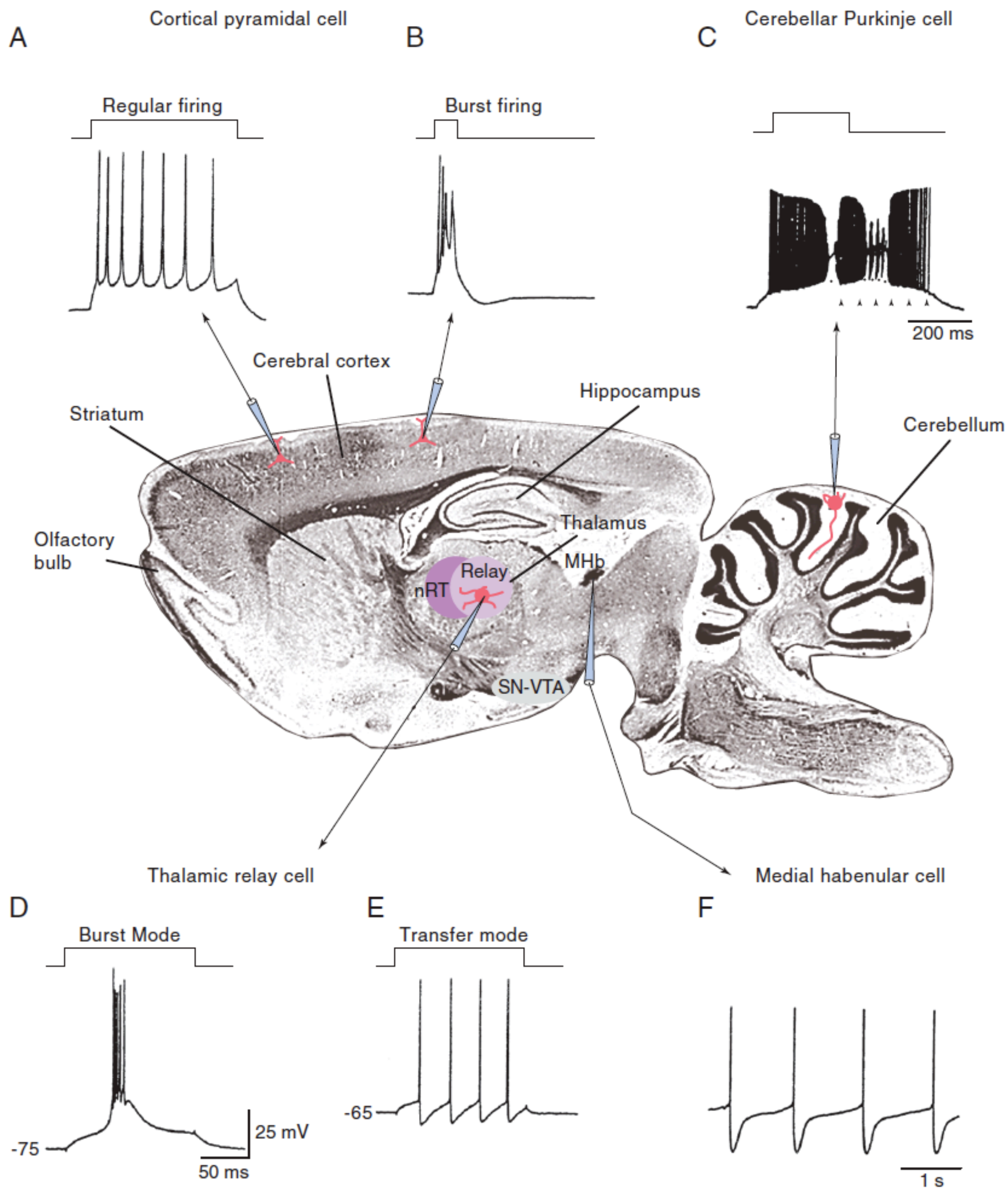
Endogenous and Exogenous Neuronal Rhythmicity

Guillaume Drion - ISSSMA | June the 25th, 2013

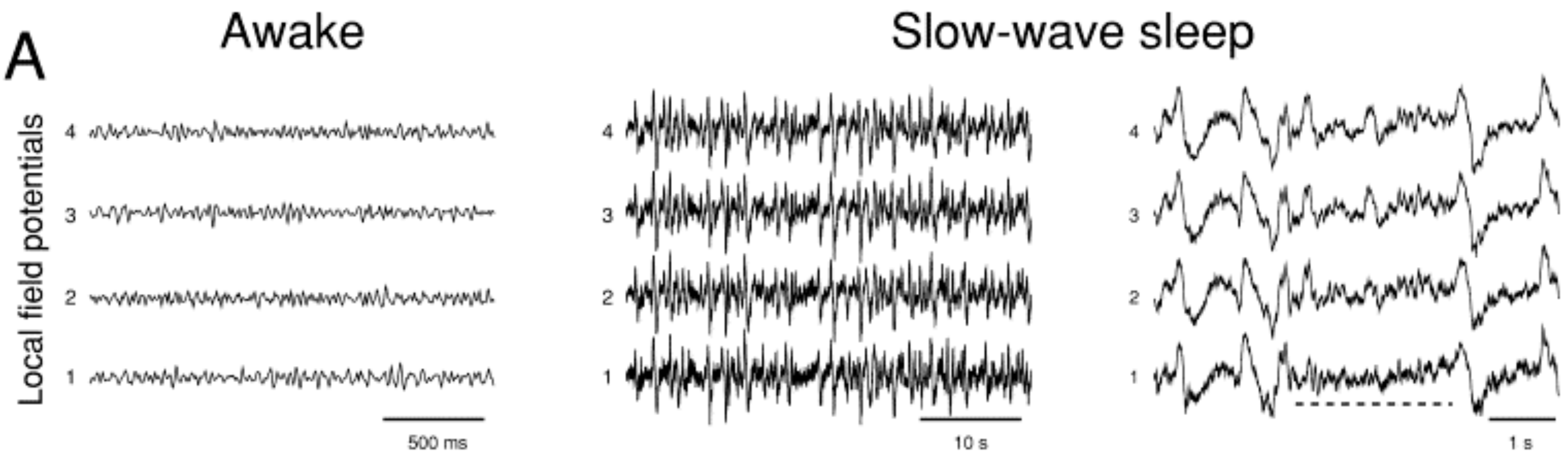
Neuronal Rhythmicity is a Key Component of Brain Information Processing



(Byrne et al., 2004)

Neuronal Rhythmicity is a Key Component of Brain Information Processing

- Example 1: Thalamic and cortical neurons during awakeness and sleep.



(McCormick and Bal, 1994)

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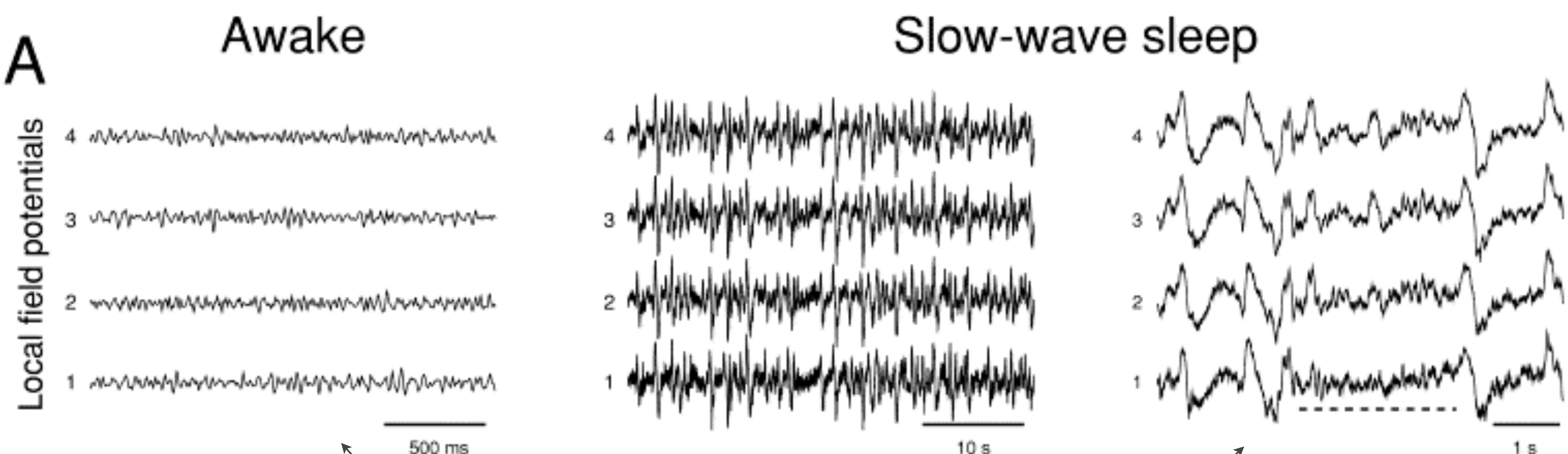
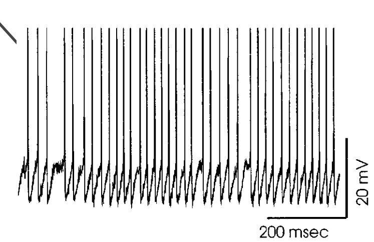
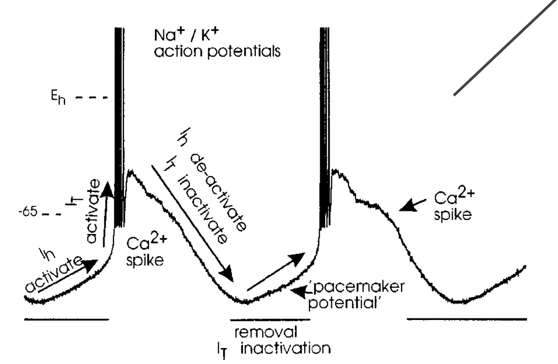




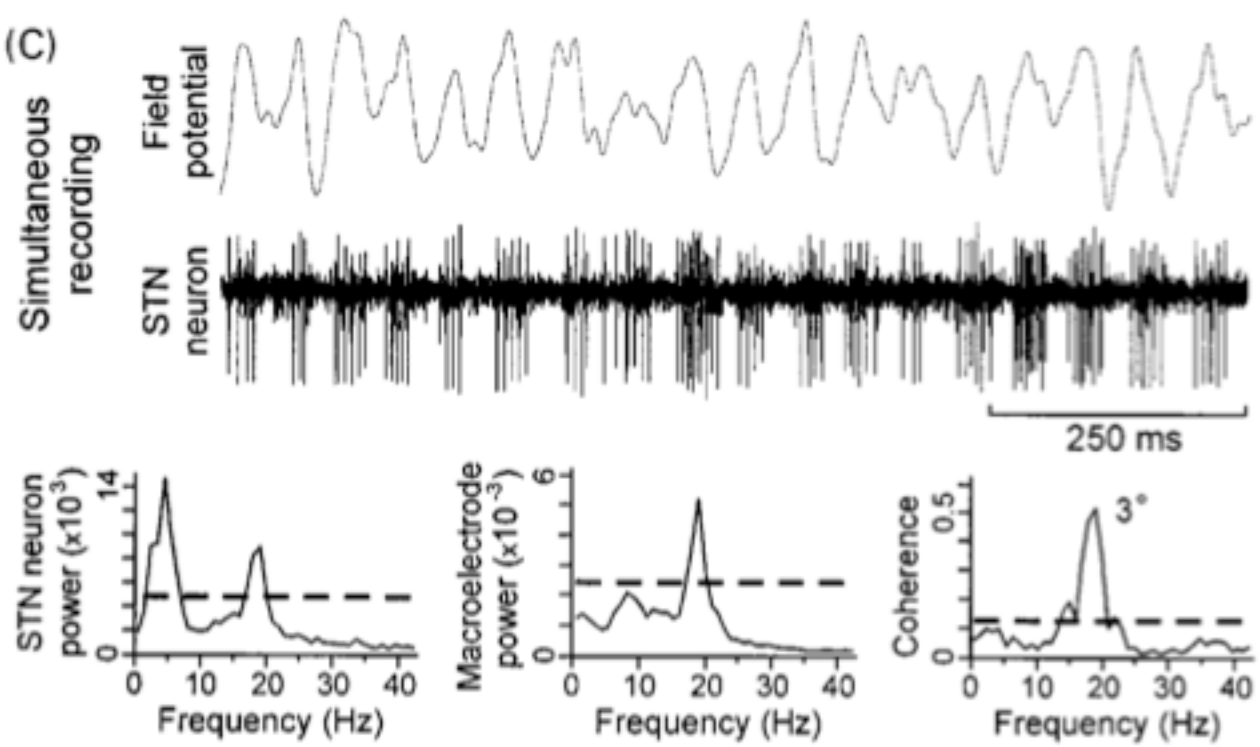


- Pathological burst firing during awakeness leads to epileptic seizures.

