Achieving robust bistability in spinal pain processing neurons

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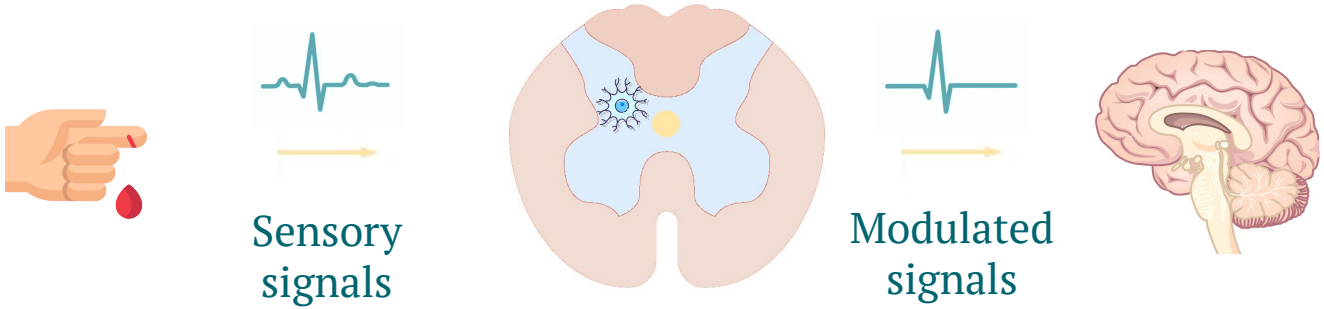
Pain processing starts in the spinal cord



Injury

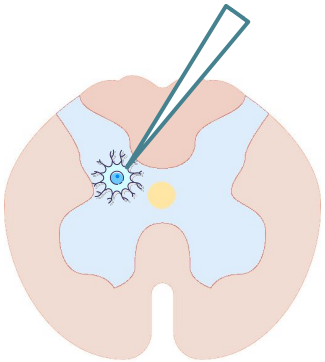
Spinal cord

Brain

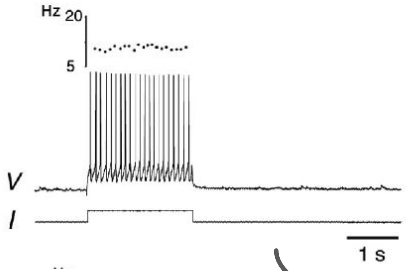
(Bear, 2007)

Spinal pain processing neurons are tunable

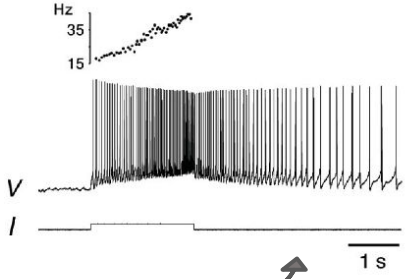
Experimental recordings of projection neurons show that these neurons can adapt their firing properties.



