Relay feedback models of biological oscillators

Rajiv Kurien

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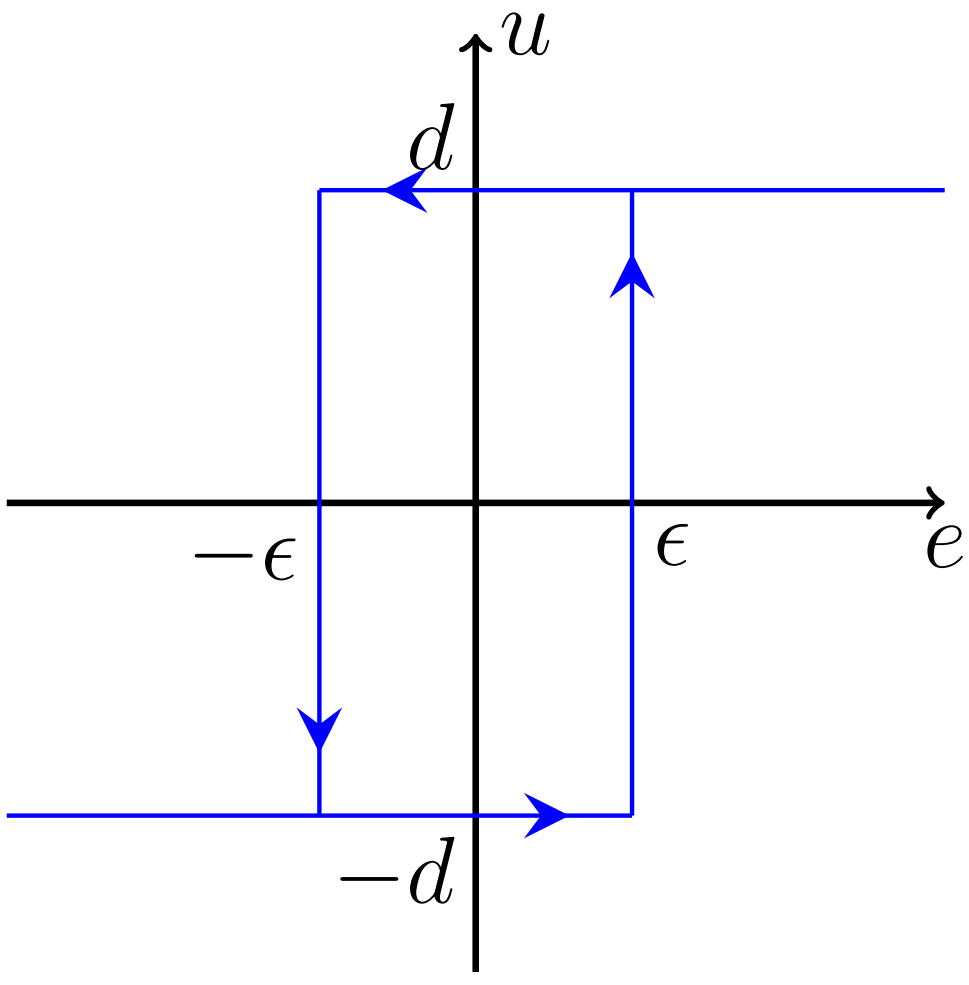
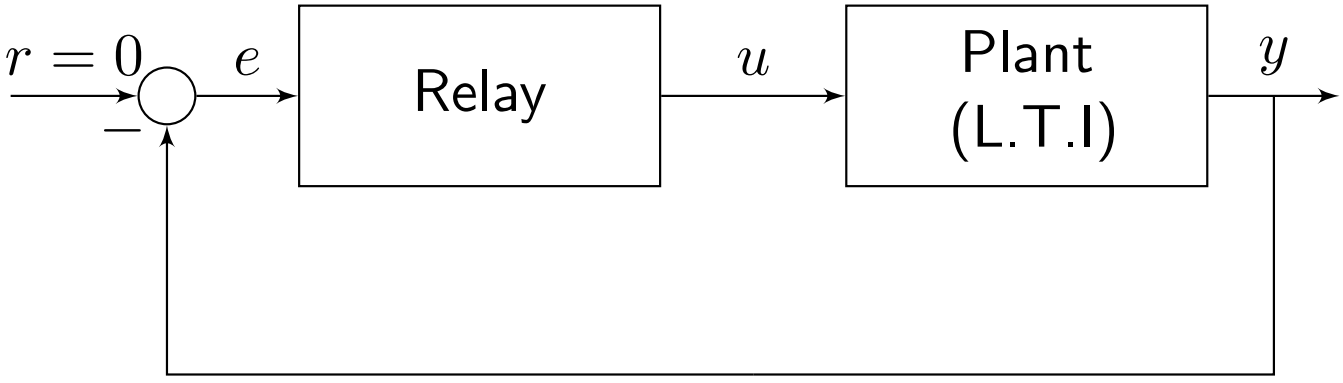
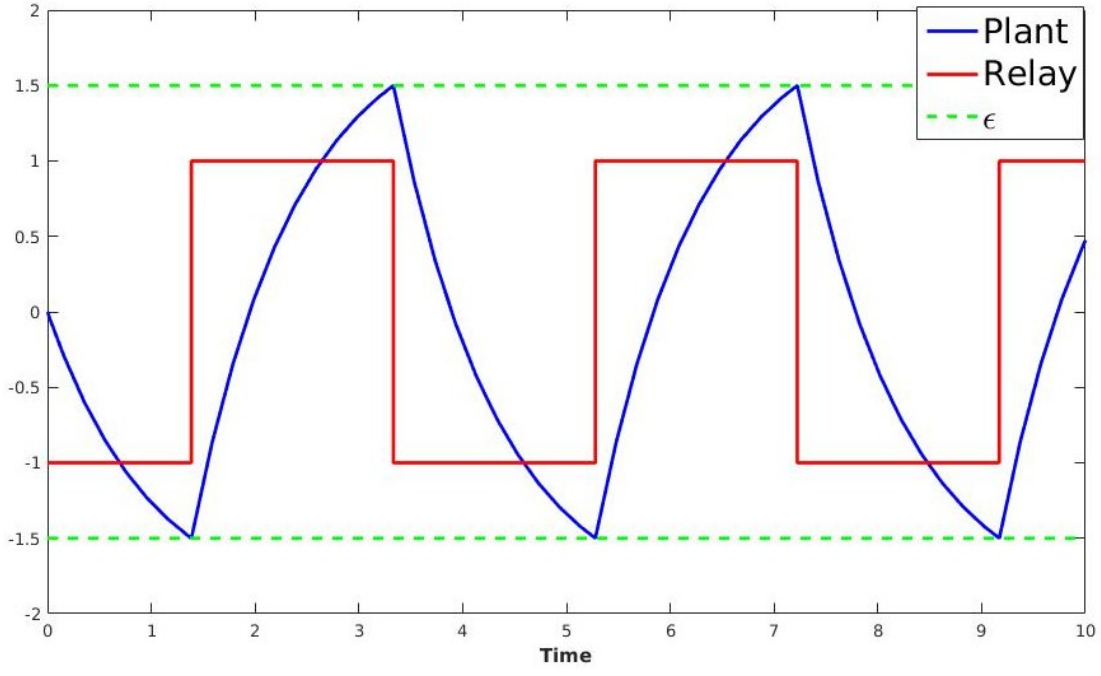
Relay