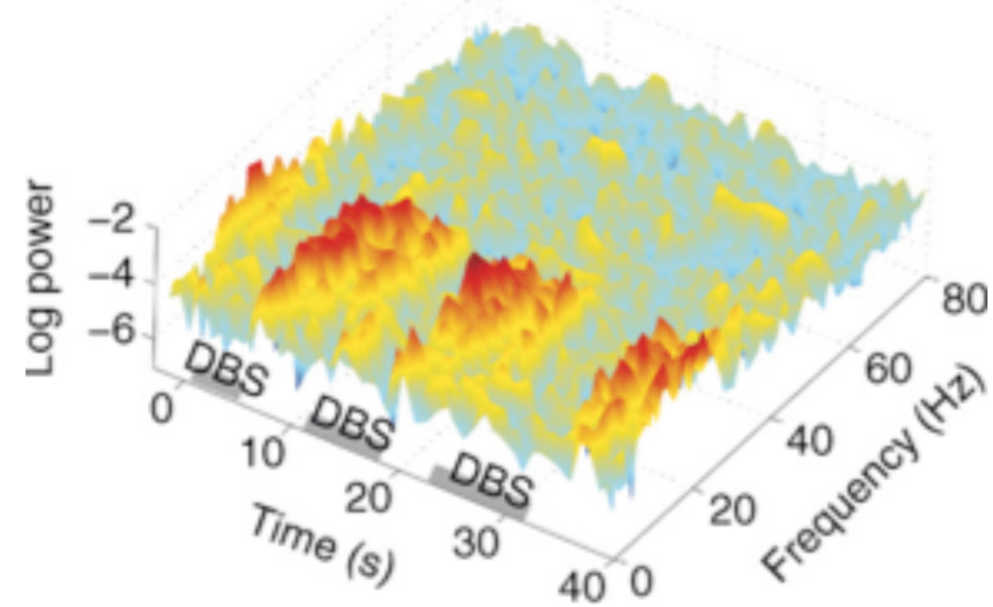
(McCormick and Bal, 1994)

Neuronal Rhythmicity is a Key Component of Brain Information Processing

- Example 2: Subthalamic nucleus (STN) neurons in control and Parkinson's disease patients



(Levy et al., 2002)

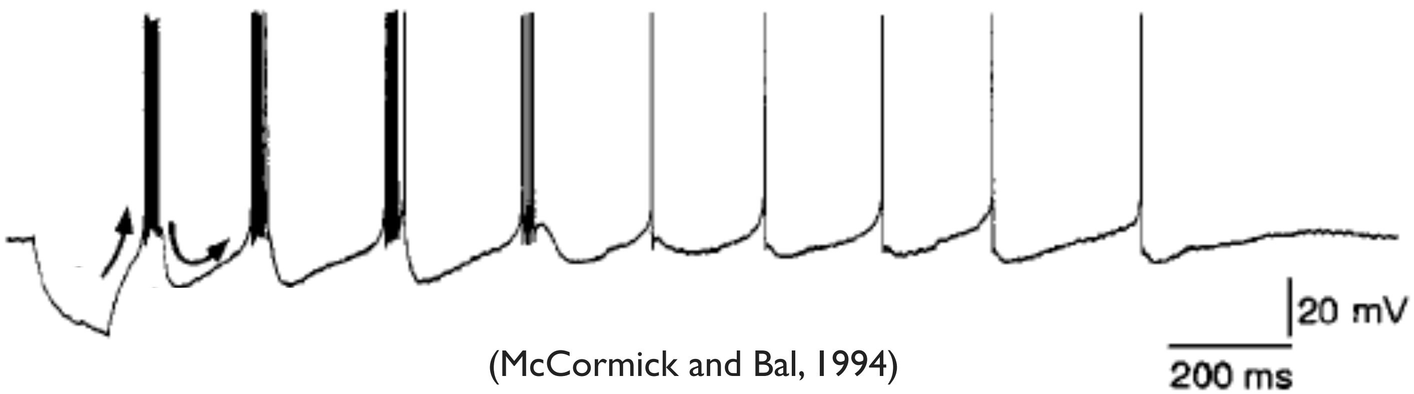


(Hammond et al., 2007)

- Many Parkinson's disease motor symptoms correlate to STN neuron pathological burst firing/STN beta oscillations.

Neuronal Rhythmicity is a Key Component of Brain Information Processing

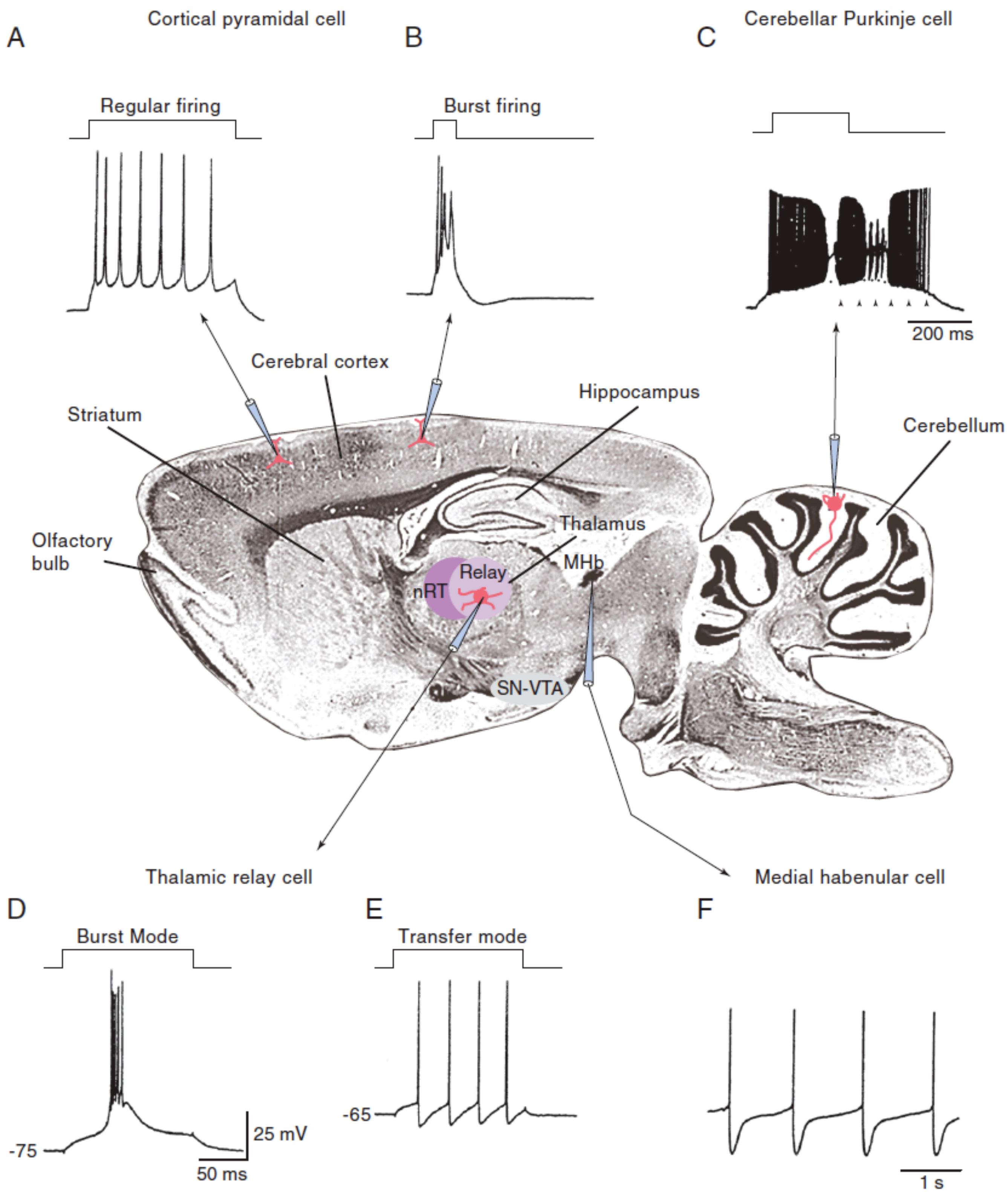
→ What are the mechanisms controlling neuronal rhythmicity?



(McCormick and Bal, 1994)

Unicellular mechanisms? (endogenous rhythmicity)
Network properties? (exogenous rhythmicity)
Both?

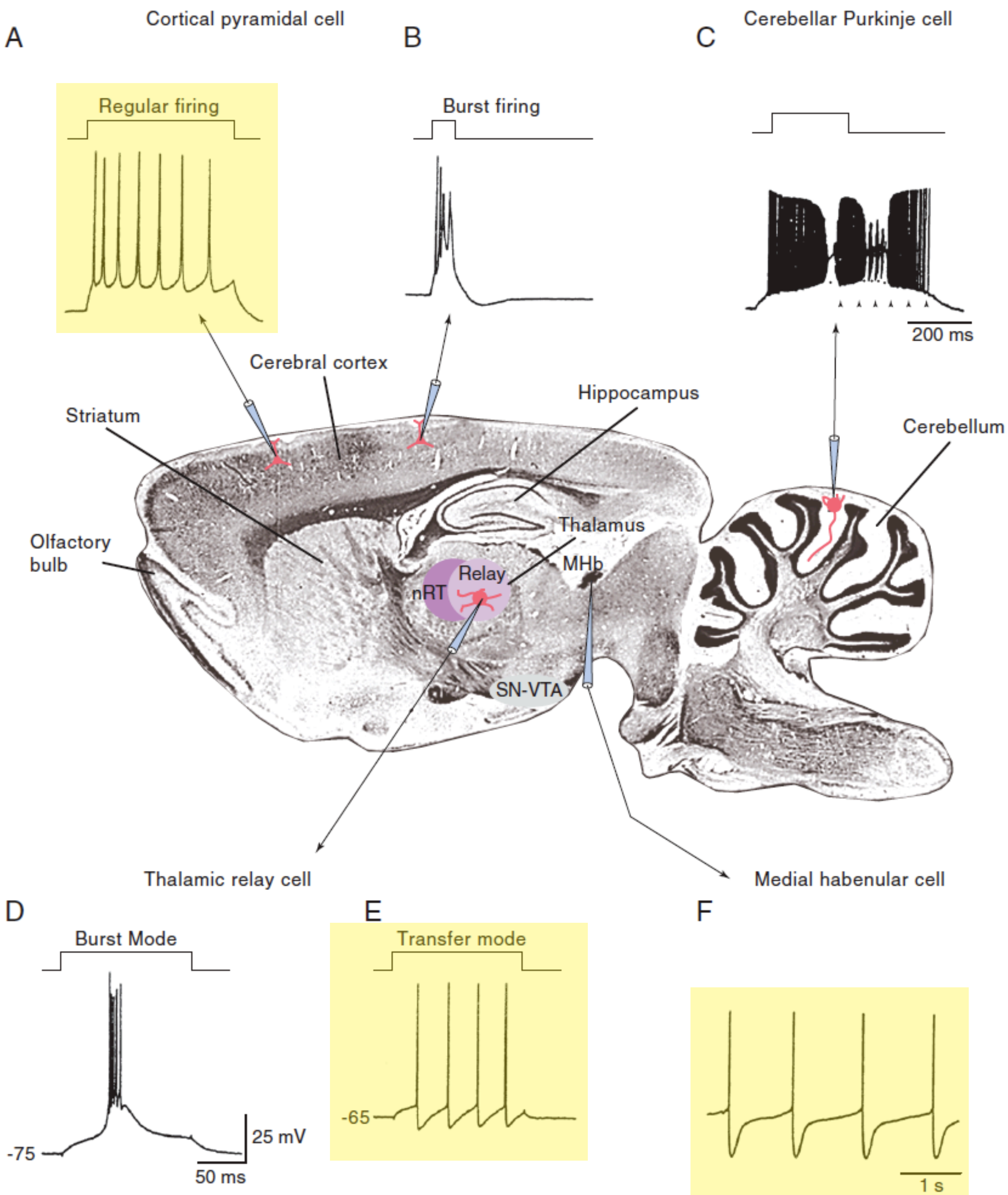
Endogenous Rhythmicity: Tonic Firing and Bursting



