Mathematical Foundations of Neuroscience - Lecture 8. Classes of excitability.

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Introduction

- We know some of the underlying geometrical mechanisms that are responsible for changing neuronal state from resting to spiking and vice versa
- It is the right moment to summarize this data and study in more detail what classes of neuronal excitability are possible.
- We will use $I_{Na,p}$ - I_K model as an example of some of the concepts.

Methodology

- There are several ways of injecting current in the neuron: pulse, ramp, step and zap and others.
- Depending on the input waveform the neuron can exhibit different dynamical behaviors
- One can imagine that a short pulse pushes the state of the system into some point in the phase space, leaving the phase portrait intact
- The ramp slowly changes the phase portrait, possibly allowing the state to accommodate
- The step suddenly changes the phase portrait leaving the state in the place of its previous steady node, which possibly becomes the attraction domain of a cycle or so.

Methodology

Definition

A **threshold** *is a minimal value of a short pulse of current that makes the neuron fire.*

Definition

A **rheobase** *is a minimal value of an infinite duration step of current that makes the neuron fire.*

As we shall se later, both the threshold an the rheobase might not be reasonably defined for some neurons.

Hodgkin Classification

- The first property used to classify neuronal responses was the frequency/current relation in responce to a step input current
- This classification was introduced by Alan Lloyd Hodgkin (the one from Hodgkin-Huxley equation) in 1948
- He was able to identify three classes
  - class I - the frequency of spikes can be arbitrarily low
  - class II - there is a cutoff frequency below which the neuron seizes to spike
  - class III - the neuron is excitable, but only spikes in response to a sudden current increase and remains quiescent no matter how large steady current is applied to the membrane

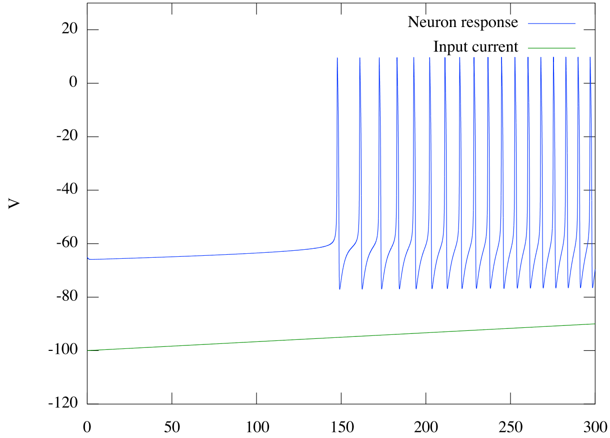
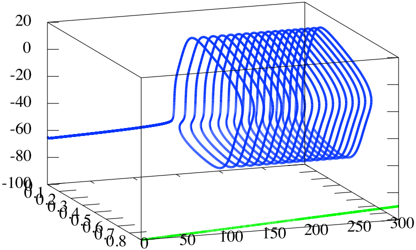


Figure: Class I excitability.



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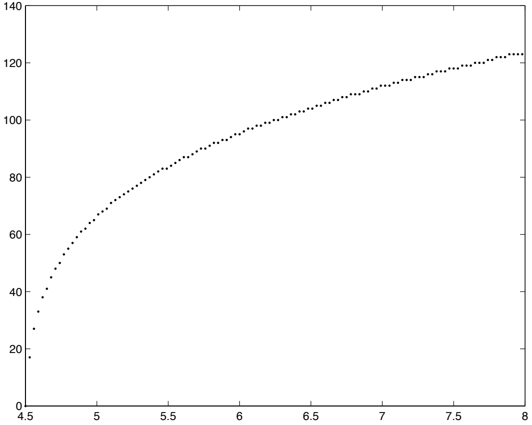


Figure: Frequency/current relation of class I excitability.

Class I

- It is quite easy to explain class I excitability in terms of phase plane geometry.
- Class I excitable neurons are precisely those which undergo a saddle node on invariant circle bifurcation, in which case the frequency/current curve scales as the square root of the bifurcation parameter

Class II

- Class II are exactly those neurons that have certain cut-off frequency and their frequency/current curve has a dicontinuity
- From our previous considerations we know that neurons that undergo any other bifurcation than the saddle node on invariant circle belong to this class
- We can see the weak point of Hodgkin classification - many interesting dynamical regimes belong to class II without being explicitly pointed out.

