Neural oscillations:

Insights from computational modeling

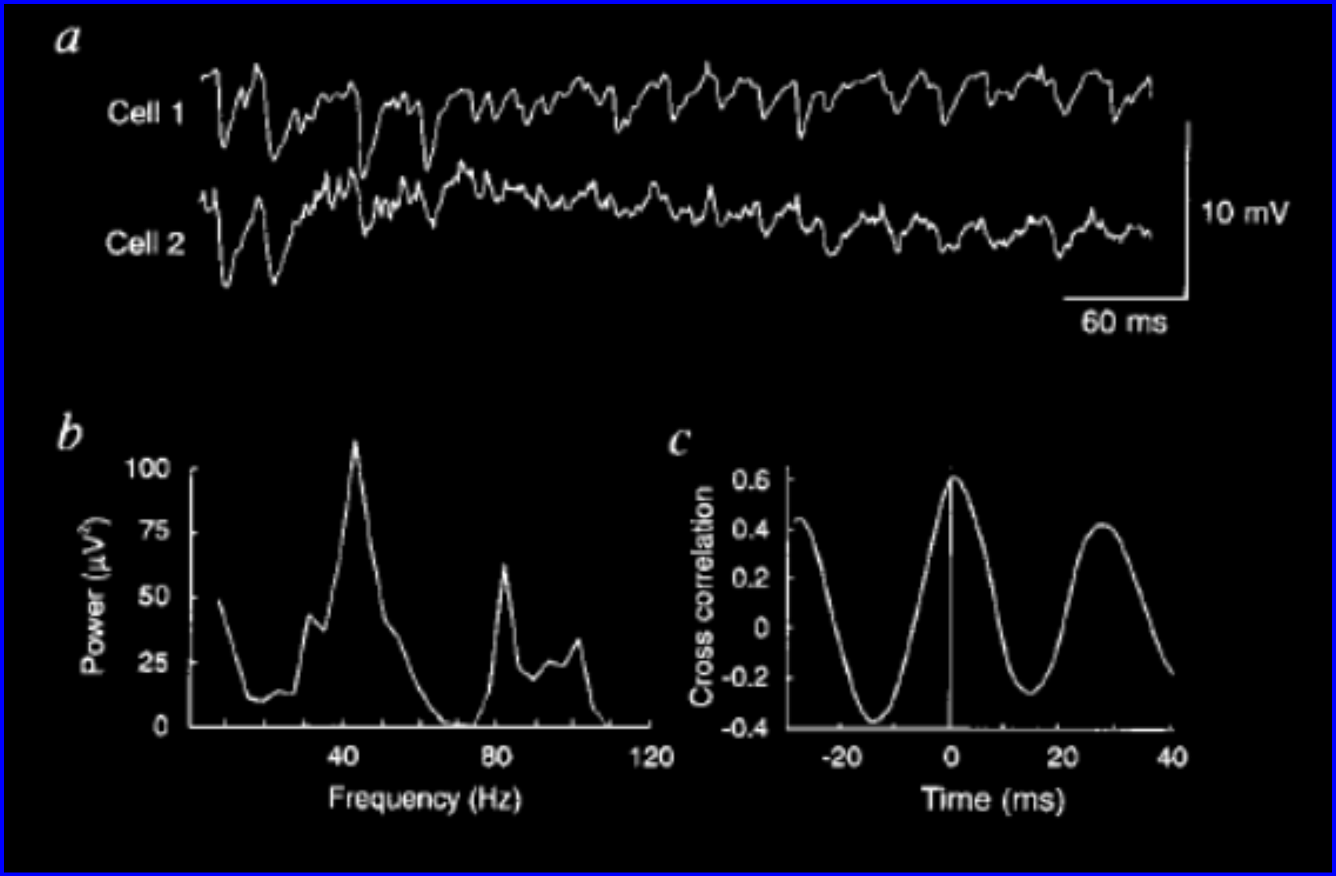
John Huguenard

Neuronal oscillations: functions

- Sleep
  - Generate activity that is independent of sensory input
  - May play roles in memory consolidation or reprioritization.
  - Spindles, delta, sharp-wave ripple complexes
- Awake behavior
  - Exploration – theta
  - Sensory binding & attention – gamma
  - Sensory discrimination – olfaction
- Pathology
  - Epilepsy
  - Parkinson's disease

Non-linearities and oscillations

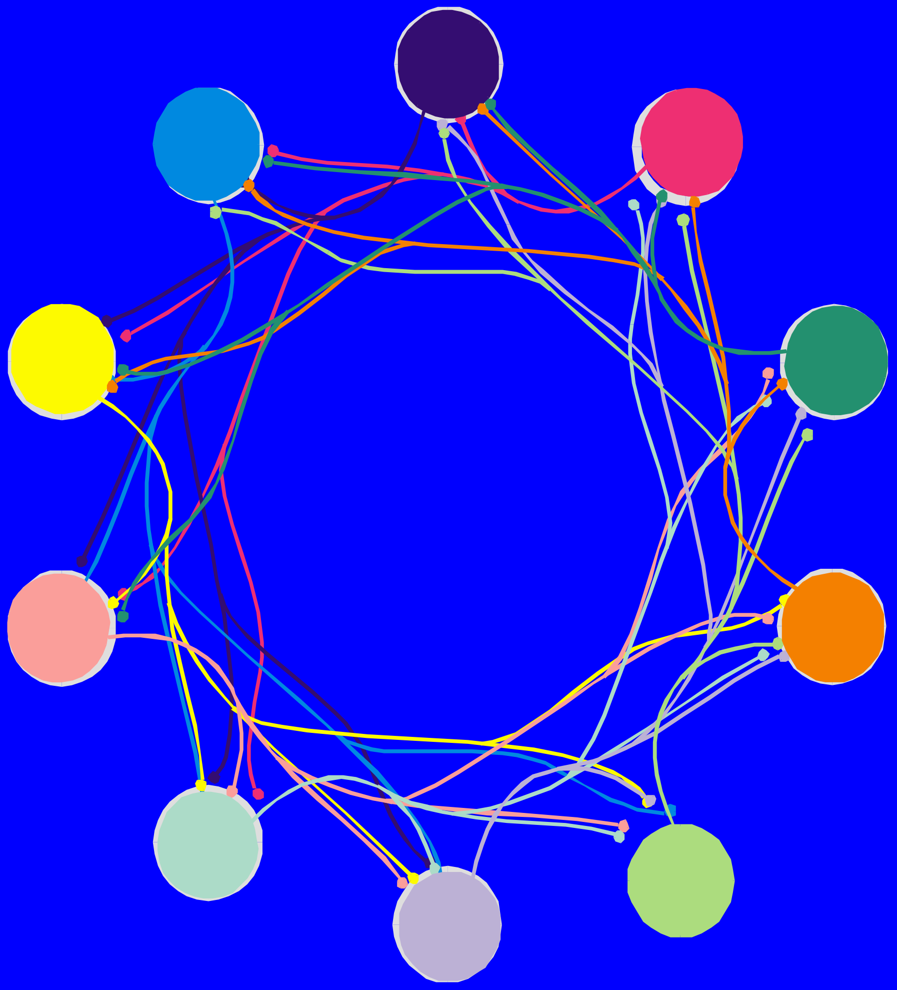
Gamma oscillations develop in cortical networks in absence of excitatory connectivity



Glutamate application, synaptic excitation blocked

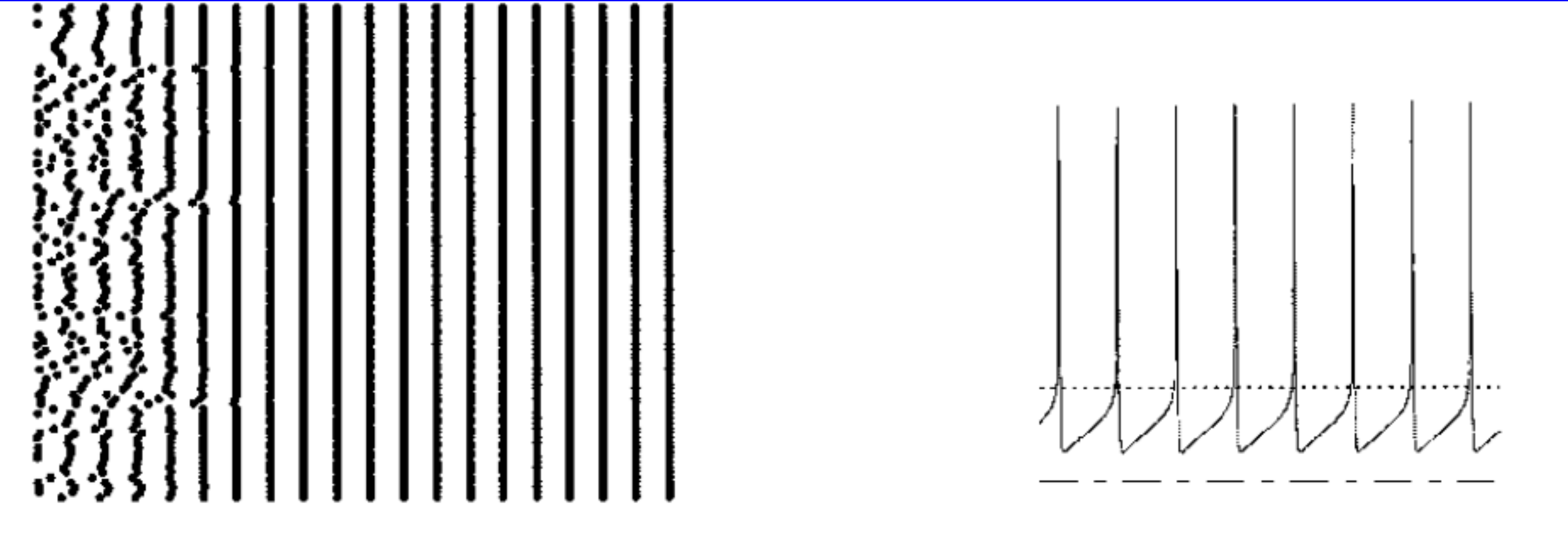
Whittington et al, 1995

Ring inhibitory networks



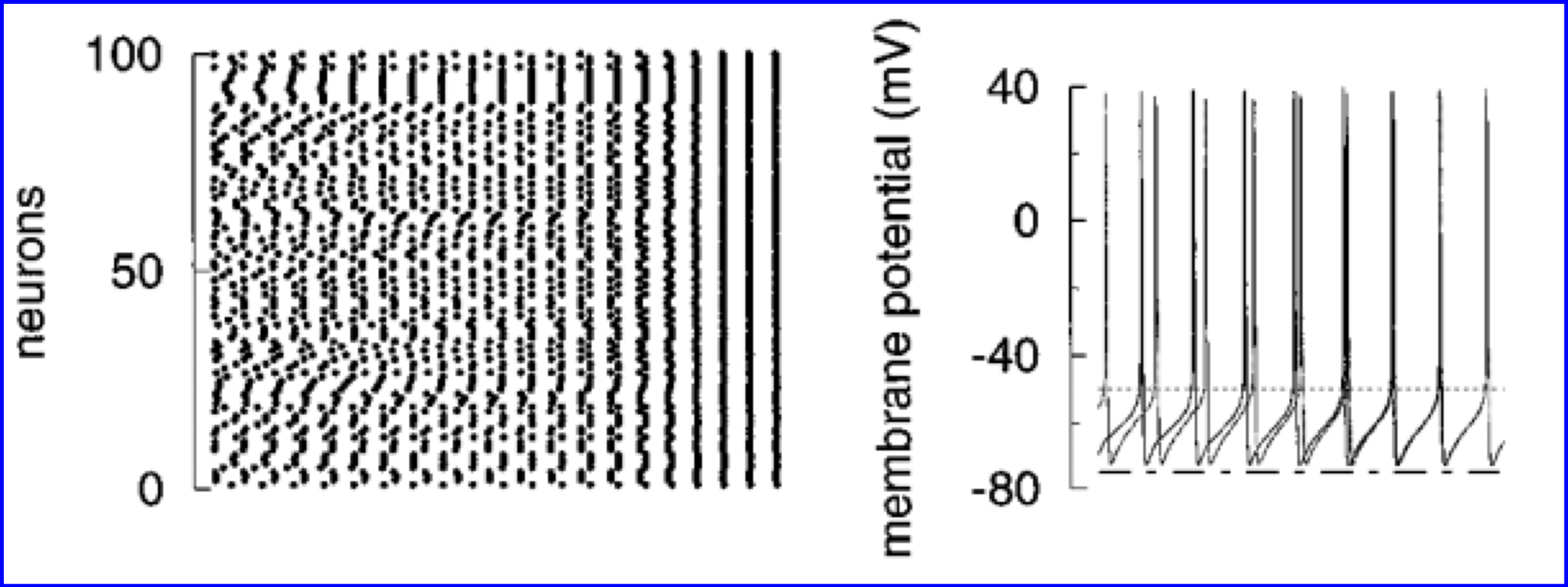
Wang and Buzsaki, J Neurosci. 16:6402-13.1996