(Byrne et al., 2004)

- Neurons can exhibit many quantitatively different firing patterns
- Qualitatively, they can be grouped in two categories:
  - Tonic (single-spike) firing
  - Bursting

Endogenous Rhythmicity: Tonic Firing and Bursting



(Byrne et al., 2004)

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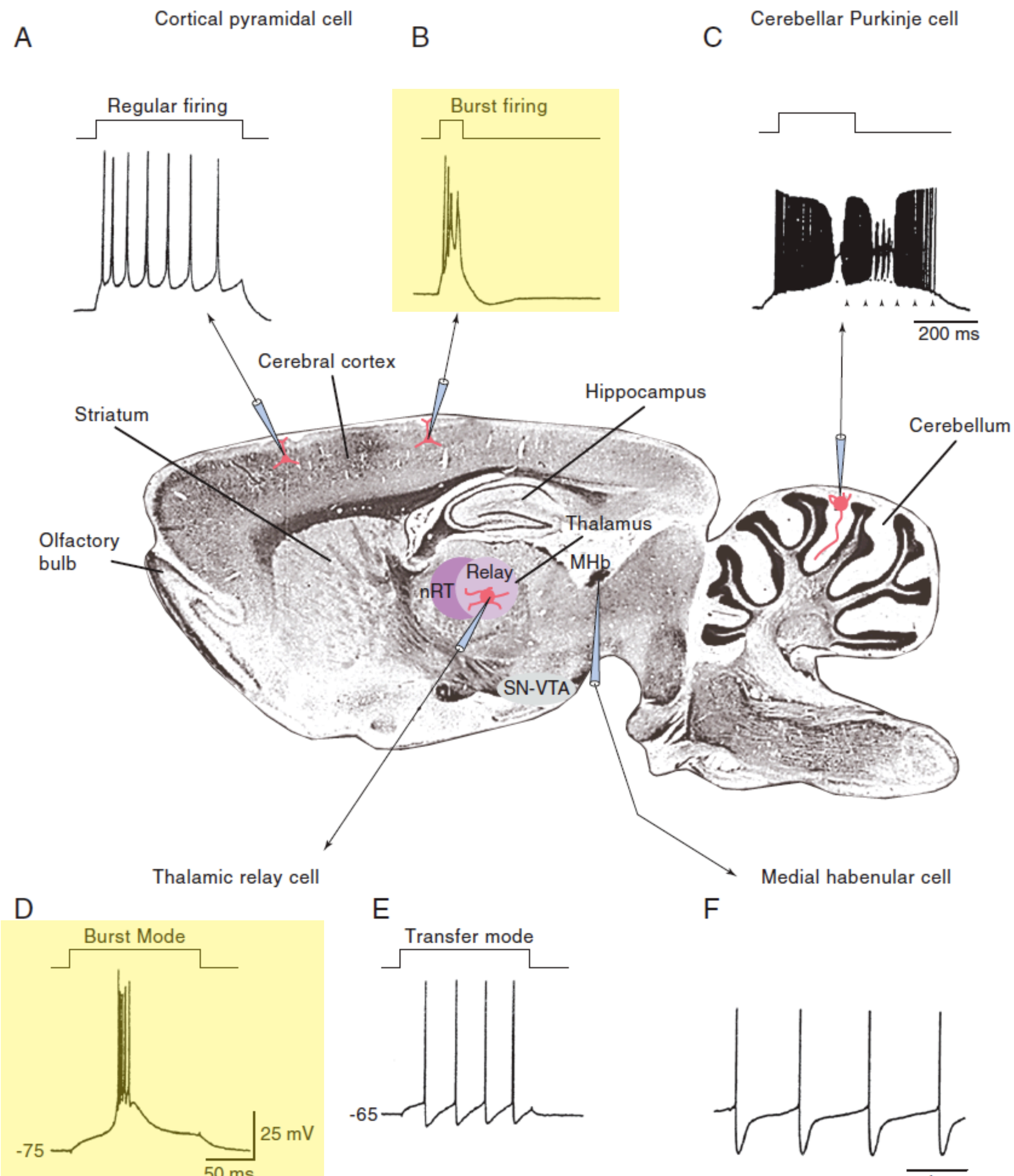
Endogenous Rhythmicity: Tonic Firing and Bursting



(Byrne et al., 2004)

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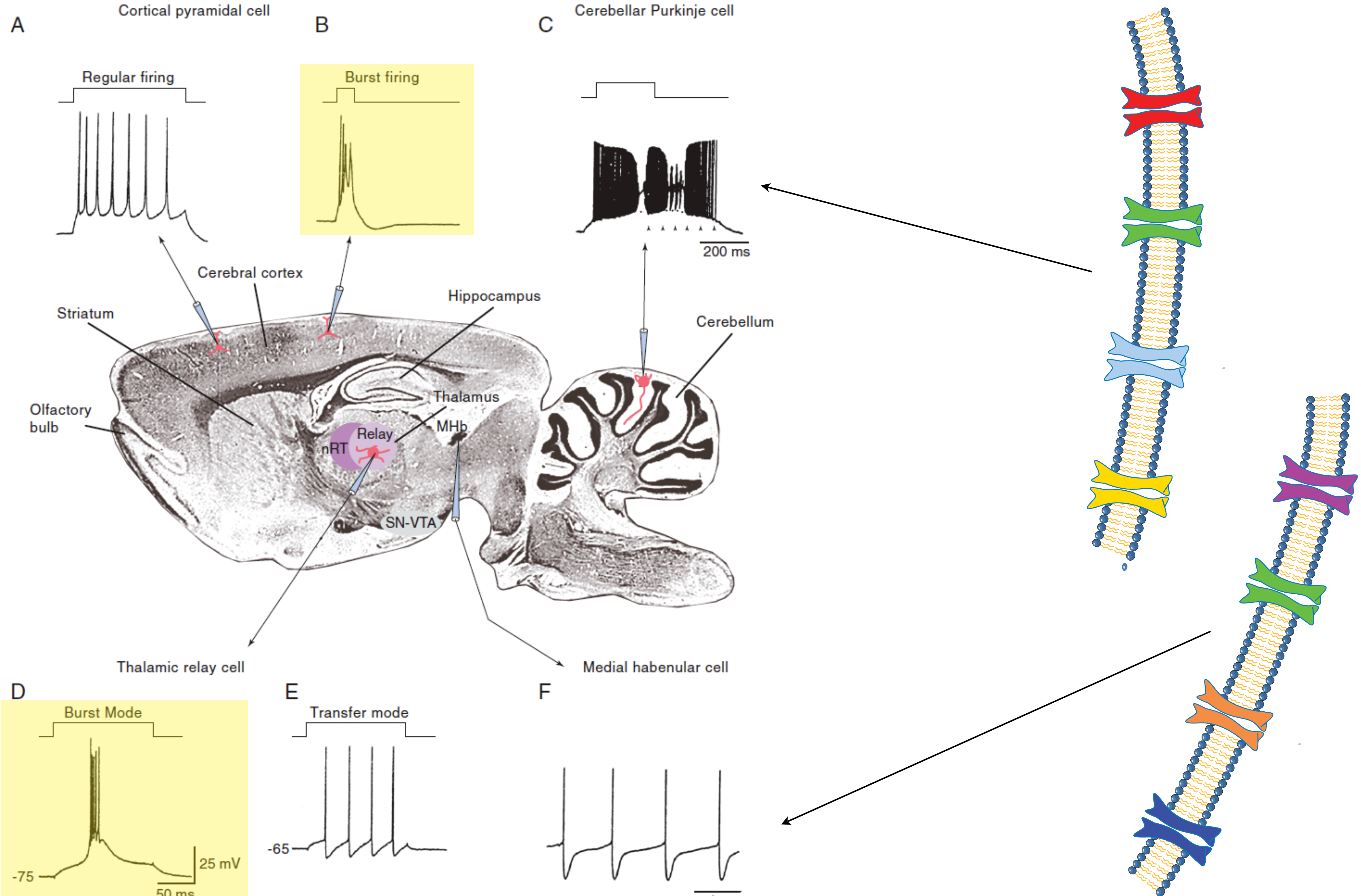
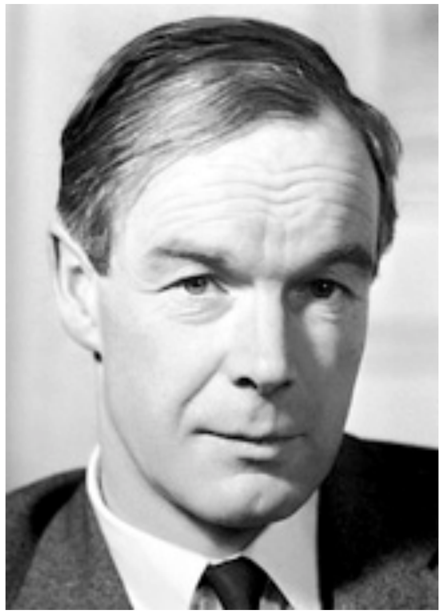
Single Neuron Rhythmicity relies on a Richness in Ion Channel Diversity

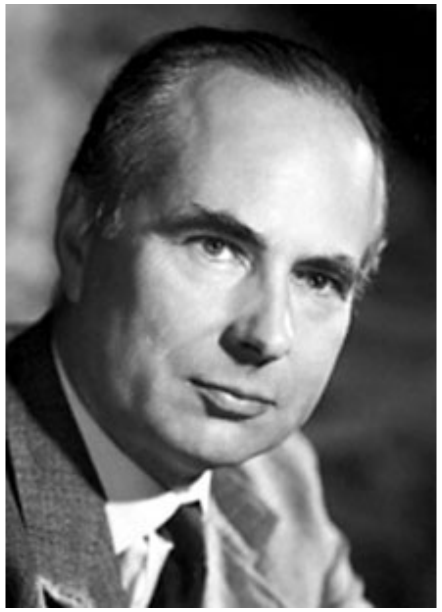


(Byrne et al., 2004)

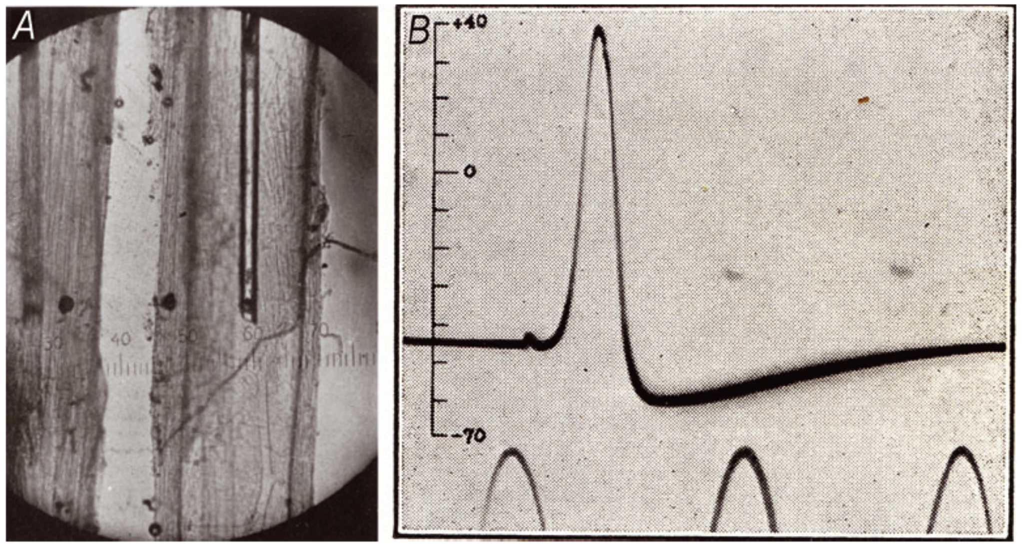
Hodgkin and Huxley were the Firsts to record, Analyze and Mathematically Model the Behavior of an Excitable Cell



