Spiking and firing rate resonance in single neurons: dynamic mechanisms of communication of subthreshold resonance to the spiking regime

Introduction to modeling and data analysis tools to capture resonance phenomena (2nd class)

Rodrigo F. O. Pena

New Jersey Institute of Technology and Rutgers University

15/10/2020

RUTGERS UNIVERSITY | NEWARK
Center for Molecular and Behavioral Neuroscience

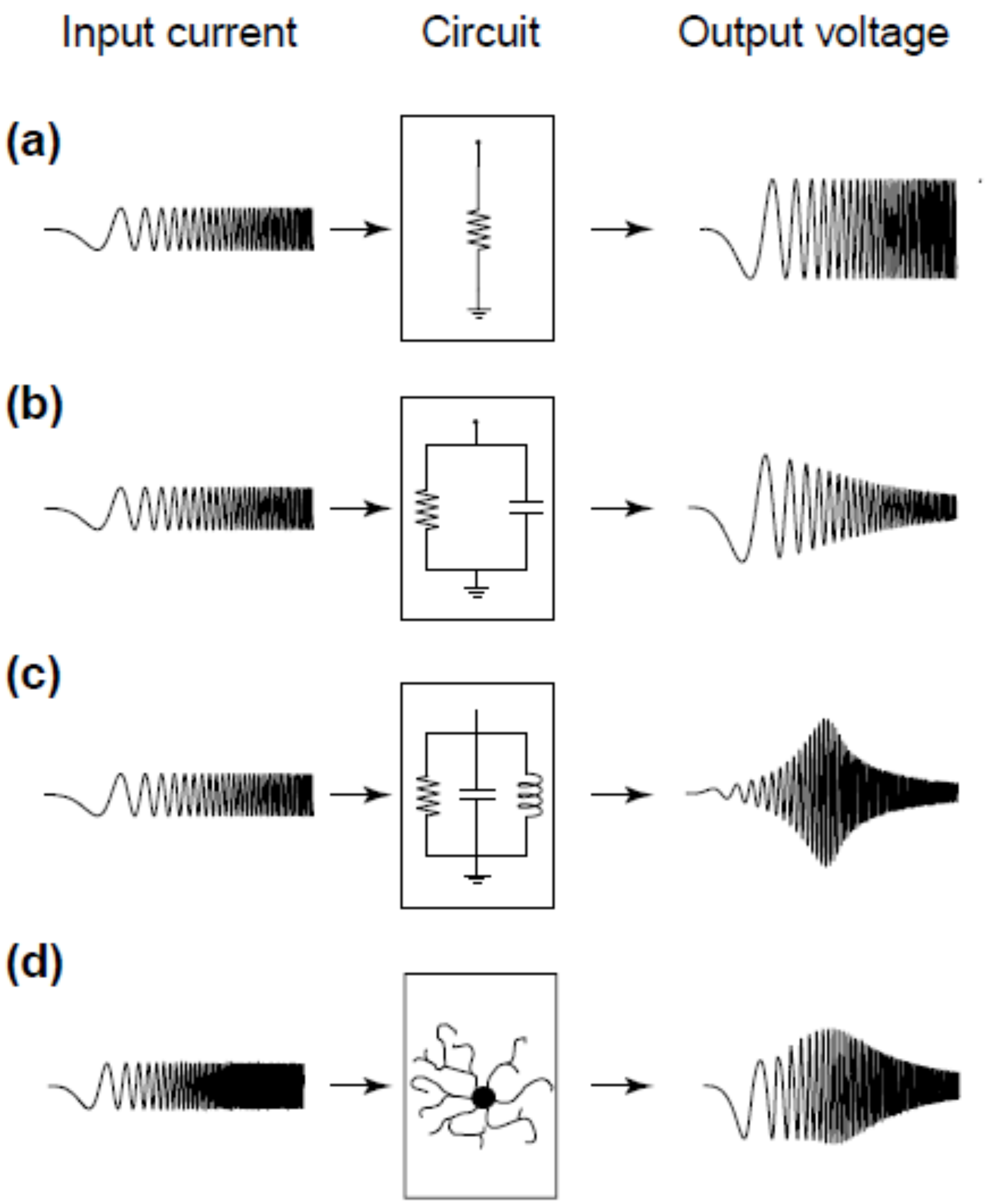
SBNeC Sociedade Brasileira de Neurociências e Comportamento

NSF DMS-1608077

NJIT New Jersey Institute of Technology

Resonance in electrical circuits

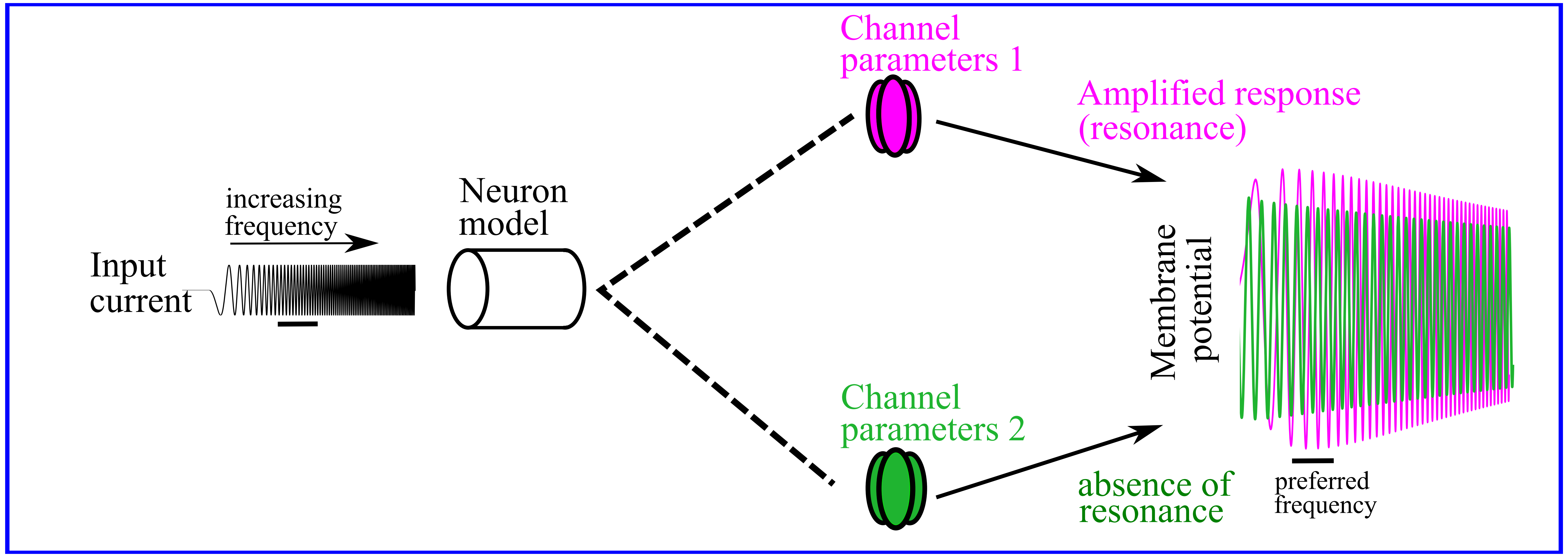
Chirp input

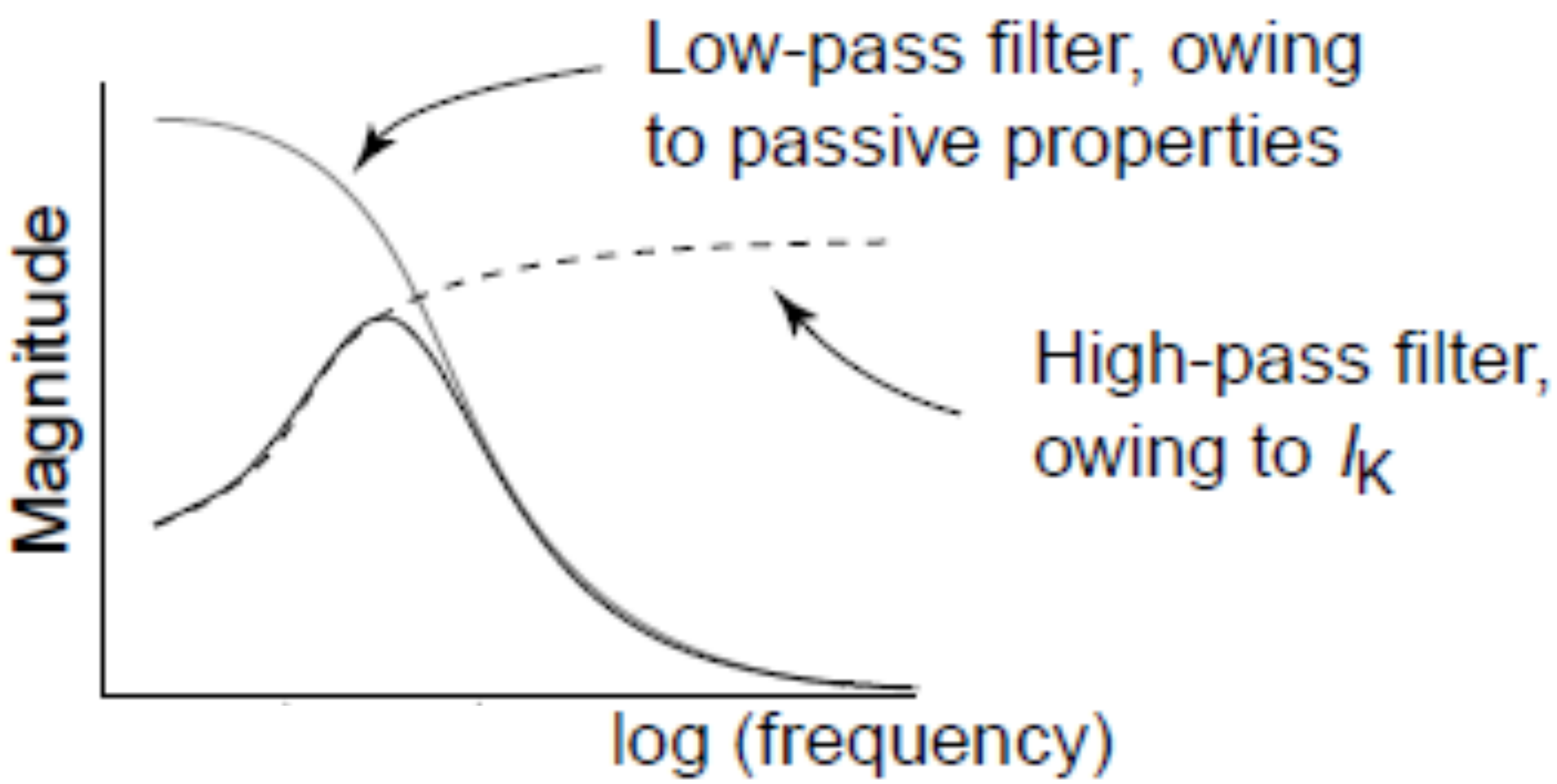


Hutcheon & Yarom (2000)

Trends Neurosci. 23:216-22

What determines sub threshold resonance in neurons?





Hutcheon & Yarom,

Trends Neurosci (2000) 23:216-22

pena@njit.edu

What determines sub threshold resonance in neurons?

- interplay of positive and negative feedback effects

slow restorative ionic currents (resonant)

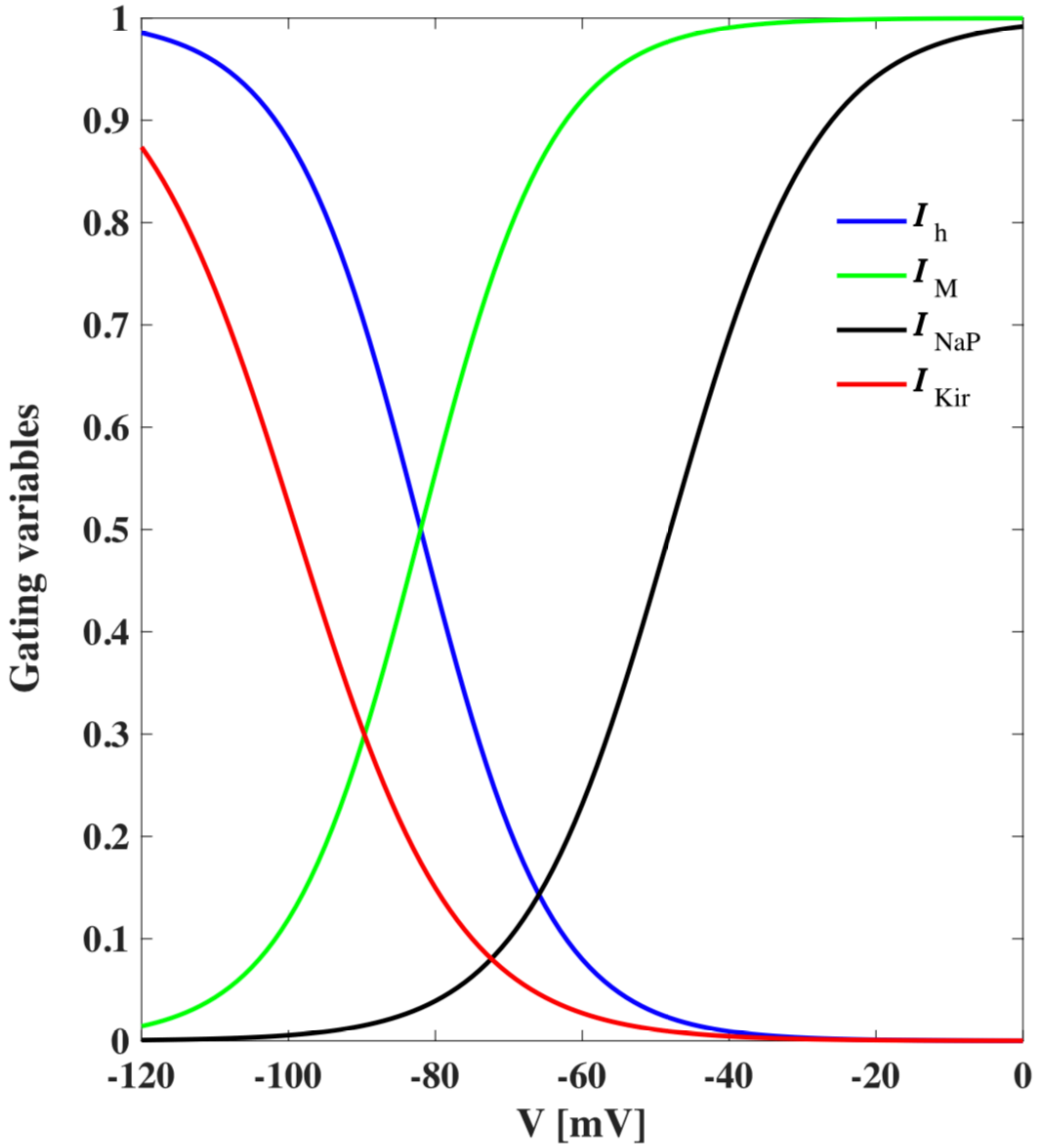
I_h (hyperpolarization-activated mixed-cation)

I_M (M-type slow-potassium)

regenerative currents (amplifying)

I_{NaP} (persistent sodium)

I_{Kir} (inward-rectifying potassium)



Pena et al., *Chaos* **29**, 103135 (2019)

The impedance profile

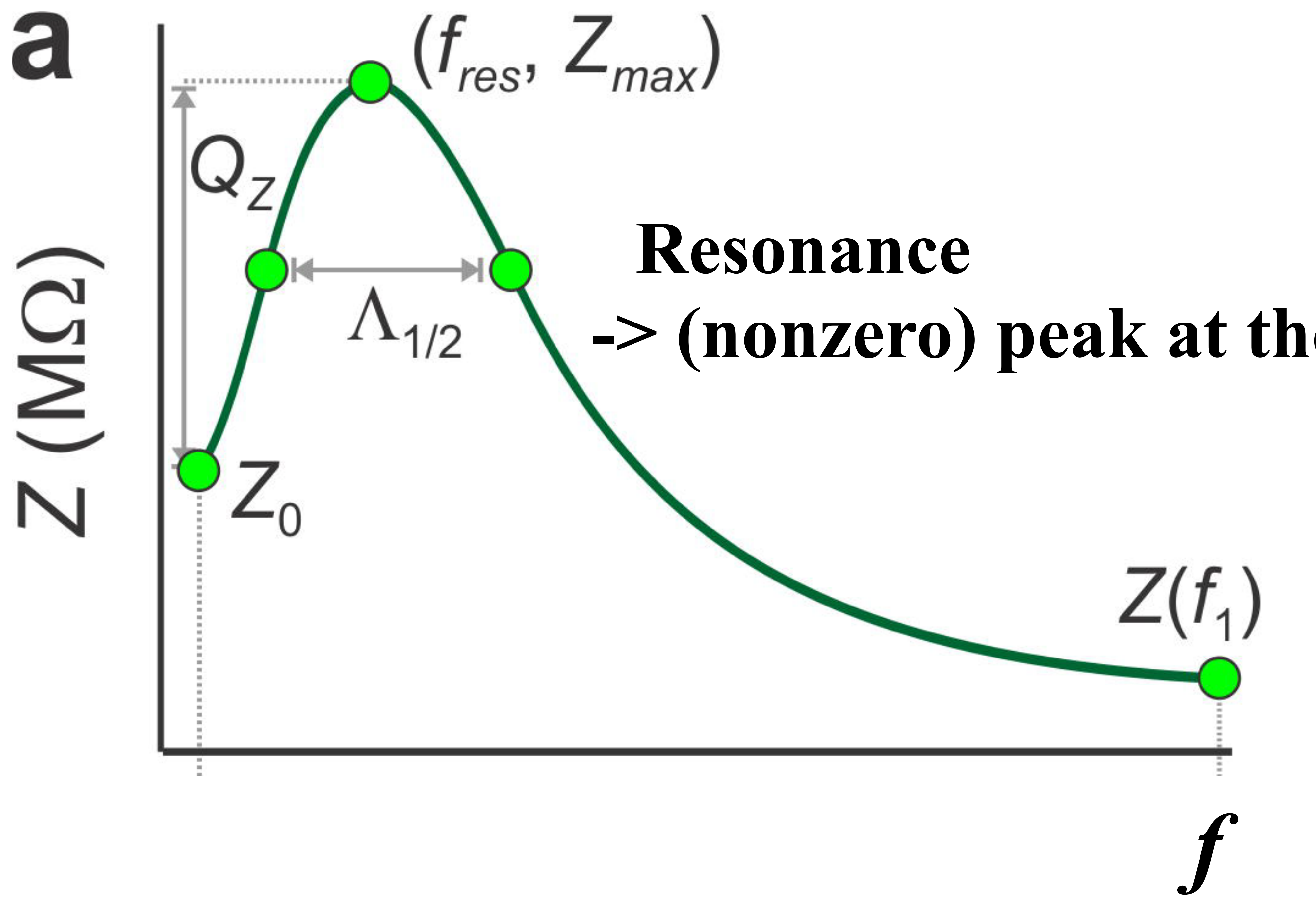
The impedance

$$Z(f) = \frac{FFT[V_{out}(t)]}{FFT[I_{in}(t)]}$$

For a **nonlinear system**, or **linear systems with non-sinusoidal inputs**,

$$Z(f) = \frac{V_{max}(f) - V_{min}(f)}{2A_{in}}$$

Assumption: output is periodic and has the same frequency as the input!



Resonance
-> (nonzero) peak at the impedance

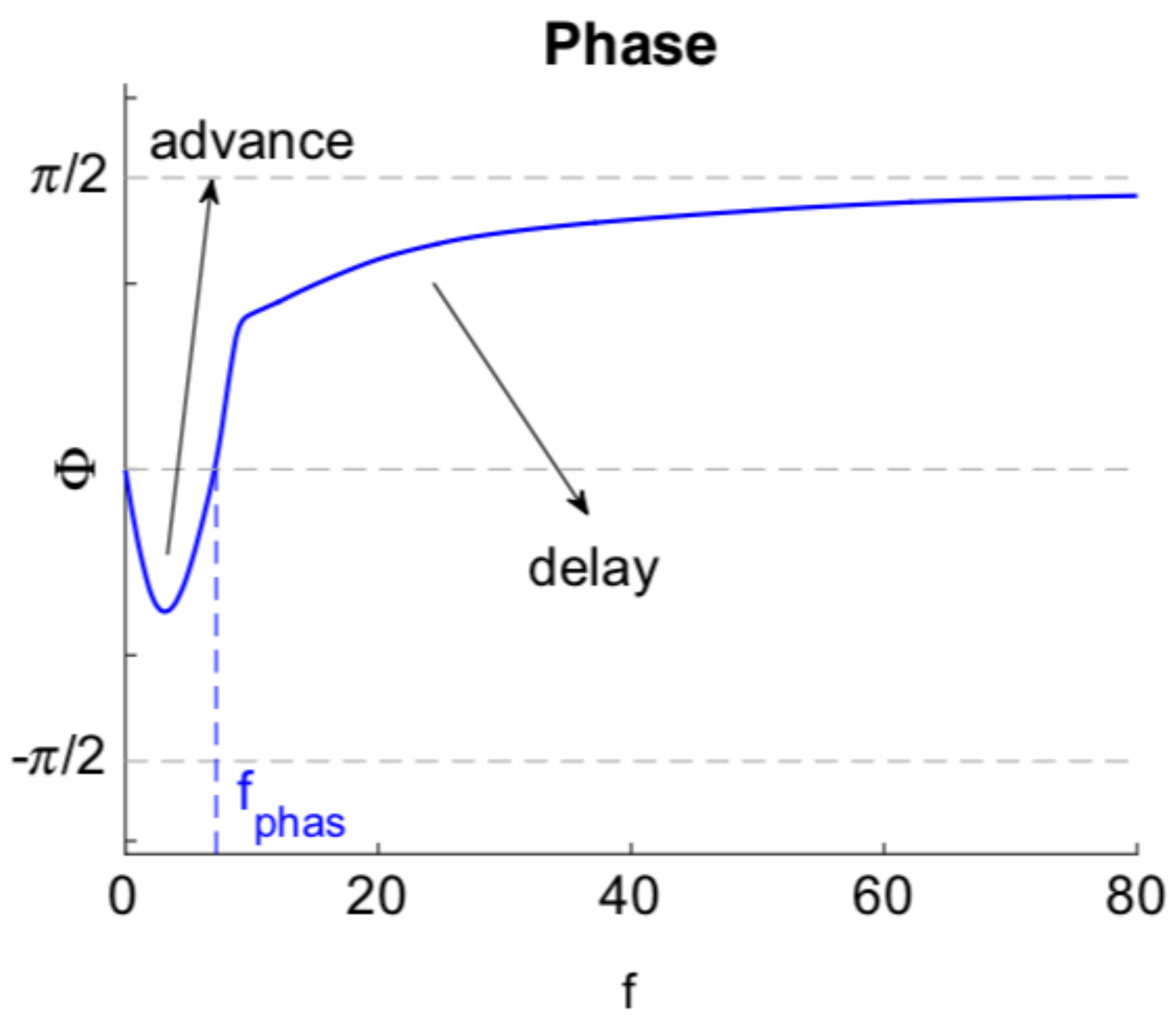
Fox et al., *PLoS Comput Biol* (2017) 13: e1005565.