1. Tonic firing



2. Plateau potentials

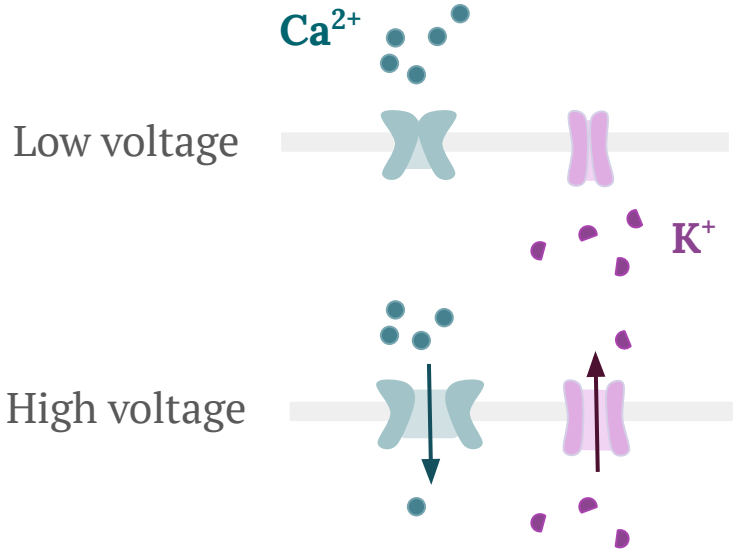


Emerging **bistability**

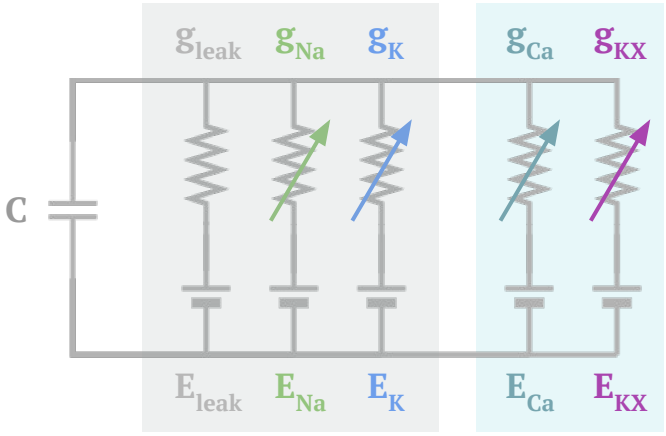
(Derjean et al., 2003)

Bistability depends on the membrane electrical properties

Biological membrane:

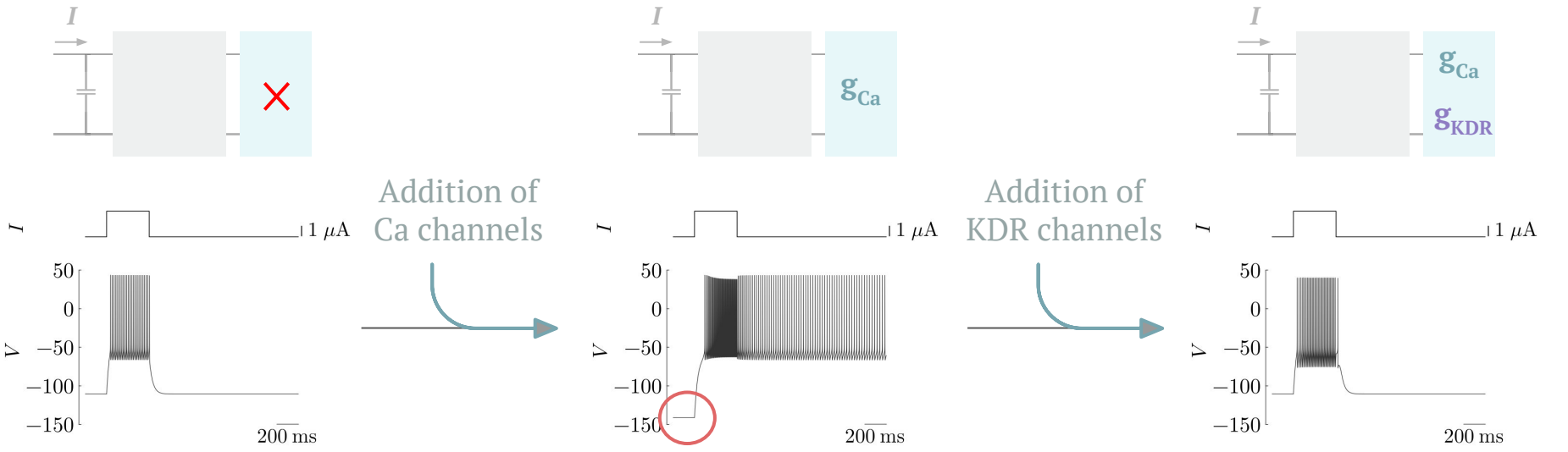


Electrical behavior:



(Hodgkin & Huxley, 1952)

Keys of robust and physiological bistability are unclear



No bistability

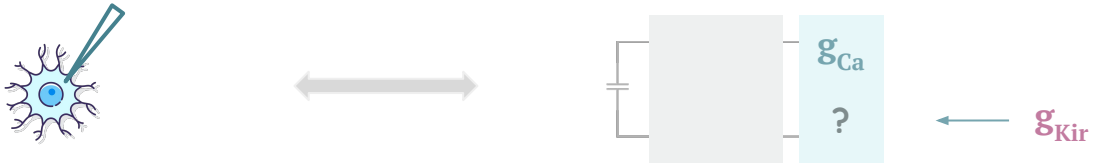
Strong bistability,
but not physiological

Physiological equilibria,
but weak bistability

(Yuen et al., 1995 ; Franci et al., 2013)

How to achieve robust bistability physiologically?