Uniform network of FS cells, random initial conditions: perfect synchrony



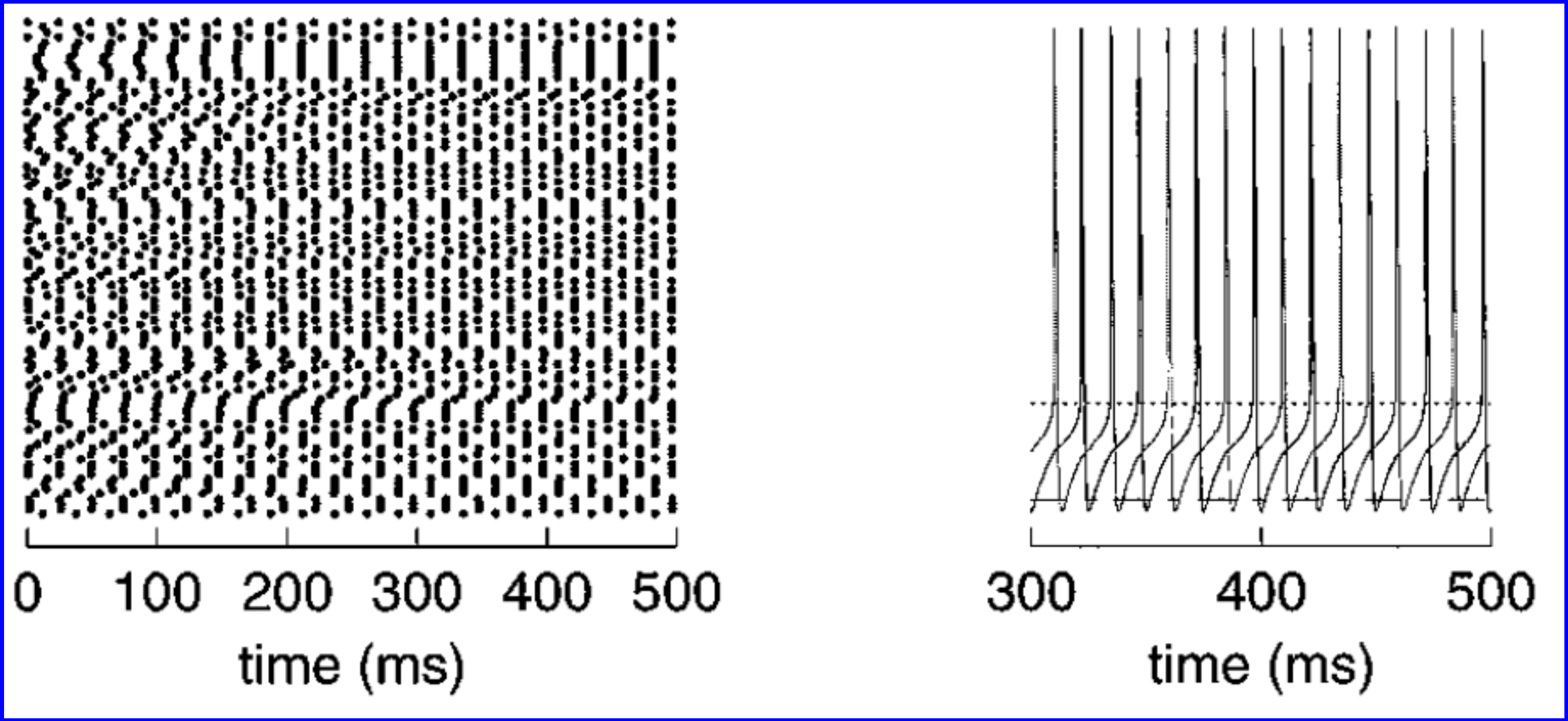
Wang and Buzsaki, 1996

Uniform network, modify AP properties to change AHP, retards synchrony



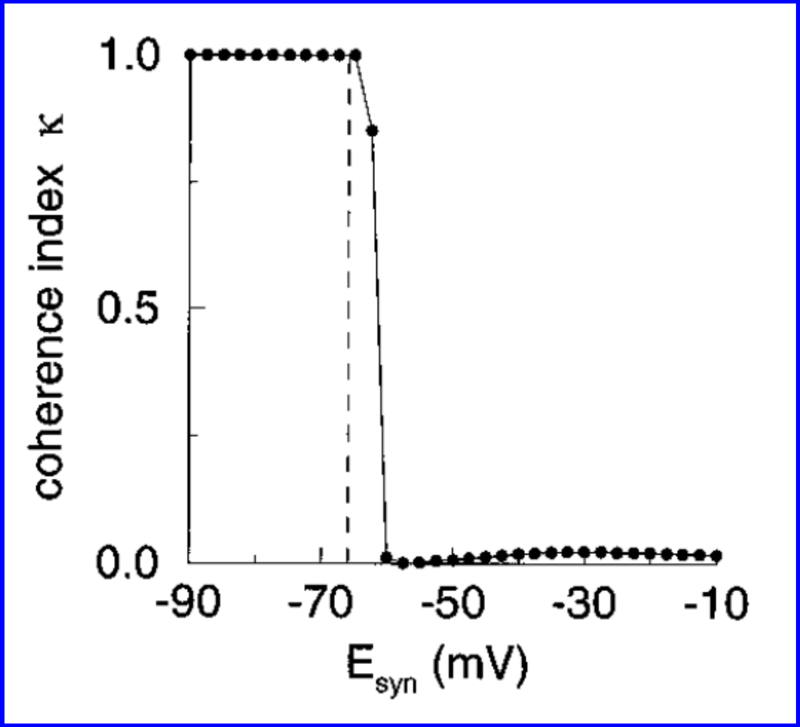
Wang and Buzsaki, 1996

Uniform network, random initial conditions, deep AHP: hemi-synchrony

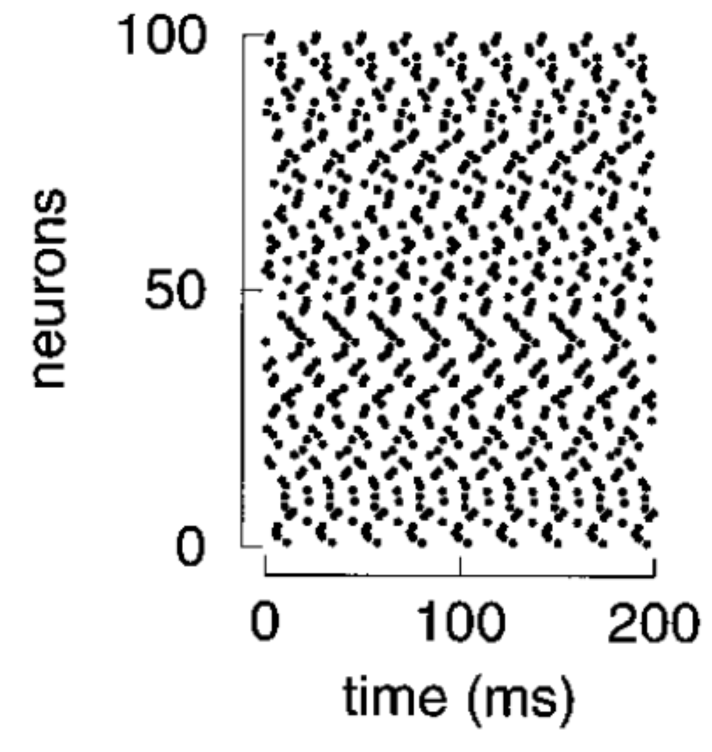


Wang and Buzsaki, 1996

Synchrony as a function of E-syn

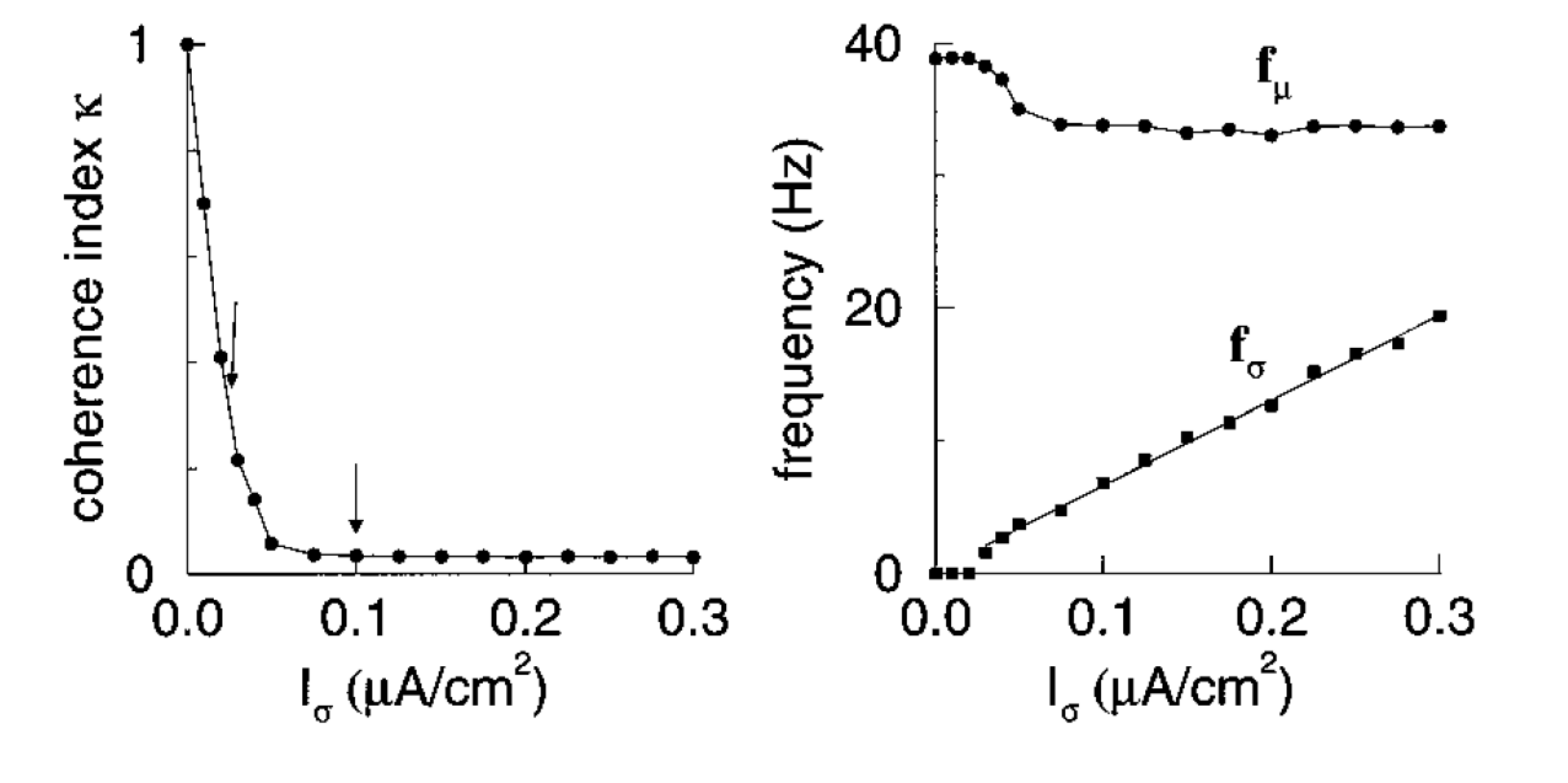


E-syn = 0 : ≈ excitatory



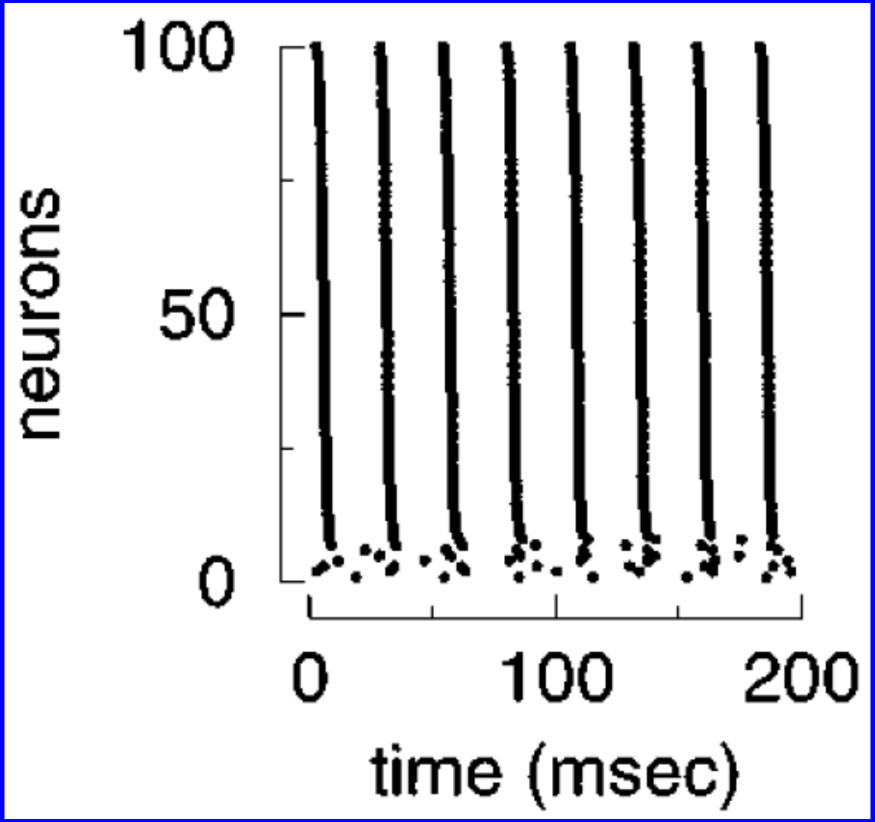
Wang and Buzsaki, 1996

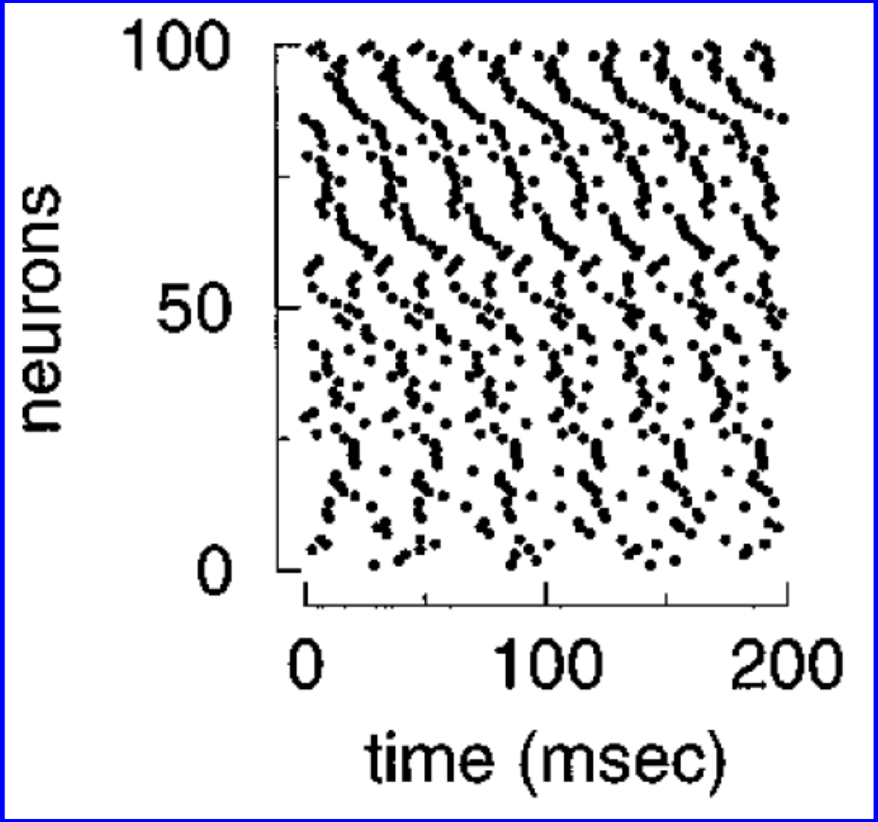
Heterogeneous network: Gamma is common output, while coherence is not