Relay feedback



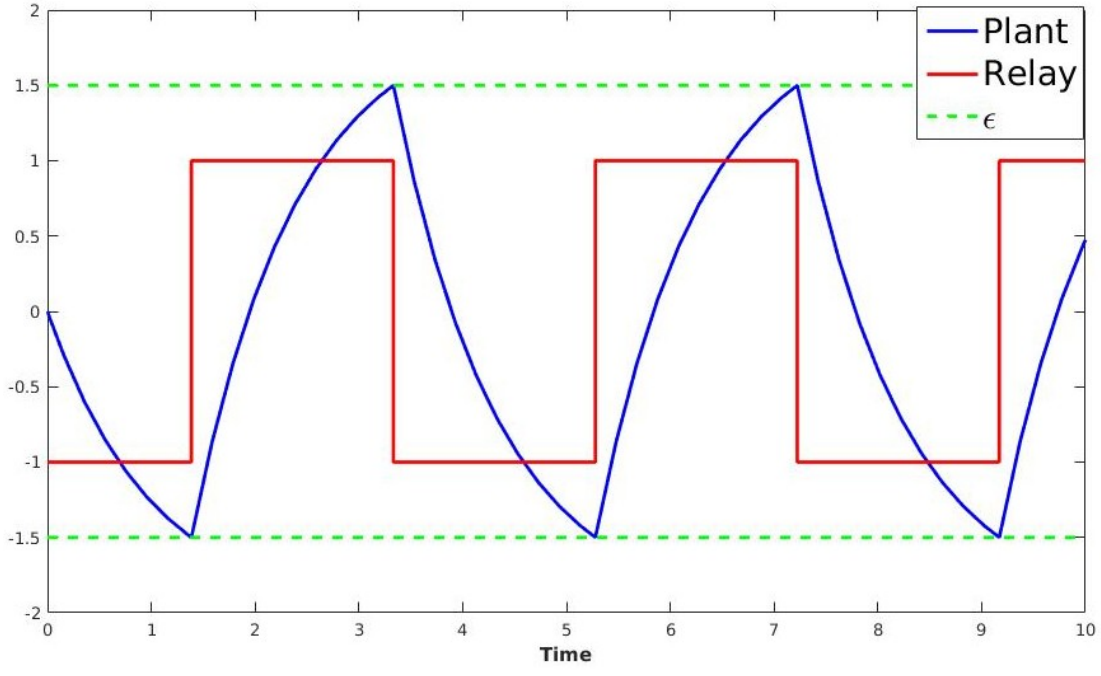


Oscillations in relay feedback systems

Åström. *Oscillations in systems with relay feedback.* (1995)

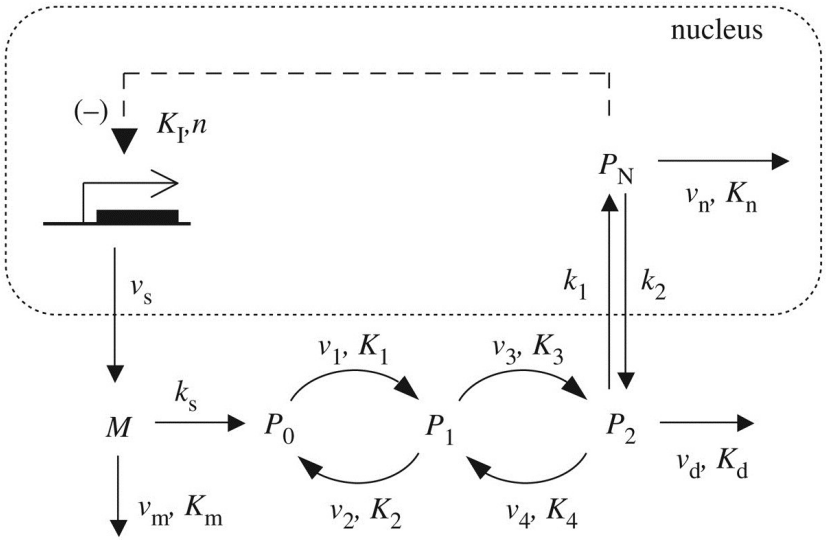
Analytical solutions for:

- Time period of oscillations
- Stability of oscillations
- Initial conditions for oscillations



Models of biological oscillations

Goldbeter. *A model for circadian oscillations in the Drosophila period protein*. (1995)



$$\frac{dM}{dt} = v_s \frac{K_I^n}{K_I^n + P_N^n} - v_m \frac{M}{K_m + M}$$

$$\frac{dP_0}{dt} = k_s M - v_1 \frac{P_0}{K_1 + P_0} + v_2 \frac{P_1}{K_2 + P_1}$$

$$\frac{dP_1}{dt} = v_1 \frac{P_0}{K_1 + P_0} - v_2 \frac{P_1}{K_2 + P_1} - v_3 \frac{P_1}{K_3 + P_1} + v_4 \frac{P_2}{K_4 + P_2}$$

$$\frac{dP_2}{dt} = v_3 \frac{P_1}{K_3 + P_1} - v_4 \frac{P_2}{K_4 + P_2} - v_d \frac{P_2}{K_d + P_2} - k_1 P_2 + k_2 P_N$$

$$\frac{dP_N}{dt} = k_1 P_2 - k_2 P_N - v_n \frac{P_N}{K_n + P_N}$$

Models of biological oscillations

- Difficult to analyse oscillations
- Tuning of parameters
- Relay feedback framework

Are relay feedback models appropriate to analyse biological oscillations?