Which channels could combine with Ca channels?



Outline

1. Is robust bistability rescued by Kir channels?
   Comparison between Kir and KM responses

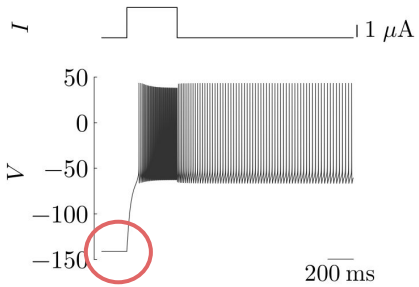
2. What promotes robust bistability?
   Properties of the tunable block channels

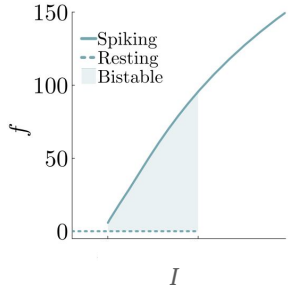
3. How robust is bistability?
   Analysis of responses to perturbations

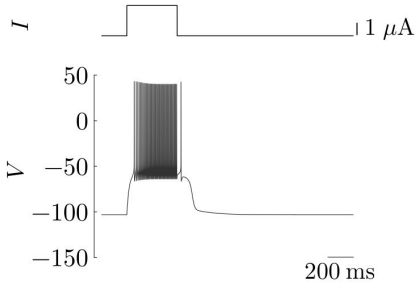
KM channels weaken Ca channels bistability

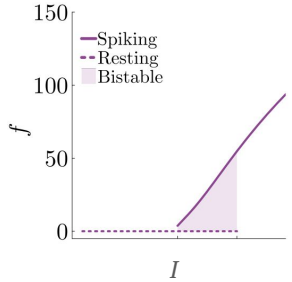
Pulse of current:

Constant current:

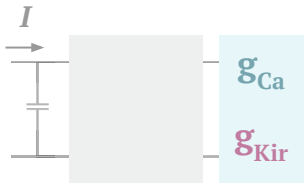




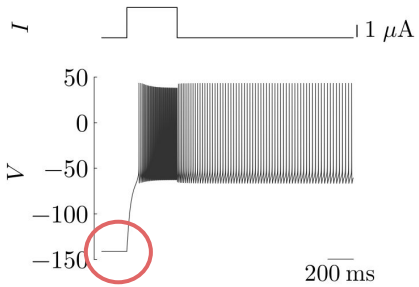


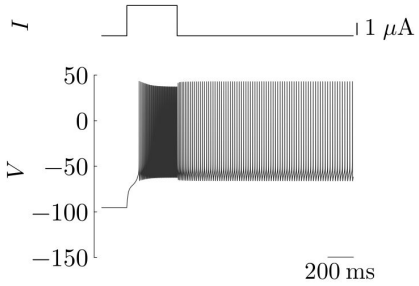


Kir channels maintain Ca channels bistability

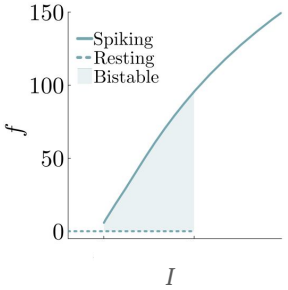


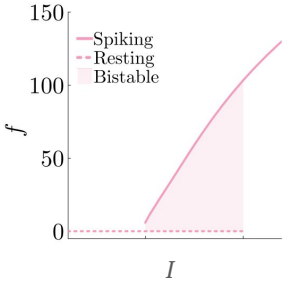
Pulse of current:



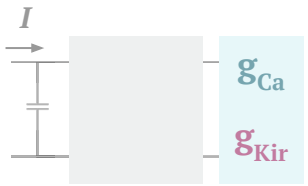


Constant current:





Kir & KM channels have opposite effect on bistability



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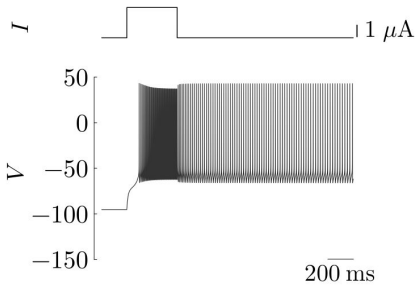
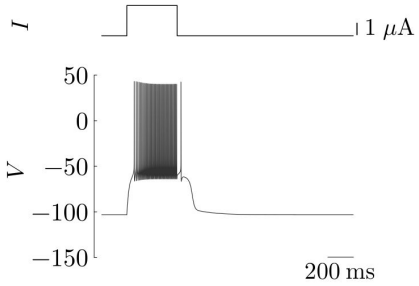
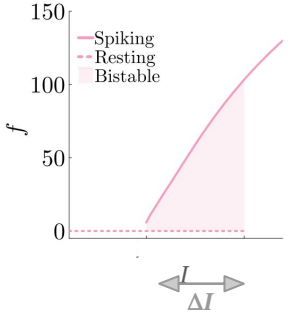
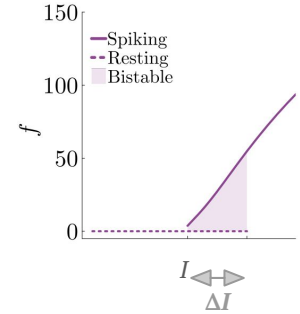


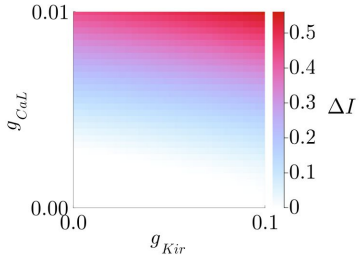


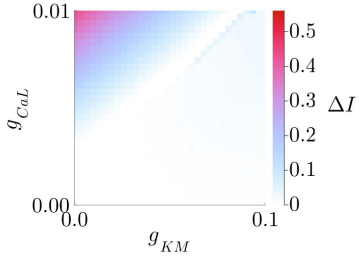
Constant current:



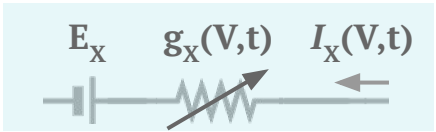


Level of bistability:





Steady-state properties of the tunable block of channels



Contribution: $C\dot{V} = -\sum I_X(V,t) + I$

Steady-state current: $I_{X,ss}(V) = g_{X,ss}(V) \cdot (V - E_X)$

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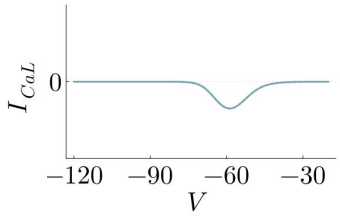
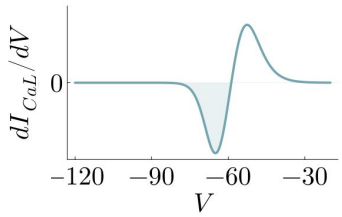
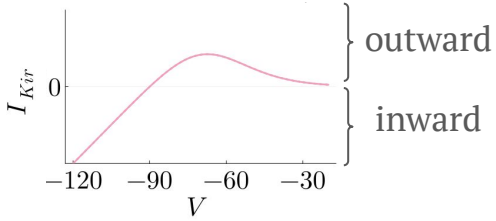
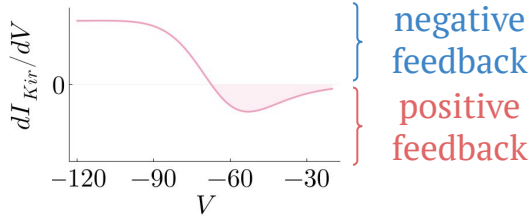
g_{Ca}