Wang and Buzsaki, 1996

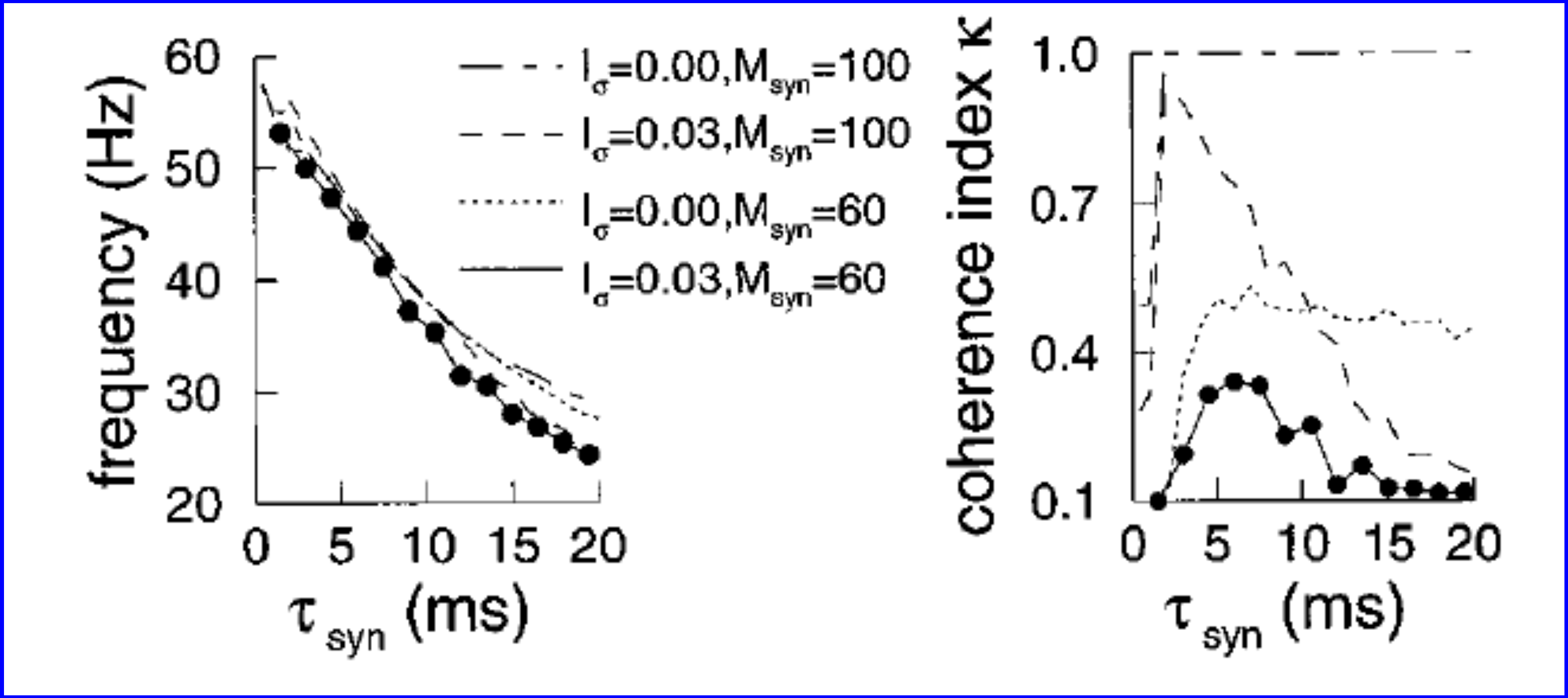
Heterogeneous network: Gamma is common output, while coherence is not





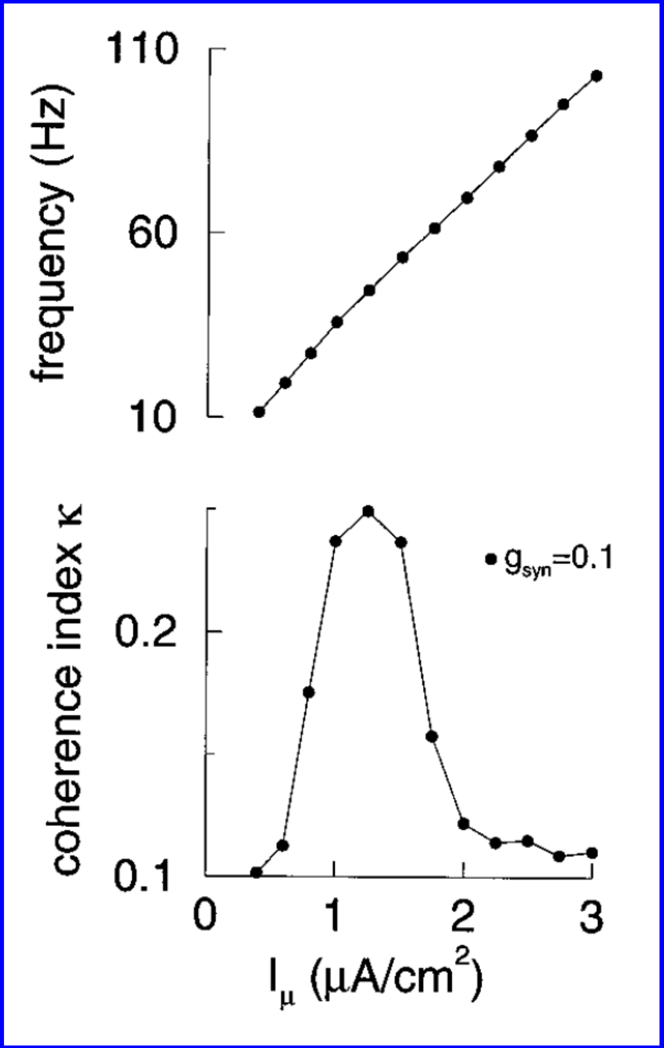
Wang and Buzsaki, 1996

Dependence on synaptic properties: Time constant of decay governs network frequency, and indirectly, coherence



Wang and Buzsaki, 1996

Coherence only in gamma frequencies



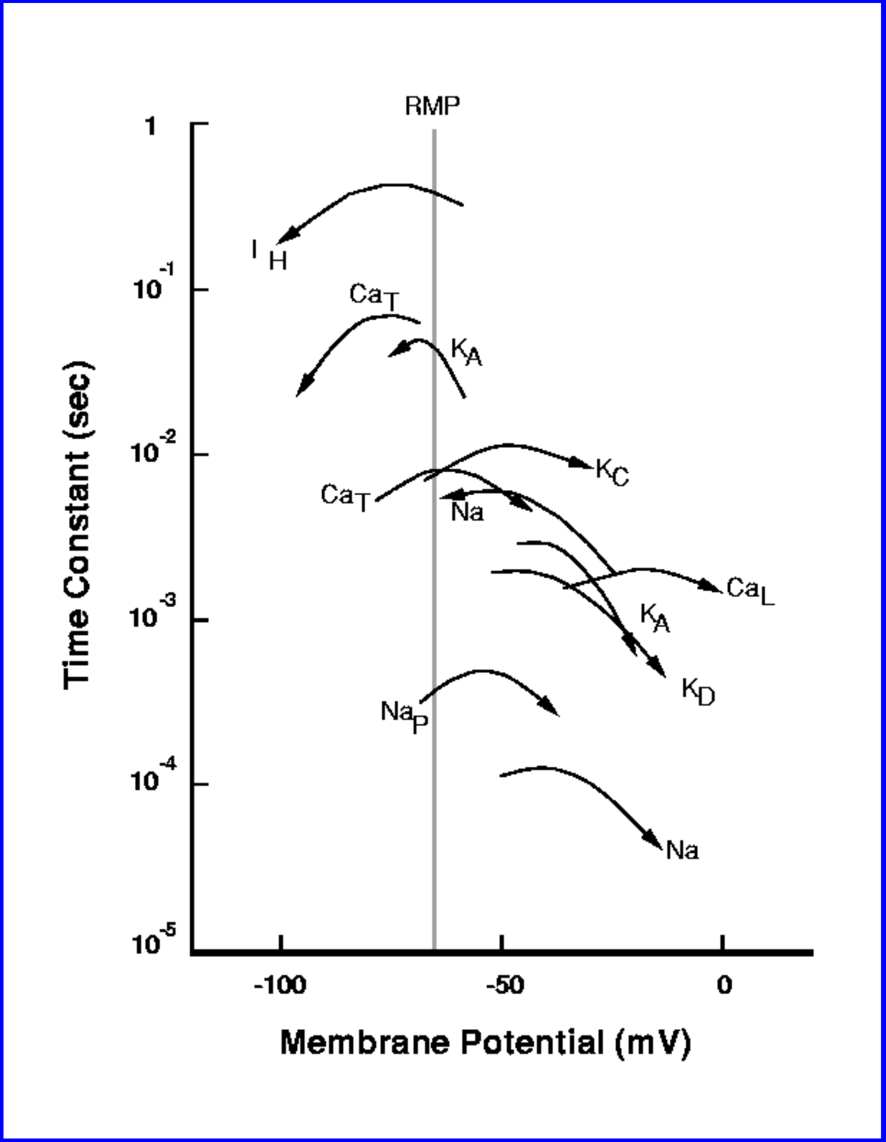
Wang and Buzsaki, 1996

Wang and Buszaki conclusions

- E-syn more negative than AP-AHP promotes synchrony
- Synaptic decay should be compatible with network frequency
- Limited heterogeneity will not break synchrony
- Connectivity must not be too sparse
- Dynamic Clamp extends this approach
  - Alex Reyes, Vikaas Sohal

Neurons as active computational devices

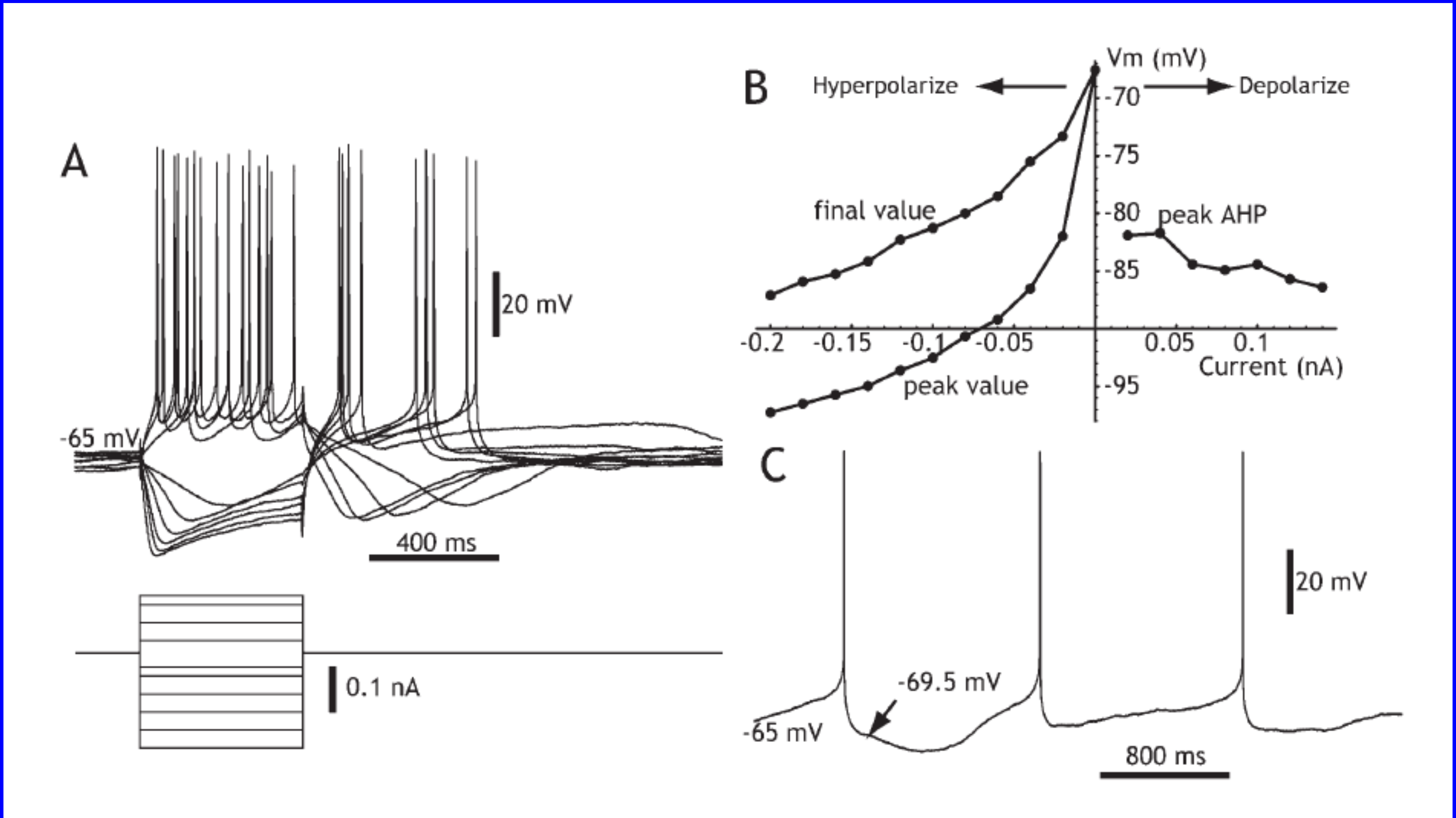
Dynamics of peri-threshold voltage gated ion channels