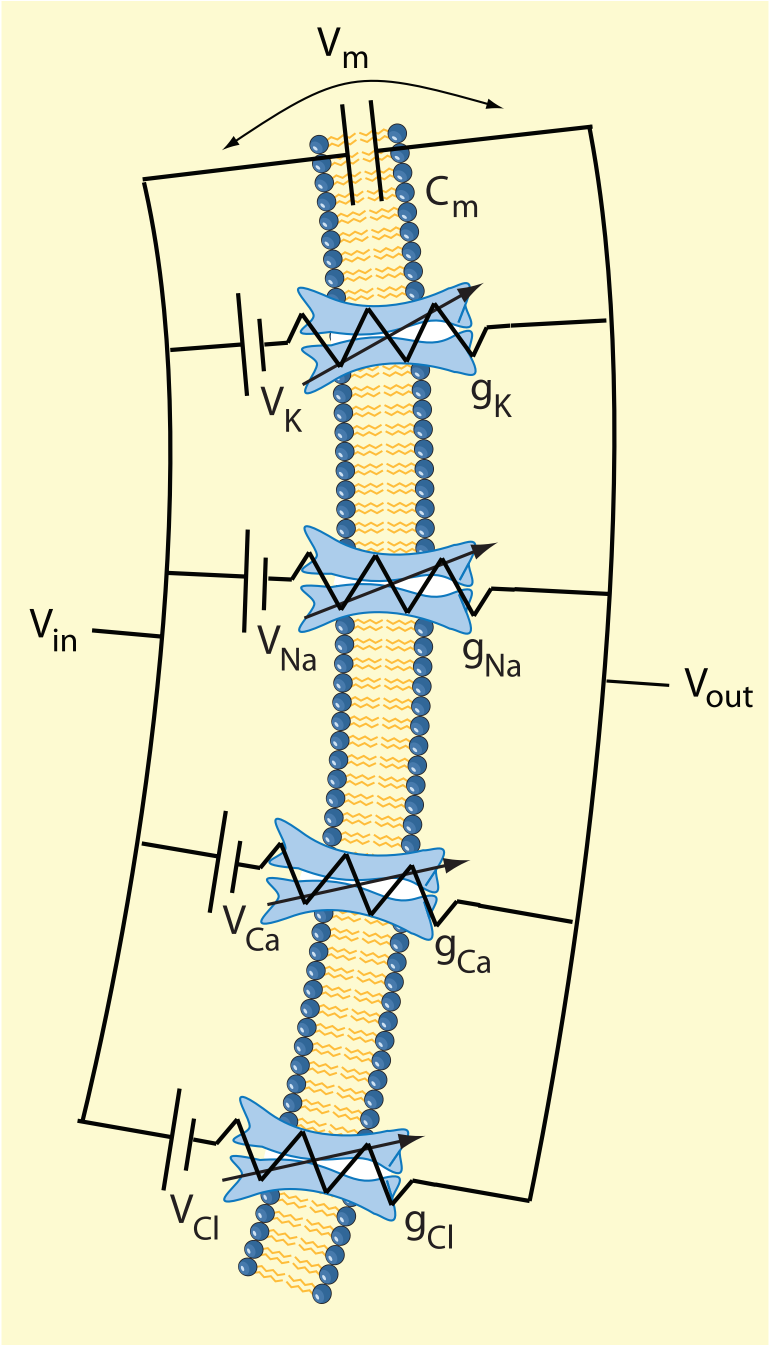
Alan L. Hodgkin



Andrew F. Huxley



$$C_m \dot{V}_m = -\sum_n I_{ion} + I_{app}$$



The HH Model Remains at the Basis of Computational Neurosciences

HH Model
(Hodgkin and Huxley, 1952)

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HH Model
(Hodgkin and Huxley, 1952) → High-Dimensional
Conductance Based Models

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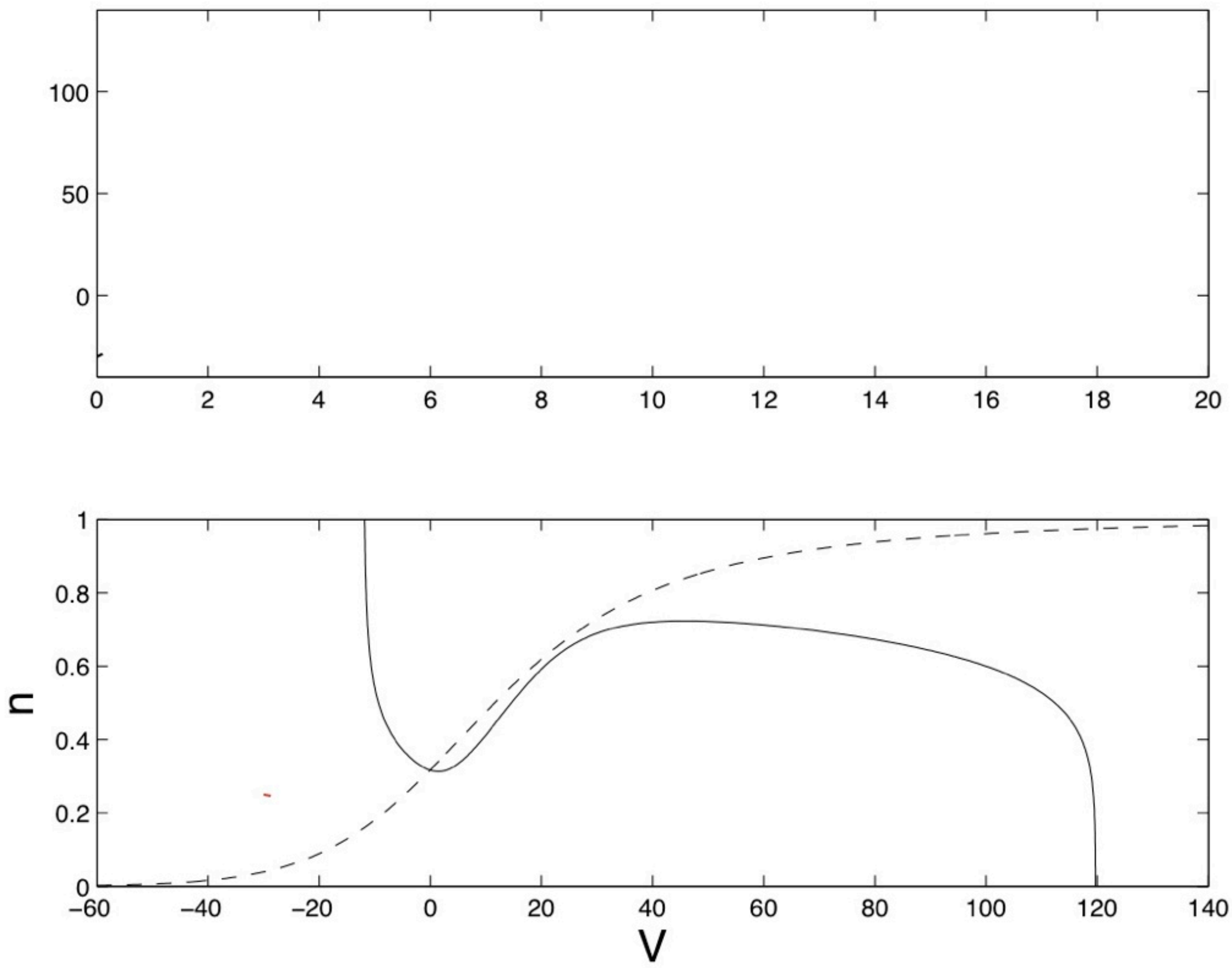
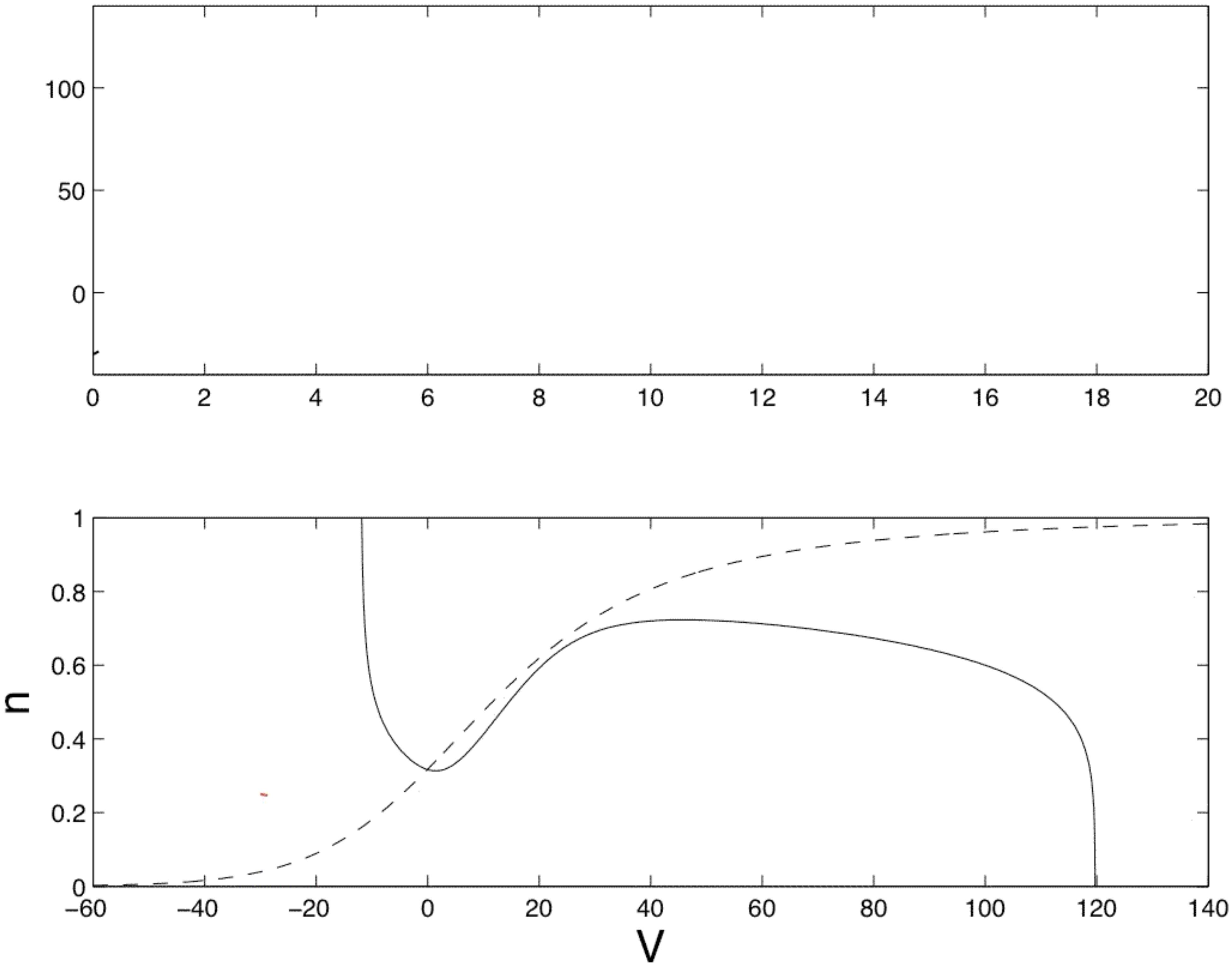
High-Dimensional
Conductance Based Models

2-D Reduction
(FitzHugh, 1961)