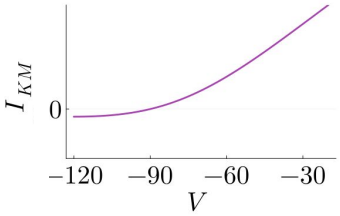


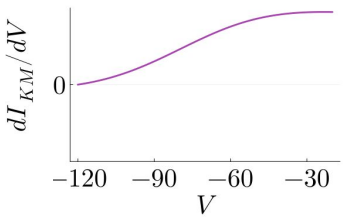
g_{Kir}



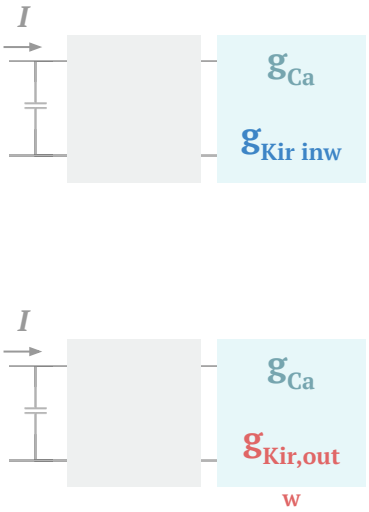


g_{KM}

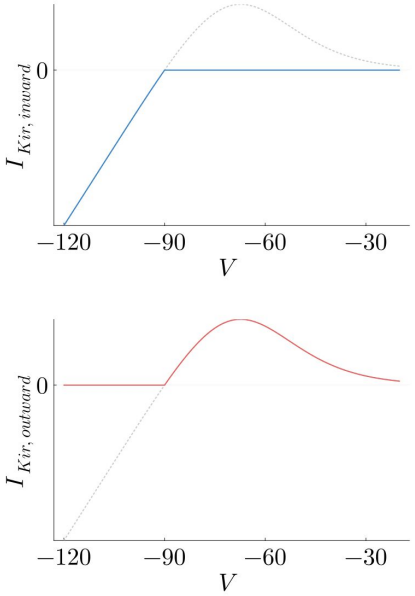




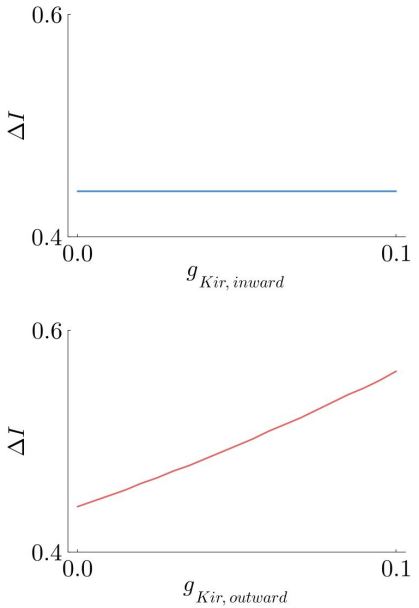
Local positive feedback promotes bistability



Modified channels steady-state current:



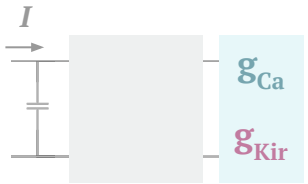
Level of bistability:

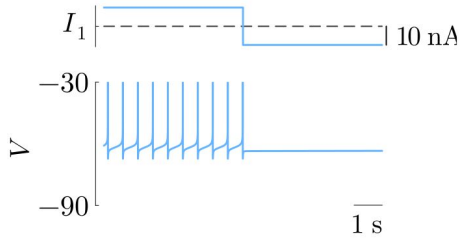


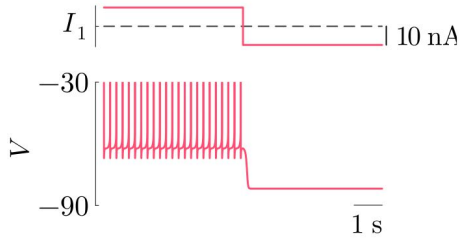
Bistability is achieved by modifying a SNIC bifurcation