Courtesy W Lytton

Bistable membranes

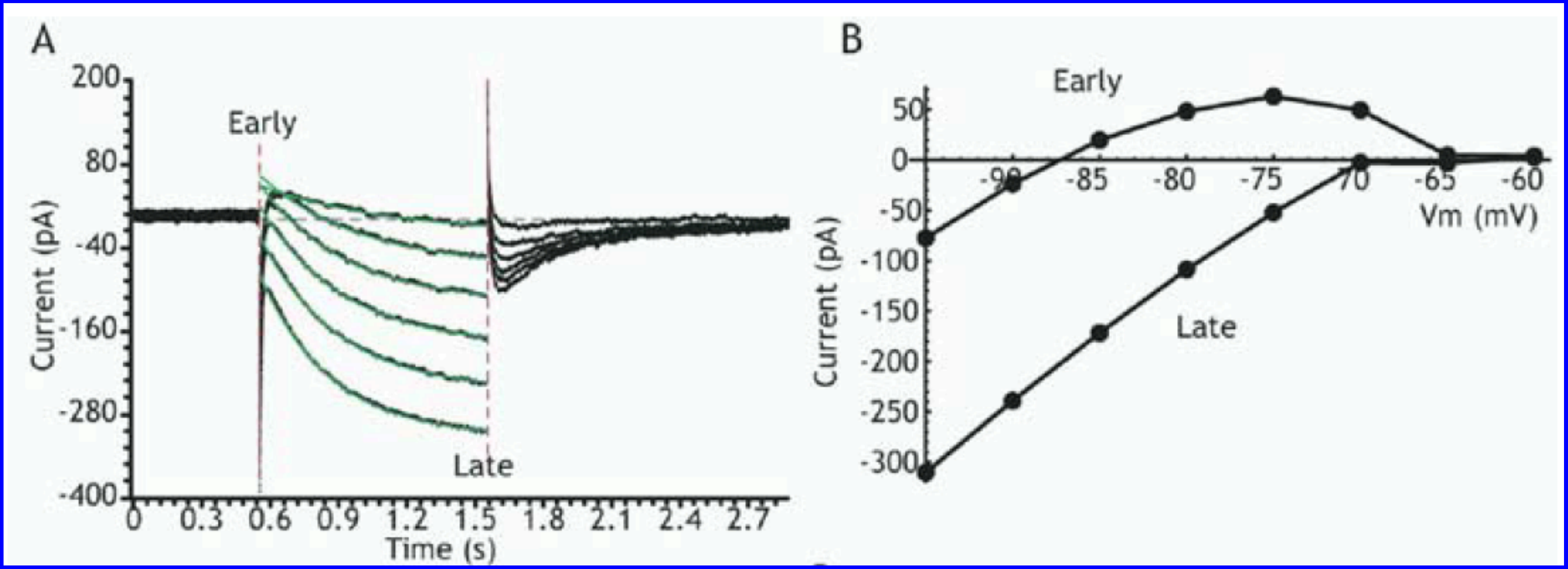
Membrane bistability from non-linearity of ion channel gating



striatal cholingeric neurons pause during relevant sensory stimuli

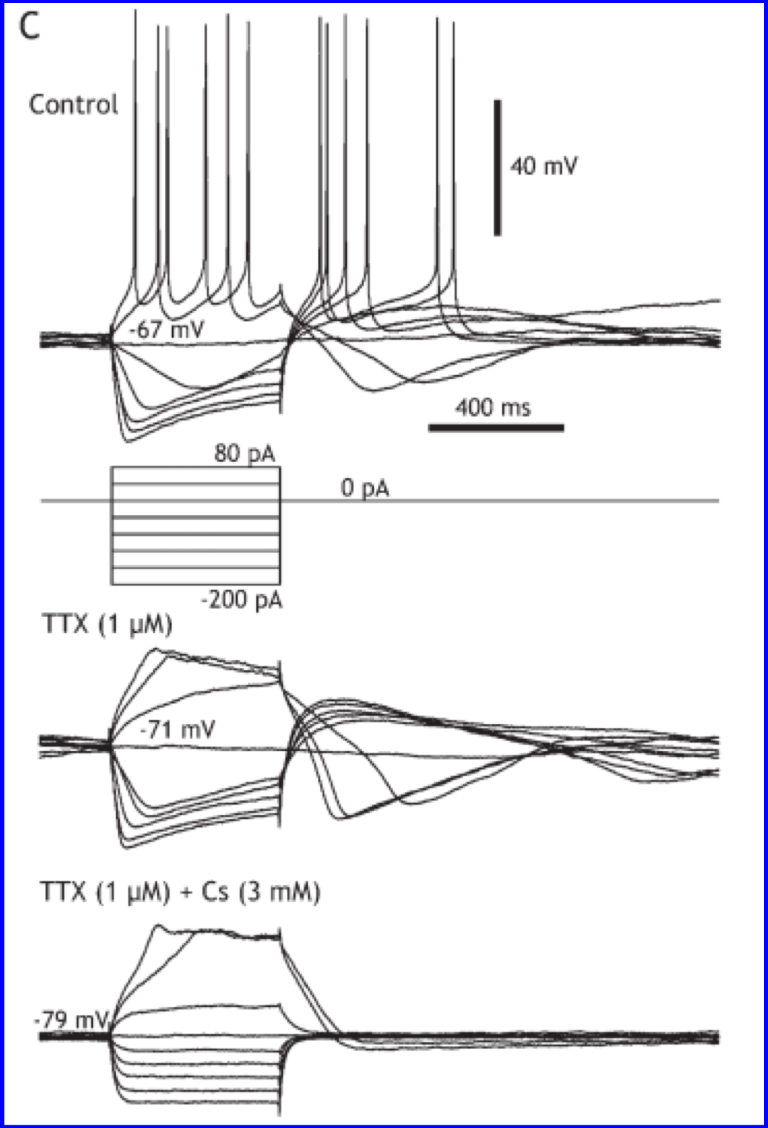
Wilson CJ. (2005) Neuron 45:575-85.

Membrane bistability from non-linearity of ion channel gating

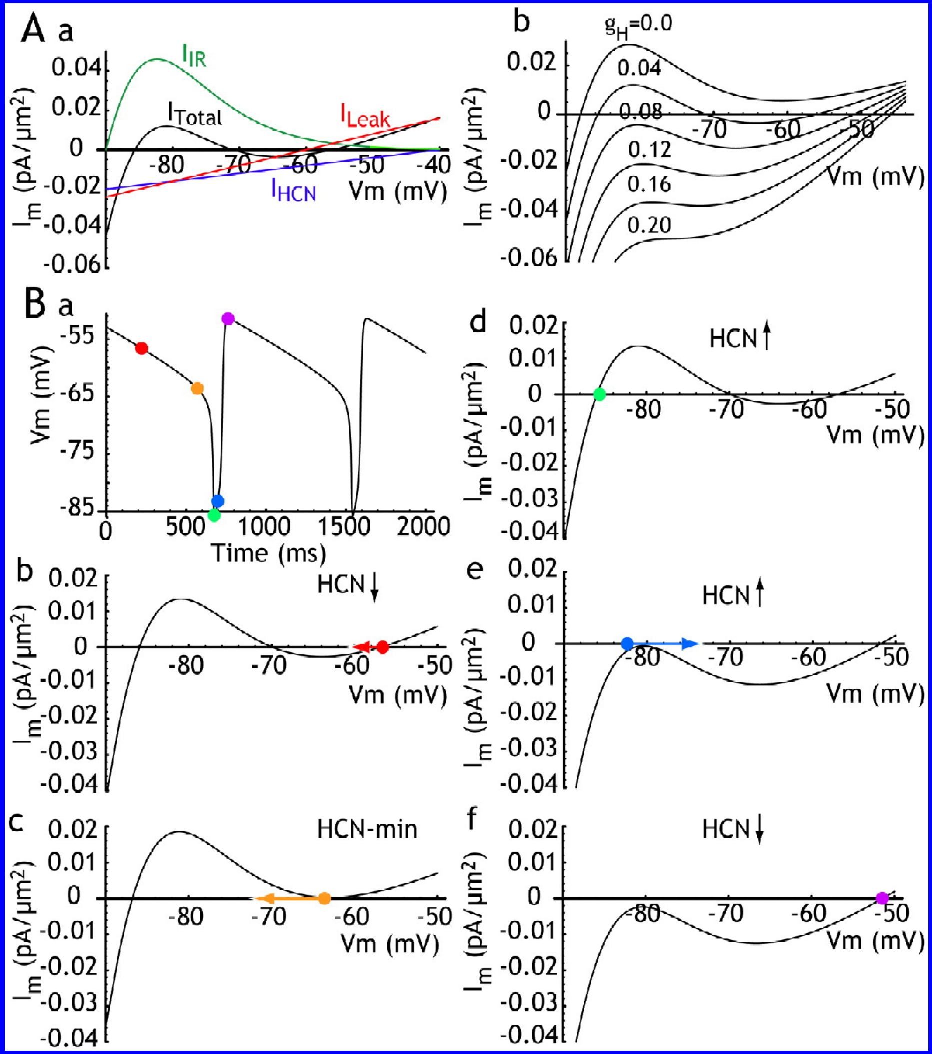


Wilson, 2005

Regenerative depolarization ionic mechanism: Cs-sensitive KIR



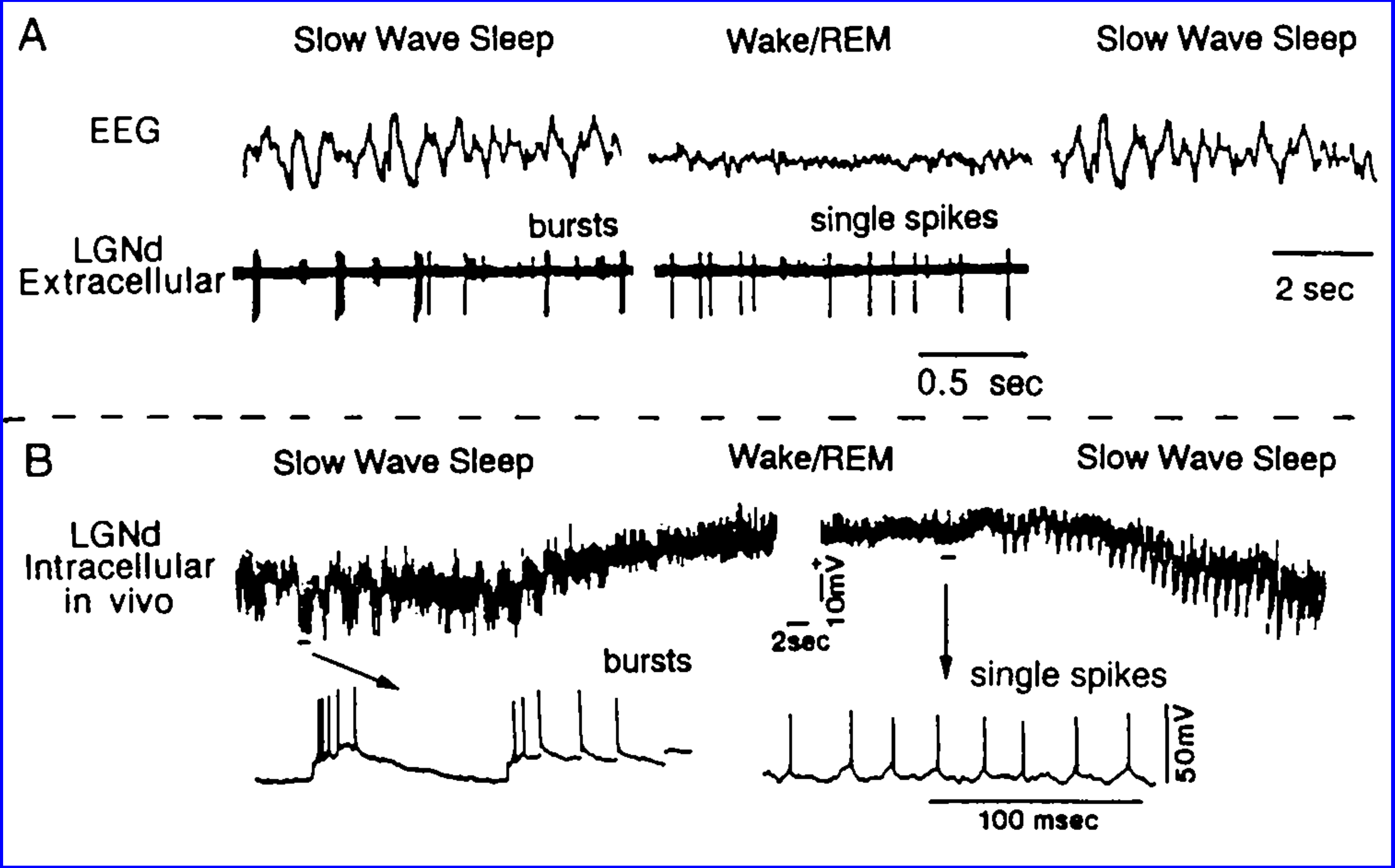
Membrane bistability from non-linearity of ion channel gating



Wilson, 2005

Thalamic oscillators, cells and circuits

Relay neuron have state dependent firing modes



McCarley, Benoit & Barrionuevo, J. Neurophysiol, 50:798, 1983. Hirsch, Fourment & Marc, Brain Res. 259:308, 1983

I-h, and its rhythogenic properties

Journal of Physiology (1990), **431**, *pp.* 291–318
With 14 figures
Printed in Great Britain

PROPERTIES OF A HYPERPOLARIZATION-ACTIVATED CATION CURRENT AND ITS ROLE IN RHYTHMIC OSCILLATION IN THALAMIC RELAY NEURONES