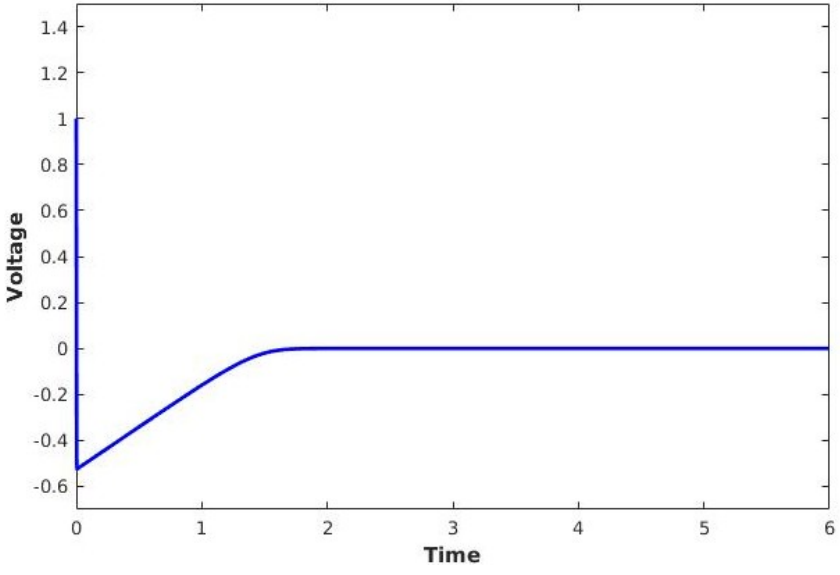
Project outline

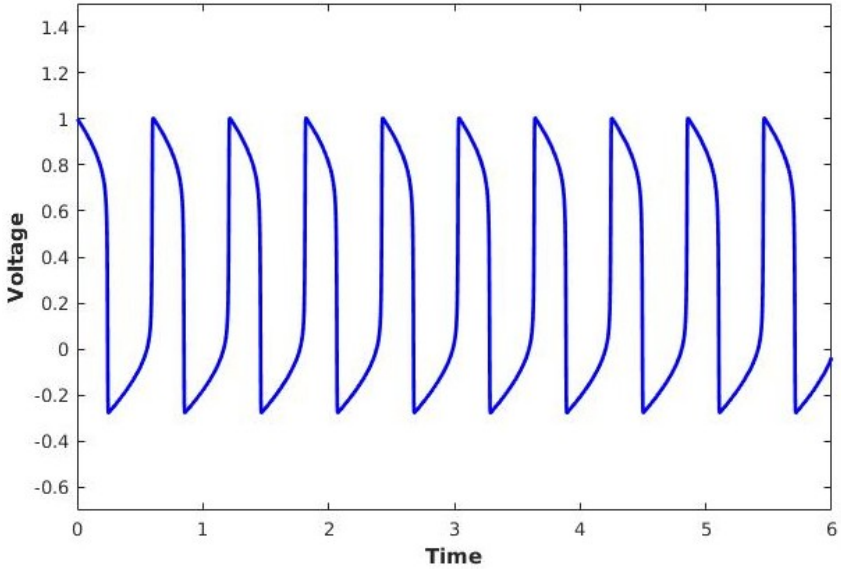
Are relay feedback models appropriate to analyse biological oscillations?

- Simple oscillations
  - Goodwin Oscillator model for circadian rhythms
  - FitzHugh-Nagumo model for action potentials
- Complex oscillations
  - Bursting normal form
  - Hindmarsh-Rose model for bursting

FitzHugh-Nagumo (1961)

- Action potential in a neuron
- Hodgkin-Huxley simplified to two variables
- Excitable system