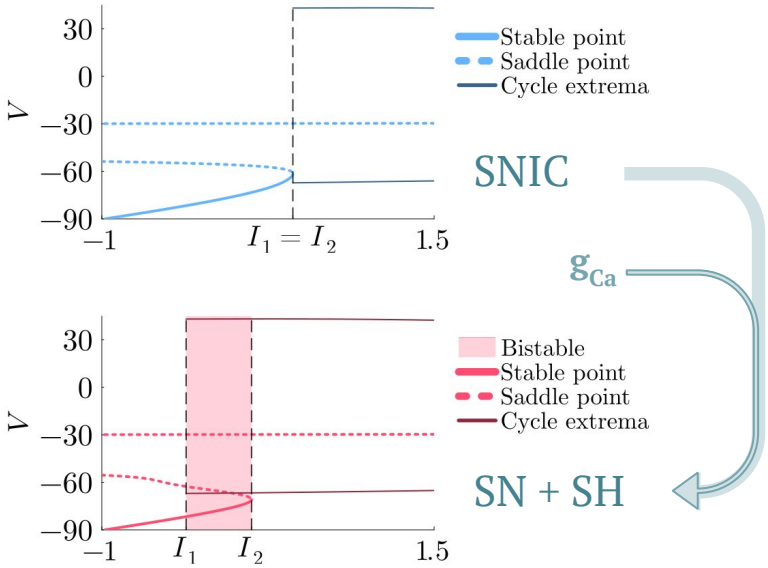
Step of current:

Bifurcation diagram:



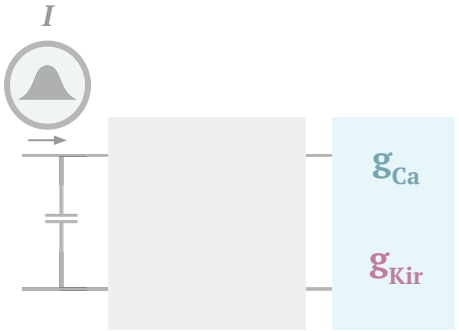




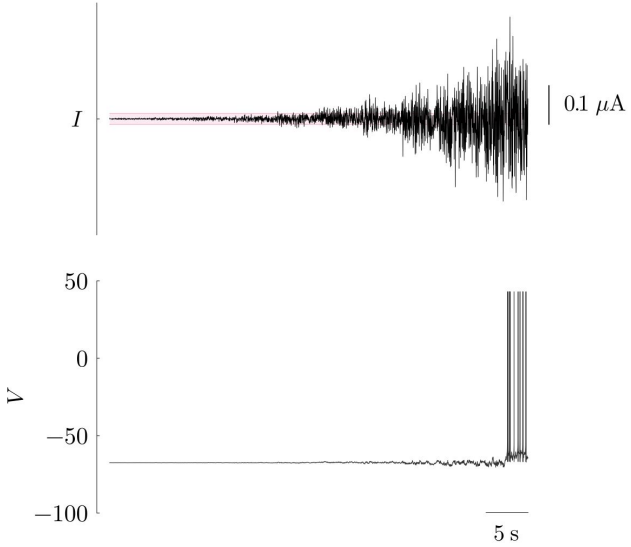


High robustness to noise in the bistability window

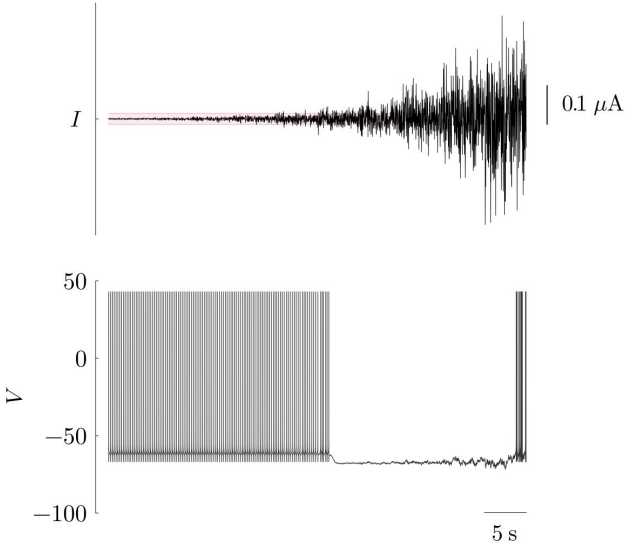
Gaussian noise superimposed on the center current of the bistability window



Initially resting



Initially spiking



Conclusion

Robust bistability can be created physiologically through local positive feedback, by combining Kir channels and Ca channels.

This pathway might be the target of modulatory mechanisms to adapt the firing properties of spinal pain processing neurons.

Future works

Analyze the mechanisms leading to a difference in robustness of the two behaviors in a reduced model.