BY DAVID A. McCORMICK* AND HANS-CHRISTIAN PAPE†

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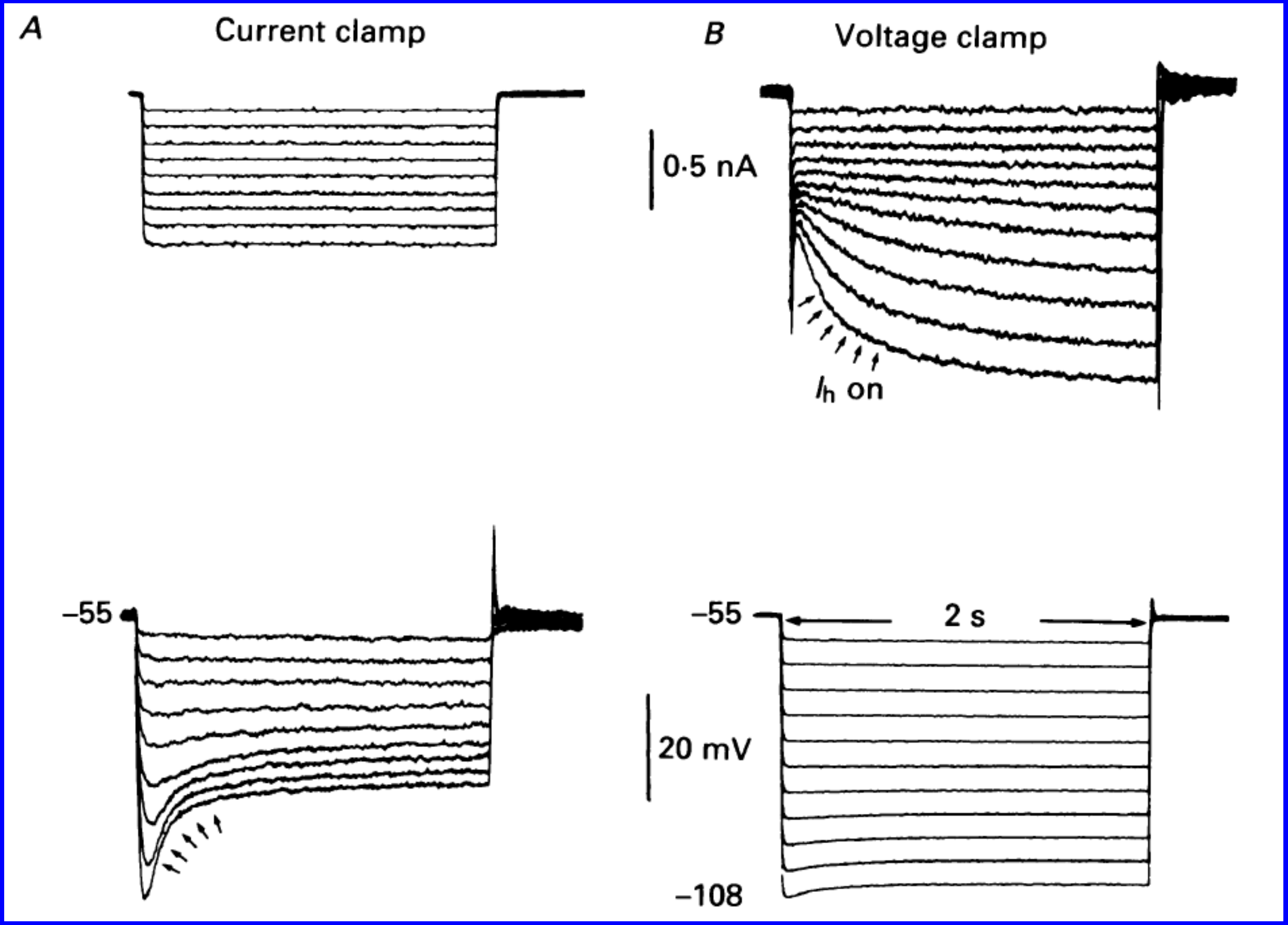
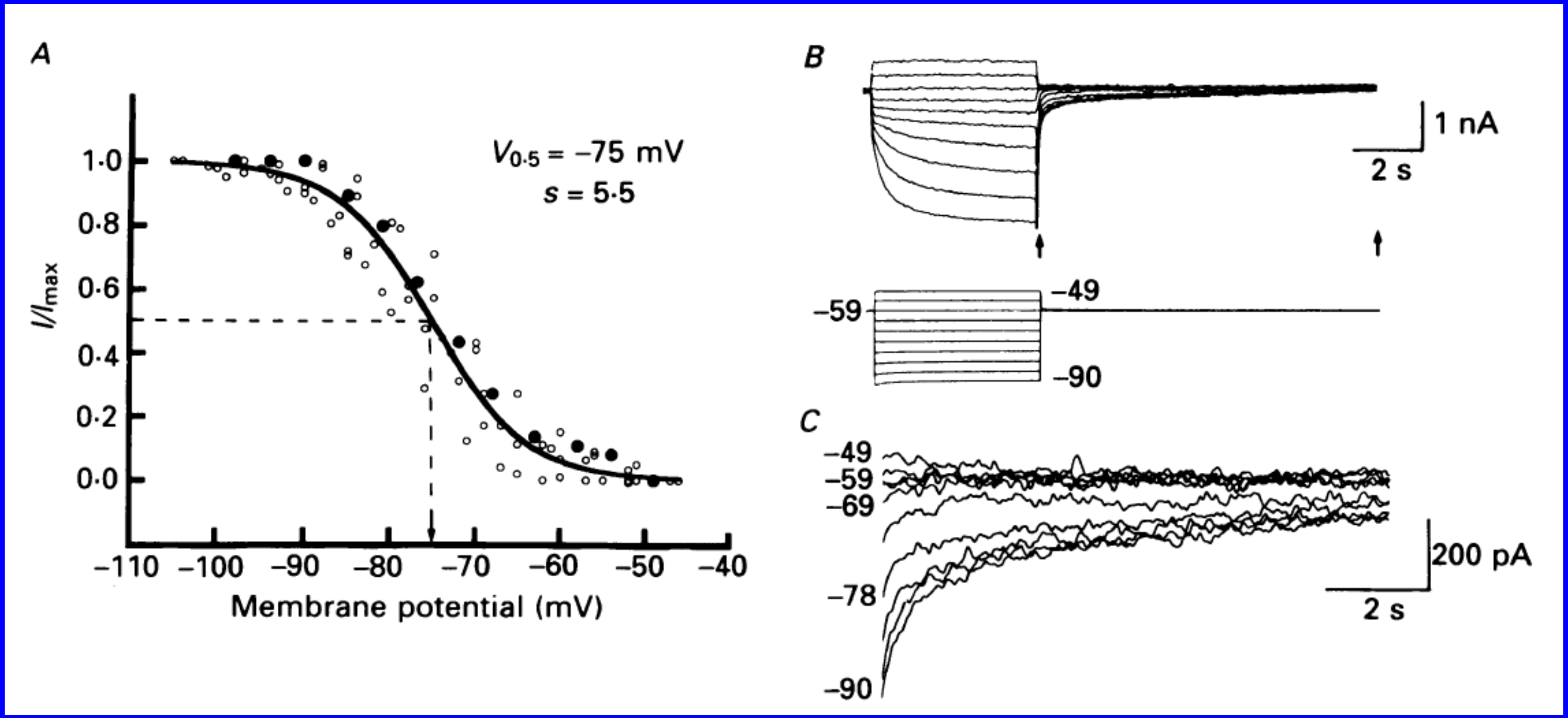
(*Received 3 April 1990*)