The phase-shift profile

The phase $\phi(f)$

$$\phi(f) = -\tan^{-1}\left(\frac{Z_{imag}(f)}{Z_{real}(f)}\right)$$

$$\phi(f) = \frac{t_{peak,out}(f) - t_{peak,in}(f)}{T_{per}(f)}$$

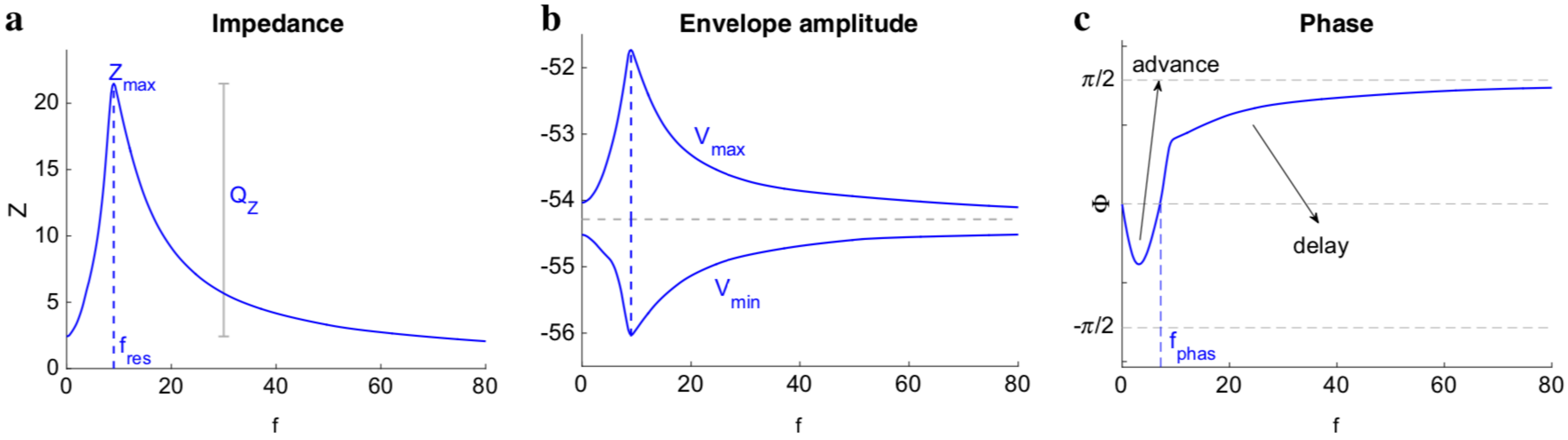


Rotstein, *J Comput Neurosci* (2017) 43:243–271

Phasonance:

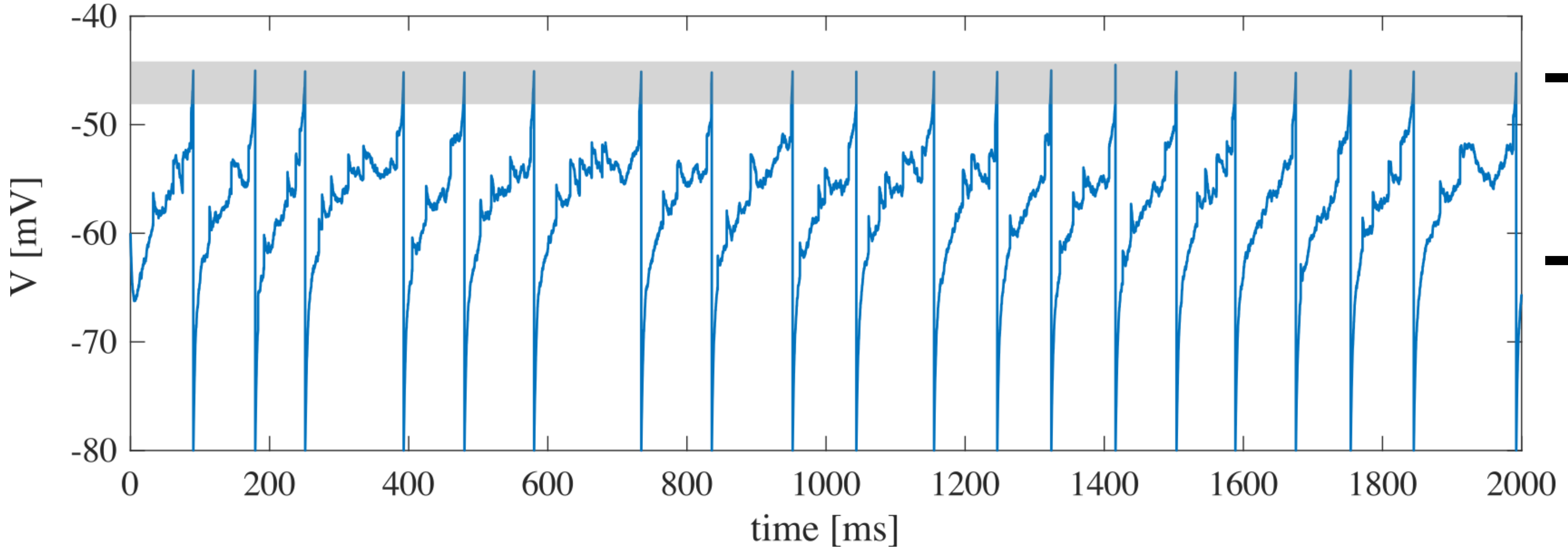
-> phase profile vanishes at a nonzero input frequency!

Basic resonance characteristics — subthreshold behavior



Rotstein, *J Comput Neurosci* (2017) 43:243–271

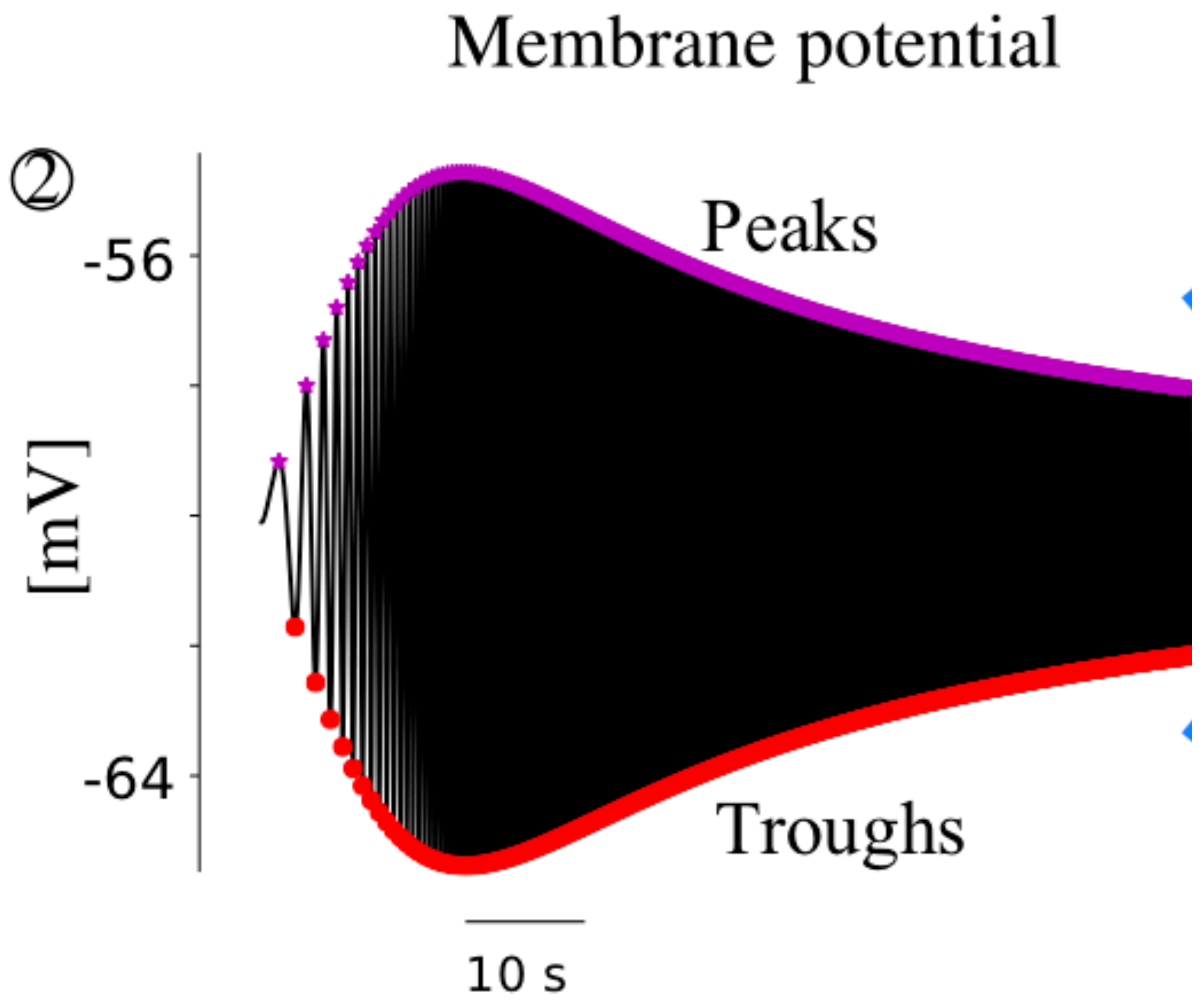
How to connect subthreshold to spiking behavior



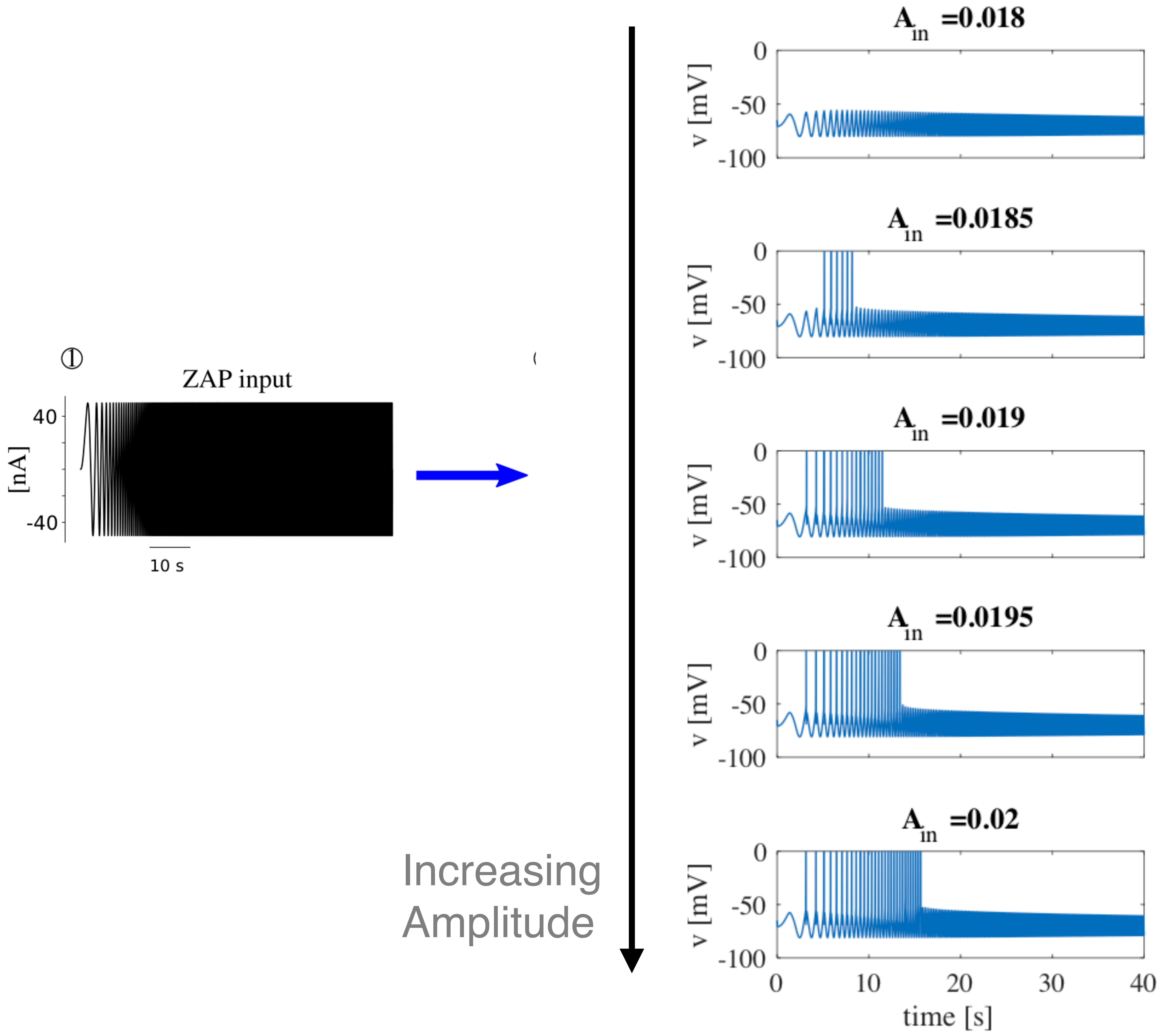
Supratreshold

Subthreshold

?



pena@njit.edu



Impedance profile when spikes are present?

Is subthreshold resonance communicated to the suprathreshold regime?

Important questions for theta (4-11 Hz) oscillations!

Mechanism that may contribute to theta generation: the resonant properties of neurons.

Outline

- Resonance for **suprathreshold** (spiking) behavior vs. **subthreshold** regime (**upper** envelope);

- Resonance for **suprathreshold** (spiking) behavior vs. subthreshold regime (**bottom** envelope);

- **Subthreshold** resonance when a neuron is **driven by spikes**.

Outline

- Resonance for **suprathreshold** (spiking) behavior vs. **subthreshold** regime (**upper** envelope);

    - **Single neuron and relation to dynamics** [Rotstein, *J Comput Neurosci* (2017) 43:243–271]
    - **Population** [Richardson et al., *J Neurophysiol* (2003) 89:2538–2554]

- Resonance for **suprathreshold** (spiking) behavior vs. subthreshold regime (**bottom** envelope);

- **Subthreshold** resonance when a neuron is **driven by spikes**.

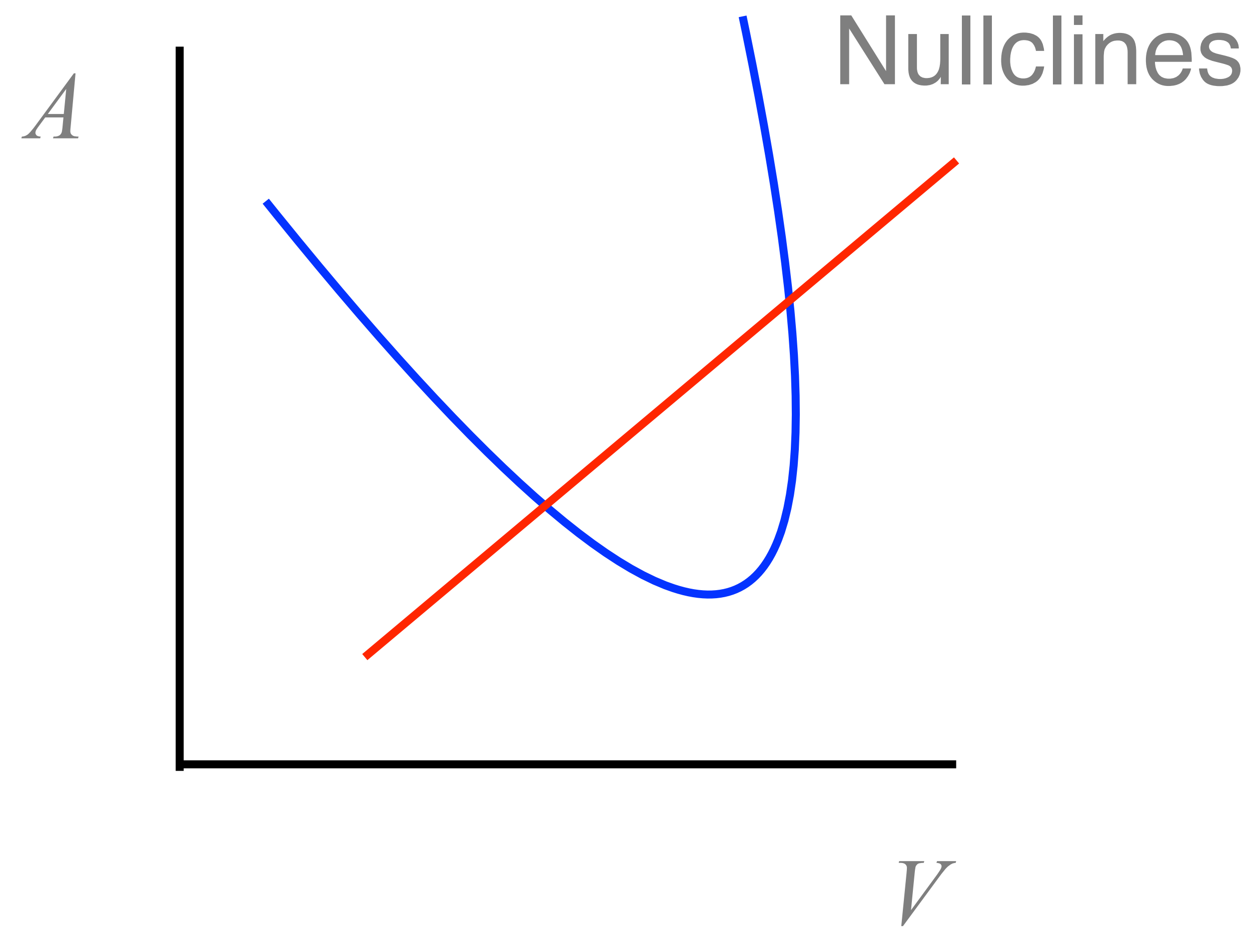
Dynamics (briefly!)

$$C_\mathrm{m}\frac{dV(t)}{dt} = -\sum_i I_i(V,t) - I_\mathrm{leak}(V) + I_\mathrm{ZAP}(t) + I_\mathrm{DC} \qquad = 0$$

$$I_i = \bar{g}_i A_i(V,t)\left(V - E_i\right)$$

$$\frac{dA_i(V,t)}{dt} = \frac{A_i^\infty(V) - A_i(V,t)}{\tau_i} \qquad = 0$$

$$A_i^\infty(V) = \frac{1}{1+\exp\left(\frac{s\left(V-V_{1/2}\right)}{k}\right)}$$