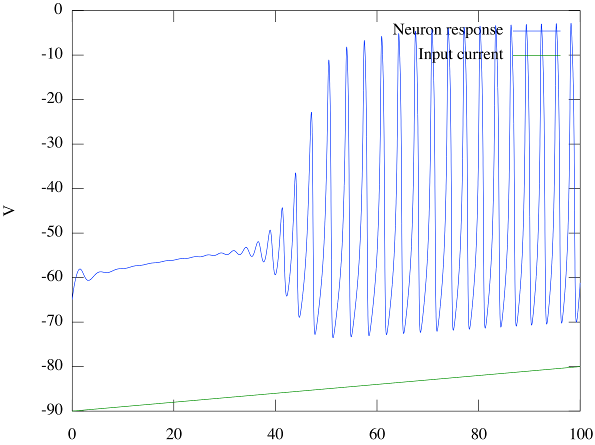


Figure: Class II excitability.

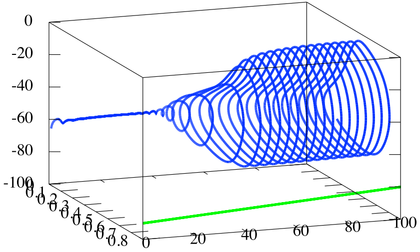


Figure: Class II excitability.

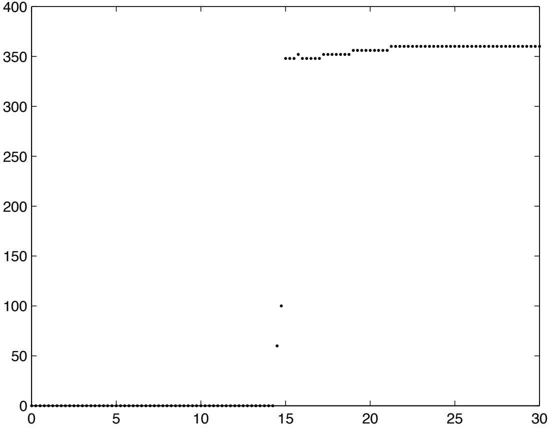


Figure: Frequency/current relation of class II excitability.

Class III

- Class III neuron is excitable, but only spikes in response to a sudden current increase and remains quiescent no matter how large steady current is applied to the membrane
- The ramp current does not induce spiking, even if the current becomes very large
- This phenomenon seems to be somewhat strange, since it doesn't seem to fit into any bifurcation we know

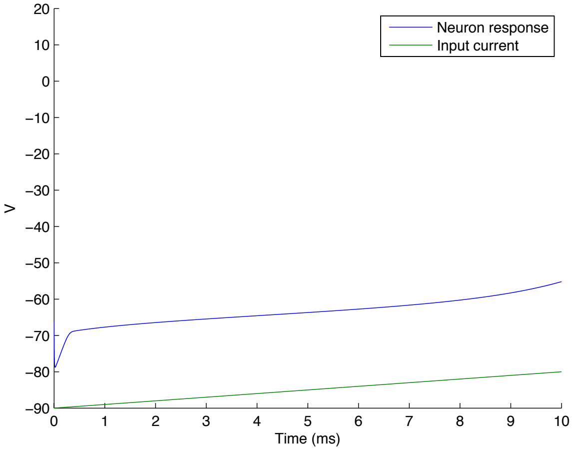


Figure: Class III excitability in response to a ramp and a set of steps.

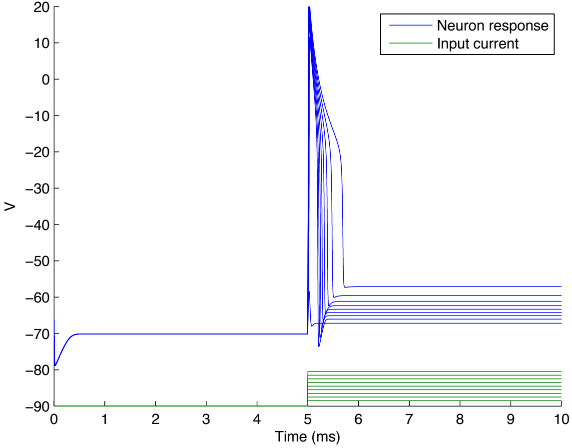


Figure: Class III excitability in response to a ramp and a set of steps.

Class III

- Class III can be simulated with $I_{Na,p}$ - I_K model with parameters: $C_d = 0.03$, $E_L = -80$, $g_L = 5$, $g_{Na} = 13$, $g_K = 6$, $E_{Na} = 60$, $E_K = -90$, $\tau(V) = 0.16$ and $n_\infty(V) = 1/\left(1 + e^{(-65-V)/2}\right)$
- As revealed by the phase plane analysis, this model does not undergo any bifurcation of the stable node for a wide range of input currents.
- It spikes right after the step, since stable node instantly changes its position and the state while converging to the new equilibrium position makes a long excursion near the right knee of the V nullcline, thus exhibiting a spike.