I-h, a hyperpolarization activated current with interesting dynamics



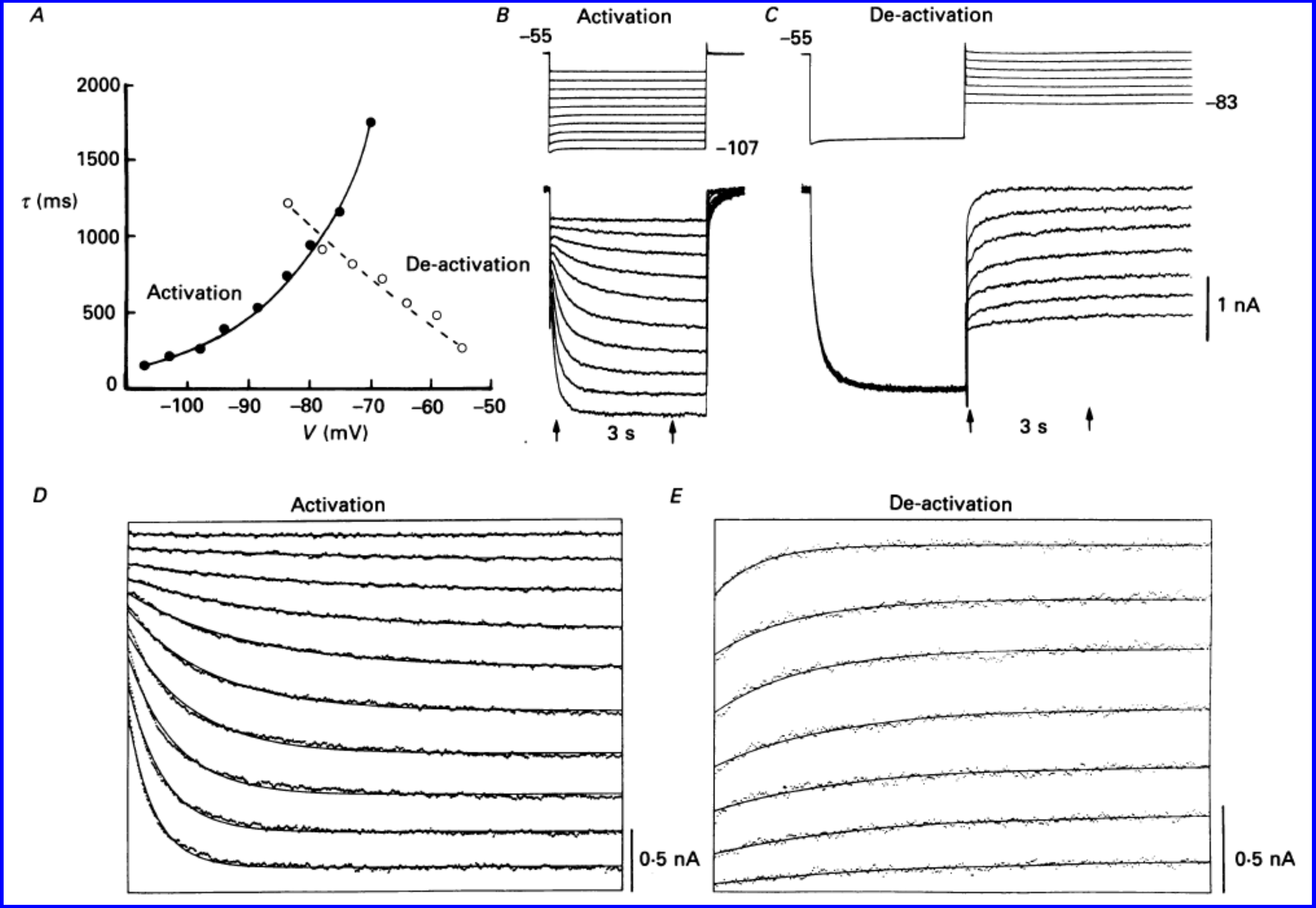
McCormick and Pape, 1990a

Properties of I-h, steady state activation



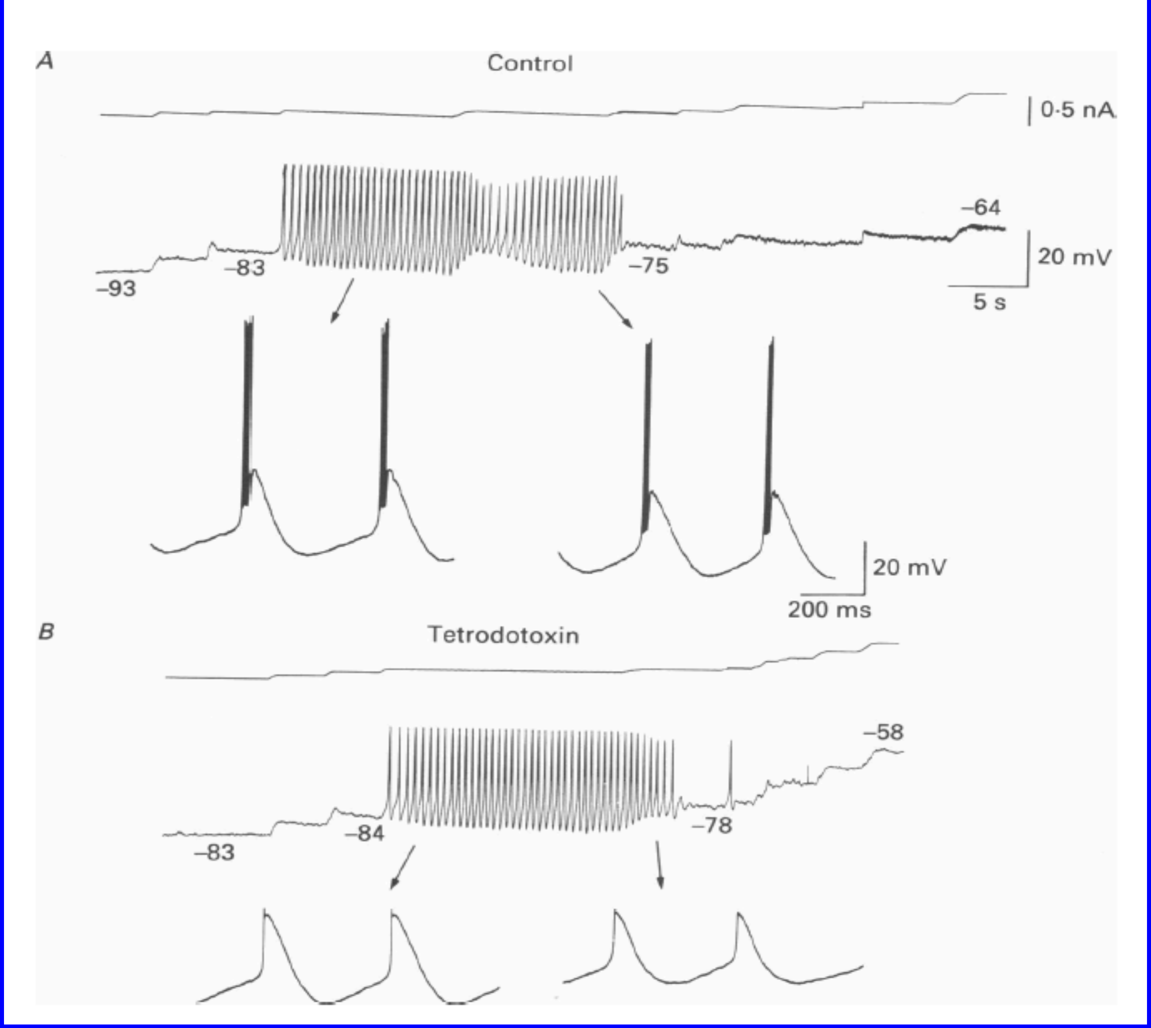
McCormick and Pape, 1990a

Properties of I-h, activation/deactivation rates



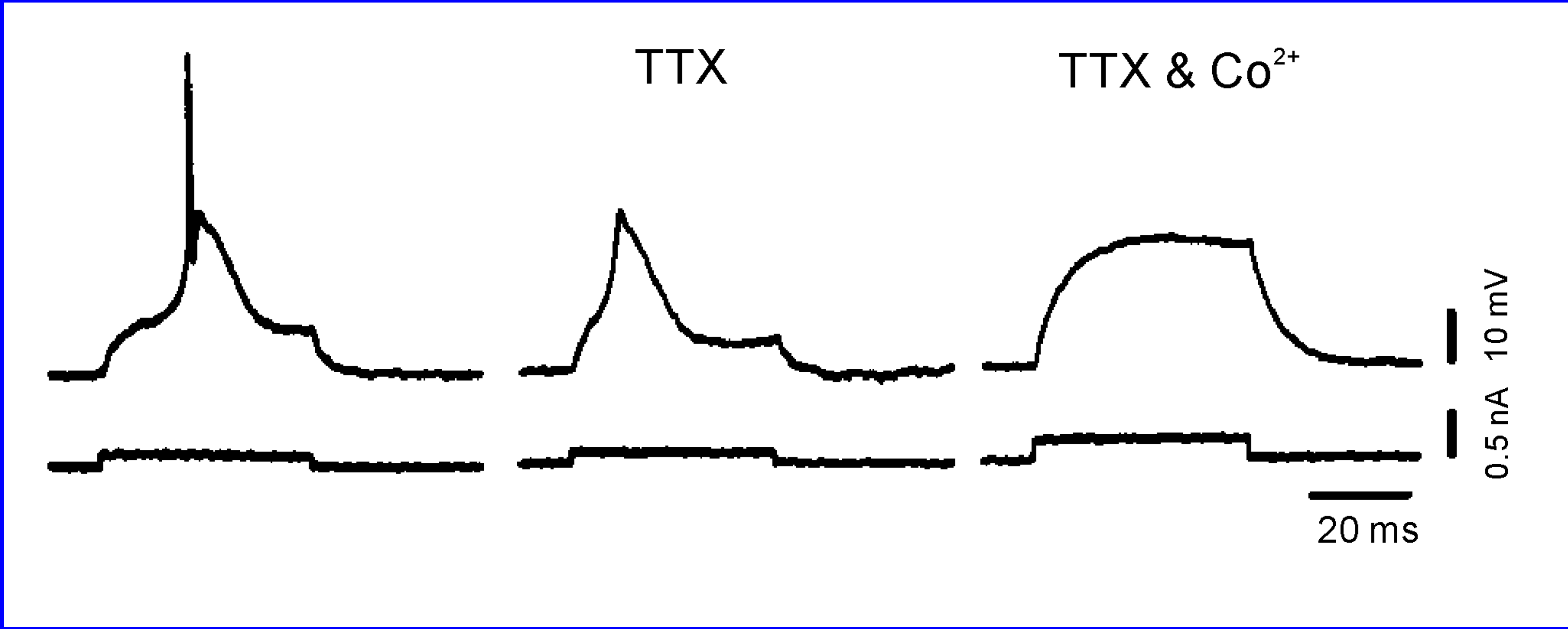
McCormick and Pape, 1990a

Thalamic relay neurons are intrinsic oscillators: dependence on sub-threshold conductances



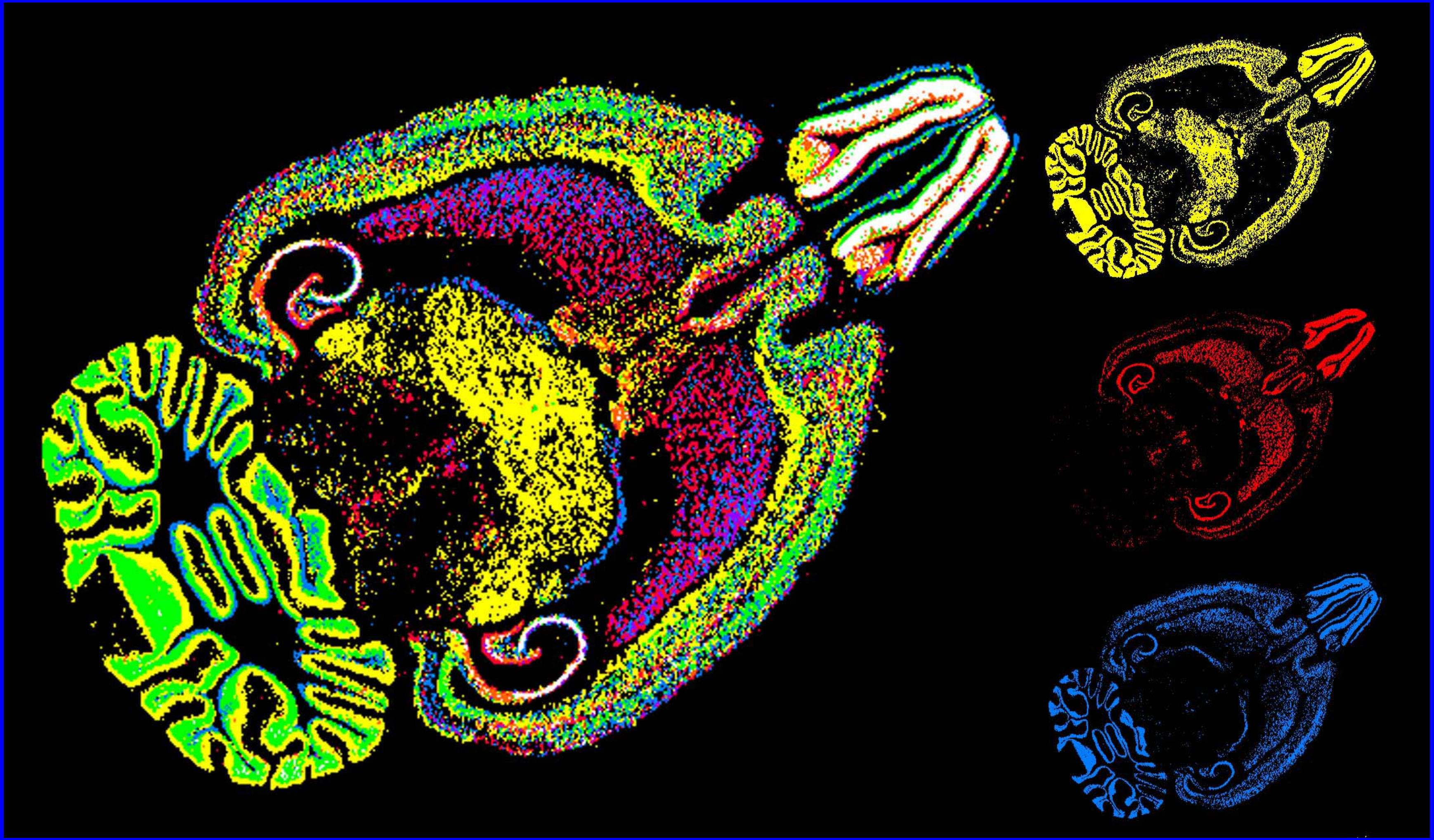
McCormick and Pape, 1990a

Basis of the burst:
the low threshold spike (LTS)



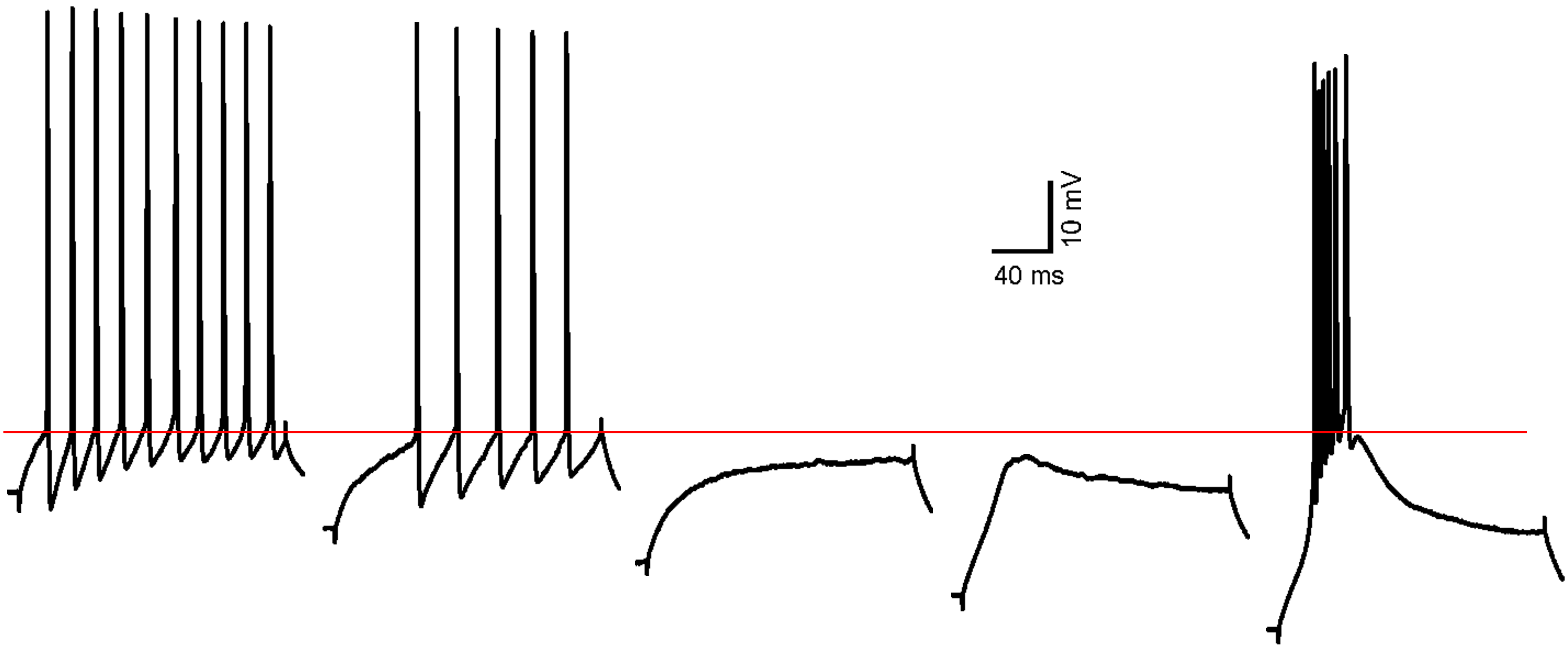
Llinás and Jahnsen, Nature 297:406, 1982