Two very similar models

I_{NaP}+I_{h} model

$$C\frac{dV}{dt} = -I_L - I_h - I_{Nap} + I_{app} + I_{in}(t)$$

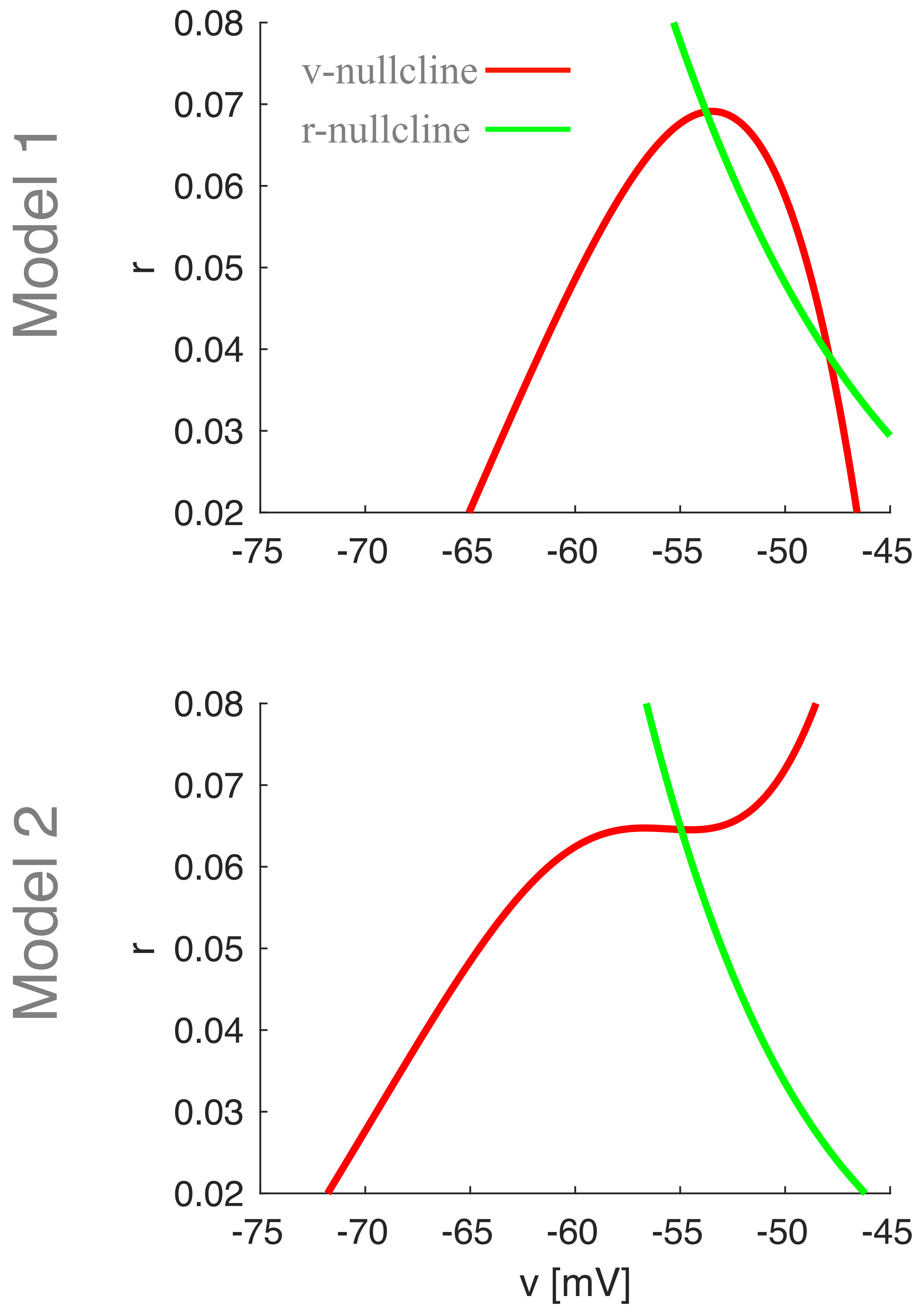
$$I_{\text{L}} = G_{\text{L}}\left(V - E_{\text{L}}\right)$$

$$I_{\text{h}} = G_{\text{h}} r\left(V - E_{\text{h}}\right)$$

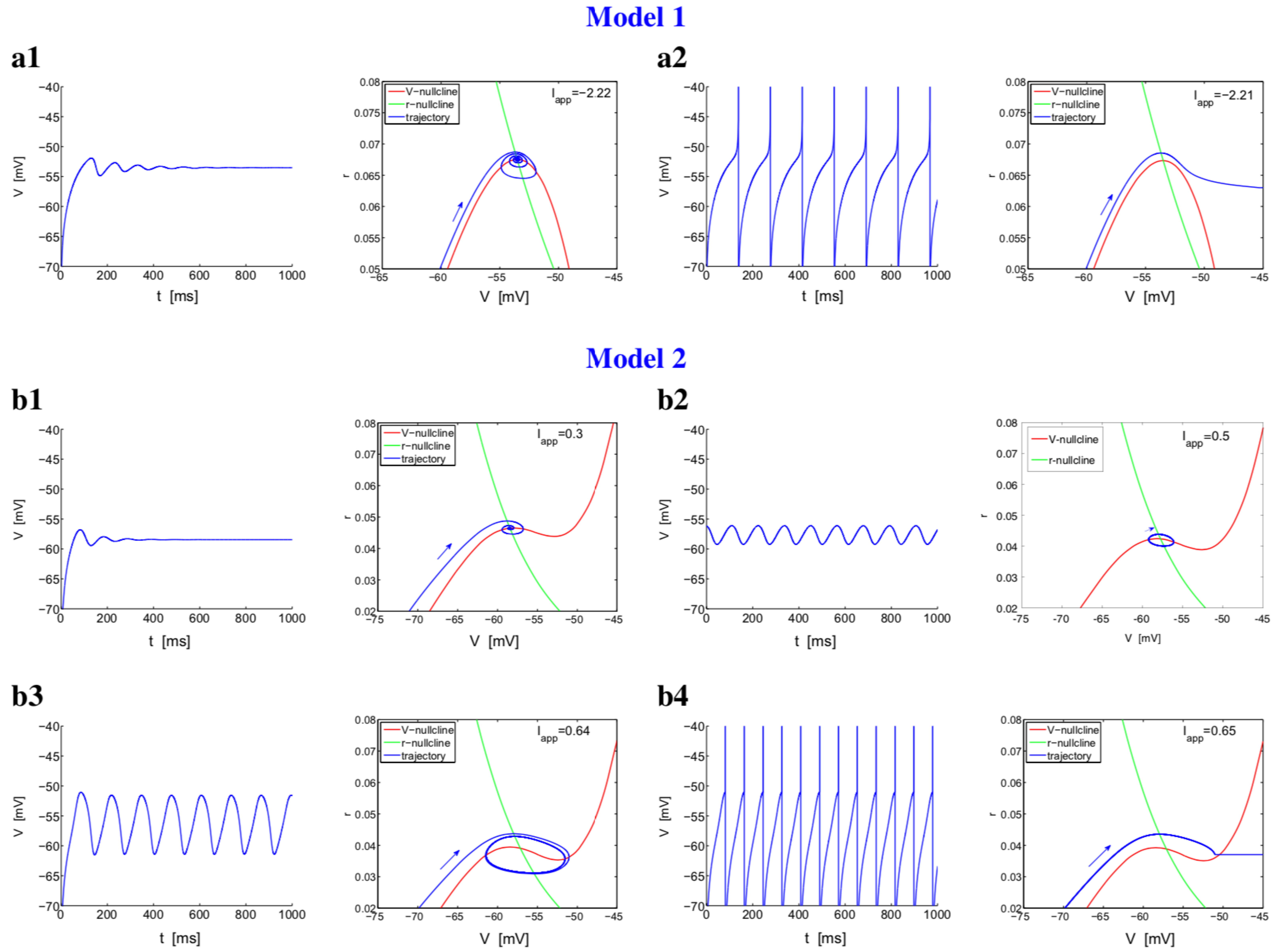
$$I_{\text{NaP}} = G_p p_\infty(V)\left(V - E_{\text{Na}}\right)$$

$x\ (= r, p)$

$$\frac{dx}{dt} = \frac{x_\infty(V) - x}{\tau_x(V)}$$



From subthreshold to spikes



Differences:

- Geometry: parabolic- and cubic-like
- Generation of STOs in the parabolic- and cubic-like
- Transition from STOs to spikes

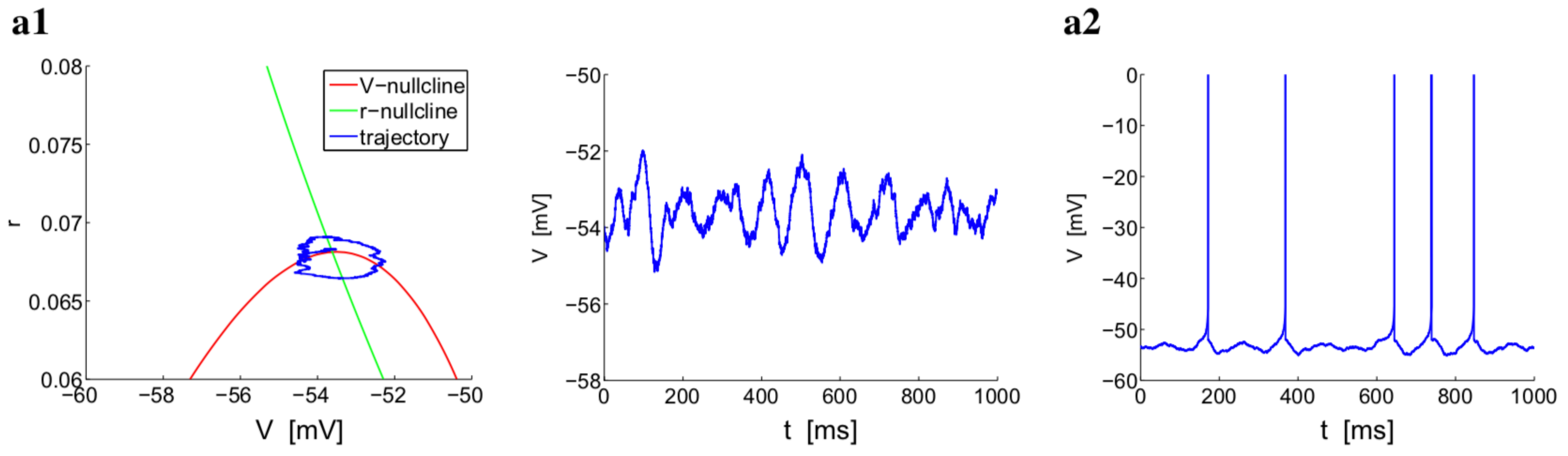
→ **model 1** generates damped STOs but not persistent (unless noise is present).

→ **model 2** generates persistent STOs
No mechanism for the onset of spikes.

pena@njit.edu

From subthreshold to spikes

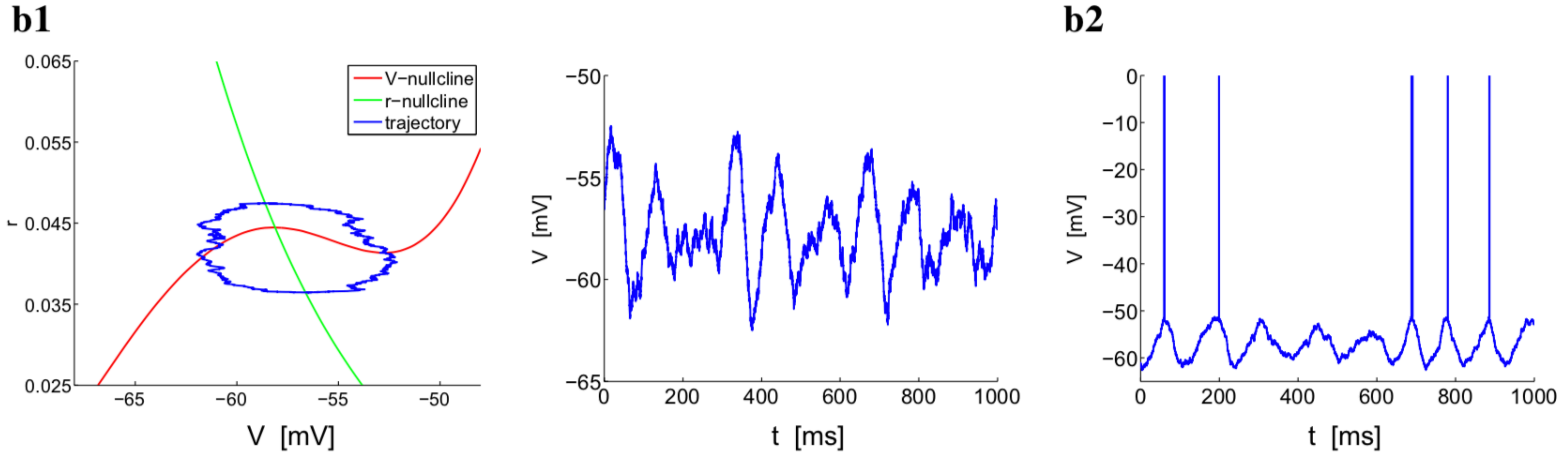
Model 1



Differences:

- Geometry: parabolic- and cubic-like
- Generation of STOs in the parabolic- and cubic-like
- Transition from STOs to spikes

Model 2



→ **model 1** generates damped STOs but not persistent (unless noise is present).

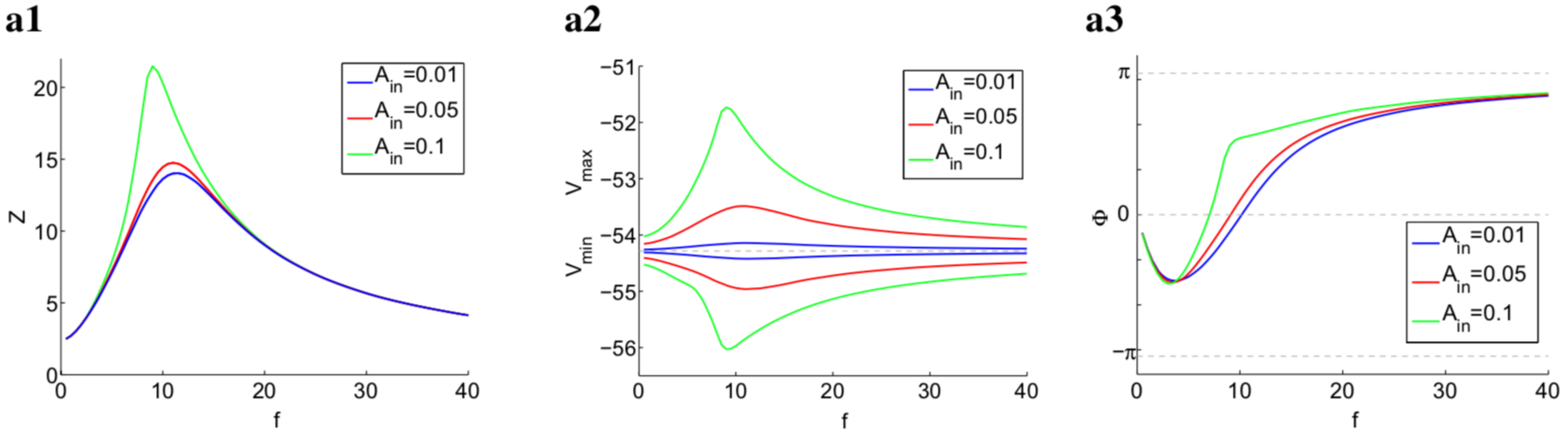
→ **model 2** generates persistent STOs

No mechanism for the onset of spikes.

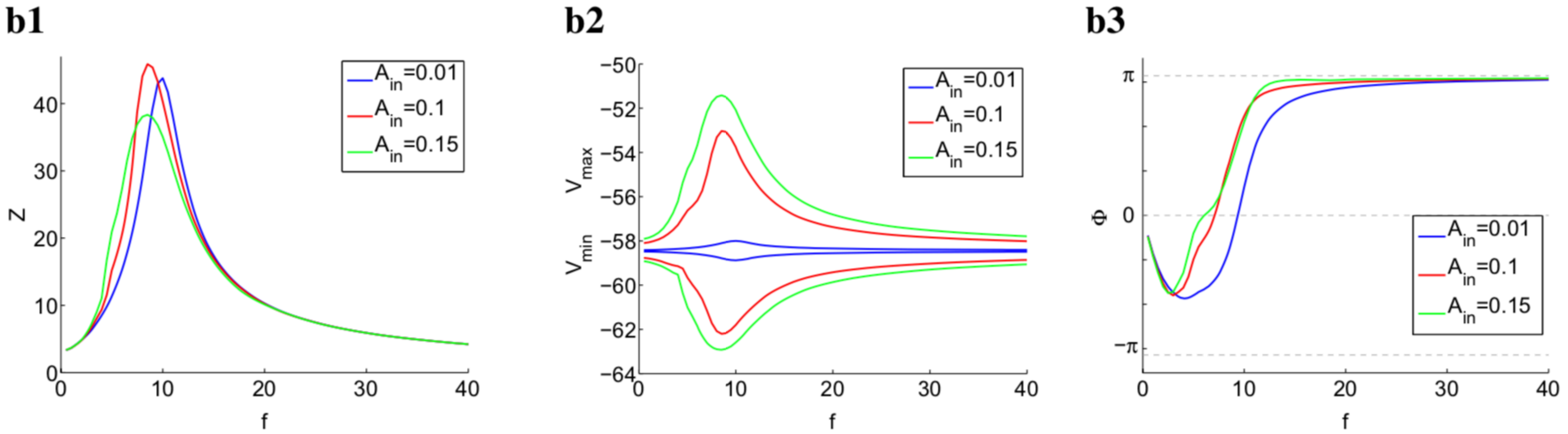
Rotstein, *J Comput Neurosci* (2017) 43:243–271

From subthreshold to spikes

Model 1 (parabolic)



Model 2 (cubic)



Both models exhibit **resonance** and **phasonance** in theta (4–12 Hz).

pena@njit.edu

How to access suprathreshold resonance

- spike-frequency (f_{spk}) response to oscillatory input currents;
- spike-phase (ϕ_{spk}) response to oscillatory input currents.

pena@njit.edu

- spike-frequency (f_{spk}) response to oscillatory input currents;

Evoked spiking resonance

spikes generated for **intermediate** (resonant) input **frequency** band $\Delta f_{res,ev}$

Output spiking resonance

output frequency belongs to an intermediate (resonant) frequency band $\Delta f_{res,out}$,
regardless of the input frequency that generated the response

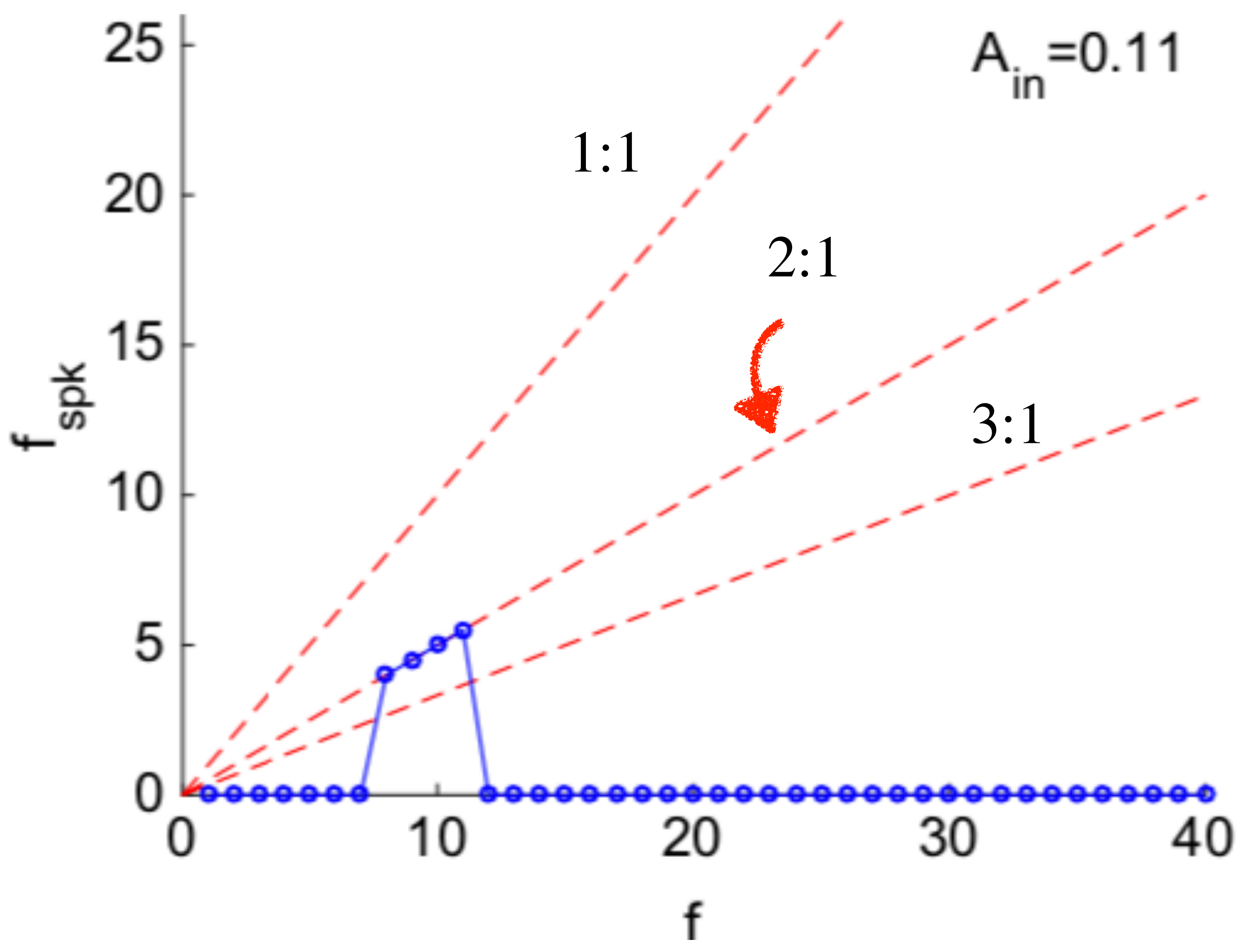
- spike-phase (ϕ_{spk}) response to oscillatory input currents.