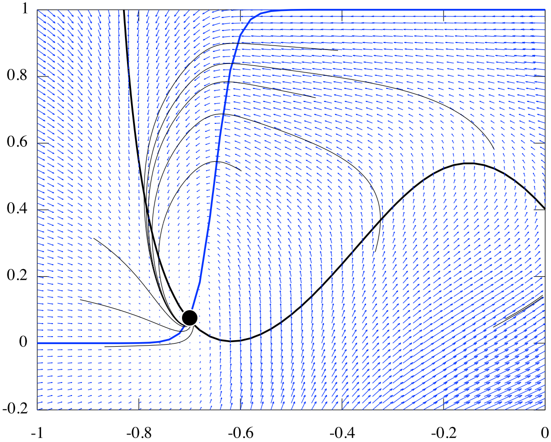
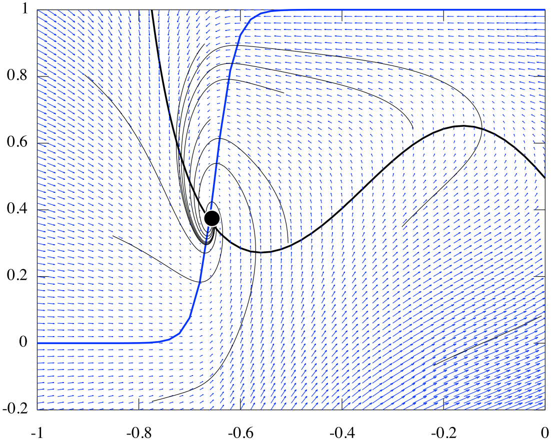


Figure: Class III excitability in $I_{Na,p}$ - I_K for $I = 0, 50, 100$.



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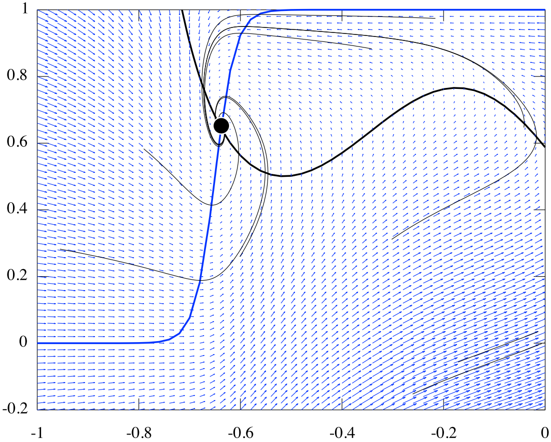


Figure: Class III excitability in $I_{Na,p}$ - I_K for $I = 0, 50, 100$.

Integrators and resonators

- Hodgkin classification, though useful, misses some of the important neuronal properties (class II is very rich)
- It is more adequate to focus on the geometrical aspects of bifurcation, in this case two lines of division emerge:
  - Bistable and monostable neurons (whether or not neuron has a range of currents at which two dynamical regimes are possible)
  - Integrators and resonators (whether or not the neuron exhibits oscillations)
- Bistability can be found by increasing and decreasing ramps
- Oscillations can be found by injecting zap current, that is sinusoidal current of increasing frequency

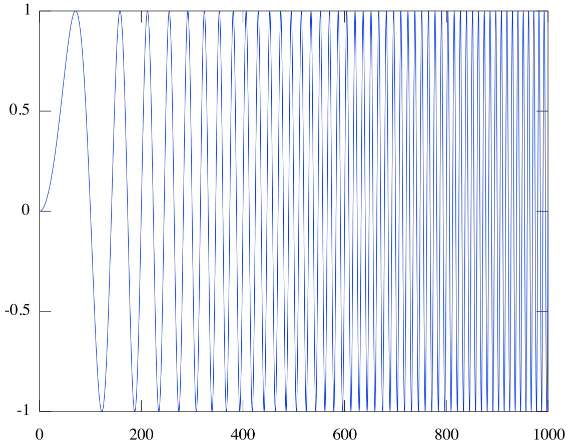


Figure: The zap current. The frequency of input steadily increases.

Monostable integrators

Monostable integrators:

- Undergo the saddle node on invariant circle bifurcation
- Prefer high frequency excitatory input
- Never spike in response to inhibition
- Have a decreasing impedance profile (response to zap current)
- Do not exhibit subthreshold oscillations
- Have a well defined threshold and the rheobase