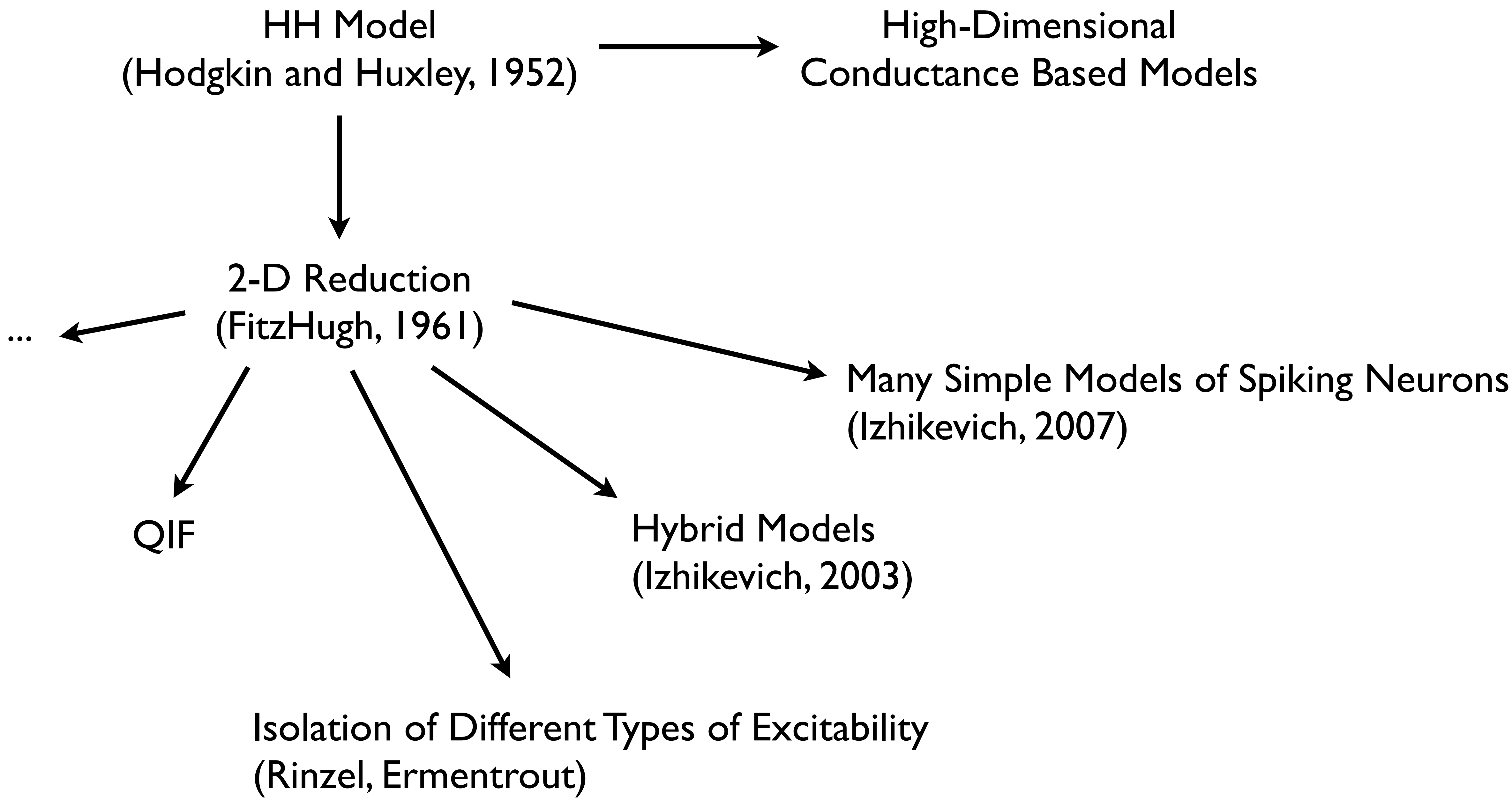
Two Dimensional Reduction of the Hodgkin-Huxley Model (FitzHugh, 1961)



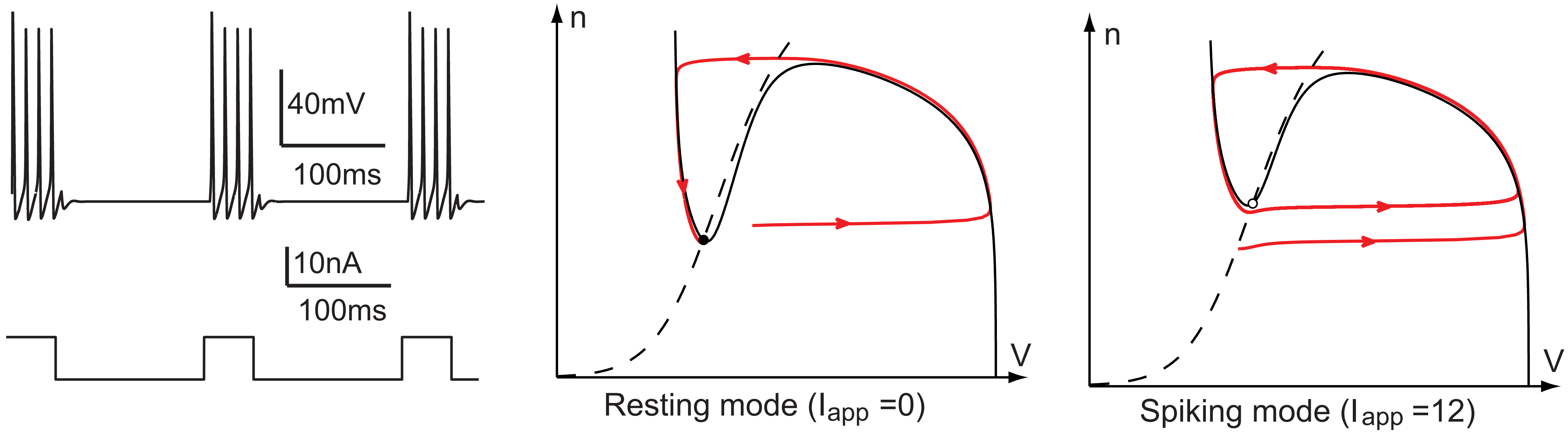
Two Dimensional Reduction of the Hodgkin-Huxley Model (FitzHugh, 1961)



The HH Model Remains at the Basis of Computational Neurosciences

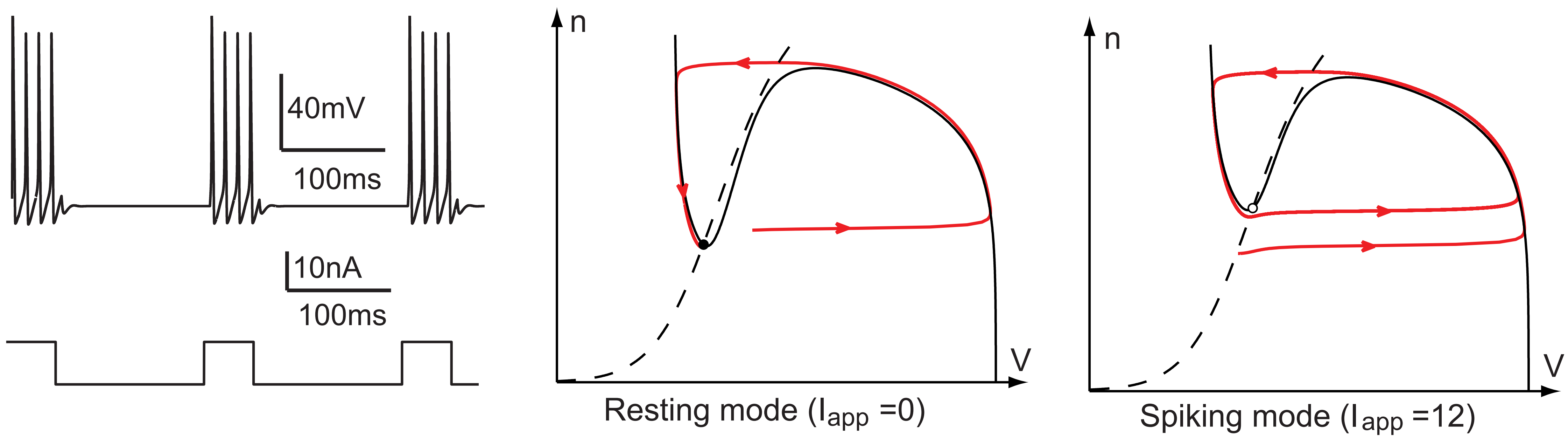


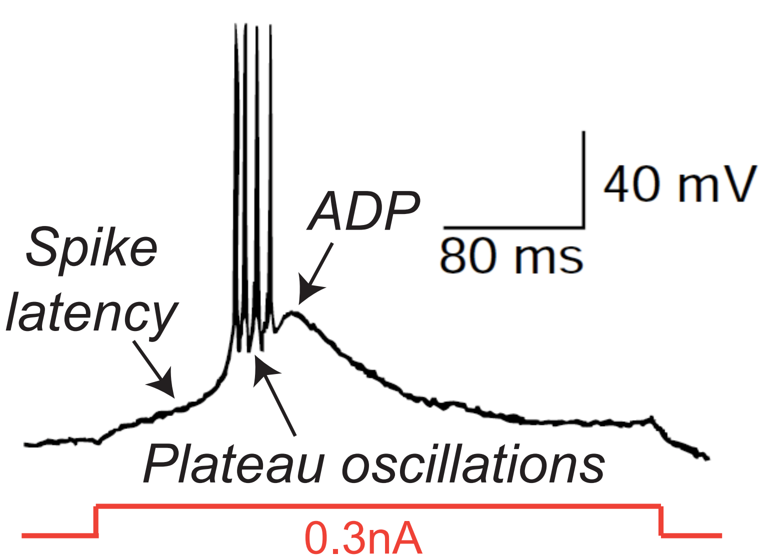
FitzHugh Reduction strongly succeeds in explaining the Geometry of Tonic Firing



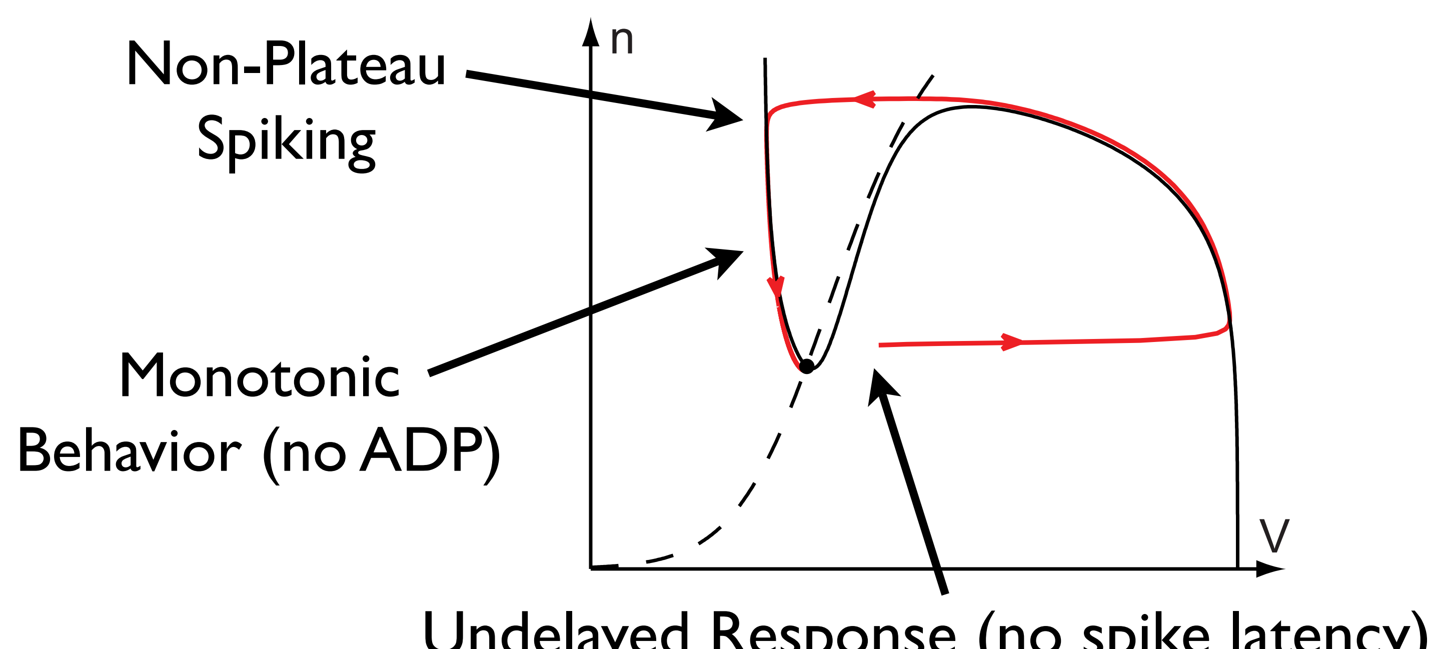
(Drion et al., 2012)

