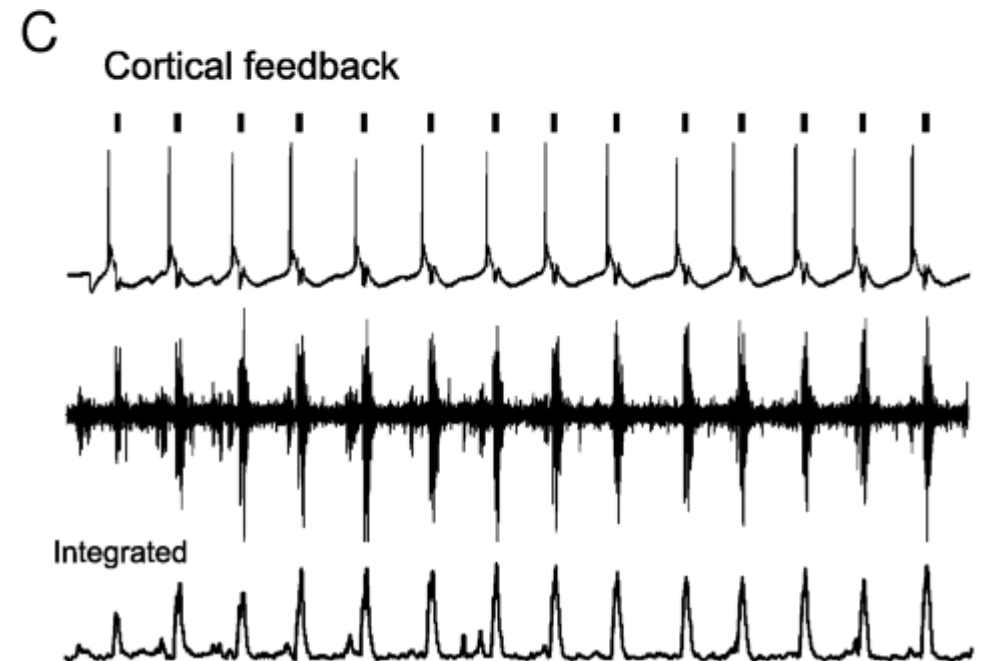
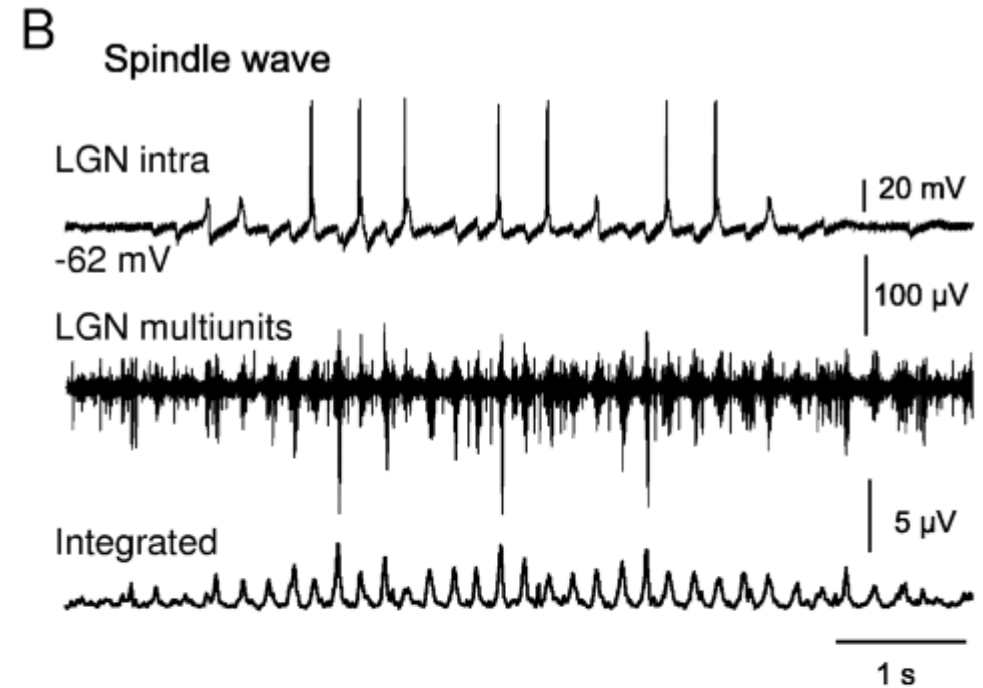
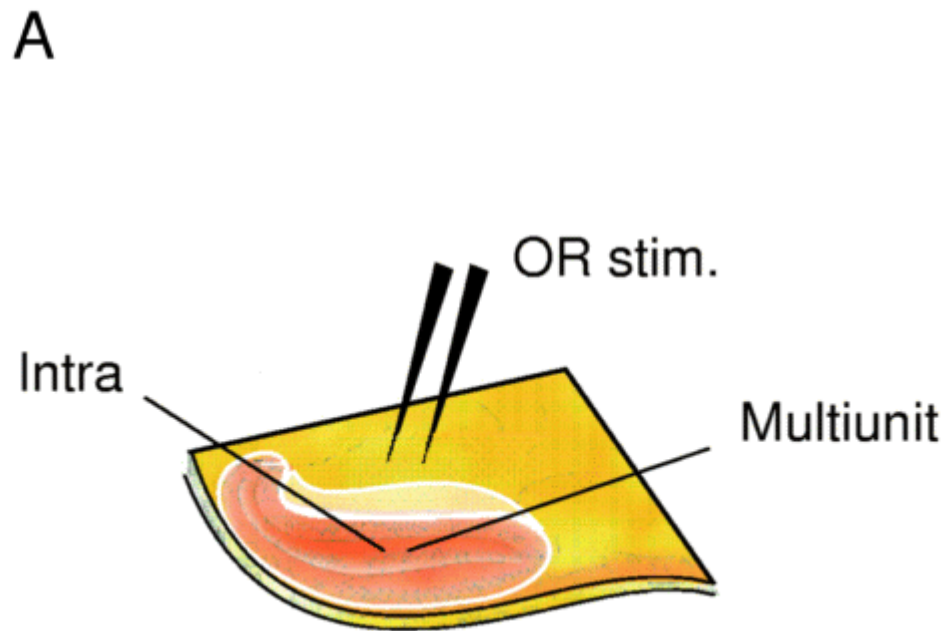
Prediction of the model



Feedback paradigm *in vitro*



Feedback paradigm *in vitro*



- Models and experiments point to a possible mechanism to explain the genesis of ~3Hz and 5-10 Hz spike-and-wave oscillations in the thalamocortical system
- This mechanism accounts for experiments on different experimental models such as the FGPE (cats), GAERS (rat), WAG-Rij (mice)
- This mechanism suggests a central role for cortico-thalamic feedback in recruiting slow, hypersynchronous oscillations in *physiologically intact* thalamic circuits