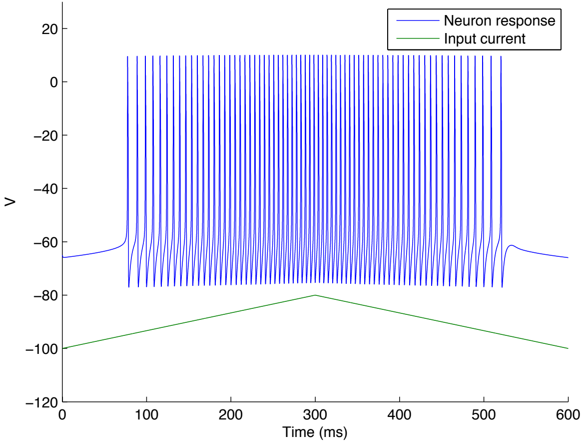
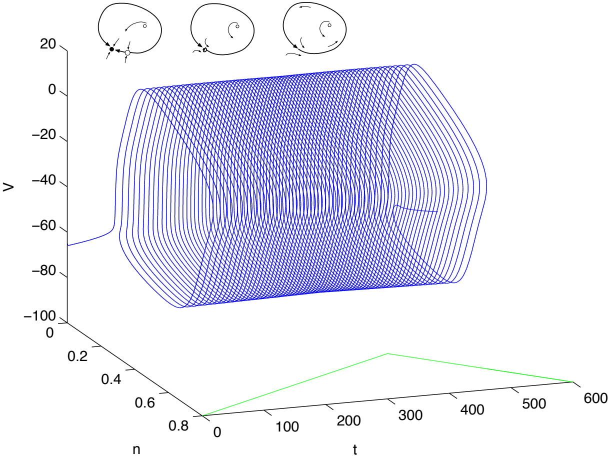


Figure: Monostable integrator undergoes a saddle node on invariant circle bifurcation.



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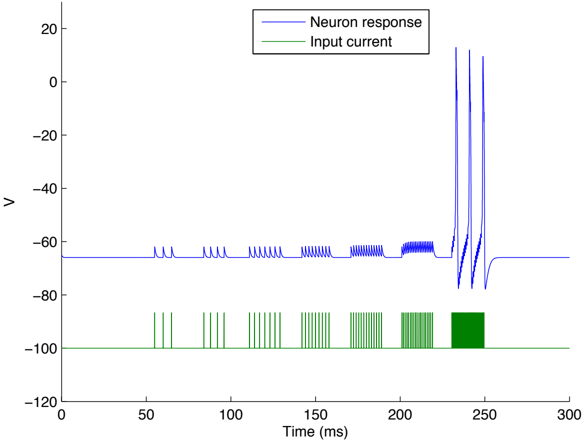
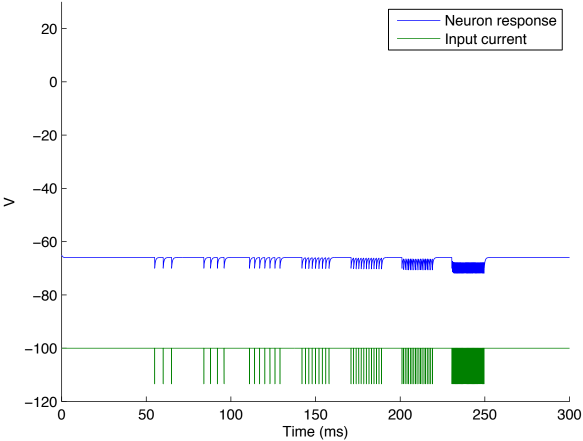


Figure: Monostable integrator prefers a high frequency excitatory input but fails to respond on an inhibitory input.



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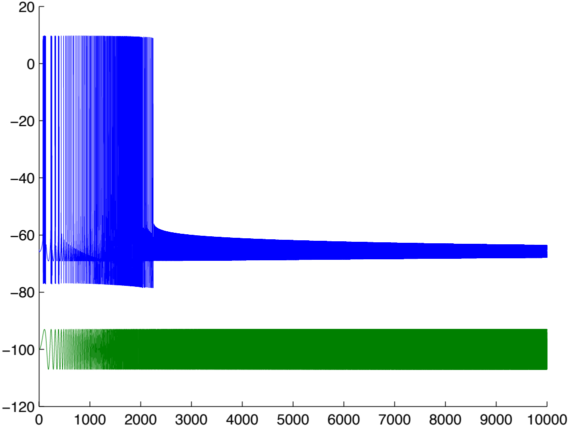


Figure: Monostable integrator has a decreasing response to the zap current (impedance profile).