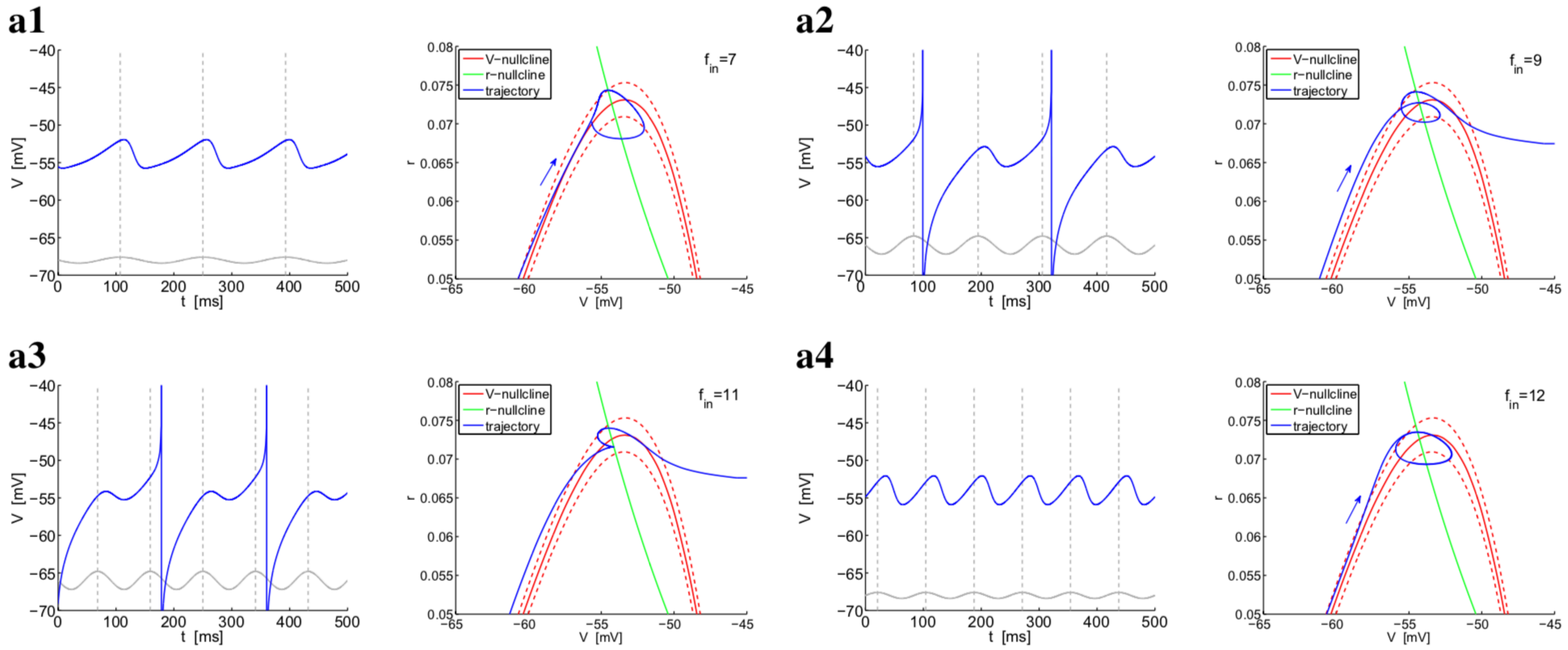
Spiking phasonance

Zero spiking phase-shift (spiking phase) ϕ_{spk} between the **output spike** and the **input peak**

Model 1 - low amplitude regime

- Subthreshold resonance is communicated to the suprathreshold regime to produce both **evoked** and **output** spiking resonance



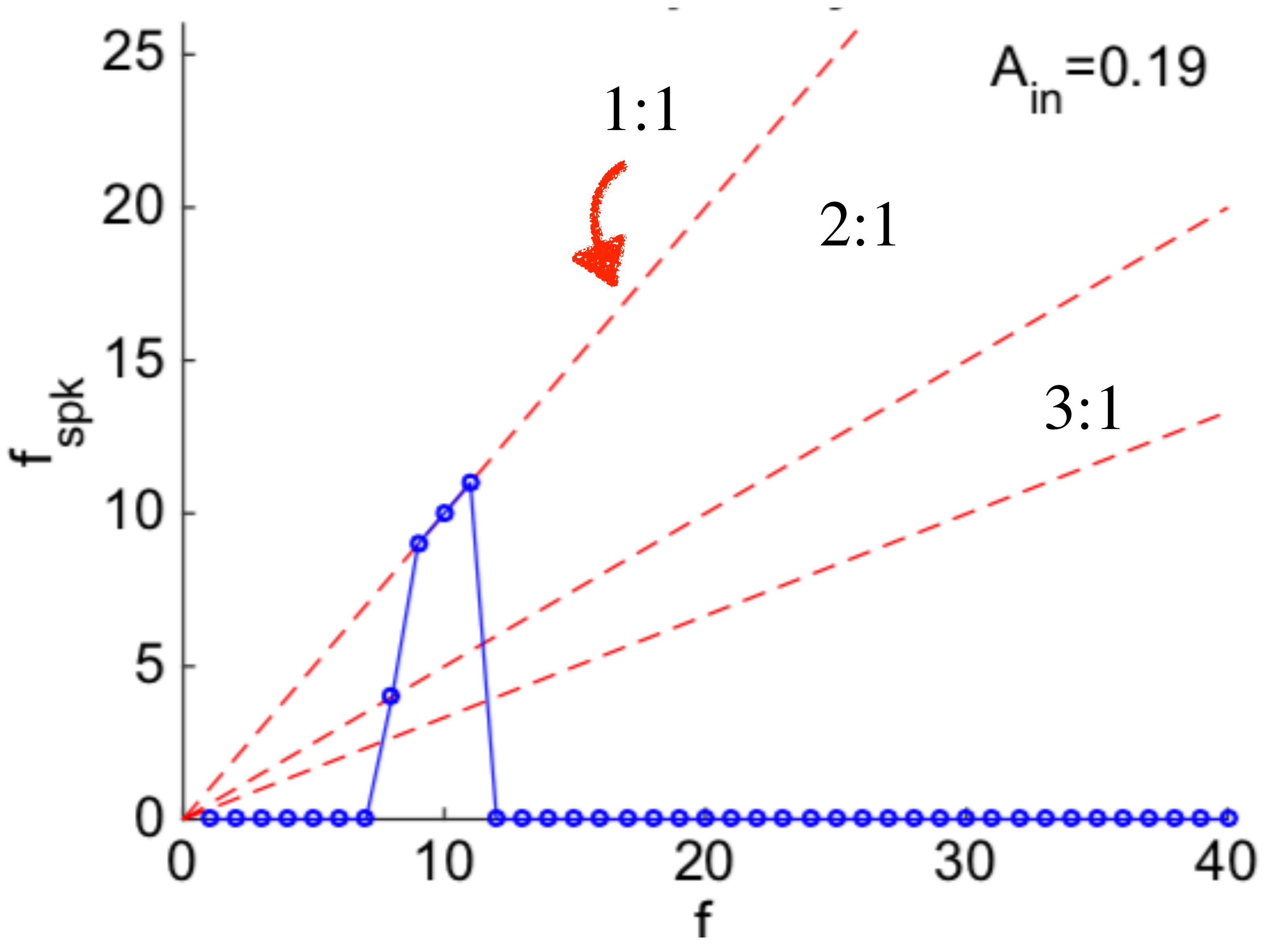


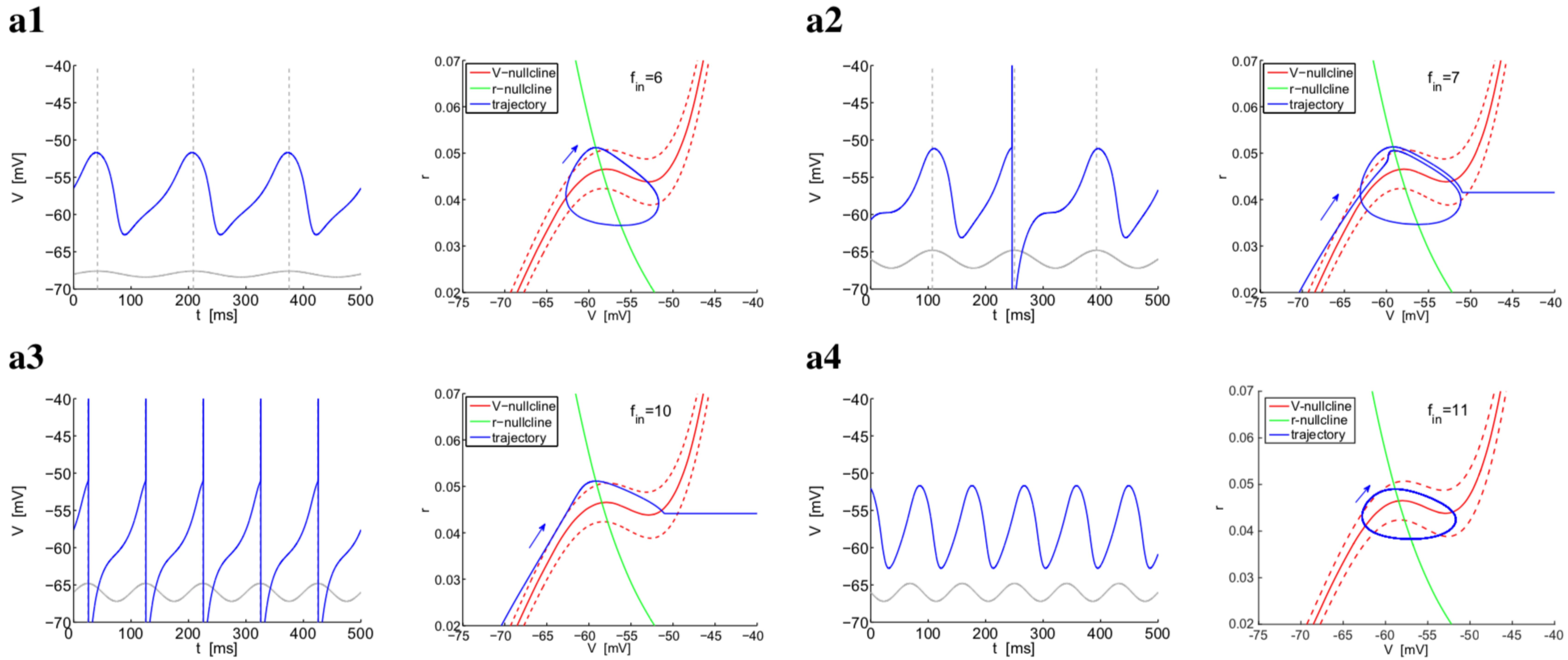
Rotstein, *J Comput Neurosci* (2017) 43:243–271

pena@njit.edu

Model 2 - low amplitude regime

- Subthreshold resonance is **also** communicated to the suprathreshold regime to produce both **evoked** and **output** spiking resonance





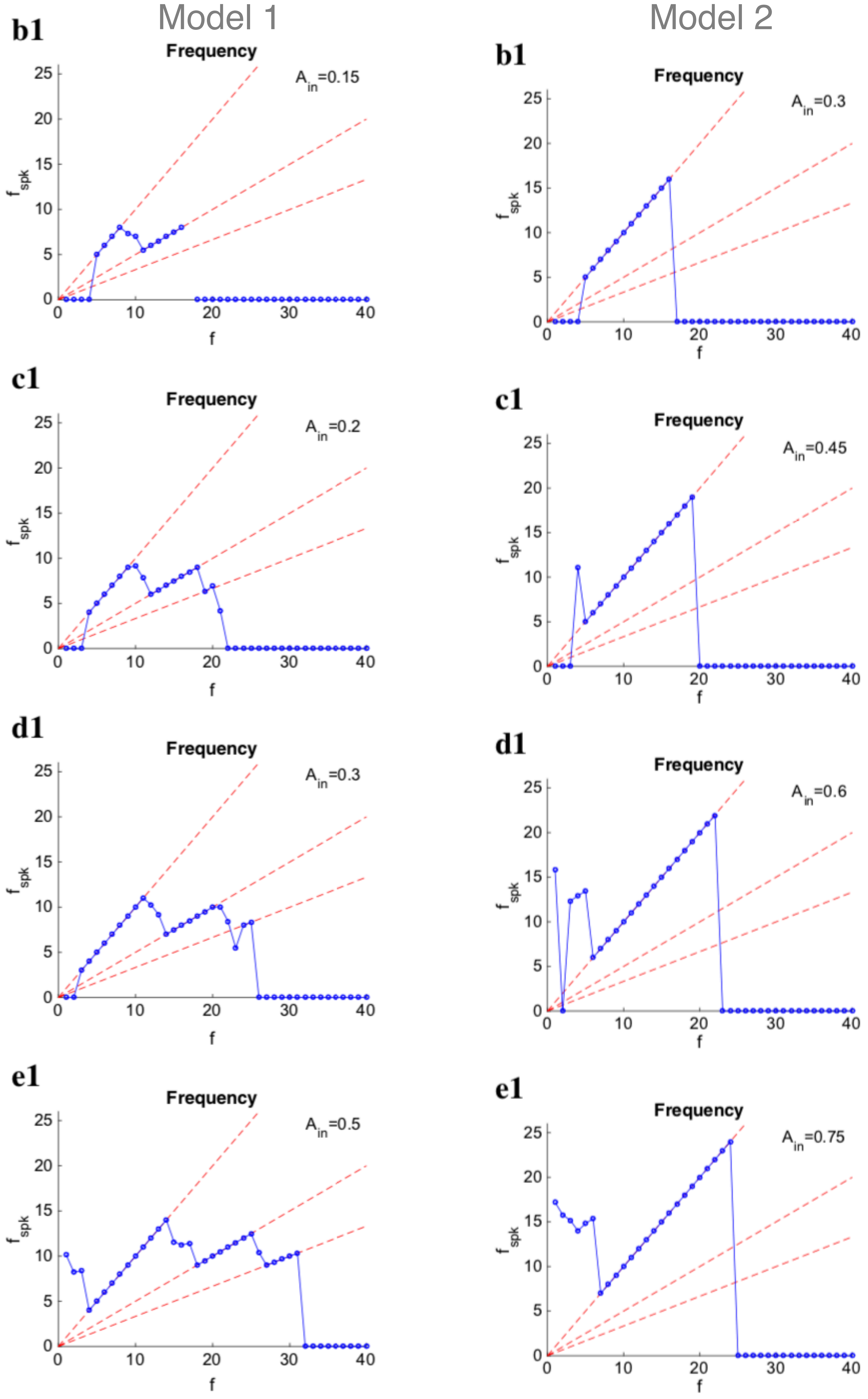
Rotstein, *J Comput Neurosci* (2017) 43:243–271

Evoked theta spiking resonance vanishes for larger amplitudes
-> low-pass filters

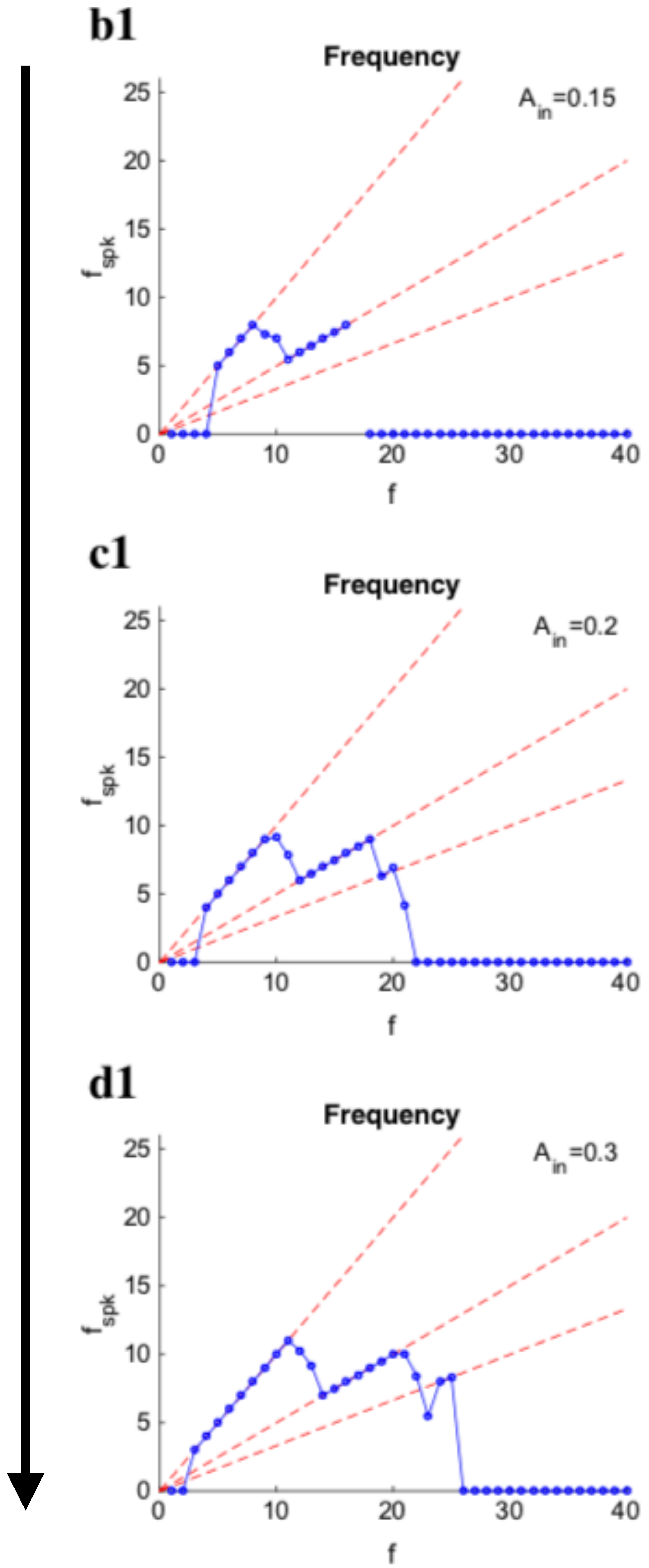
- **evoked spiking** resonance for low amplitude due to **subthreshold upper envelope**

- evoked spiking **low-pass filter** for **higher amplitudes**

Increasing Amplitude

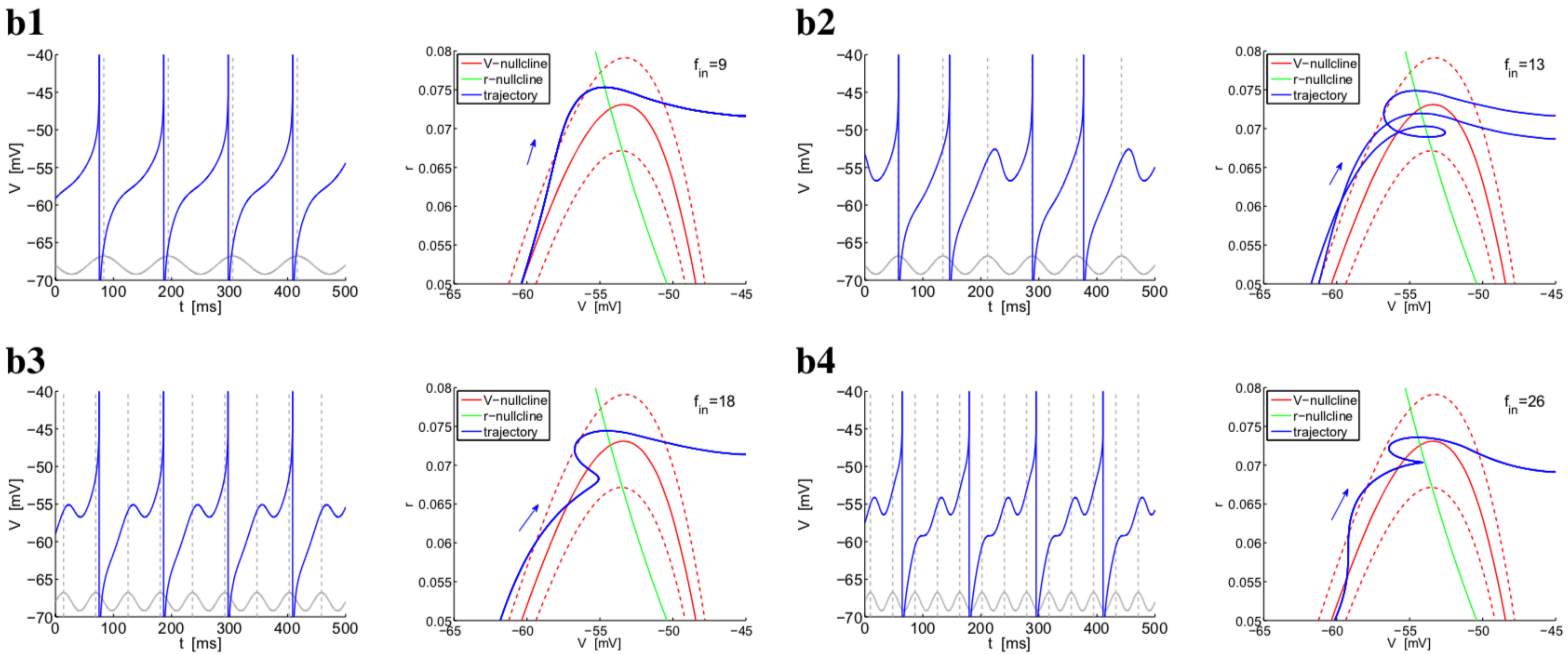


Model 1 - intermediate amplitude regime



Increasing Amplitude

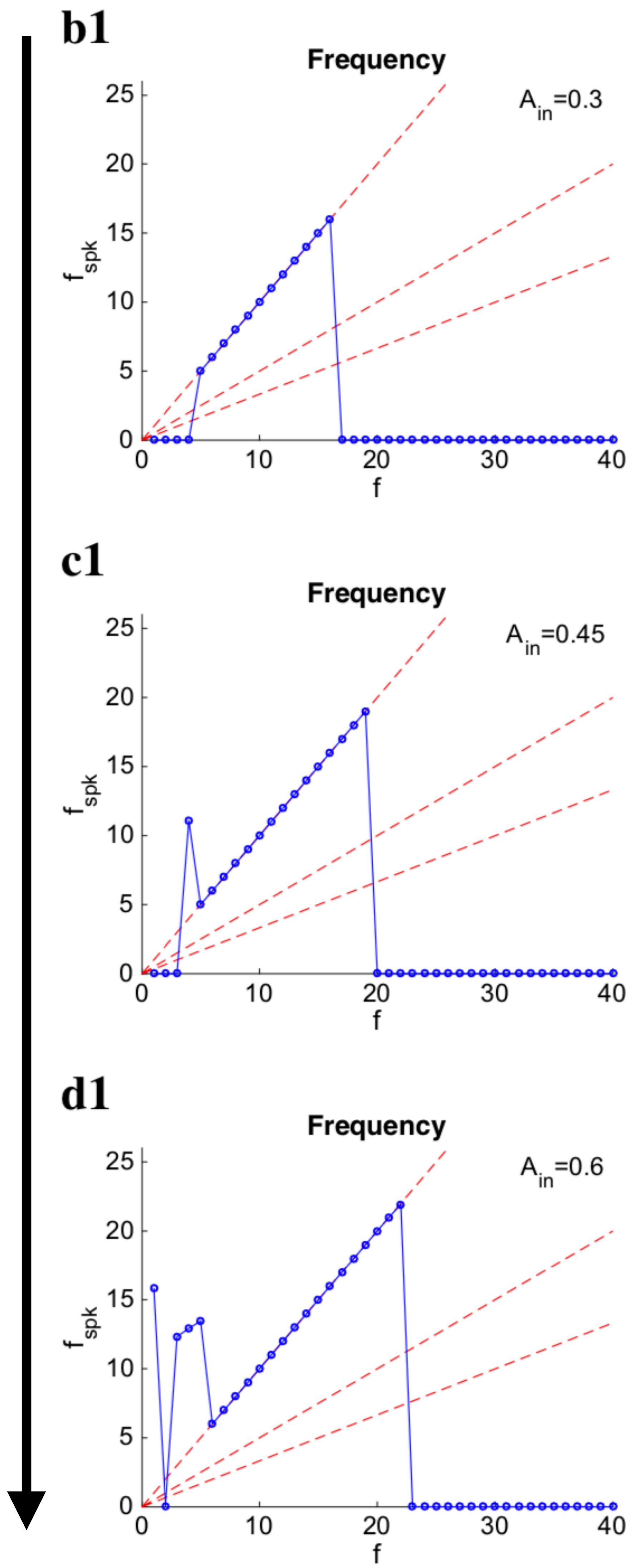
- theta output resonance for intermediate values of Ain