However, Many Neuronal Behavior, including Bursting, cannot be Reproduced on the Basis of this Picture





VS



(Drion et al., 2012)

The HH Model Remains at the Basis of Computational Neurosciences

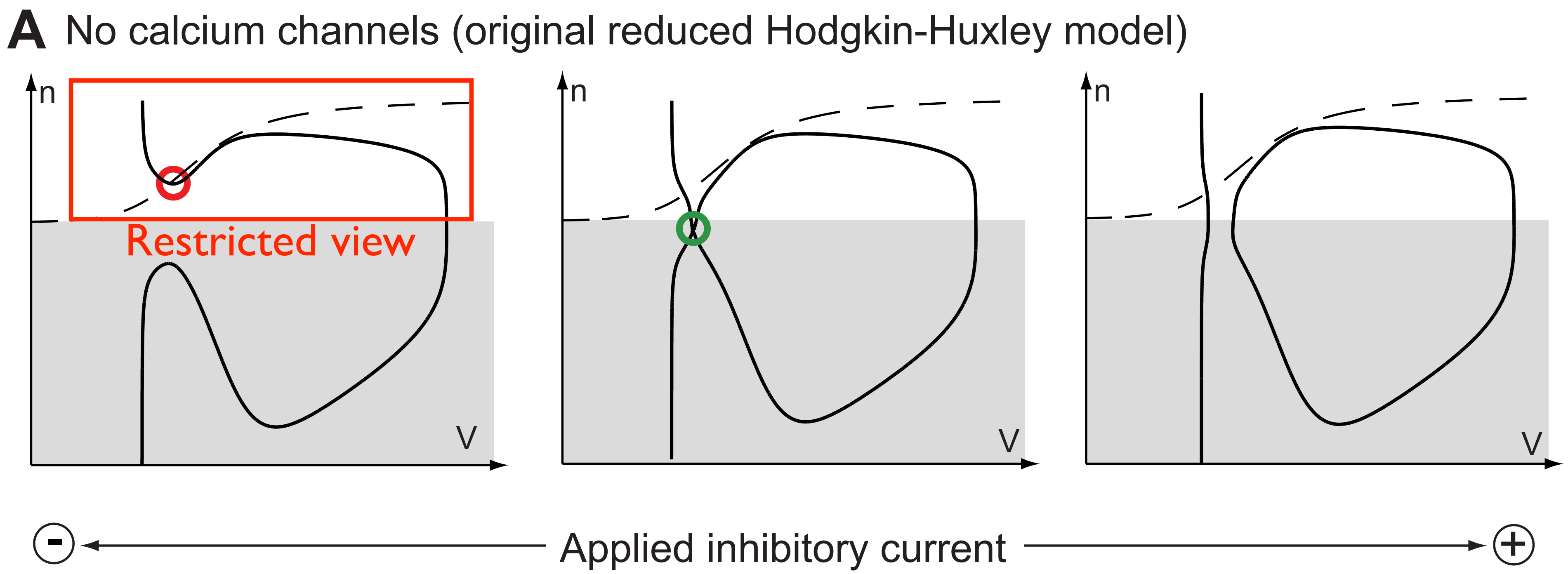
HH Model
(Hodgkin and Huxley, 1952)

High-Dimensional
Conductance Based Models

2-D Reduction
(FitzHugh, 1961)

2-D Reduction
(Drion et al., 2011)

The Classical Picture of Neuronal Excitability is only one Half of the Story



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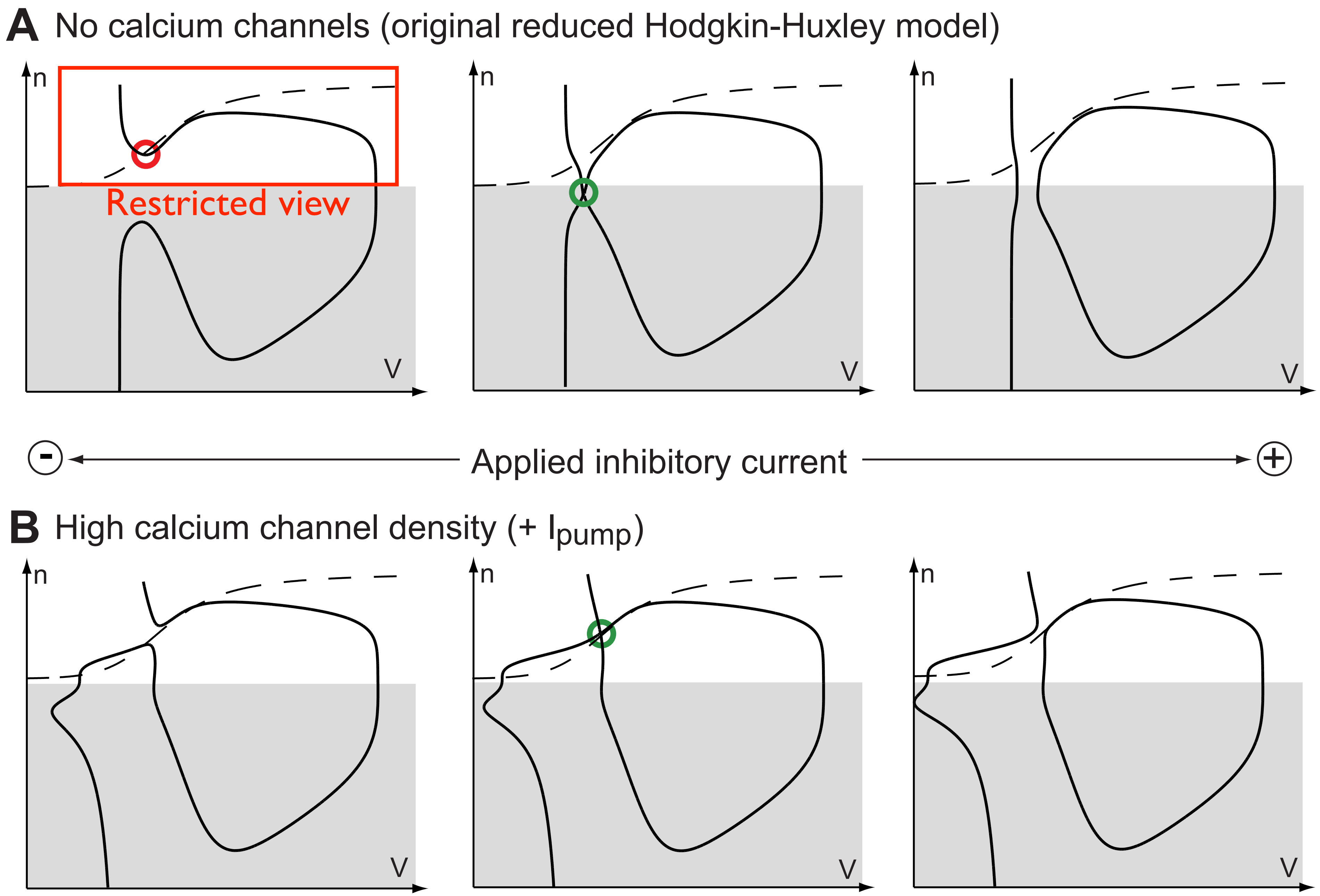

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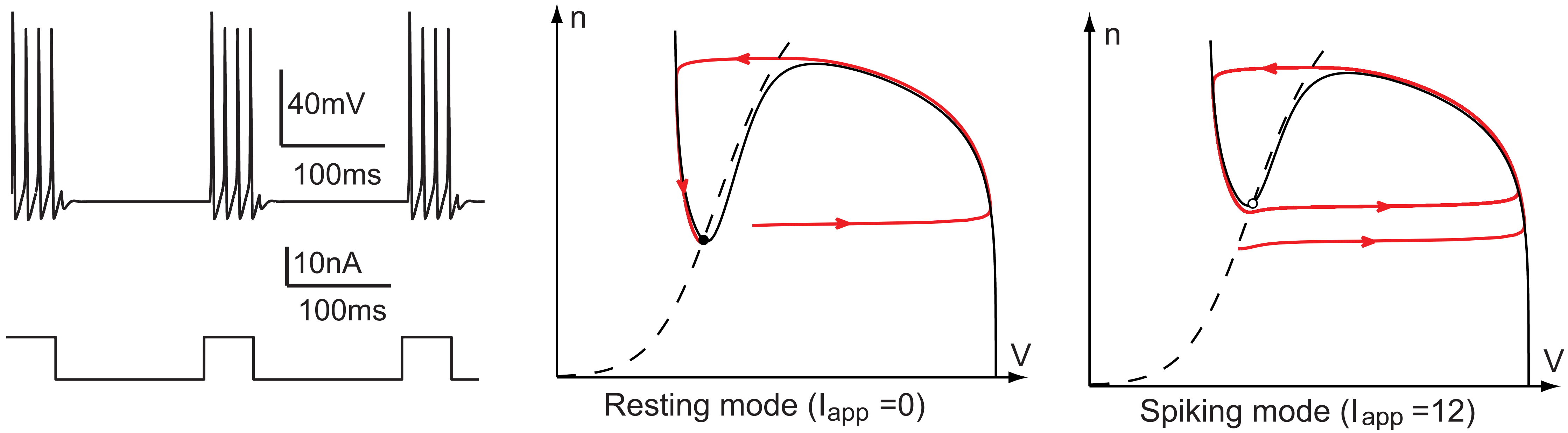
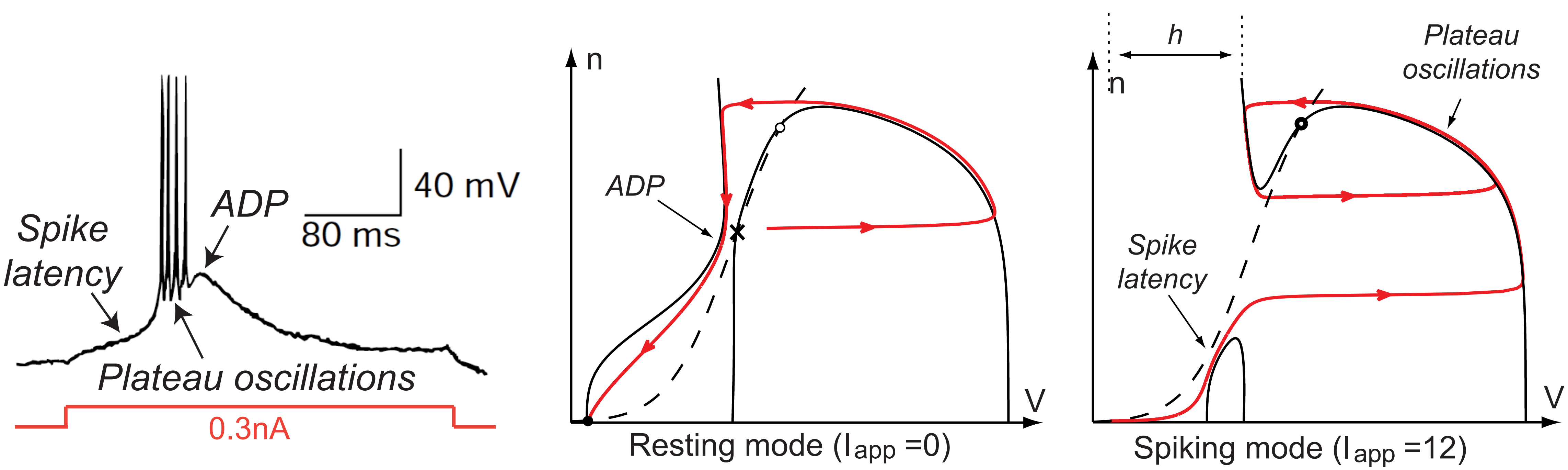
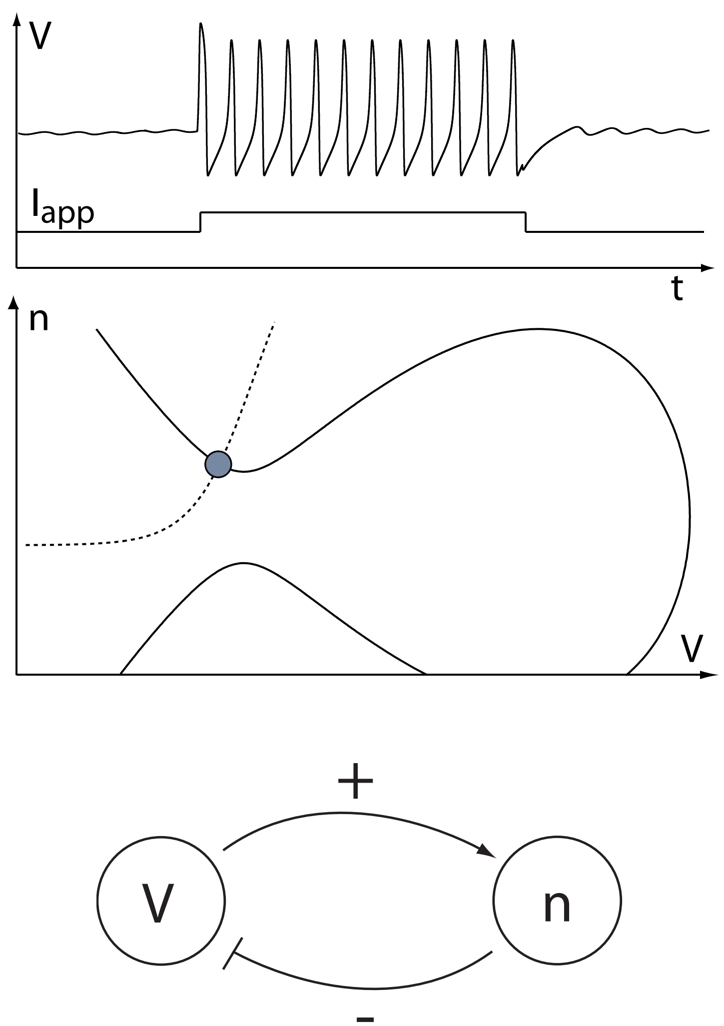