Bistable integrators

Bistable integrators:

- Undergo the saddle node bifurcation
- Prefer high frequency excitatory input
- Never spike in response to inhibition
- Have a decreasing impedance profile (response to zap current)
- Do not exhibit subthreshold oscillations
- Have a well defined threshold and the rheobase
- Can be turned on by excitatory current and turned off by inhibitory current

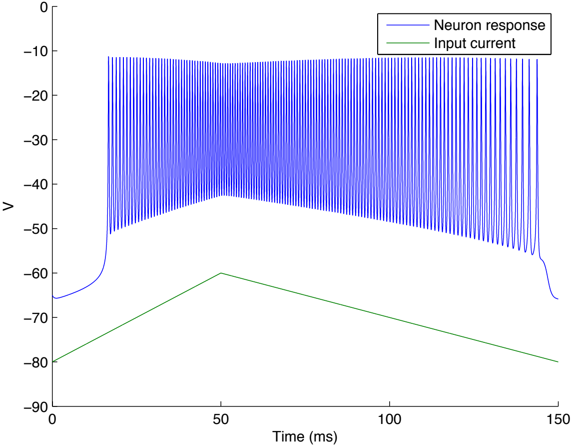
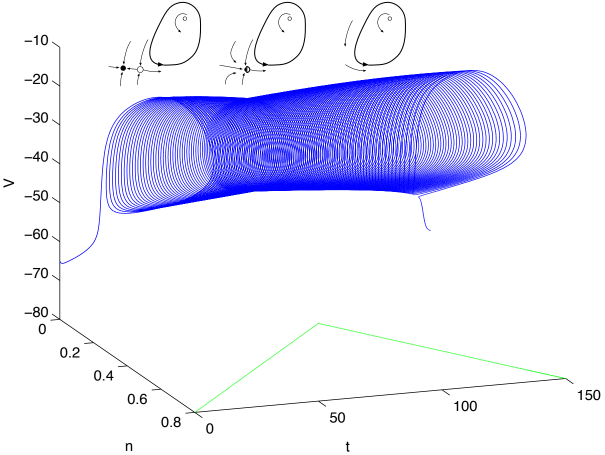


Figure: Bistable integrator undergoes a saddle node bifurcation.



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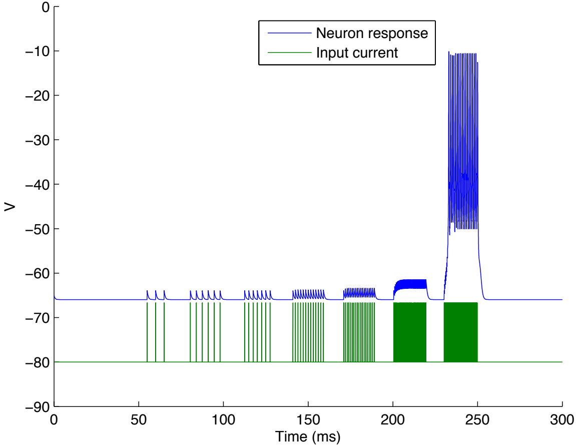

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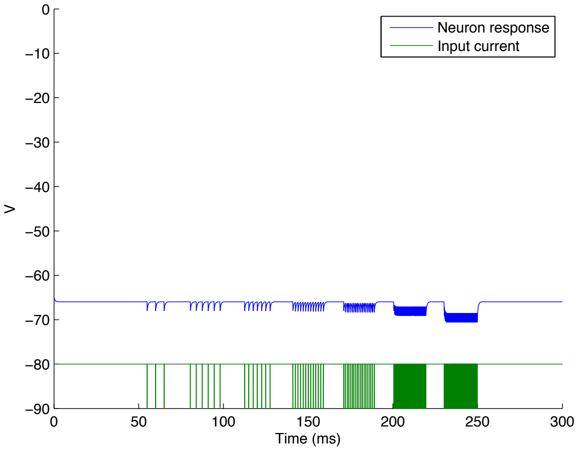

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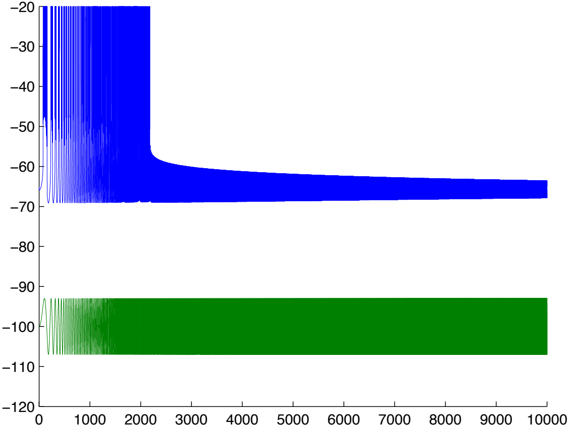


Figure: Bistable integrator has a decreasing response to the zap current (impedance profile).