- cycle skipping mechanisms allows patterns 2:1 and 3:1 in addition to the 1:1

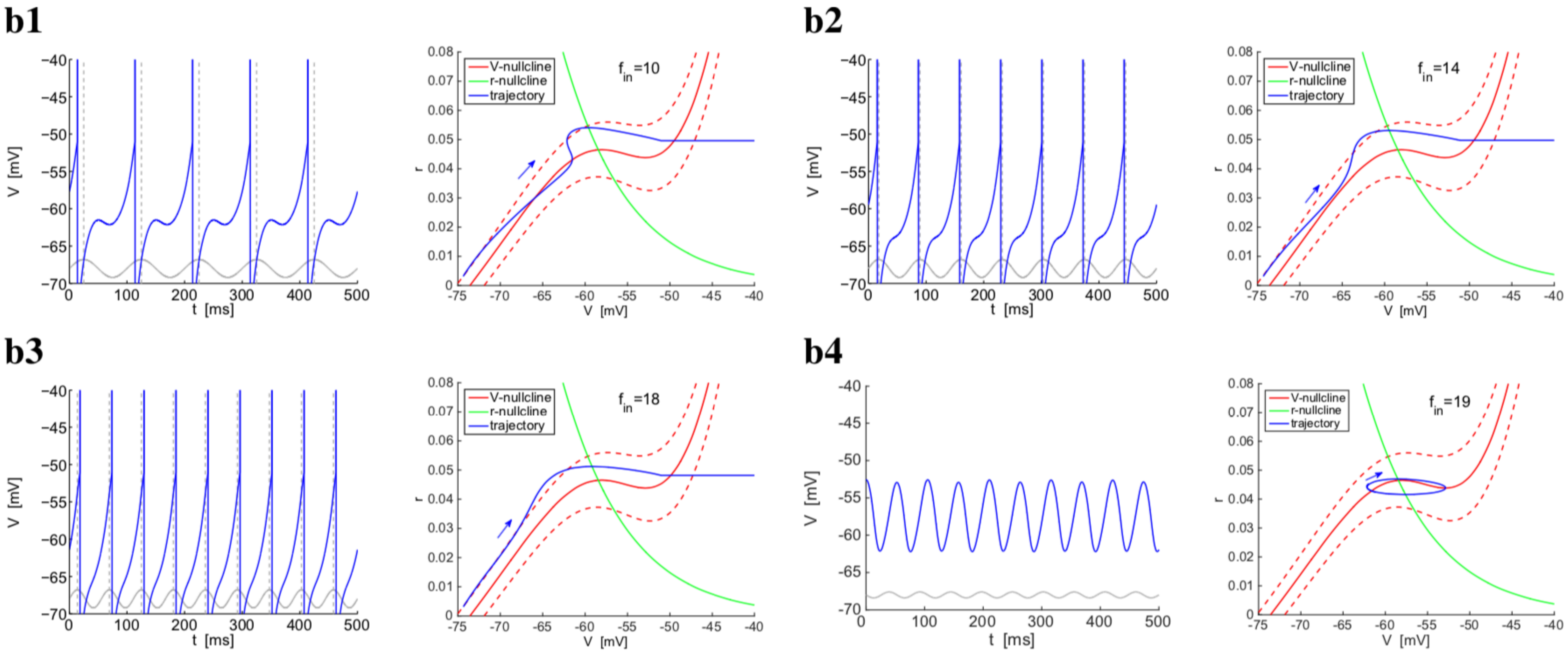
pena@njit.edu

Model 2 - intermediate amplitude regime



Increasing Amplitude

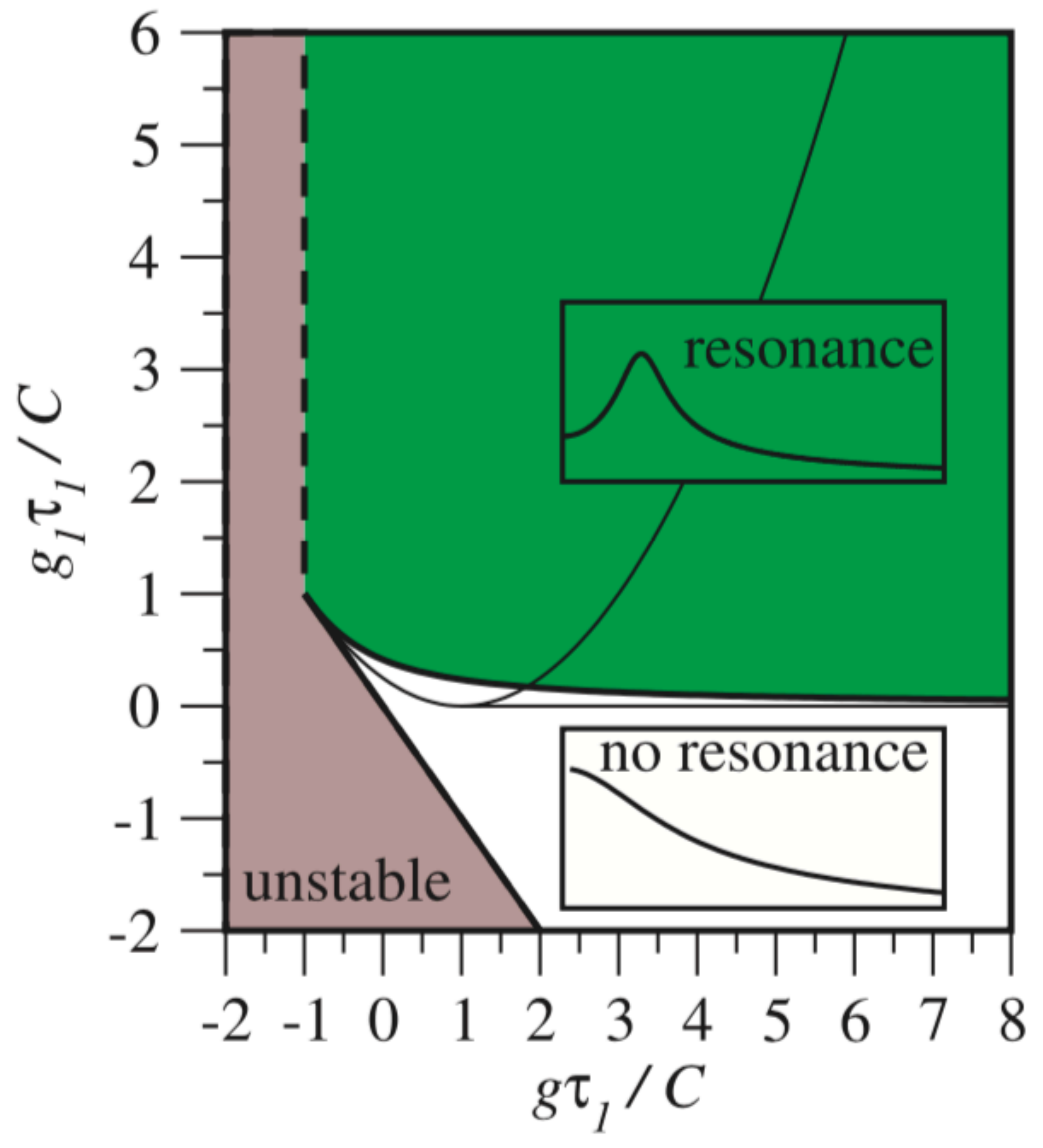
- Broad-band output response for intermediate amplitudes

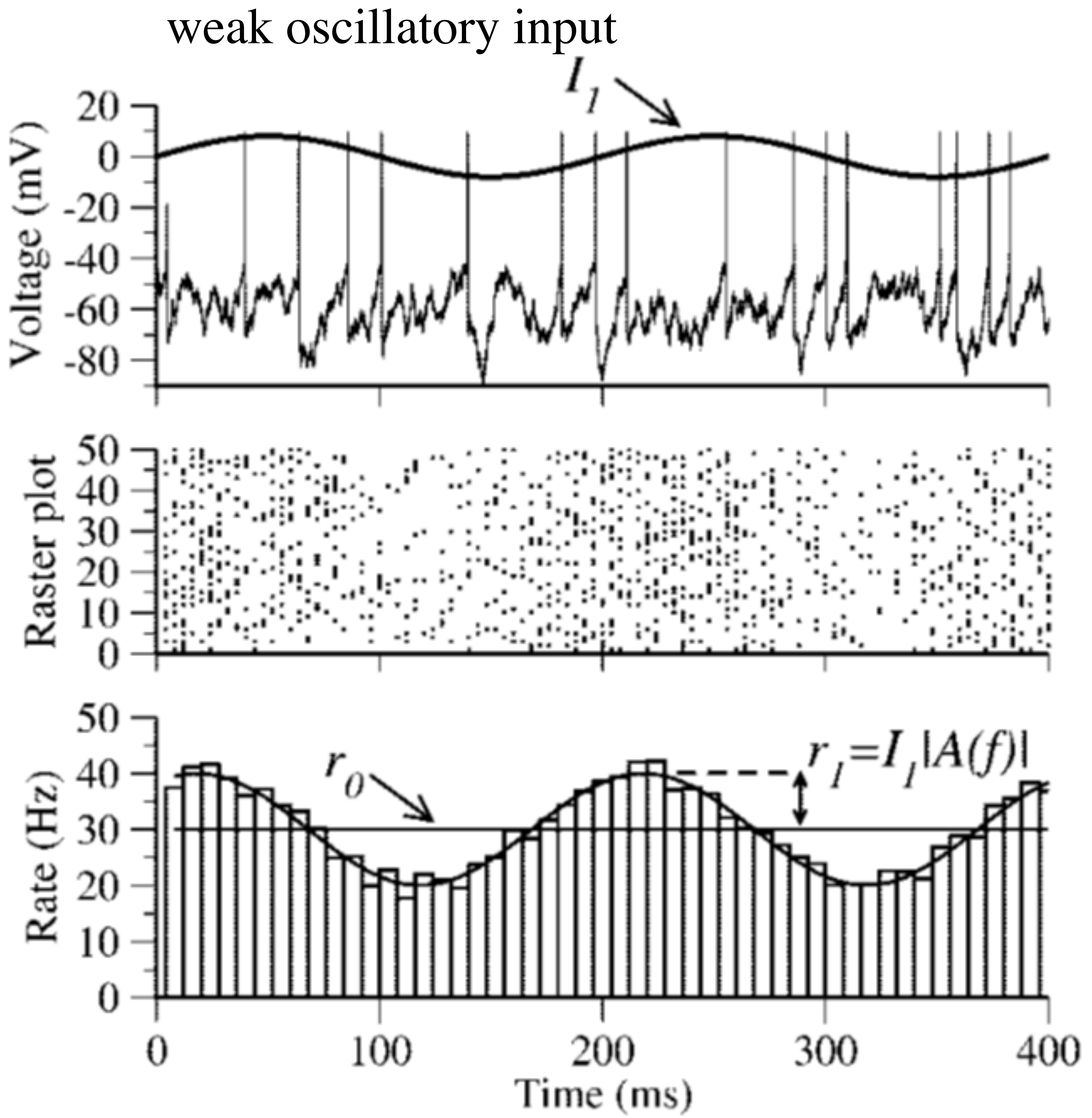


- No cycle skipping mechanisms, patterns continue 1:1 even for higher frequencies

$$C\frac{dv}{dt} = -gv - g_1 w + I_{app}(t)$$

$$\tau_1 \frac{dw}{dt} = v - w$$





Richardson et al., *J Neurophysiol* (2003) 89:2538–2554

Two distinct and independent frequency scales:

Subthreshold resonant frequency f_R

subthreshold dynamics of the membrane potential

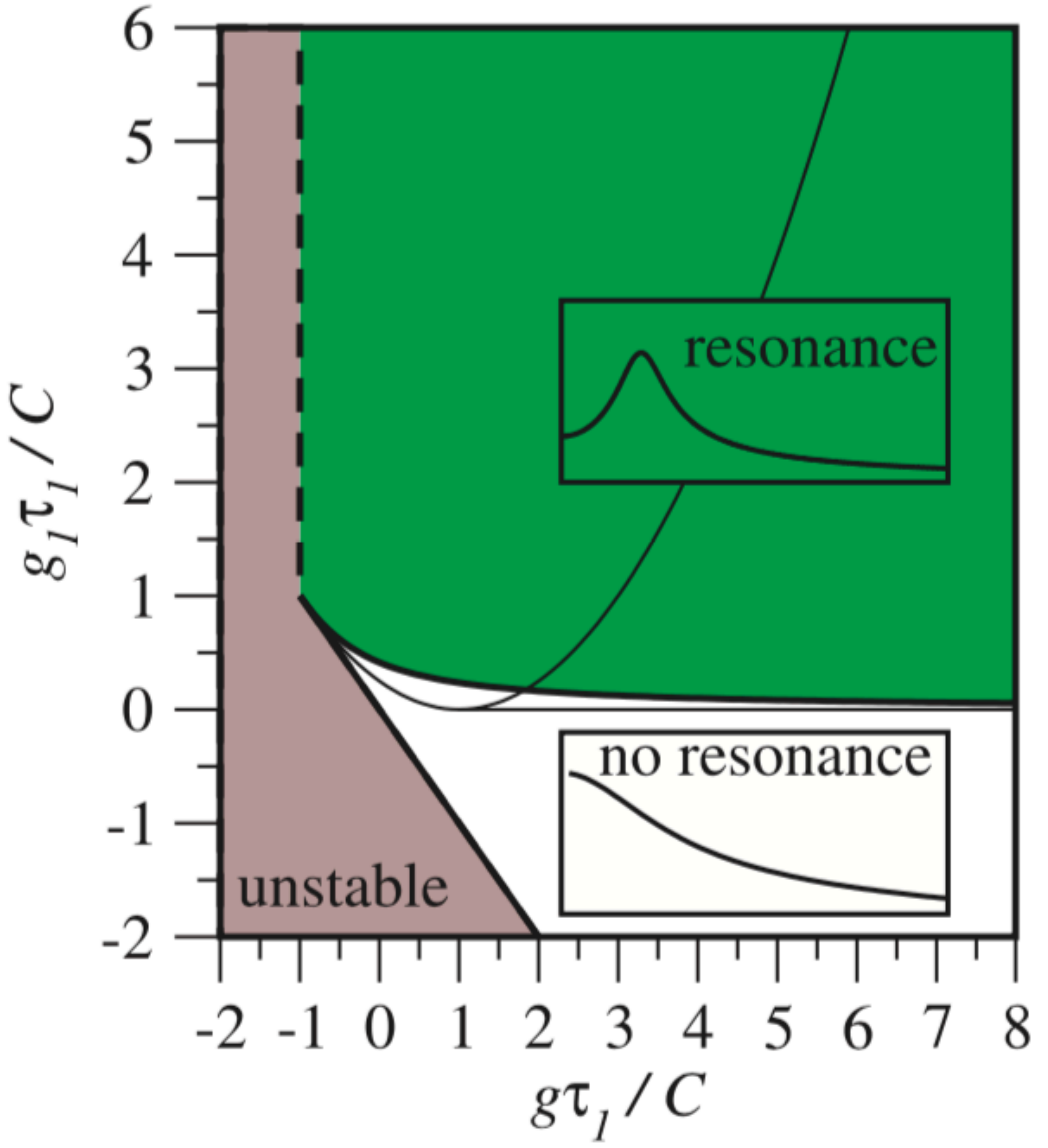
Background firing frequency r_0

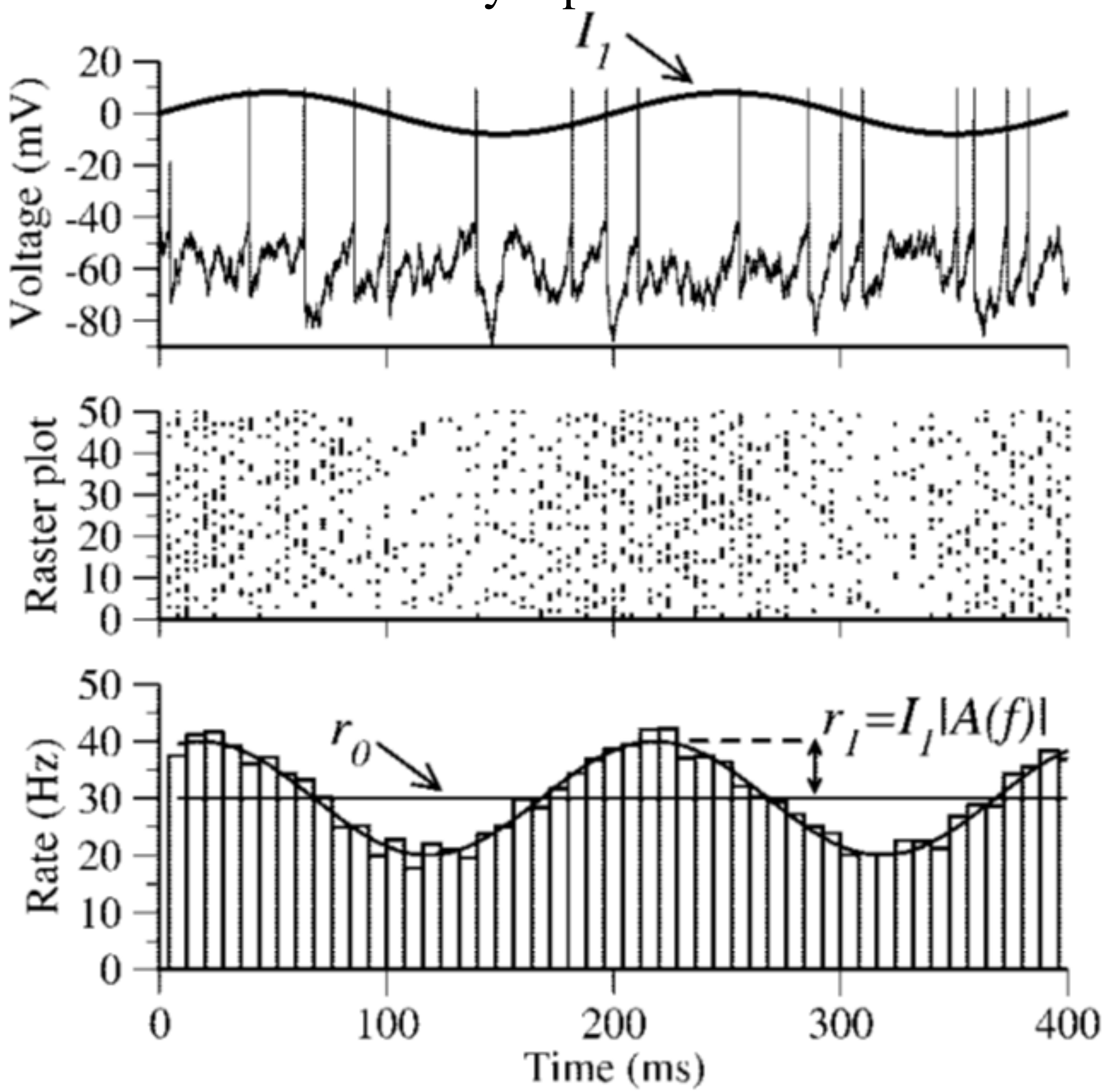
externally applied noisy current

pena@njit.edu

$$C\frac{dv}{dt} = -gv - g_1 w + I_{app}(t)$$

$$\tau_1 \frac{dw}{dt} = v - w$$





Richardson et al., *J Neurophysiol* (2003) 89:2538–2554

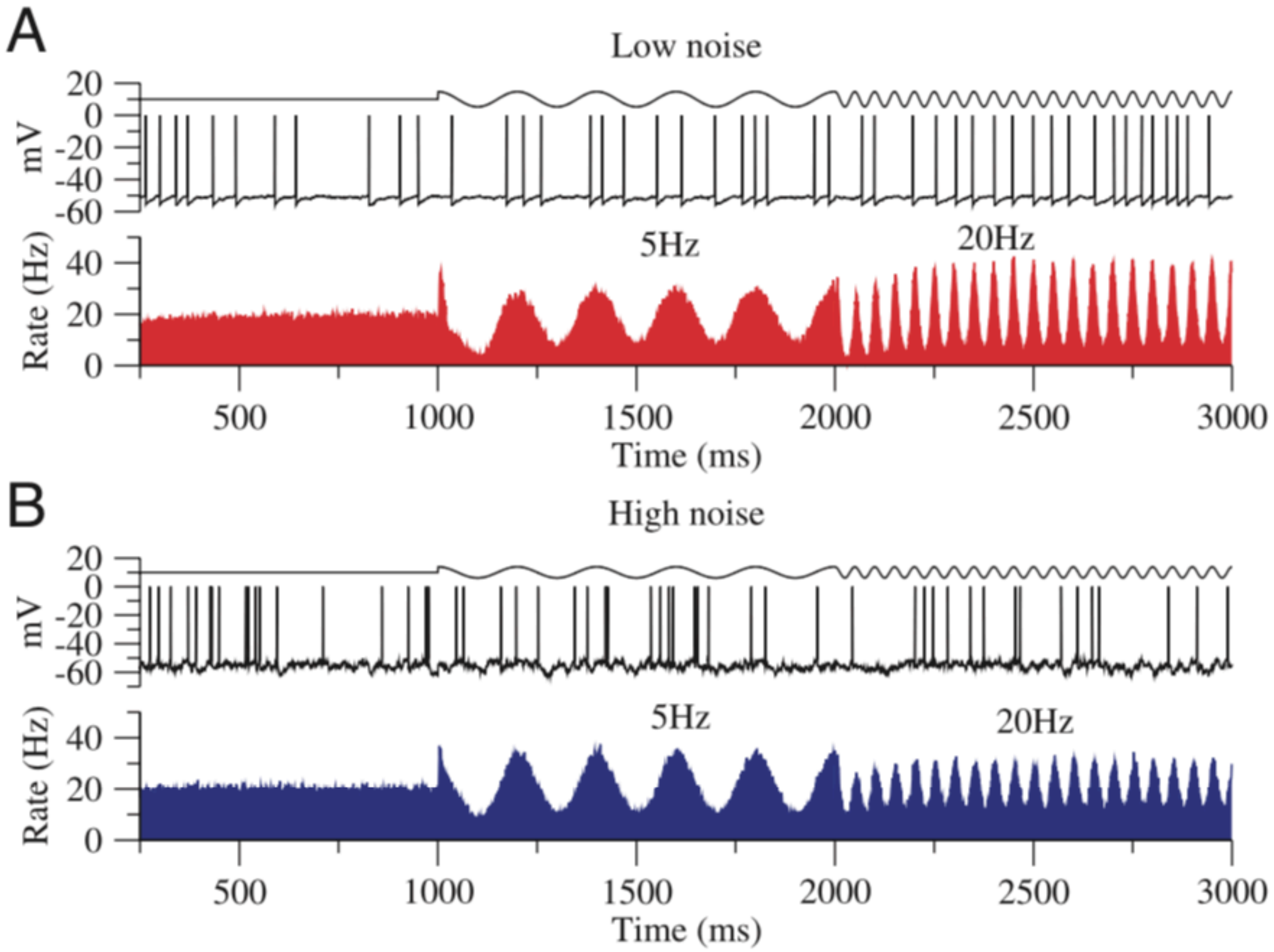
signal gain

$$|A(f)| = r_1(f)/I_1$$

Note similarity with impedance

$$|Z(f)| = V_1(f)/I_1$$

pena@njit.edu

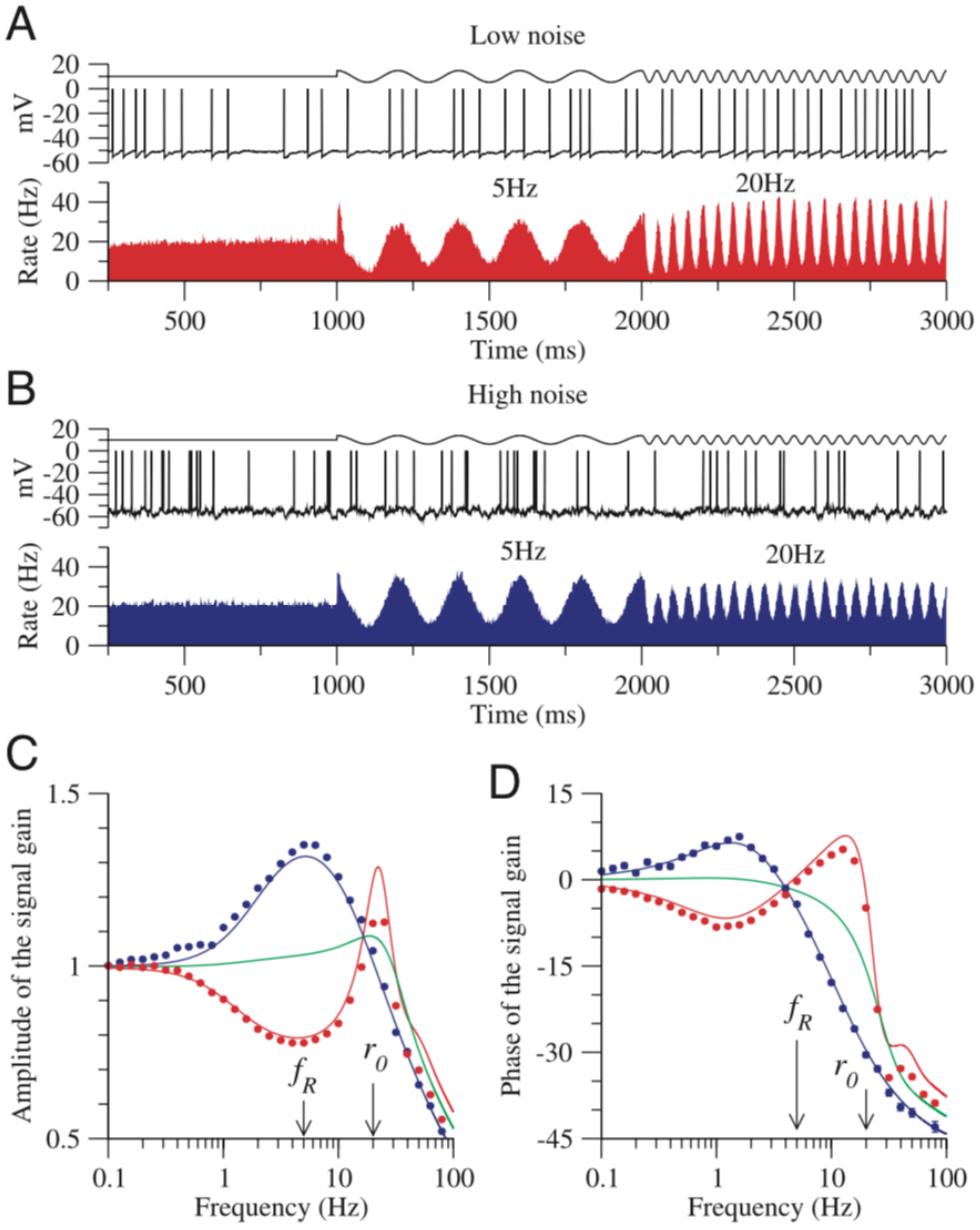


Richardson et al., *J Neurophysiol* (2003) 89:2538–2554

Two distinct modes of behavior

- regular firing (*low noise*);
- irregular firing (*high noise*).

pena@njit.edu

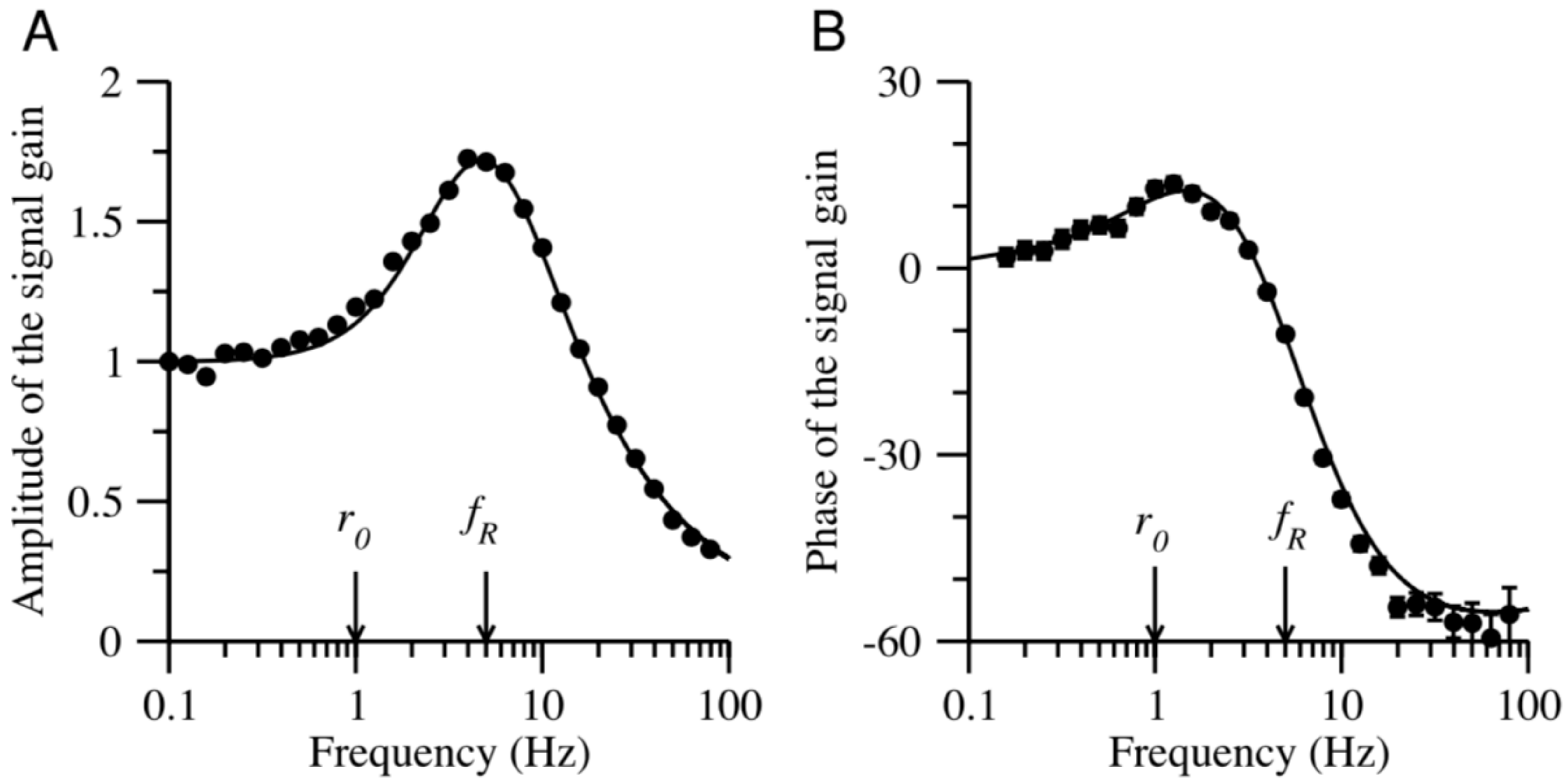


Richardson et al., *J Neurophysiol* (2003) 89:2538–2554

Two distinct modes of behavior

- regular firing (*low noise*);
- irregular firing (*high noise*).

pena@njit.edu



Richardson et al., *J Neurophysiol* (2003) 89:2538–2554

For $r0 < fR$, high noise is necessary to achieve lower frequencies

(type II neuron starts firing at finite frequency)

inter-spike interval is long:

neuron has time to explore subthreshold regime and begin to “resonate” before firing.

Outline

- Resonance for **suprathreshold** (spiking) behavior vs. **subthreshold** regime (**upper** envelope);

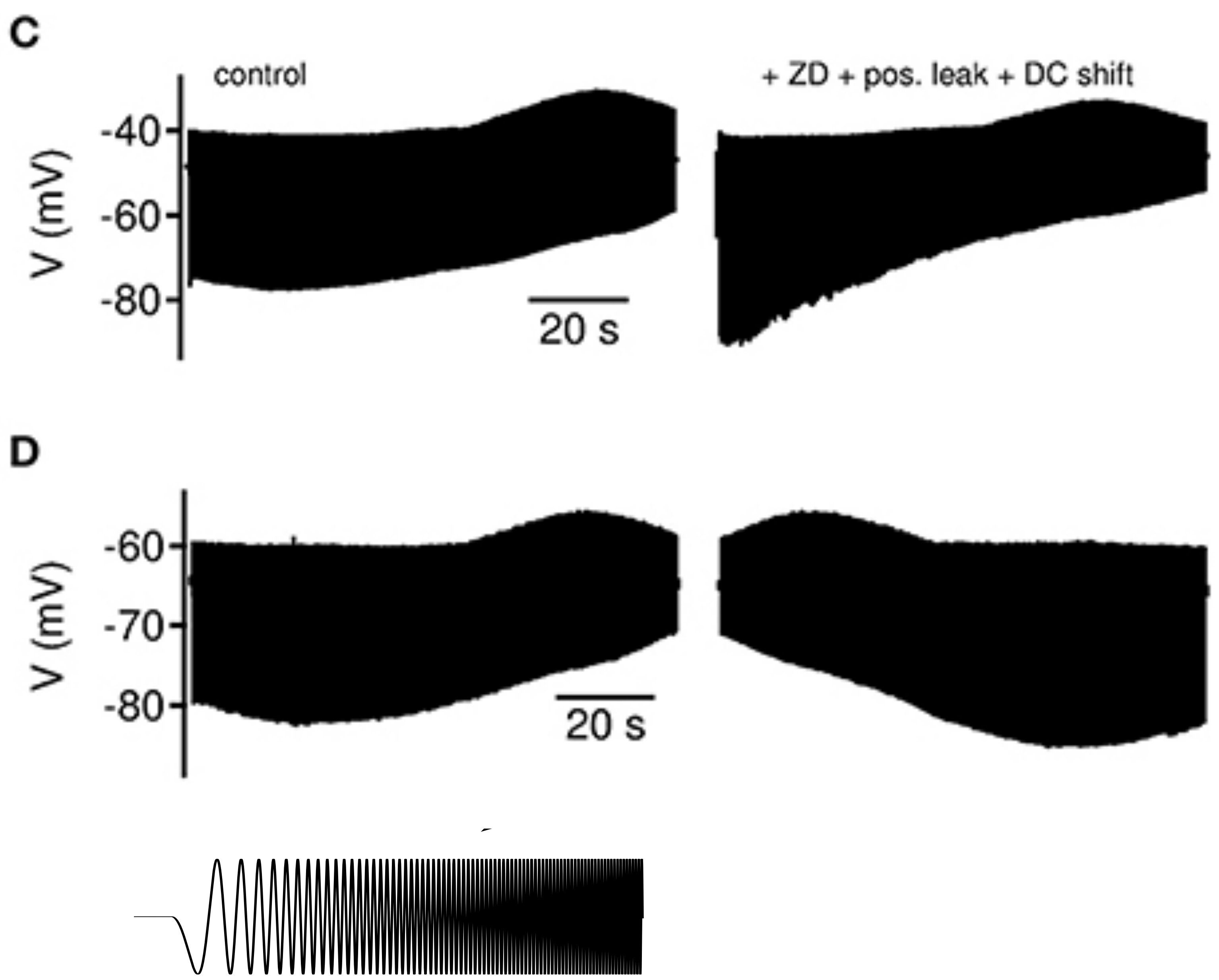
- Resonance for **suprathreshold** (spiking) behavior vs. subthreshold regime (**bottom** envelope);

- **Subthreshold** resonance when a neuron is **driven by spikes**.

pena@njit.edu

Experimental observations (asymmetries)

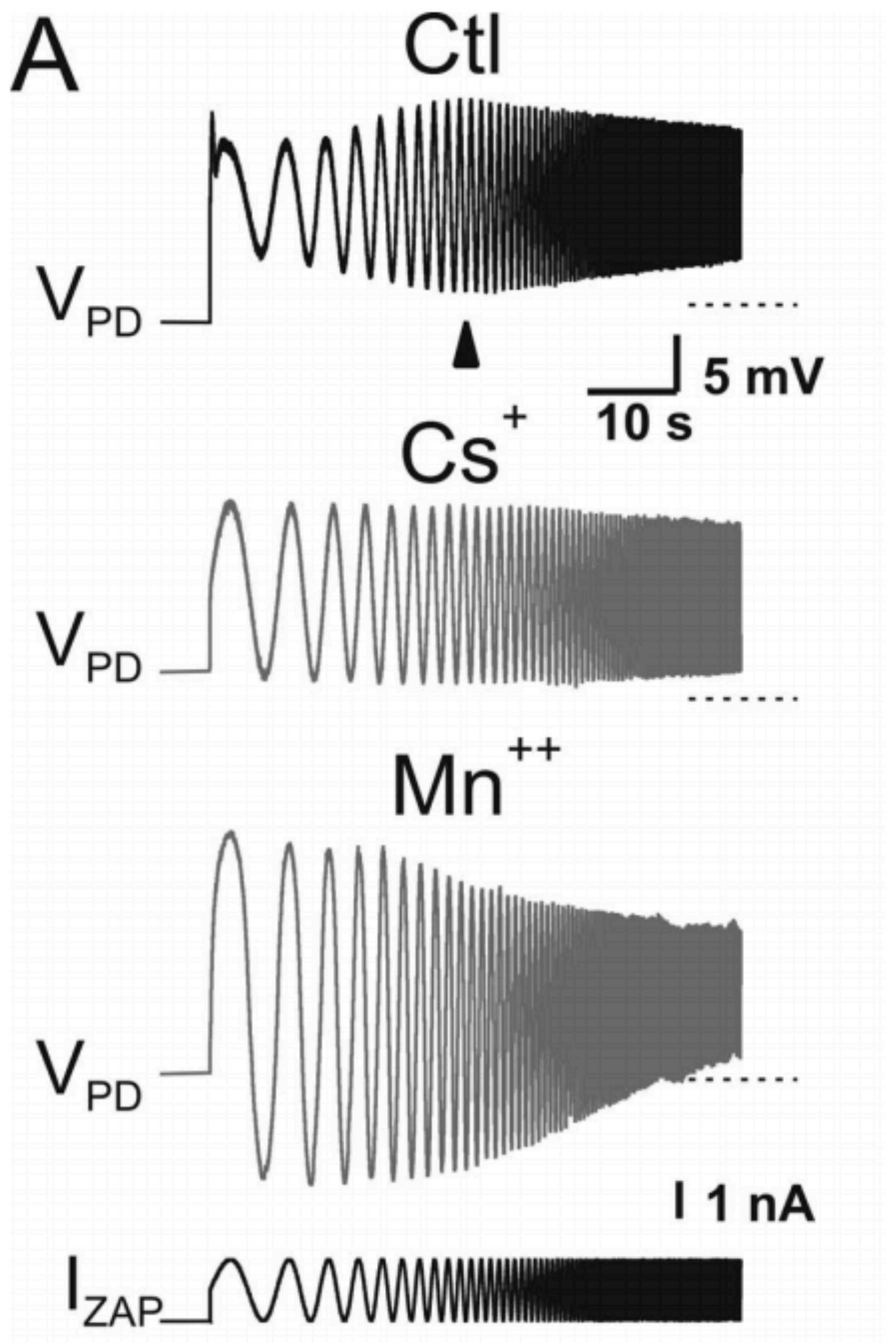
auditory brainstem neurons (mice)



Fischer et al. (2018)

Front Cell Neurosci 12:9

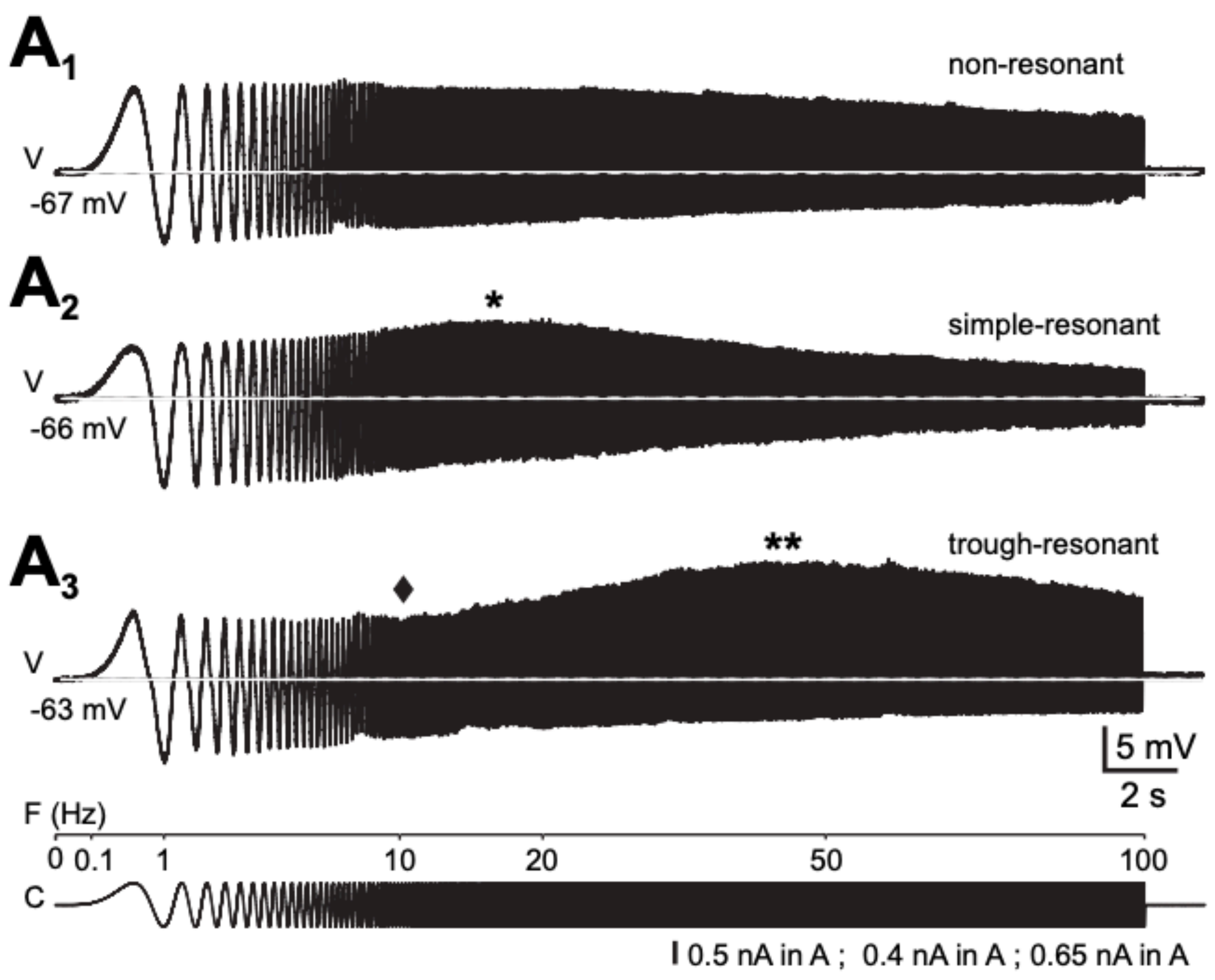
crab pyloric CPG



Tohidi and Nadim (2009)