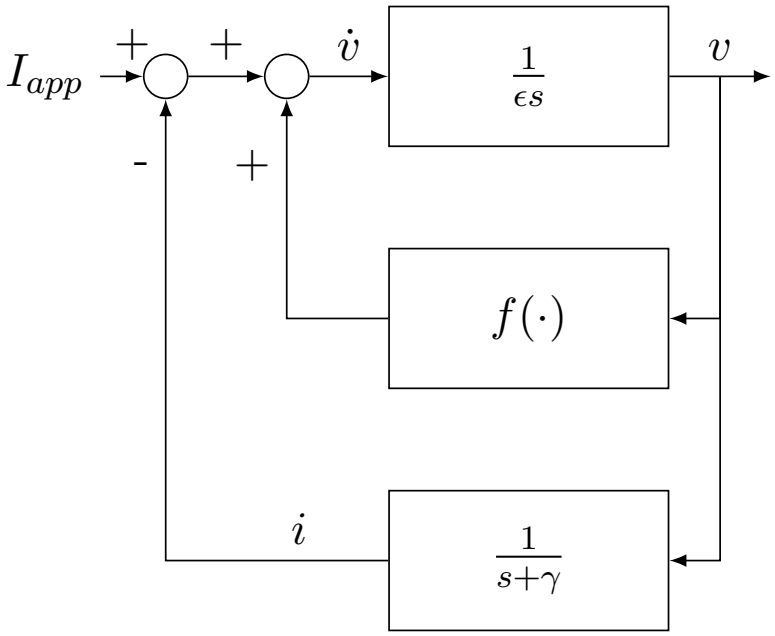




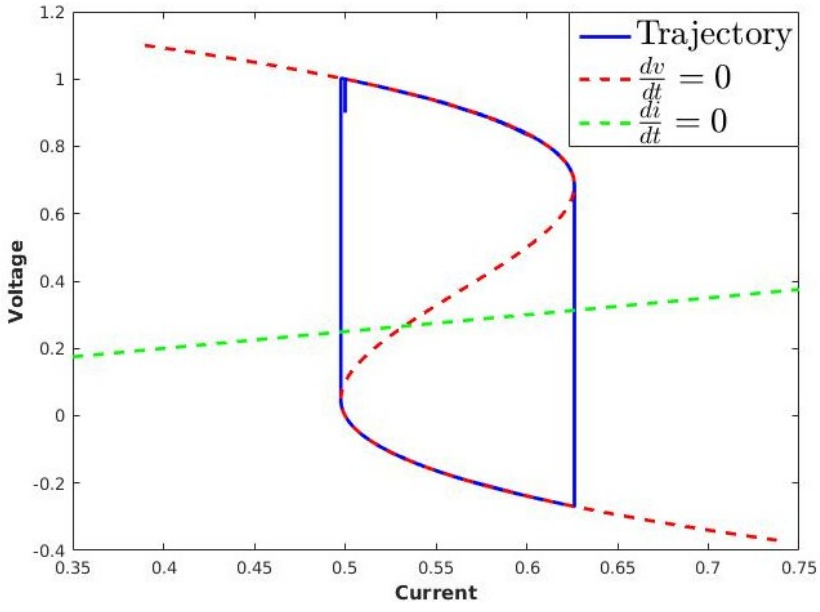
FitzHugh-Nagumo (1961)

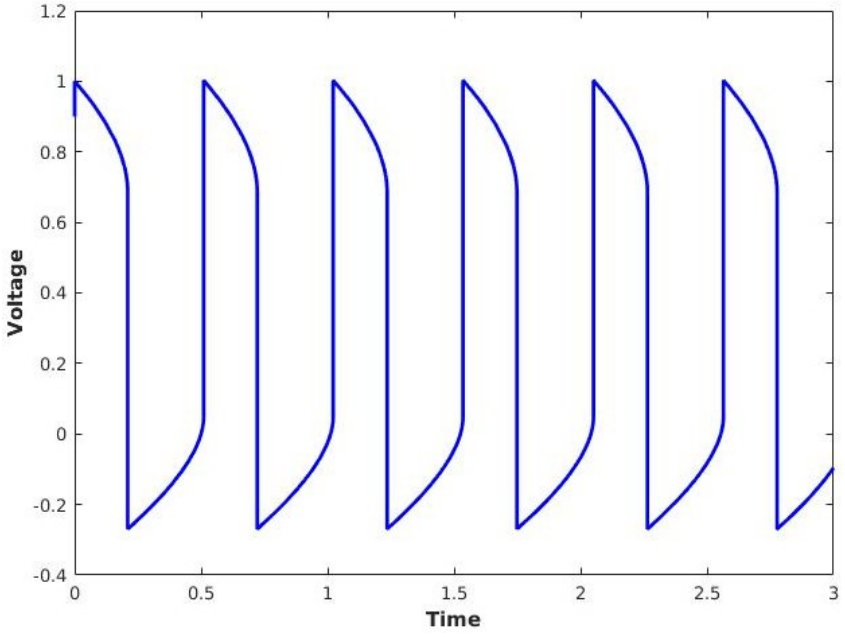
Voltage $$\epsilon \frac{dv}{dt} = f(v) - i + I_{\text{app}}$$