Monostable resonators

Monostable resonators:

- Undergo the supercritical Andronov-Hopf bifurcation
- Have a frequency preference (resonant frequency)
- Can spike in response to inhibition
- Have a non monotonic impedance profile (response to zap current)
- Do exhibit damped subthreshold oscillations
- May not have a well defined threshold and the rheobase

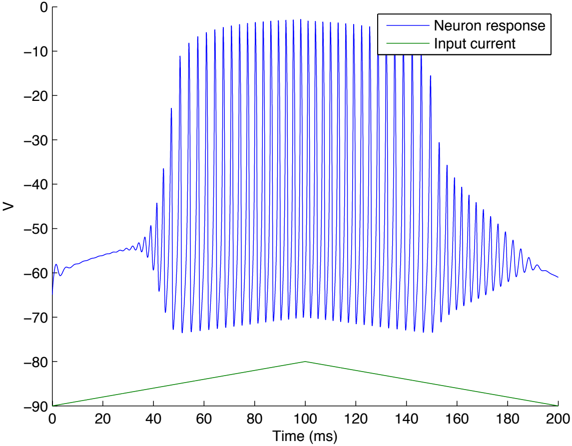
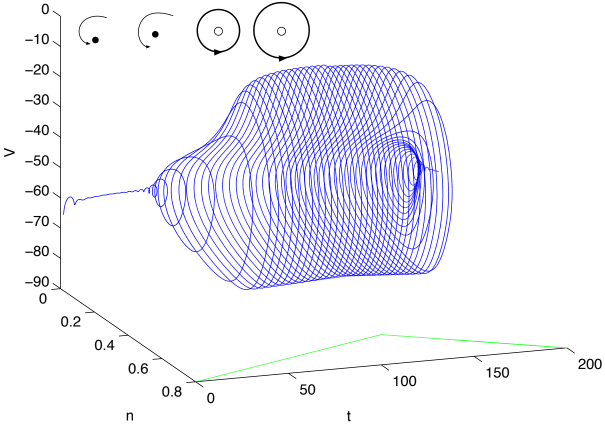


Figure: Monostable resonator undergoes a supercritical Andronov-Hopf bifurcation.



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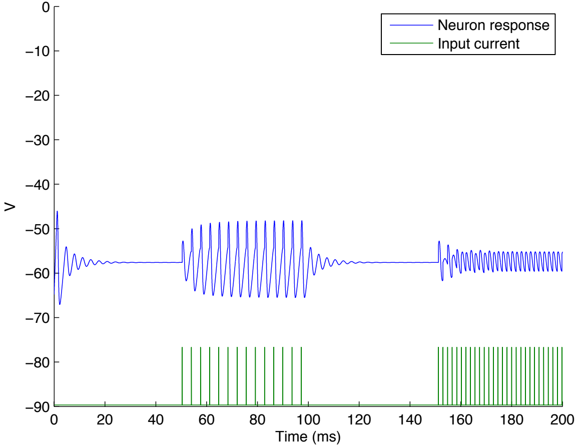
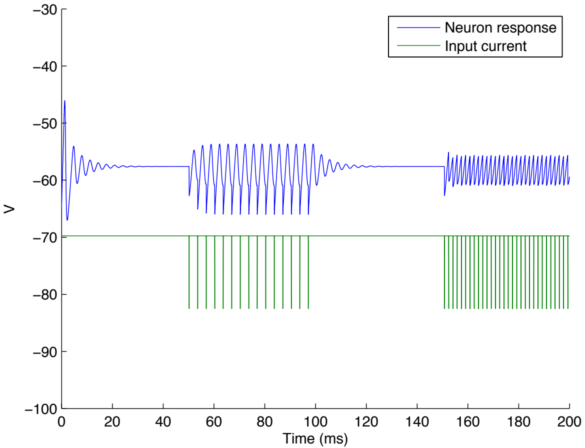


Figure: Monostable resonator has a frequency preference. Either excitatory and inhibitory input of the right frequency causes a potent response.



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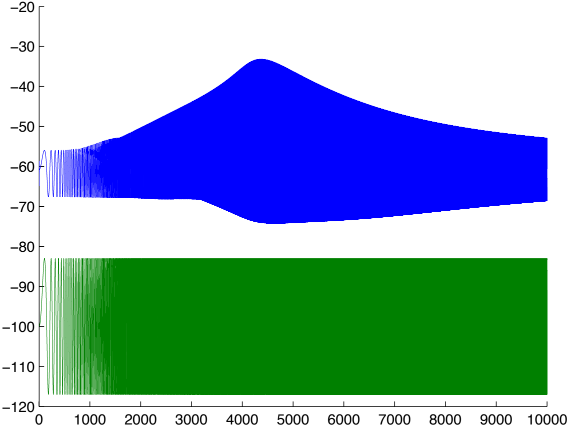

Figure: Monostable resonator has the highest response to the zap current at a particular frequency range, which corresponds to the frequency of oscillations near the stable focus.