J Neurosci 29:6427– 6435

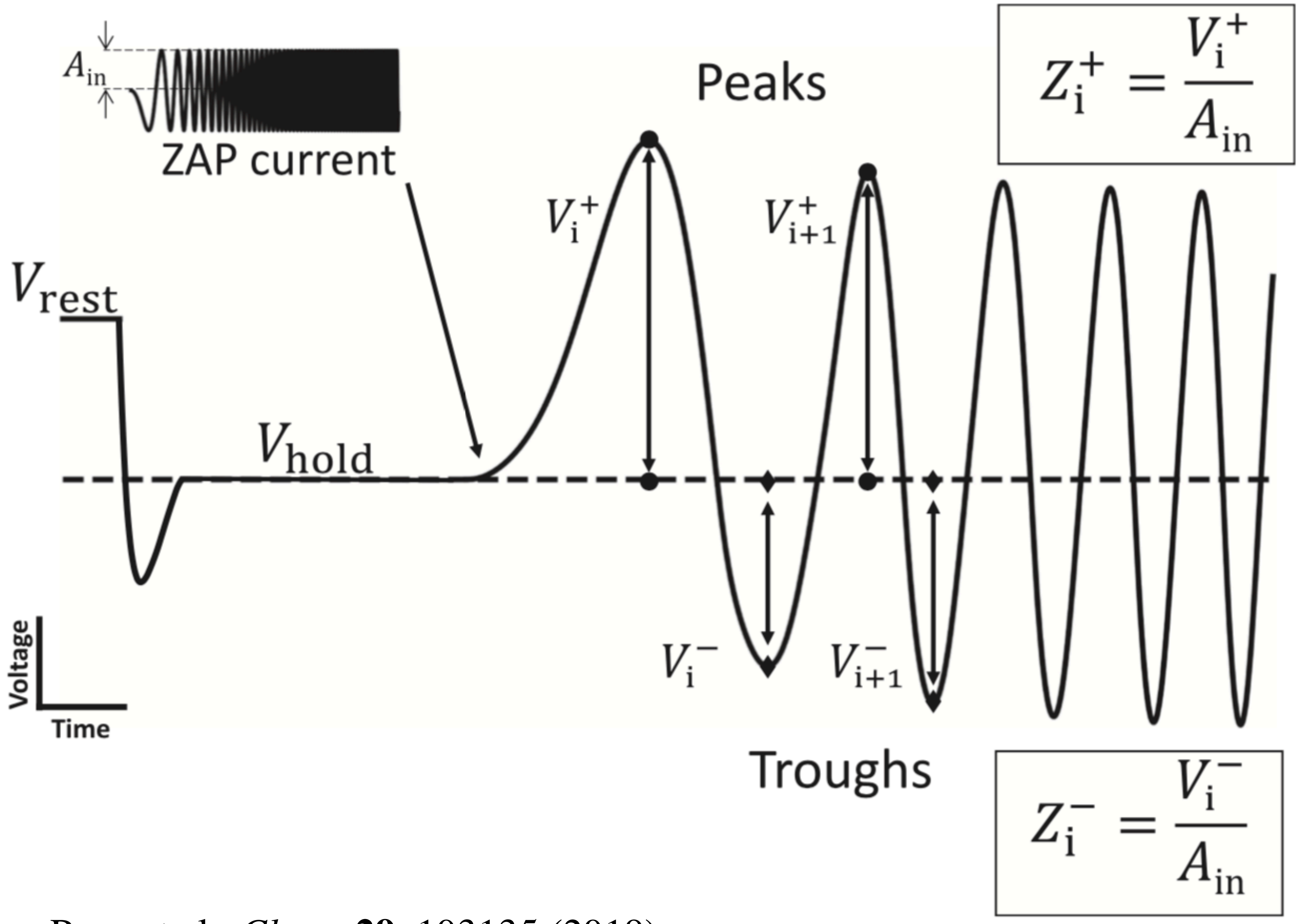
Frog Vestibular Neuron



Beraneck et al. (2007)

J Neurosci 27:4283– 4296

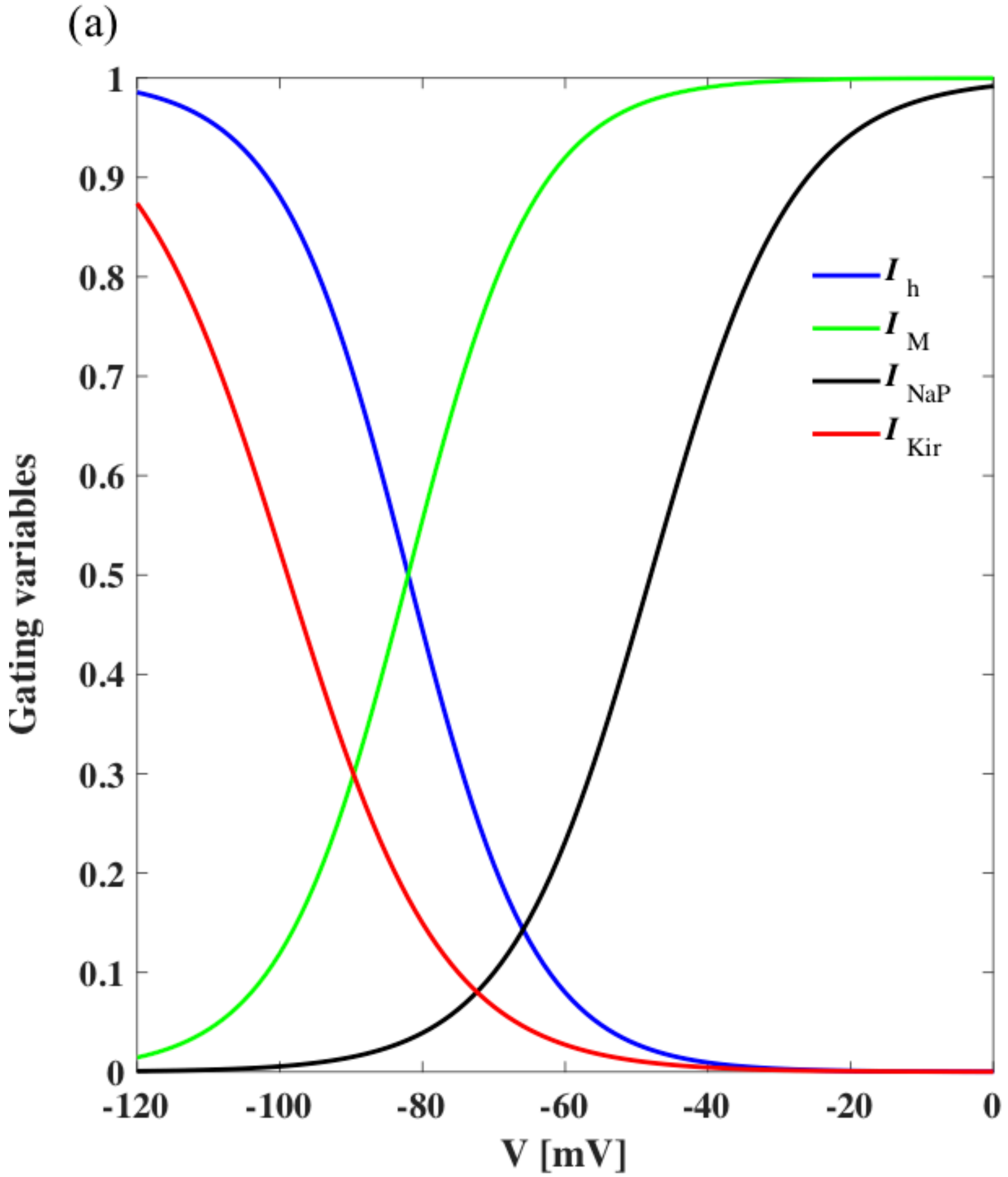
Measuring asymmetries

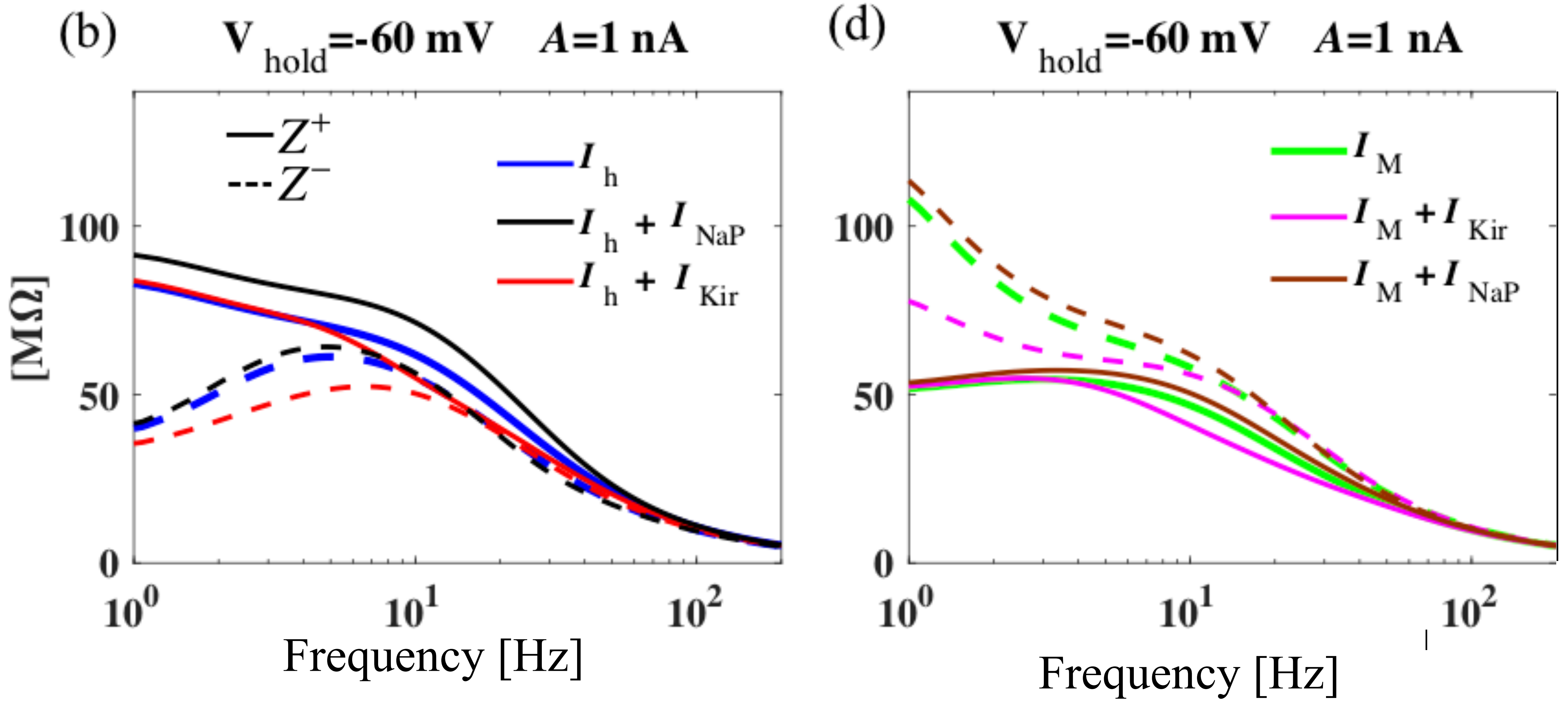


Pena et al., *Chaos* **29**, 103135 (2019)

Why asymmetries emerge?

Biophysical explanation



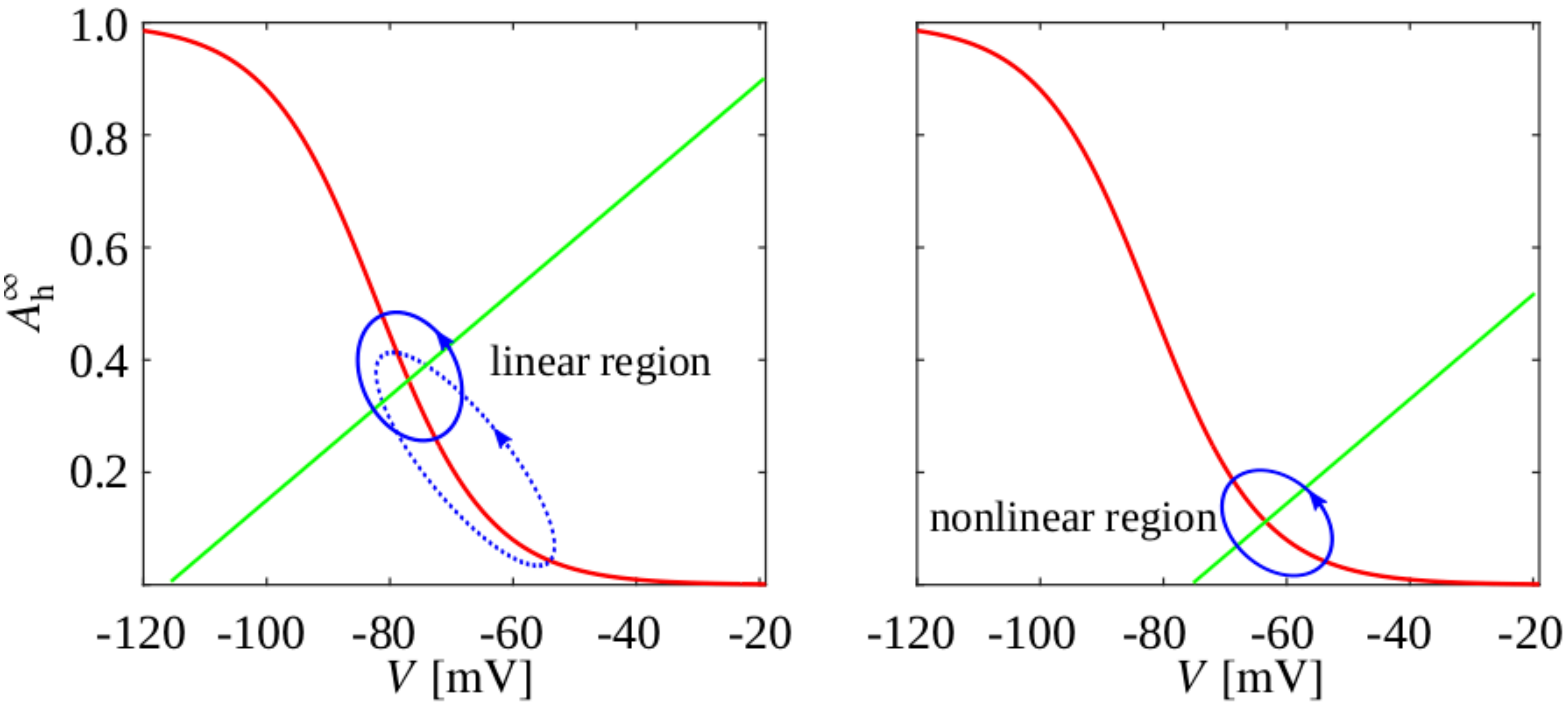


- Activation curves are related to $Z^{+/-}$ resonance

Pena et al., *Chaos* **29**, 103135 (2019)

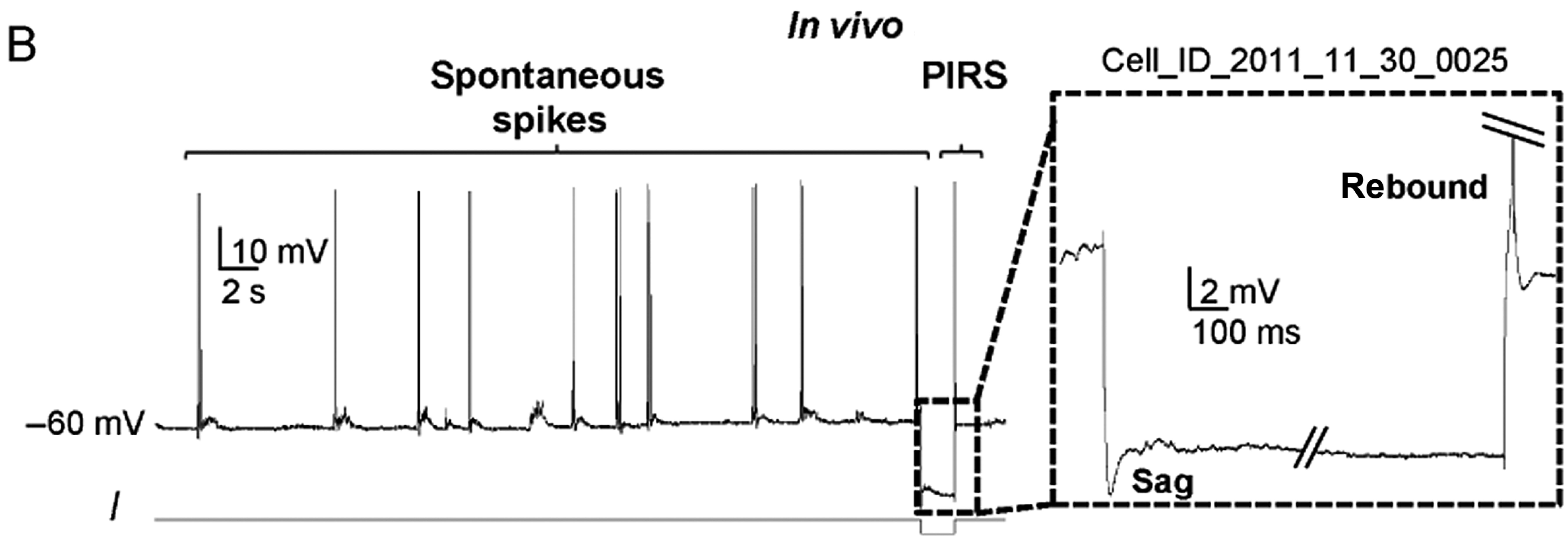
Why asymmetries emerge?