(Drion et al., 2012)

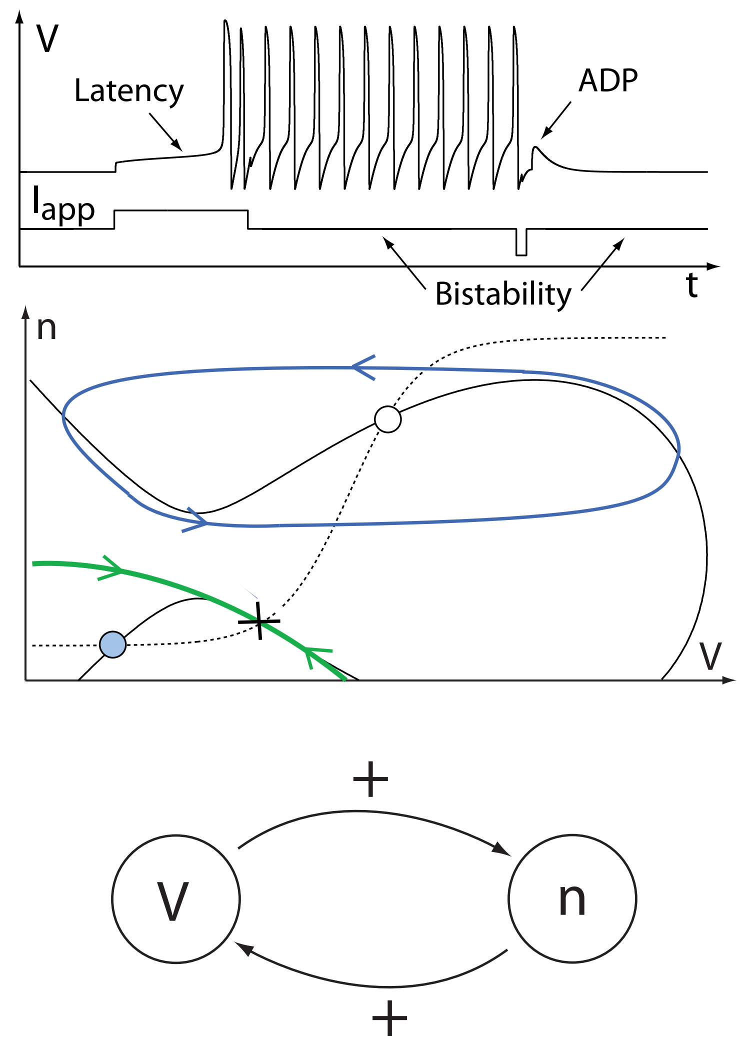
Restorative and Regenerative Excitability in Planar Models

Restorative Excitability (Type I,II,III)



TC

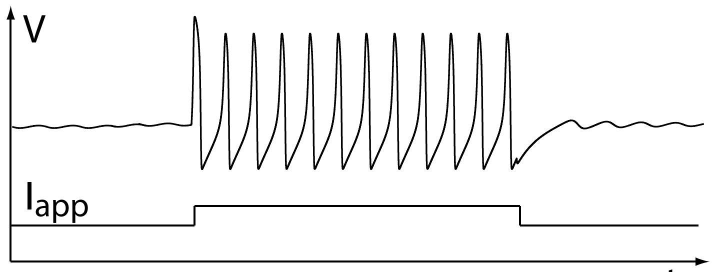
Regenerative Excitability (Type IV,V)



(Franci et al., 2012)

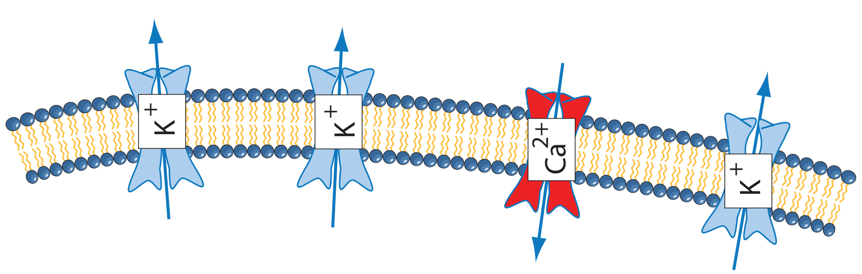
Restorative and Regenerative Excitability in Conductance-Based Models

Restorative Excitability (Type I,II,III)

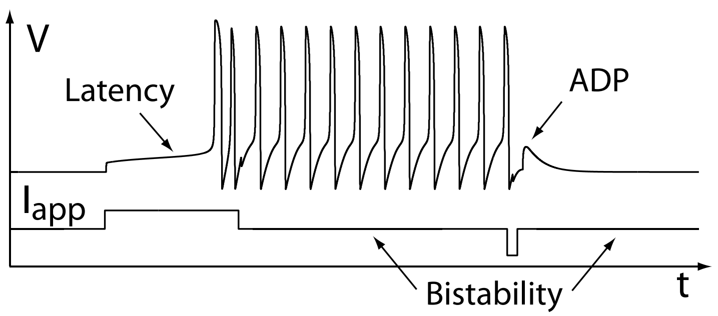


"Restorative" ion channels have a dominant role at rest.

Ex: Many potassium channels

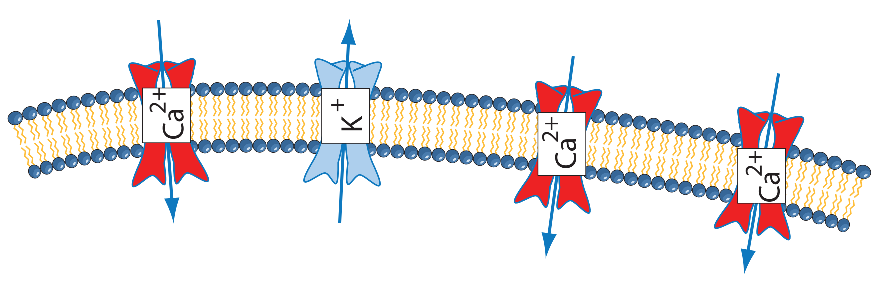


Regenerative Excitability (Type IV,V)



"Regenerative" ion channels have a dominant role at rest.

Ex: Calcium channels



TC

(Franci et al., 2013)

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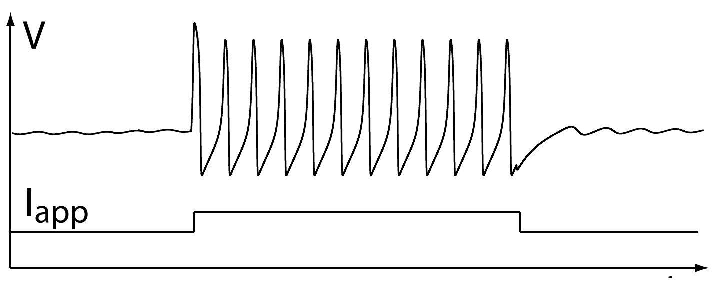
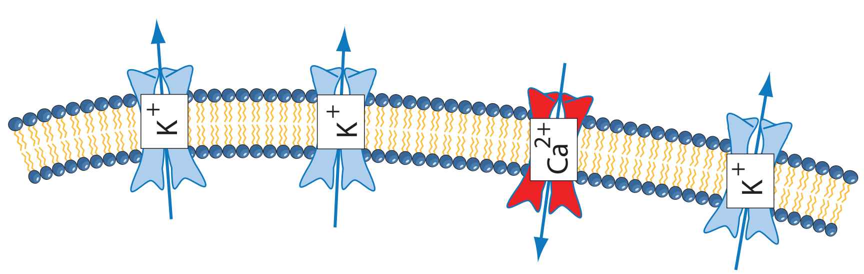


(Almost) Monostable

→ Tonic firing



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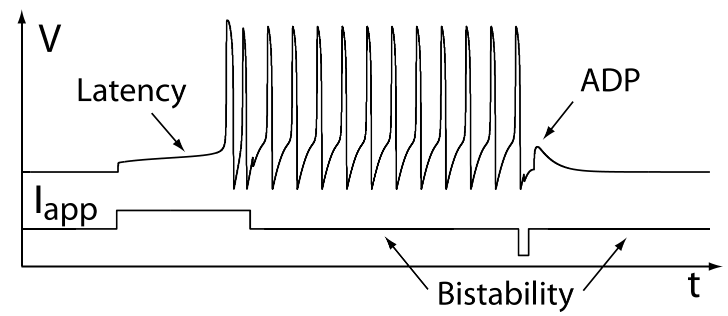
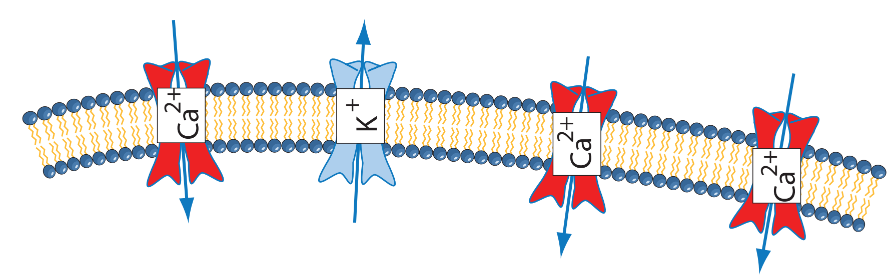