Bistable resonators

Bistable resonators:

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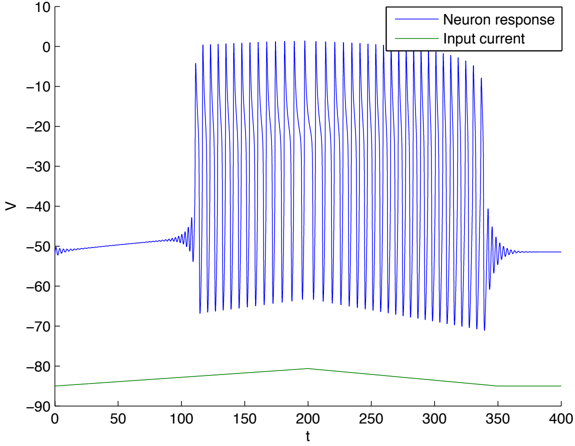
- Have a frequency preference (resonant frequency)
- Can spike in response to inhibition
- Have a non monotonic impedance profile (response to zap current)
- Do exhibit damped subthreshold oscillations
- May not have a well defined threshold and the rheobase
- Can be turned on and off by a resonant/non resonant input.



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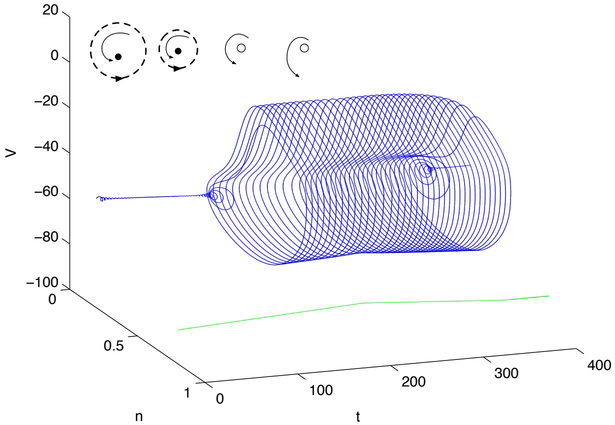

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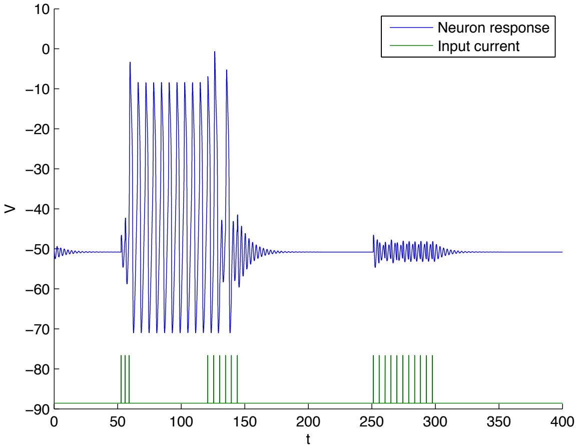
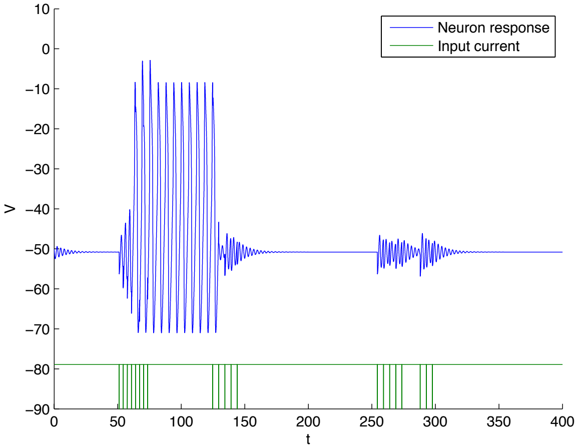


Figure: Bistable resonator has a frequency preference. Either excitatory and inhibitory input of the right frequency causes a potent response. Bistability results in an interesting phenomenon - the neuron can be switched on by a certain input and then turned off, by a non resonant input.



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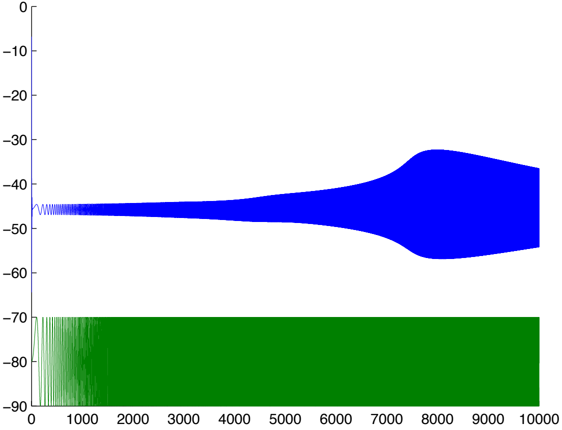

Figure: Bistable resonator has the highest response to the zap current at a particular frequency range, which corresponds to the frequency of oscillations near the stable focus.