T type calcium channel genes in thalamus

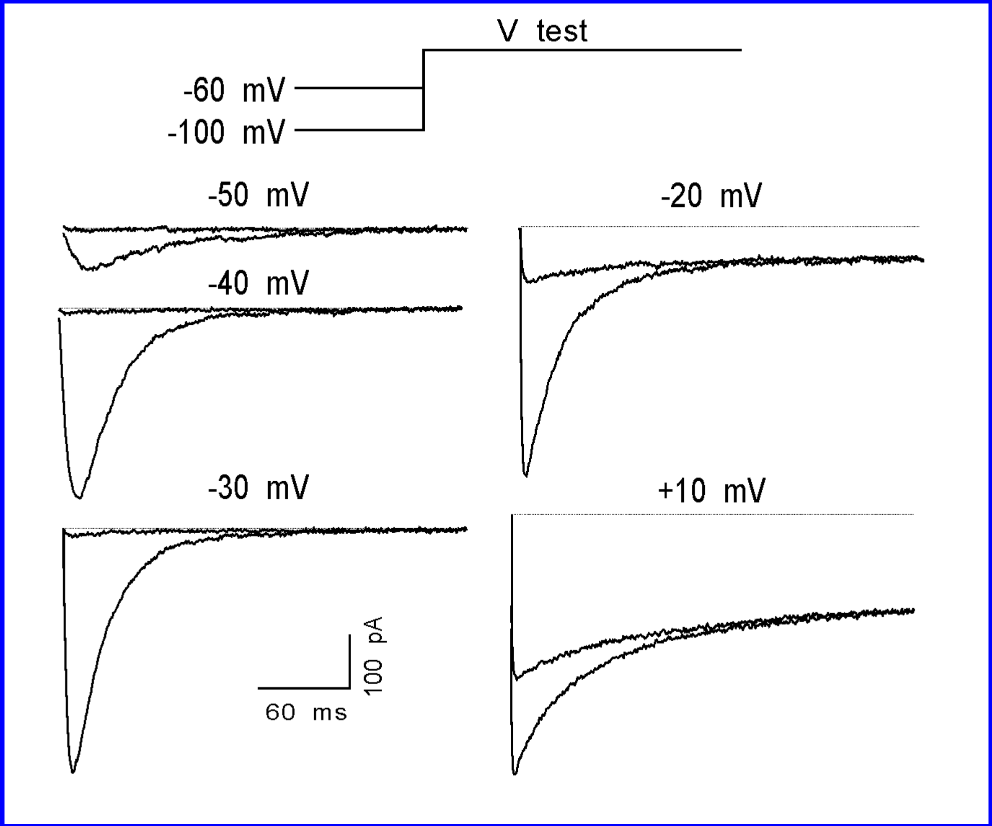


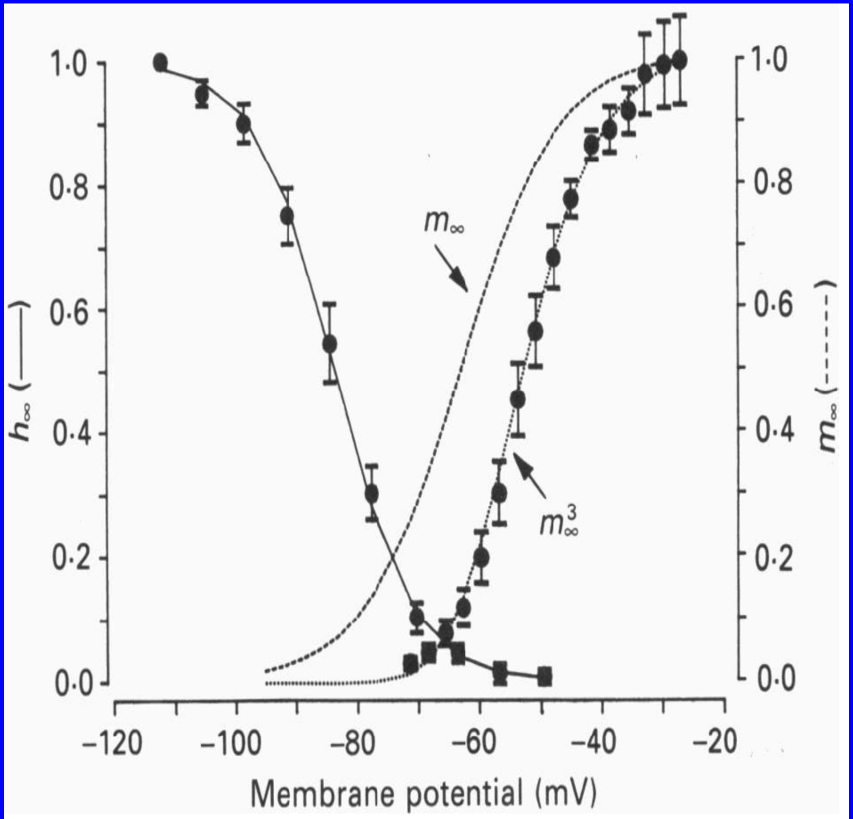
Talley, E.M., Cribbs, L.L., Lee, J.H., Daud, A., Perez-Reyes, E., and Bayliss, D.A. *J.Neurosci.* 19:1895-1911, 1999.

Paradoxical excitability in thalamic relay neurons



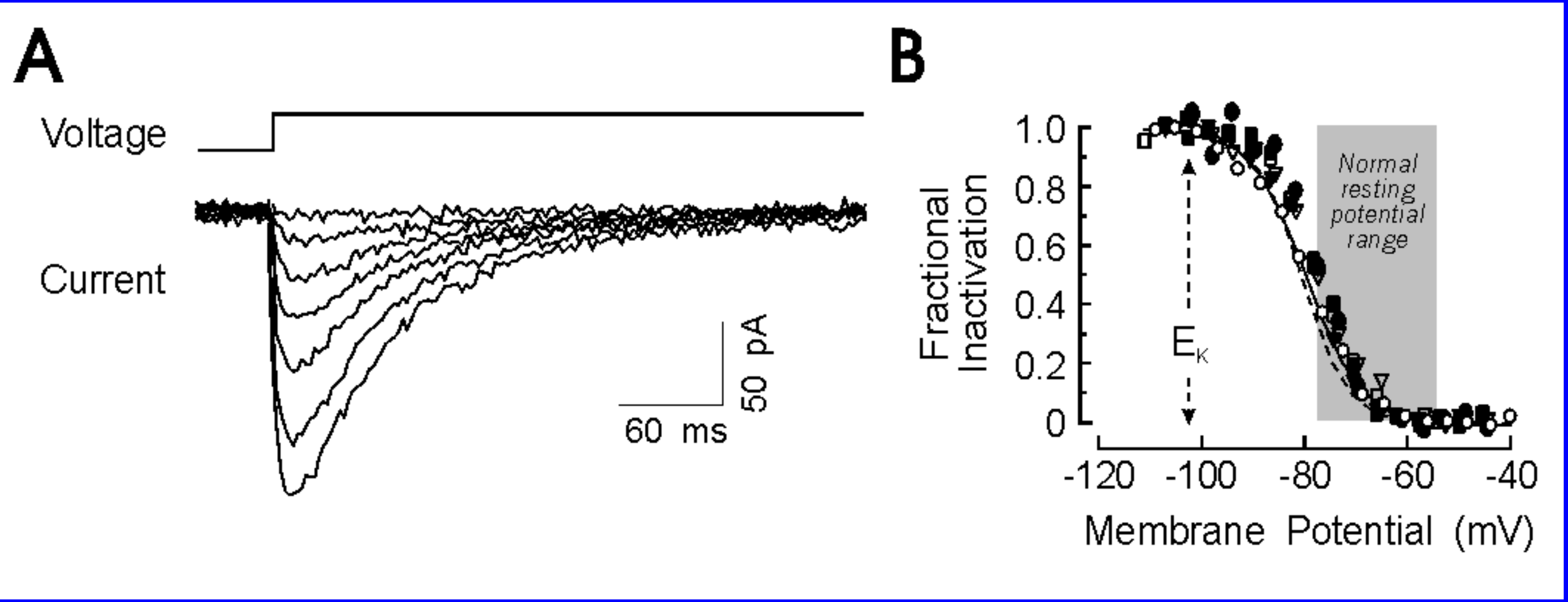
Isolation of I_T based on voltage clamp protocols: Hodgkin-Huxley-esque approach



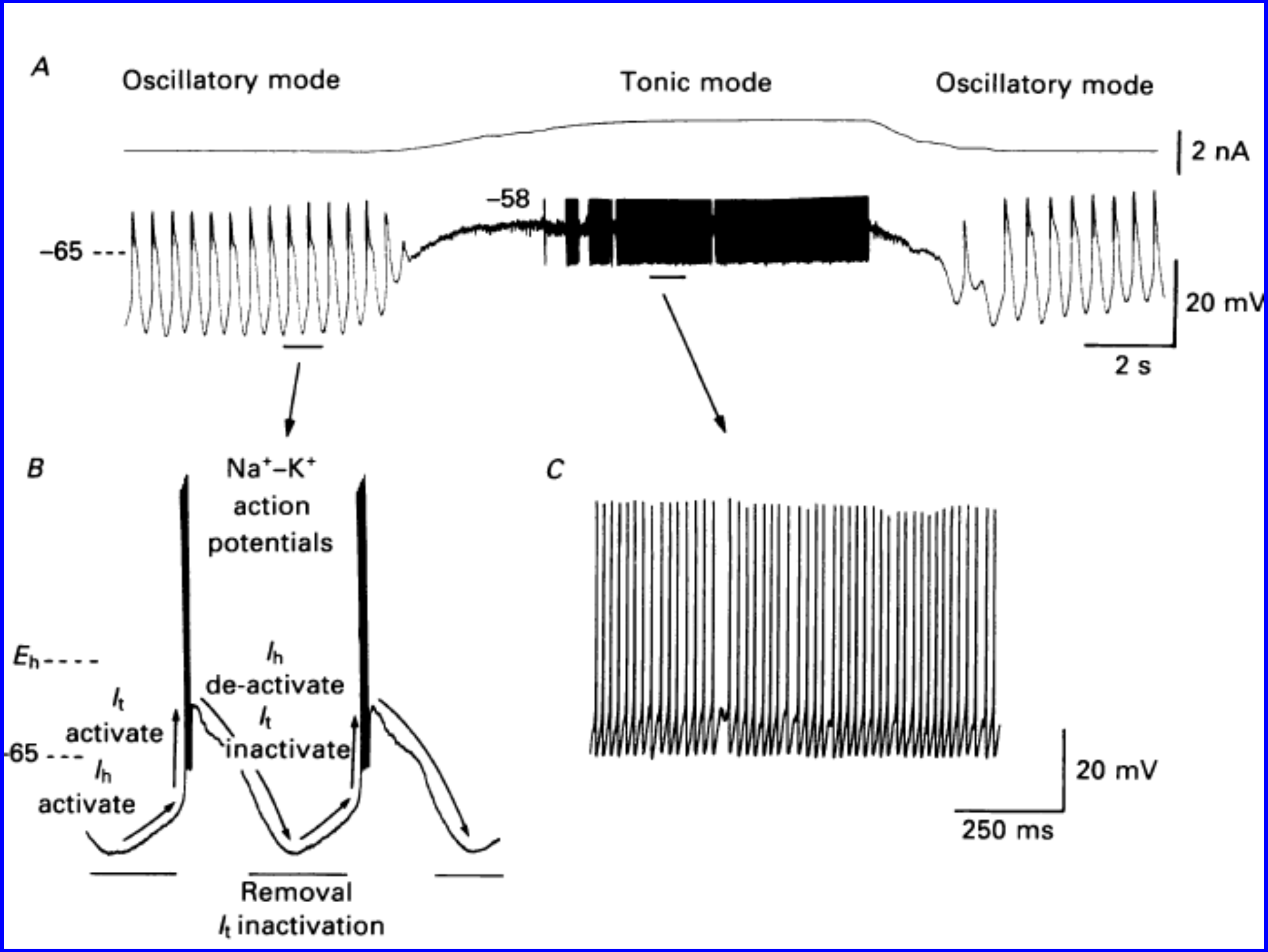


Huguenard and Prince, J Neurosci 1992,
Coulter, *Huguenard and Prince, J. Physiol 1989

I-t is significantly inactivated at rest



I-h is partner with I-t in intrinsic oscillations



McCormick and Pape, 1990a

I-h is modulable

Journal of Physiology (1990), **431**, *pp.* 319–342
With 13 *figures*
Printed in Great Britain

NORADRENERGIC AND SEROTONERGIC MODULATION OF A HYPERPOLARIZATION-ACTIVATED CATION CURRENT IN THALAMIC RELAY NEURONES

BY DAVID A. McCORMICK* AND HANS-CHRISTIAN PAPE†

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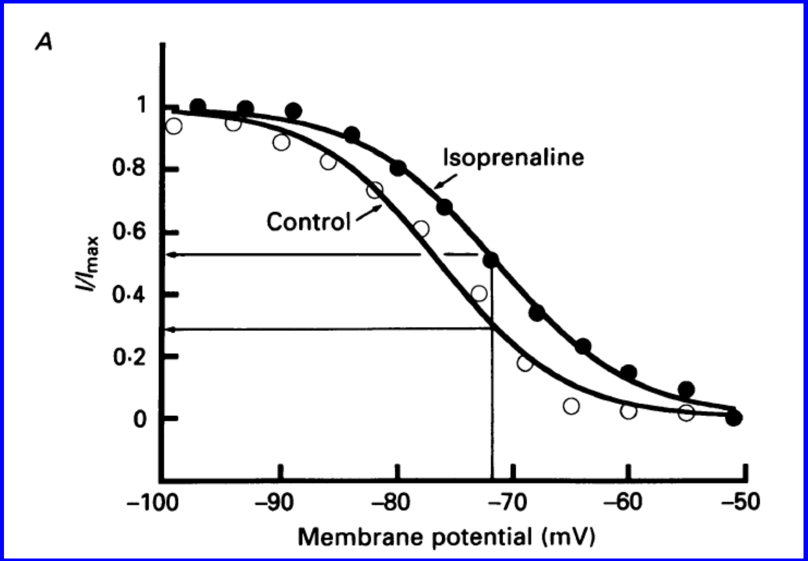


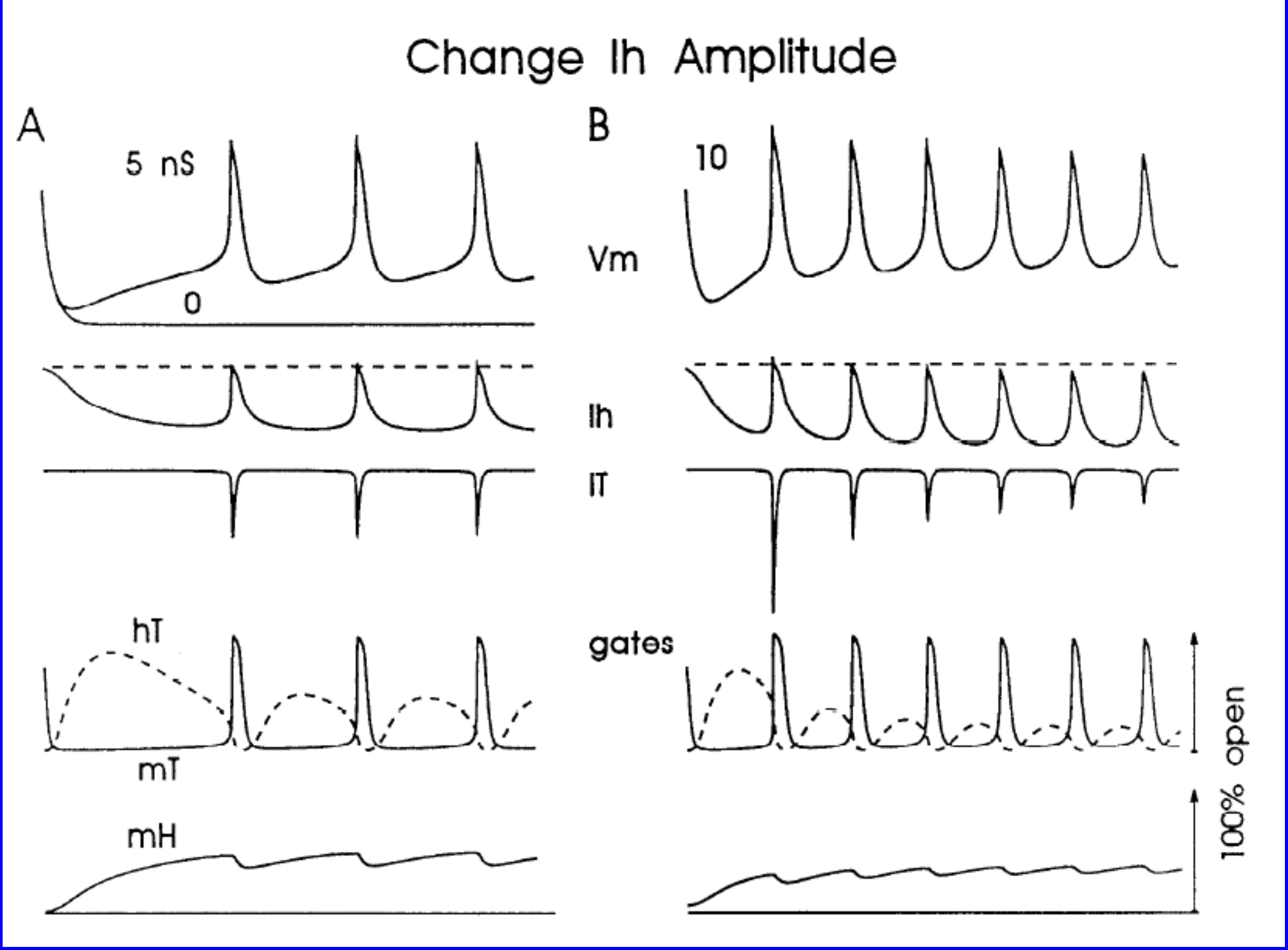
There are models available for cells with complex properties