Robustly Bistable

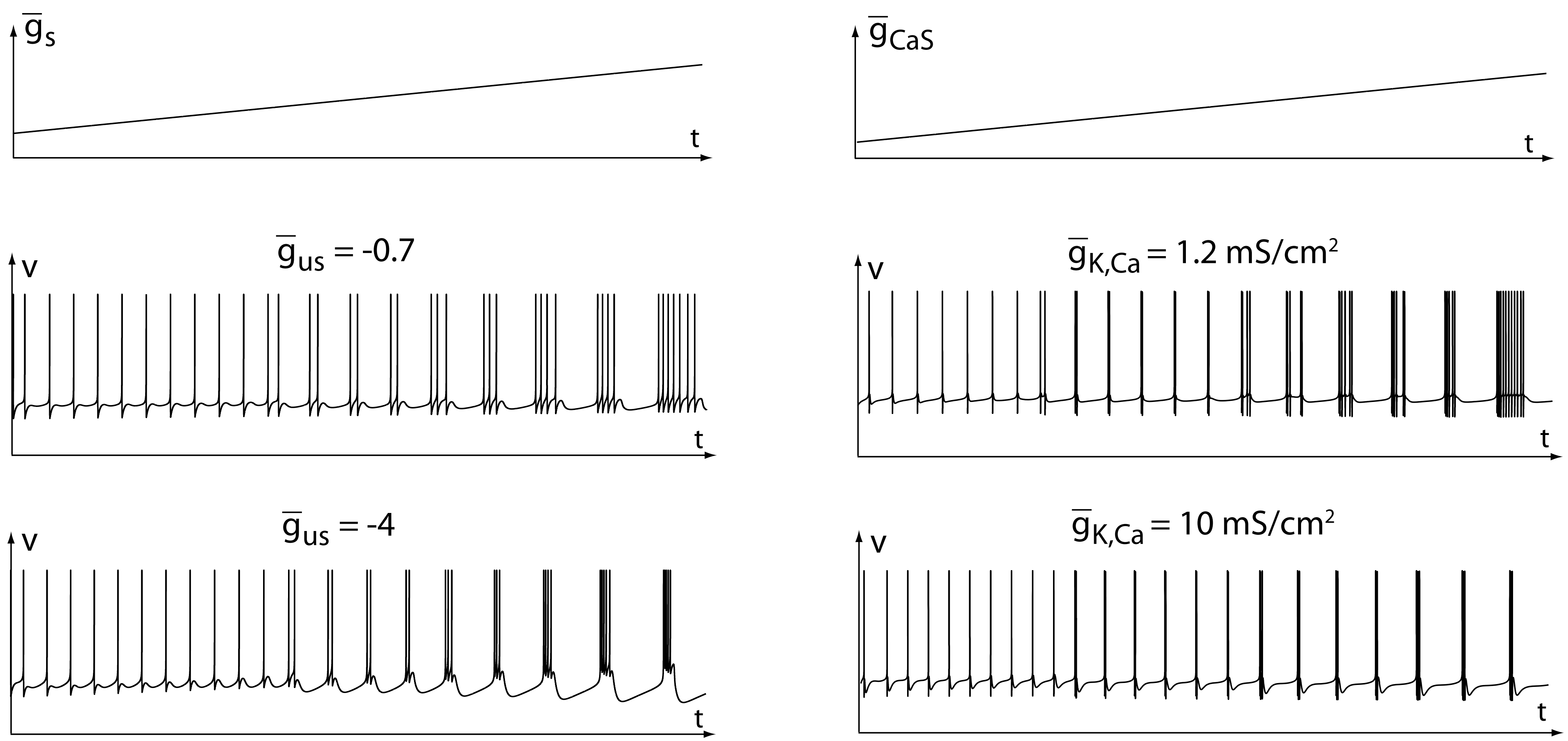
→ Bursting



(Franci et al., 2013)

A Switch from Restorative to Regenerative Excitability provides a Physiological Route to Bursting

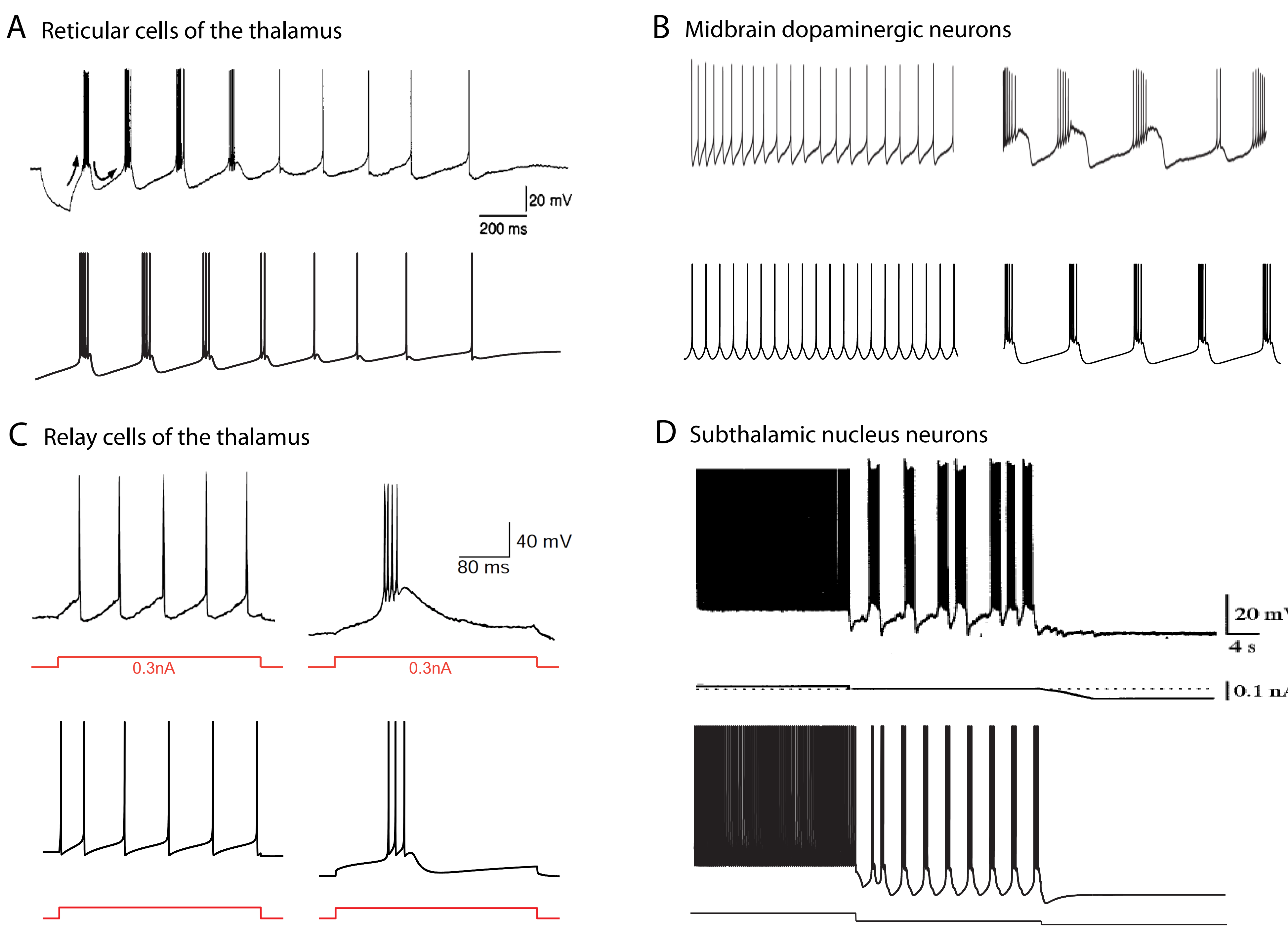
Planar model | **Conductance-based model**



(Franci et al., submitted)

A Switch from Restorative to Regenerative Excitability provides a Physiological Route to Bursting

- Some physiological examples (top: experimental trace, bottom: reduced model):



(Franci et al., submitted)

Summary

I. The switch from tonic to burst firing is a fundamental signaling mechanism in neurons

1. Sleep and arousal in thalamocortical neurons
2. Healthy vs Parkinson's disease state in STN neurons

II. Reduced modeling and bifurcation theory provides new insights on the mechanisms underlying this switch

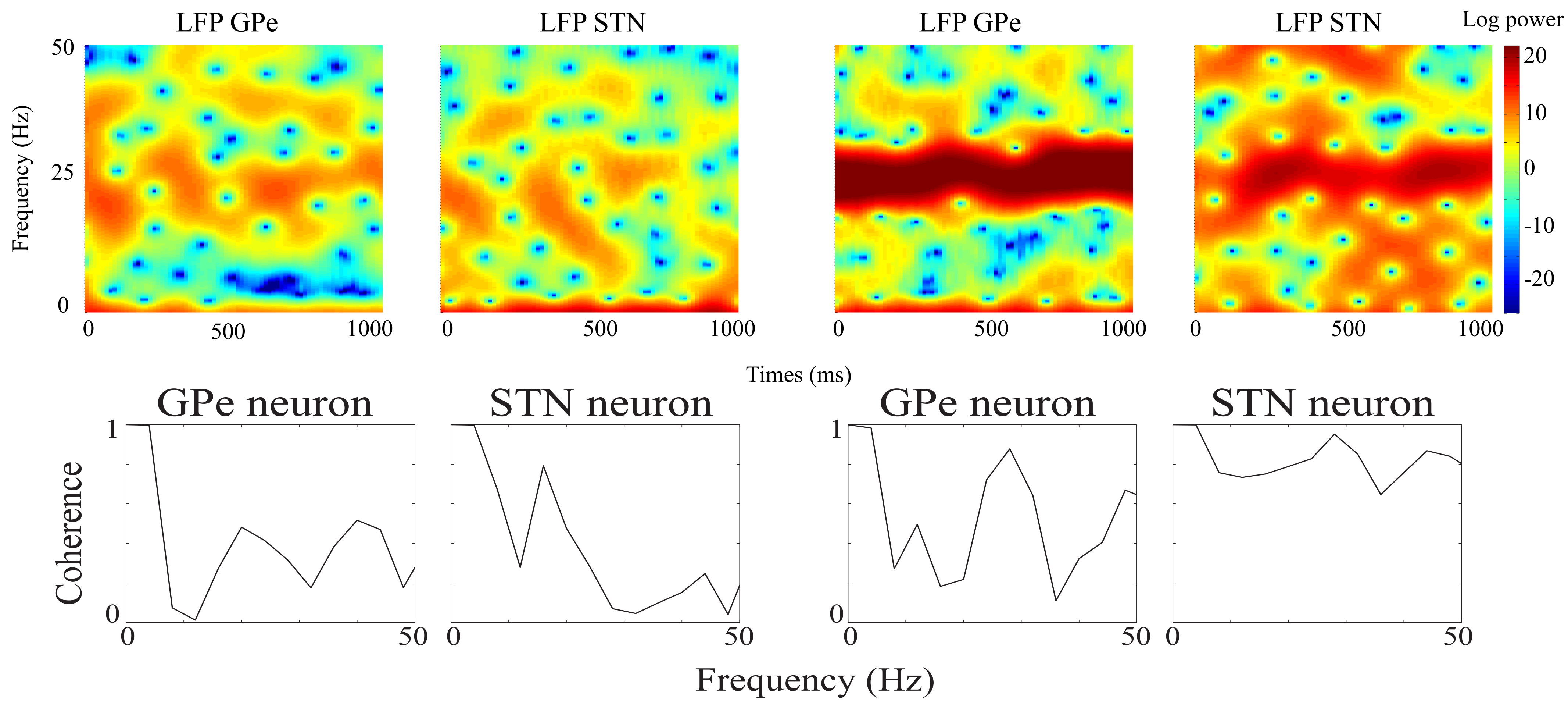
1. The organizing center of neuronal excitability is a transcritical bifurcation
2. Physiologically, the bifurcation corresponds to a balance between restorative and regenerative channels

III. A physiological route to bursting

1. The proposed reduced model is able to switch from tonic to burst firing by modulation of physiologically relevant parameters
2. The same transition is observed in high-dimensional conductace-based model via modulation of the balance between restorative and regenerative channels

Impact of Neuron Endogenous Rhythmicity at the Network Level?

- Back to example 2: Subthalamic nucleus (STN) neurons in control and Parkinson's disease patients



- See Julie Dethier's poster:
  "<u>Oscillations in the basal ganglia: illustration of a cellular effect at the network level</u>"

Acknowledgments

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