Current $$\frac{di}{dt} = v - \gamma i$$

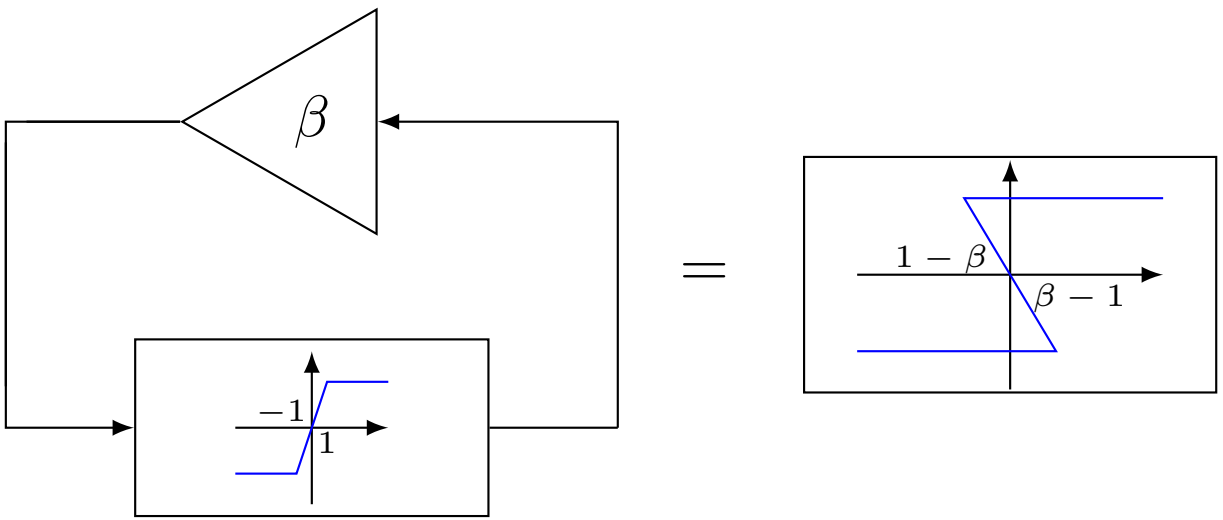


FitzHugh-Nagumo

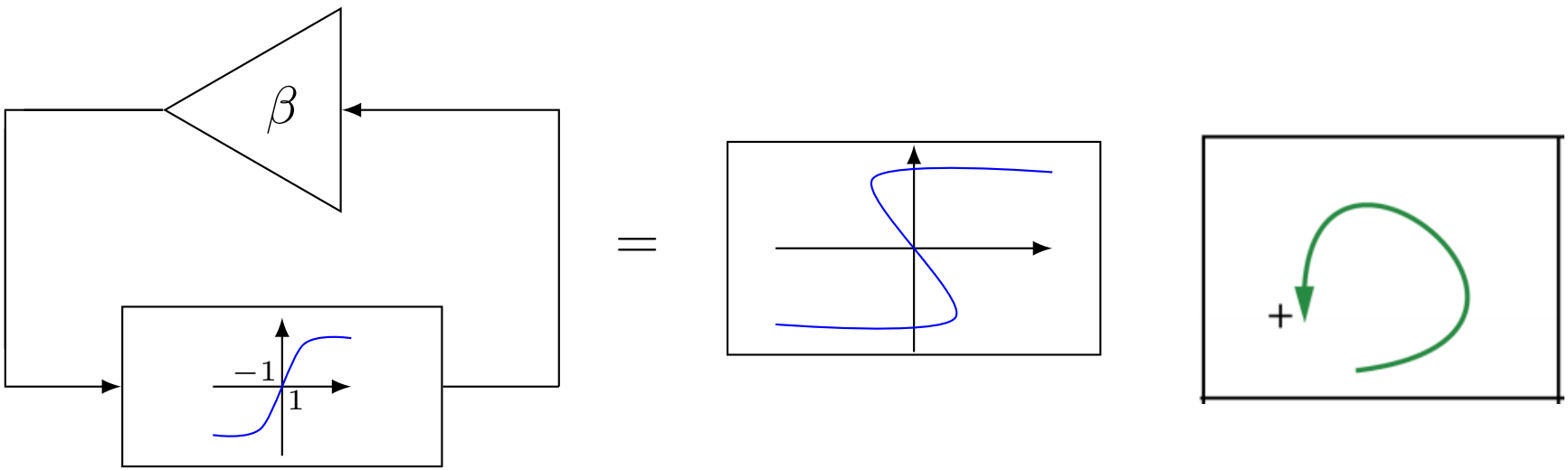