JOURNAL OF NEUROPHYSIOLOGY
Vol. 68, No. 4, October 1992. *Printed in U.S.A.*

A Model of the Electrophysiological Properties of Thalamocortical Relay Neurons

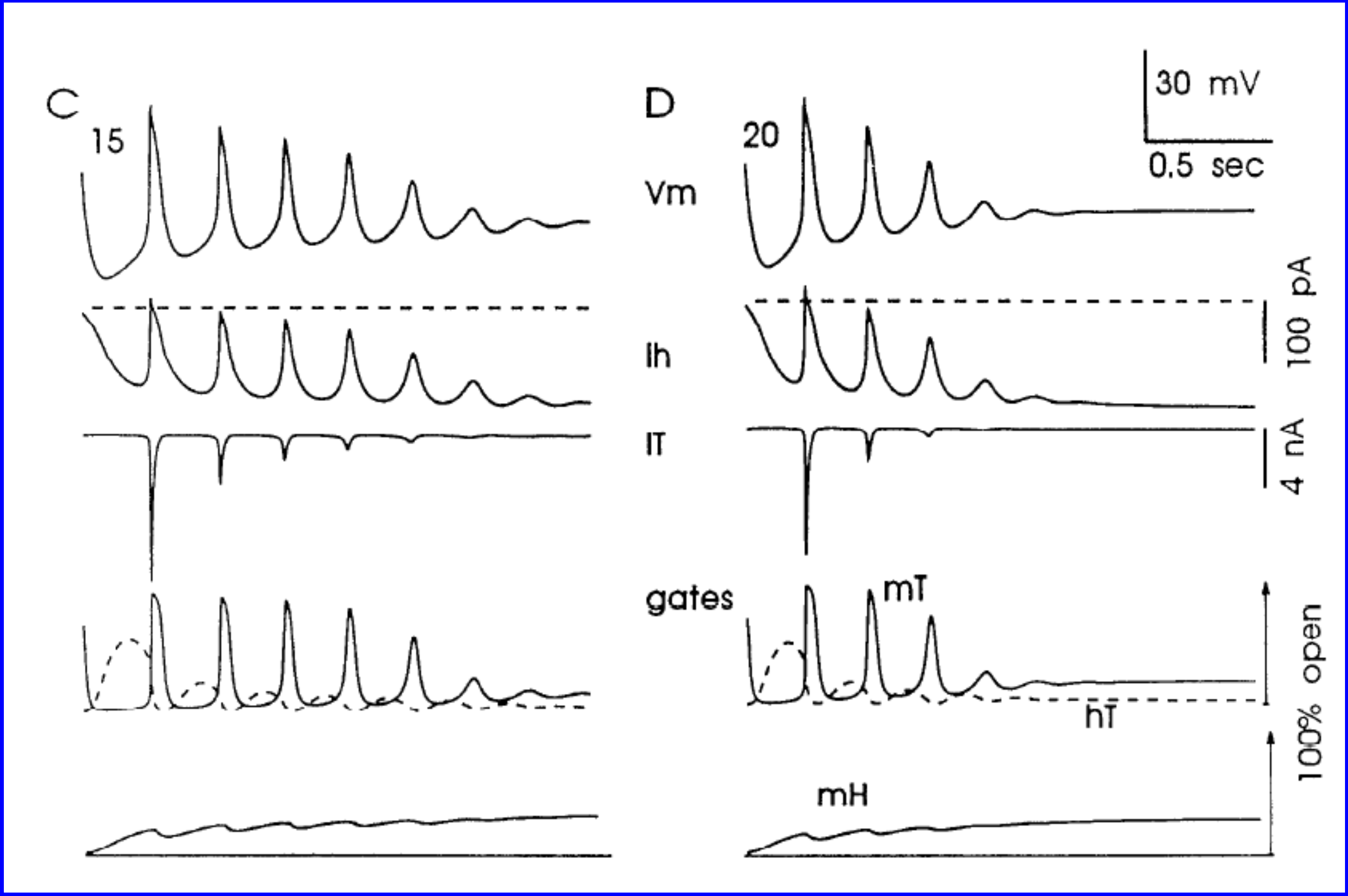
DAVID A. McCORMICK AND JOHN R. HUGUENARD
Section of Neurobiology, Yale University School of Medicine, New Haven, Connecticut 06510; and Department of Neurology, Stanford University Medical School, Stanford, California 94305

Can systematically vary different parameters to determine, e.g. sensitivity and necessity



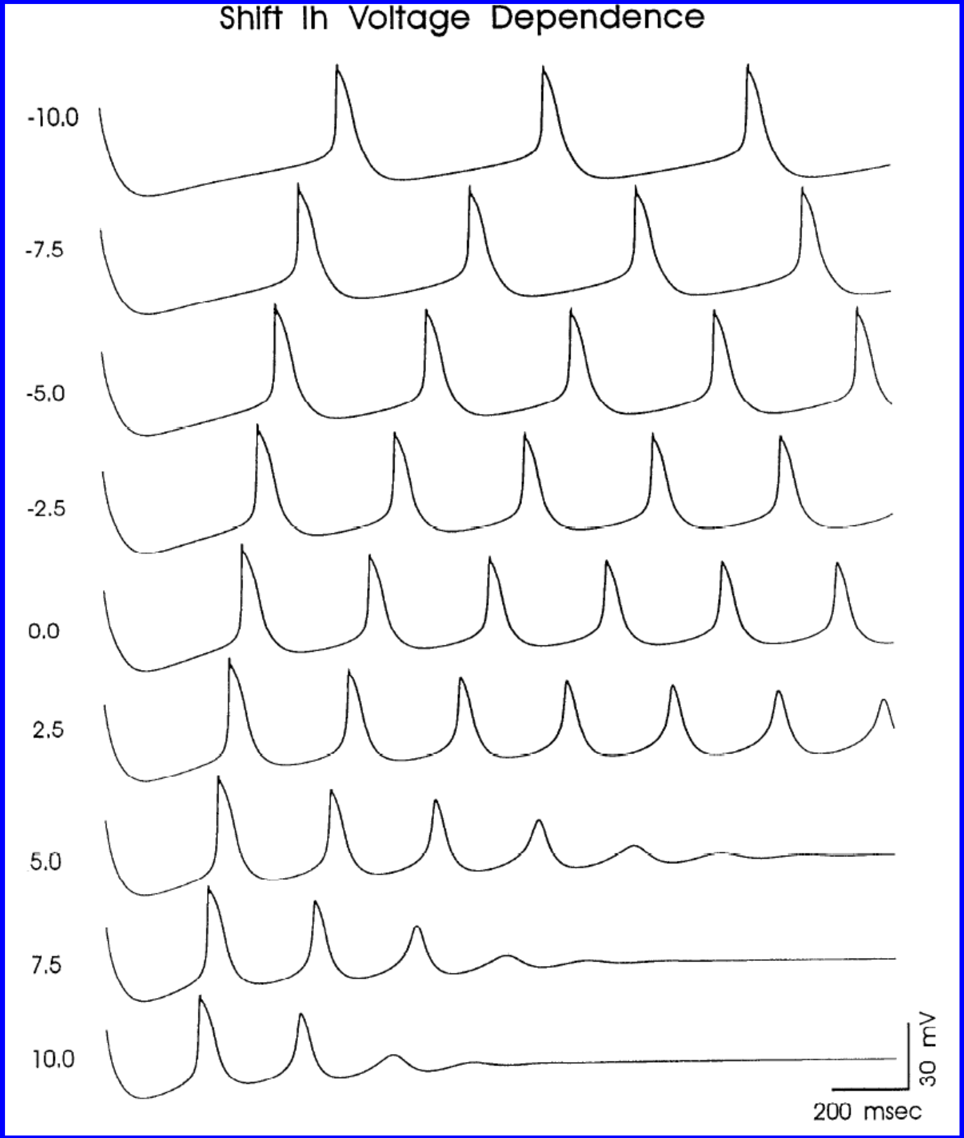
McCormick and Huguenard, 1992

Too much of a good thing?



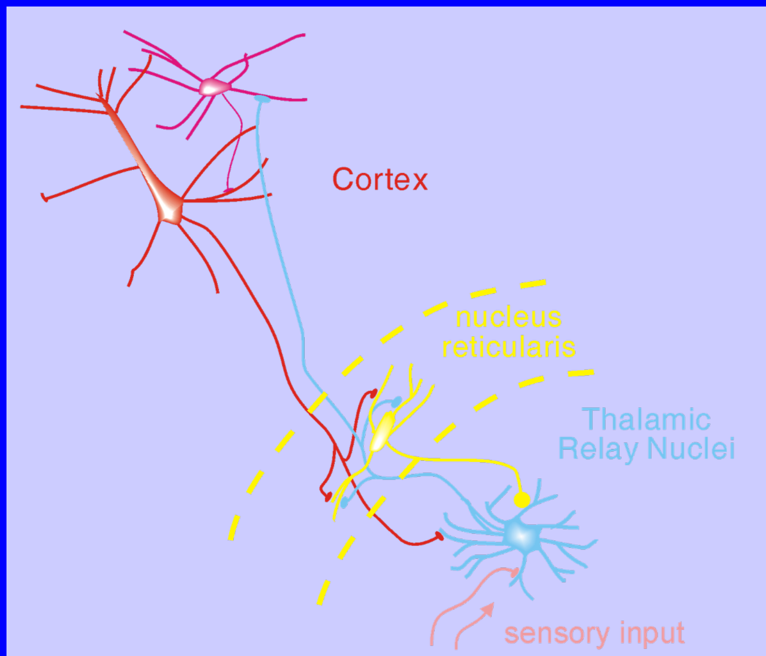
McCormick and Huguenard, 1992

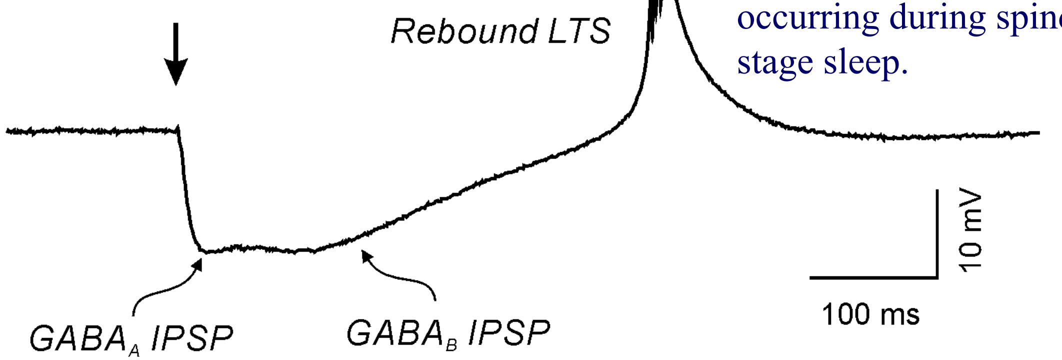
Modulation of I-h modifies network strength and structure



McCormick and Huguenard, 1992

Post inhibitory rebound in thalamus and sleep rhythms





When active, thalamocortical cells receive recurrent (feedback) inhibition from neurons of the thalamic reticular nucleus (TRN). The inhibitory feedback in turn, leads to post-inhibitory rebound low threshold spike, re-excitation of TRN, and recurrent network oscillations, such as those occurring during spindle-stage sleep.

Summary, oscillations

- Oscillations can be generated in neural networks
  - through synaptic interactions, usually inhibitory
  - Through the intrinsic voltage dependent properties of neural elements

Summary, oscillations

- Recurrency promoted by membrane bistability
  - Between depolarized and hyperpolarized states
    - » The latter is associated with activity
    - » the former is generally associated with quiescence
  - Bistability is a result of non-linearities in the V/I relationship of neurons

Summary, oscillations

- Non-linearities in neural membranes
  - N-shaped I/V curves
    - » Different from passive cells with largely linear I/V curves
  - N-shaped I/V curves with more than one positive crossing of current axis will have more than one stable point
  - Interactions with synapses (e.g. inhibition) or voltage gated ion channels (H-channels) result in reentrant transitions between stable states, and ultimately, oscillations

References

- Wang XJ, Buzsáki G. (1996) Gamma oscillation by synaptic inhibition in a hippocampal interneuronal network model. J Neurosci. 16:6402-13.
- Wilson CJ. (2005) The mechanism of intrinsic amplification of hyperpolarizations and spontaneous bursting in striatal cholinergic interneurons. Neuron 45:575-85.
- McCormick DA, Pape HC (1990) Properties of a hyperpolarization-activated cation current and its role in rhythmic oscillation in thalamic relay neurones. J Physiol. 431:291-318.