Short summary

	Monostable	**Bistable**
Resonator	Supercritical Andronov-Hopf	Subcritical Andronov-Hopf
Integrator	Saddle node on invariant circle	Saddle node

Short summary

	Integrators		Resonators	
Bifurcation	SNIC	SN	Subcritical AH	Supercritical AH
Excitability	Class I	Class II	Class II	Class II
Oscillations	No		Yes	
Frequency preference	No		Yes	
Coexistance of resting and spiking	No	Yes	Yes	No
Threshold and rheobase	Well defined		Not well defined	

From integrators to resonators

- Integrators are separated from resonators by the Bogdanov-Takens bifurcation.
- Neurons which are near the bifurcation can exhibit interesting mixed regimes, like being an integrator at some currents and resonator at some other currents.
- Such mixed type neurons are rare, but not negligible.
- The wierd mixed behavior can be observed in $I_{Na,p}$ - I_K model with $C_d = 1$, $E_L = -79.42$, $g_L = 8$, $g_{Na} = 20$, $g_K = 10$, $E_{Na} = 60$, $E_K = -90$, $\tau(V) = 0.16$ and $n_\infty(V) = 1/\left(1 + e^{(-31.64-V)/7}\right)$

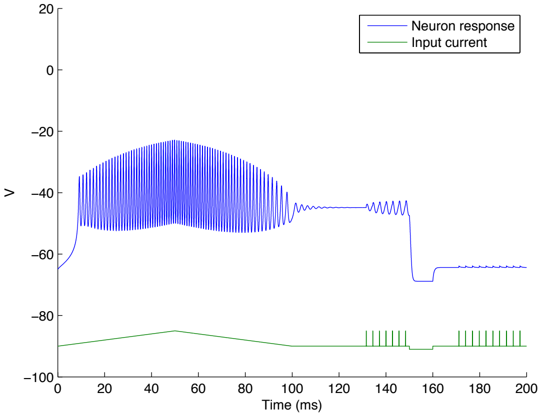

Figure: A neuron ($I_{Na,p}$ - I_K model parameters as above) near Bogdanov-Takens bifurcation has a stable node and a focus. It therefore exhibits two regimes, when the state rests at the focus, the neuron is a resonator. If the state rests in the stable node, the neuron becomes and integrator.

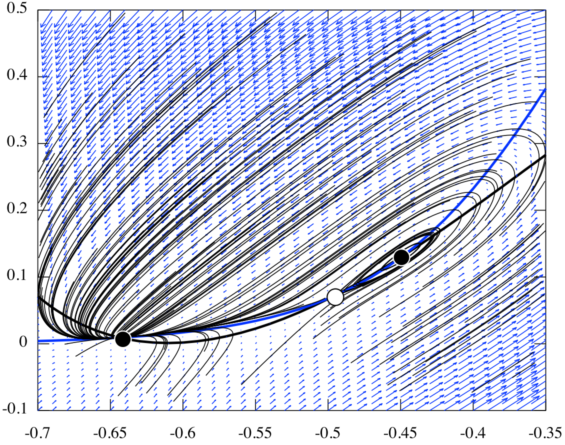

Figure: Phase plane of the $I_{Na,p}$ - I_K model near Bogdanov-Takens bifurcation.

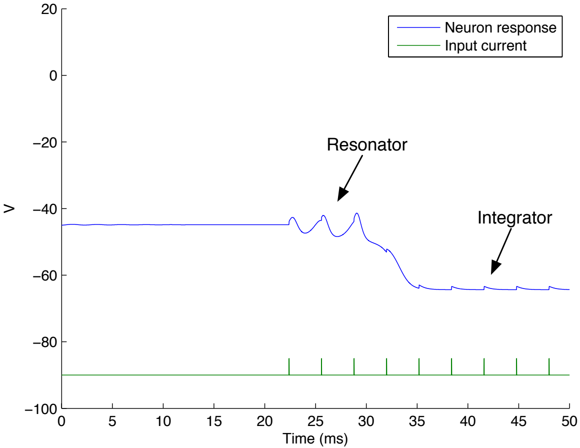

Figure: Transition from resonator to integrator.

Recapitulation

- Neurons can classified based on their frequency/current curve - Hodgkin classes
- A somewhat more useful classification takes into account bi/monostability and the existence of oscillations
- Based on that neurons can be divided into mono/bi stable integrators and resonators
- Bogdanov-Takens bifurcation separates integrators from resonators. Neurons near the bifurcation can exhibit features of both species.
- Saddle-node homoclinic orbit bifurcation separates monostable and bistable integrators.
- Bautin bifurcation separates monostable and bistable resonators.