Dynamical explanation



Pena et al., *Chaos* **29**, 103135 (2019)

Post-inhibitory rebound spikes in medial entorhinal cortex Layer-II stellate cells



Ferrante et al., *Cereb. Cortex* 27 (2017): 2111-2125.

pena@njit.edu

Outline

- Resonance for **suprathreshold** (spiking) behavior vs. **subthreshold** regime (**upper** envelope);

- Resonance for **suprathreshold** (spiking) behavior vs. subthreshold regime (**bottom** envelope);

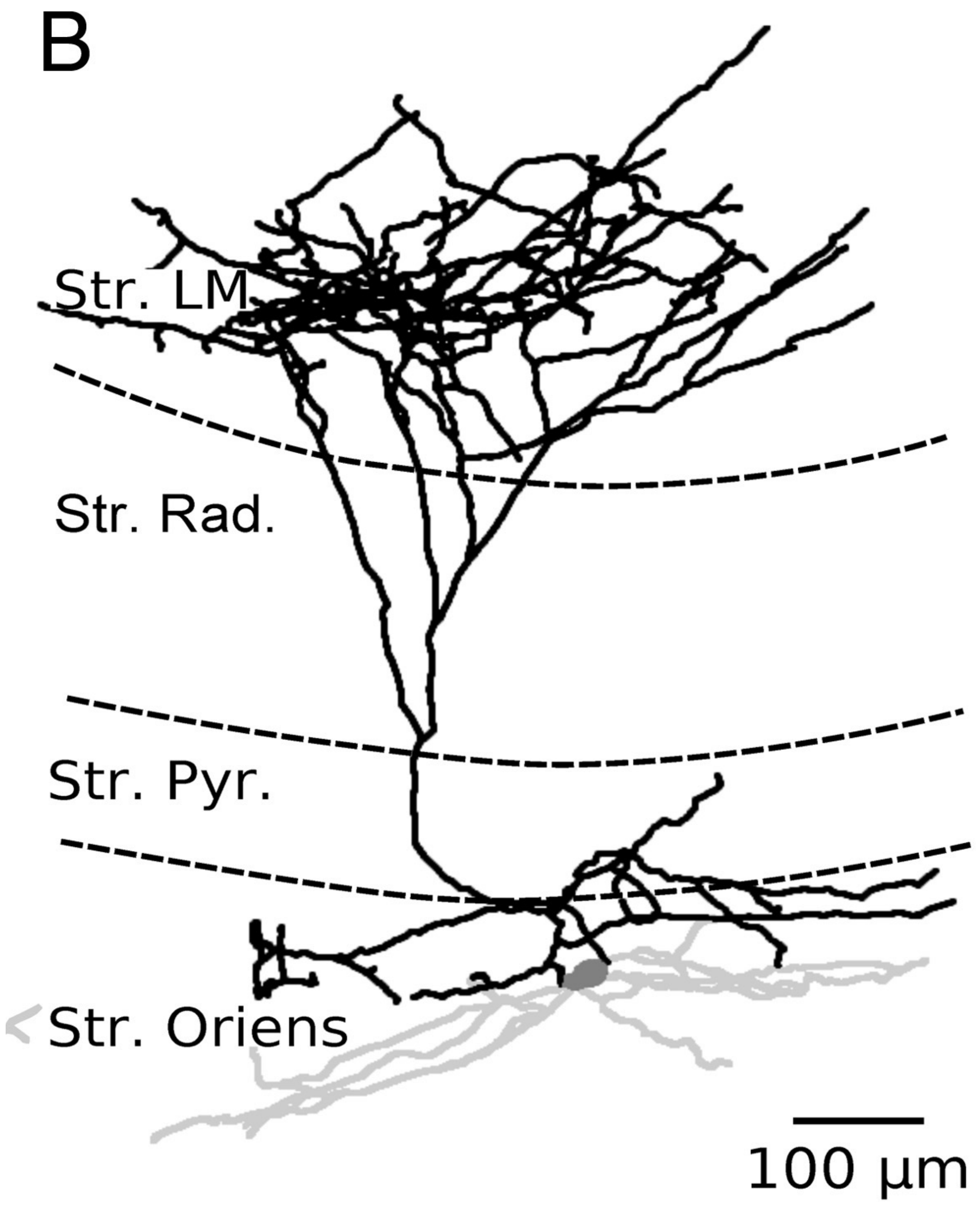
- **Subthreshold** resonance when a neuron is **driven by spikes**.

pena@njit.edu

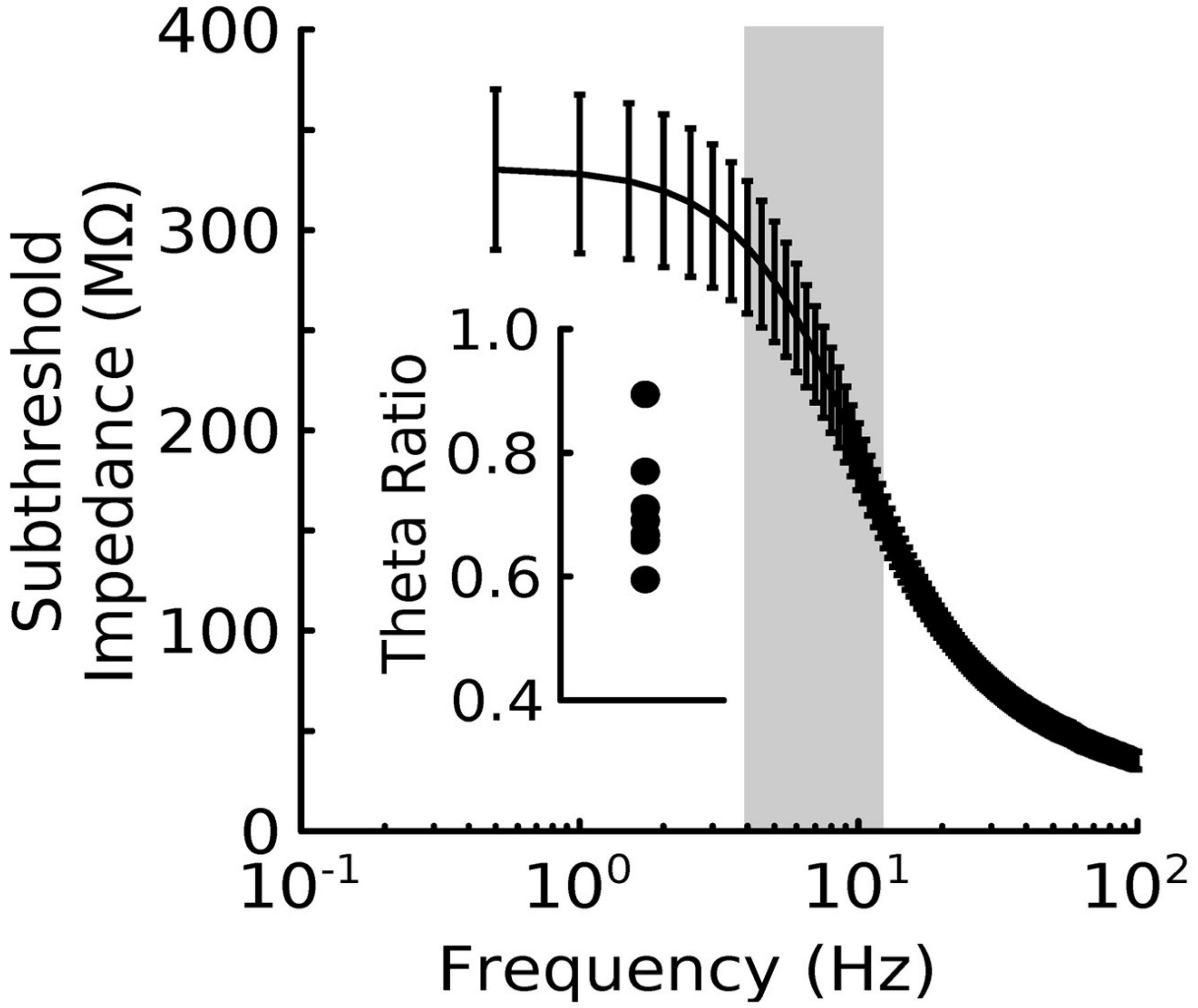
Experimental observations (O-LM cell in hippocampus)

Kispersky et al. (2012)

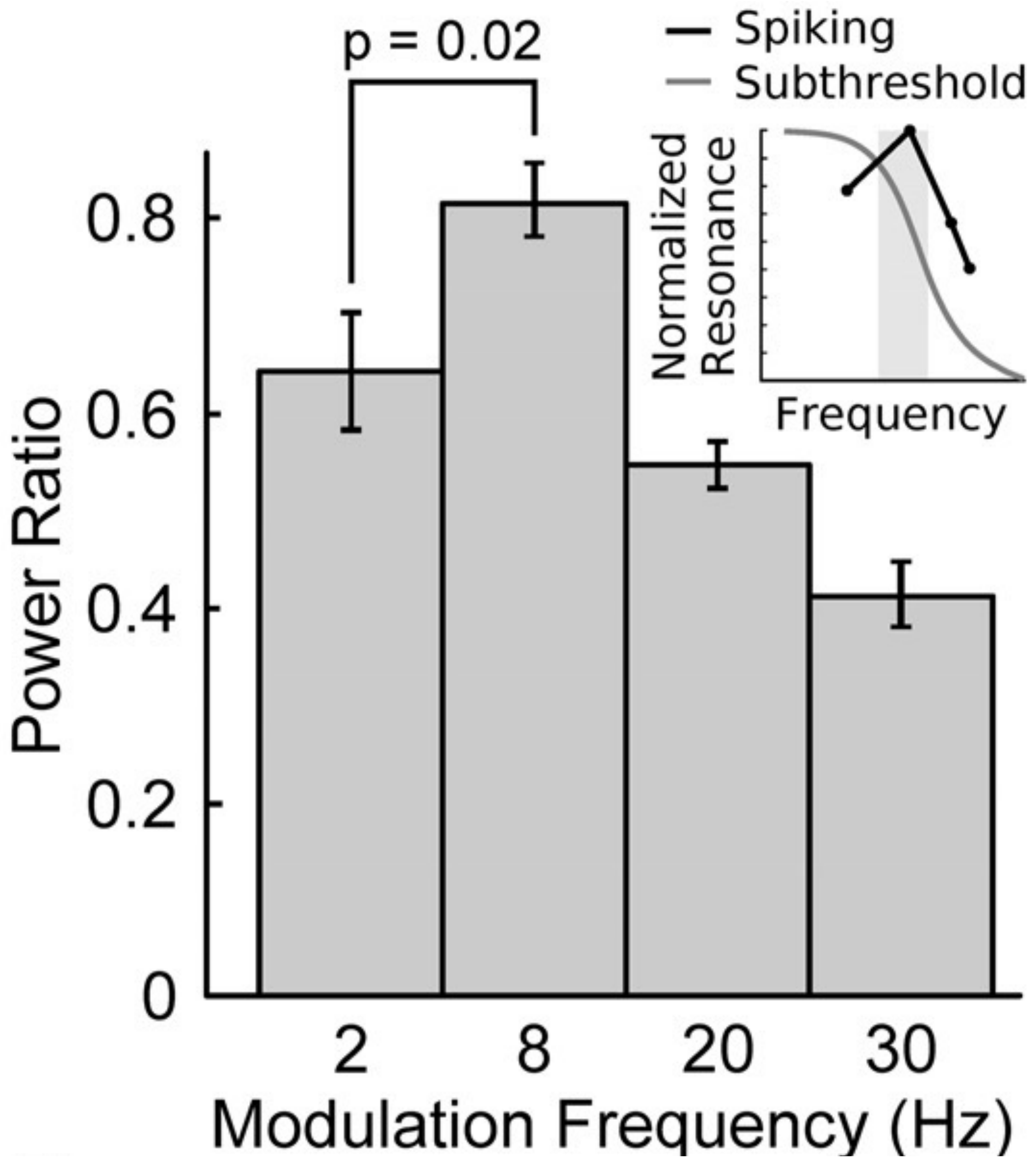
J Neurosci 32:3637-3651



Subthreshold impedance $Z(f)$ (under white Gaussian noise)



Low-pass behavior



Spiking resonance

pena@njit.edu

What does literature say about how to test resonance patterns?

"Unlike resistance, impedance is a frequency-dependent relationship between the amplitudes (and phases) of **oscillatory signals**."

Hutcheon & Yarom (2000)

Trends Neurosci. 23:216-22

Impedance as a property of oscillatory signals?

J Comput Neurosci (2015) 39:349–370
DOI 10.1007/s10827-015-0580-6

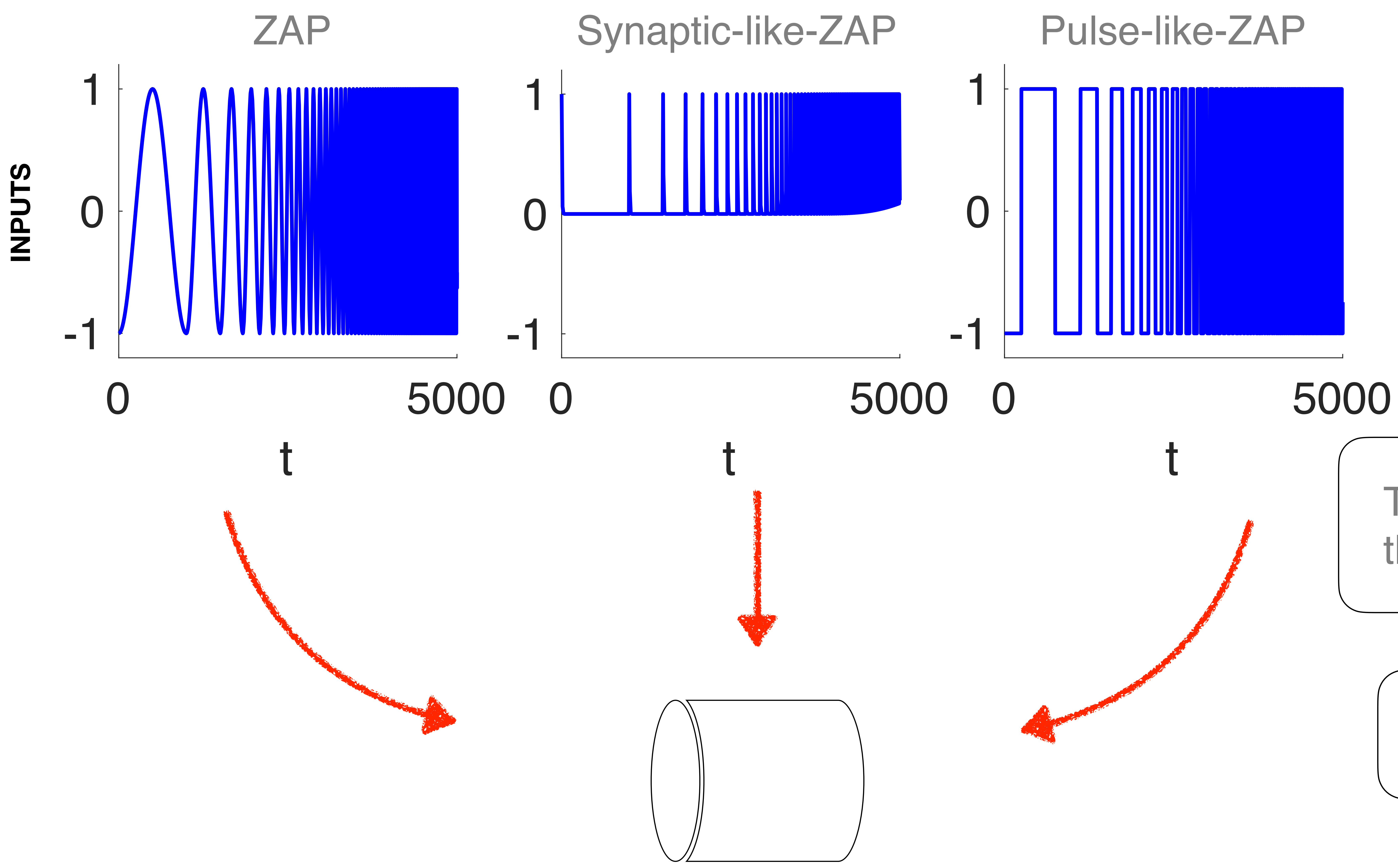
Information filtering in resonant neurons

Sven Blankenburg[1,2,3] · Wei Wu[4] · Benjamin Lindner[1,3] · Susanne Schreiber[1,2]

To test for resonances, stimulation can be based on any time-dependent stimuli that exhibit power in the frequency range of interest. In experiments, it is common practice to use pure sine waves or sine waves whose frequency is modulated in time (such as ZAP stimuli, see, for example Gimbarzevsky et al. 1984). Alternatively, time-dependent noise stimuli can be used as well (yielding mathematically equivalent results in linear systems). We here adopt the latter approach and model and the external current signal $s(t)$ as an Ornstein-Uhlenbeck (OU) process

$$\tau_{OU} \frac{d}{dt} s(t) = -s(t) + \xi_{OU}(t),$$

Simple experiment with a linear neuron model



These inputs cover
the same frequency range!

$$C\dot{v} = -g_L v - g_1 w + I$$
$$\tau_1 \dot{w} = v - w$$

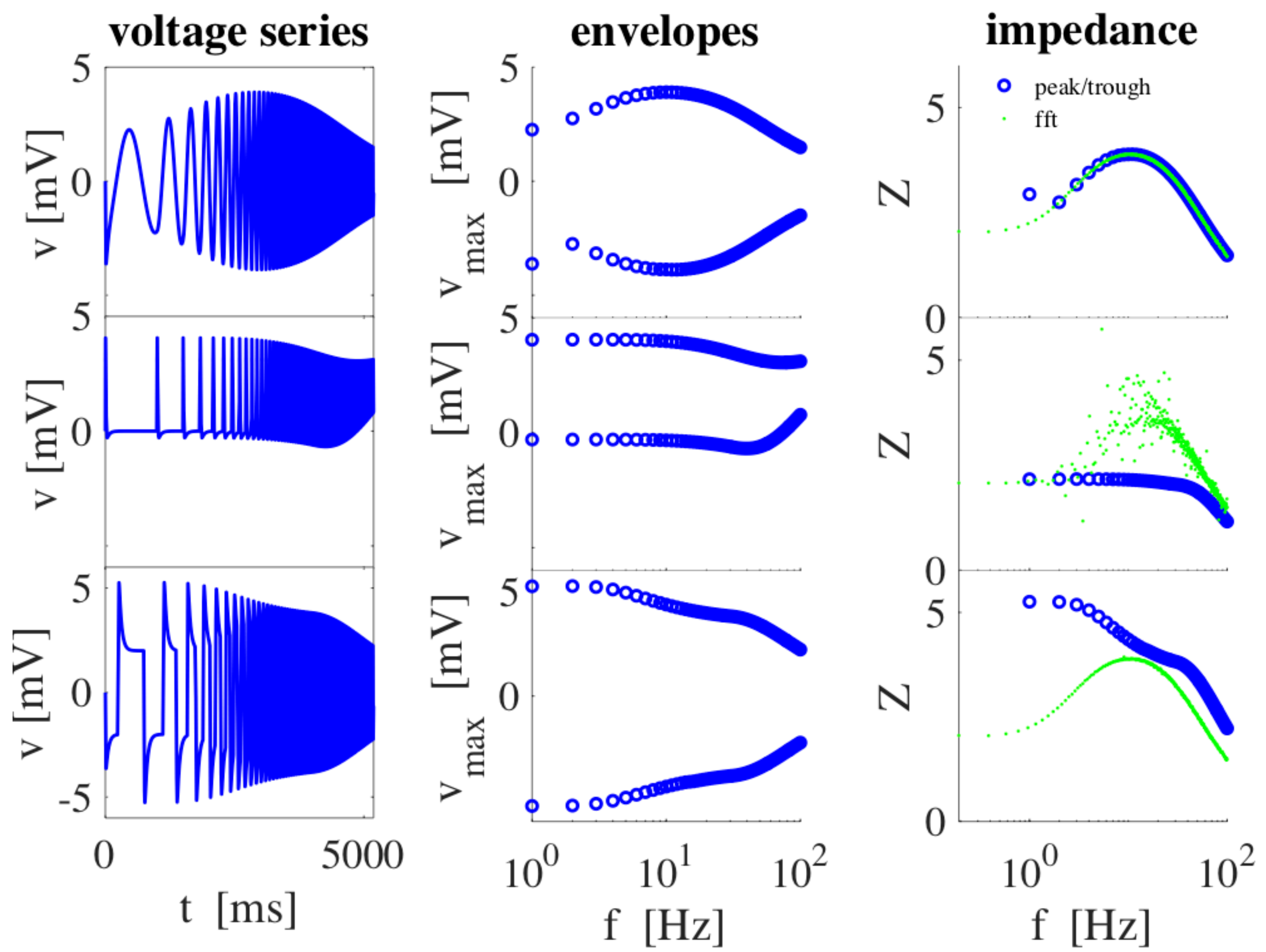
Rotstein (2003)
Chaos 23:046104

Simple experiment with a linear neuron model

ZAP

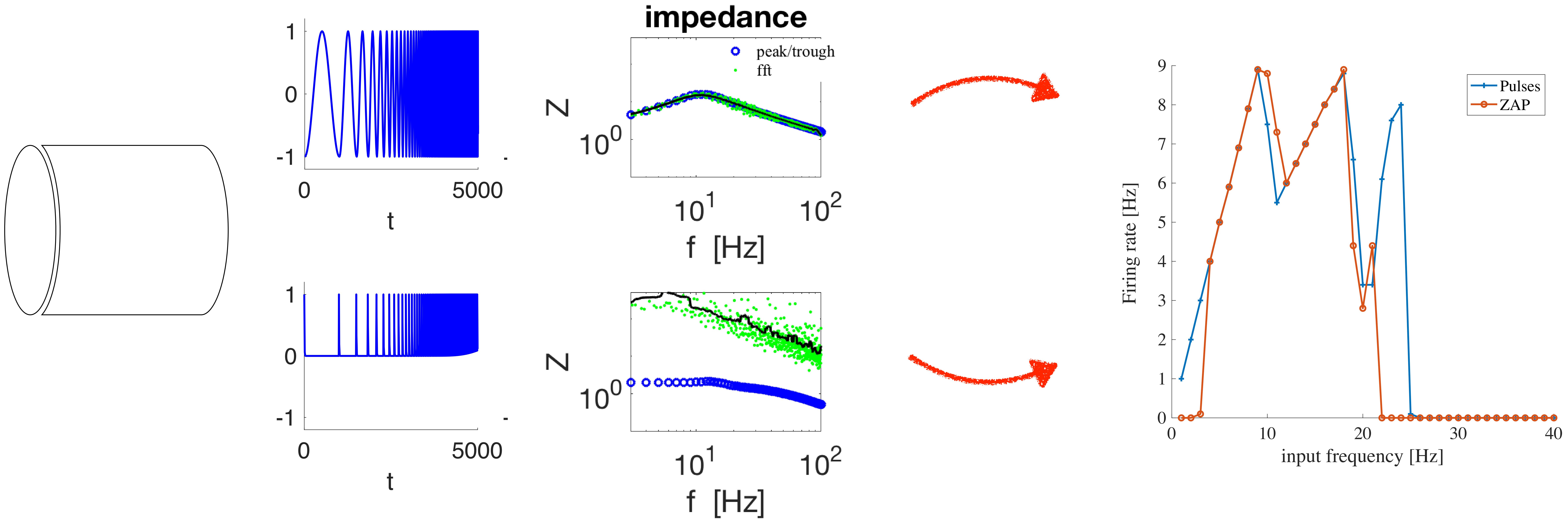
Synaptic-like-ZAP

Pulse-like-ZAP



What about spiking resonance?

Which one matters for spiking?



pena@njit.edu

Suggested literature

Subthreshold resonance

- Hutcheon & Yarom, *Trends Neurosci* (2000) 23:216-22

Spiking resonance

- Rotstein, *J Comput Neurosci* (2017) 43:243–271
- Richardson et al., *J Neurophysiol* (2003) 89:2538–2554

Asymmetries

- Pena et al., *Chaos* **29**, 103135 (2019)

Thank you very much!