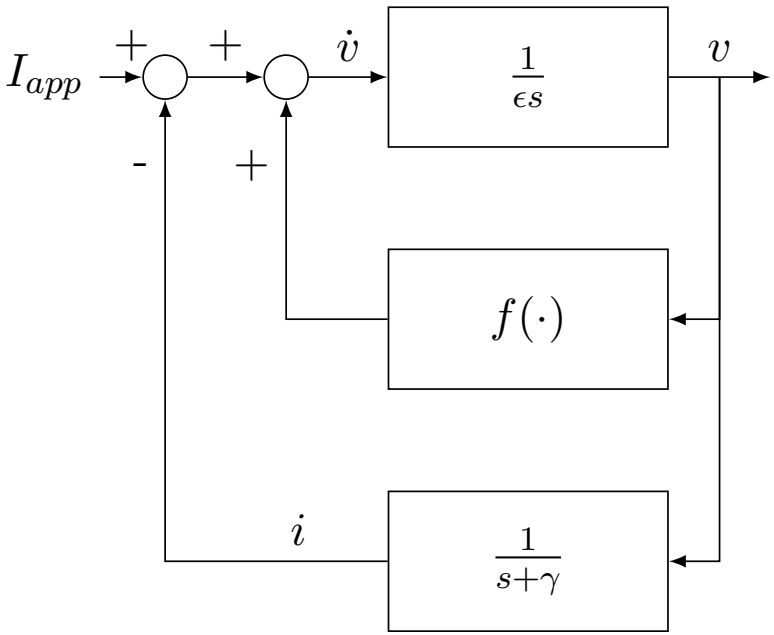
Positive feedback

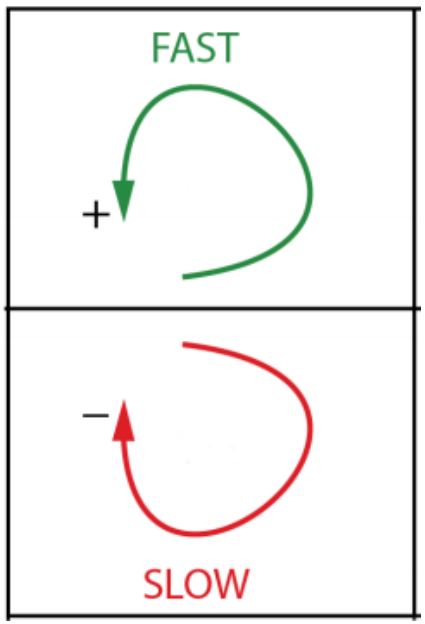


Positive feedback

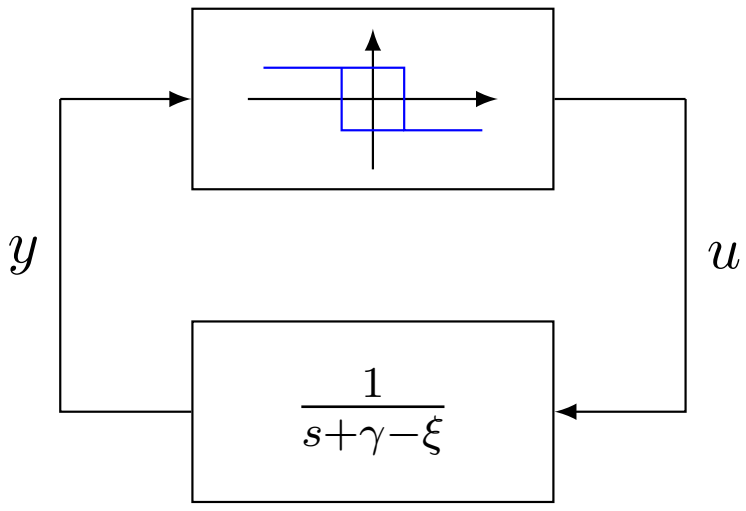


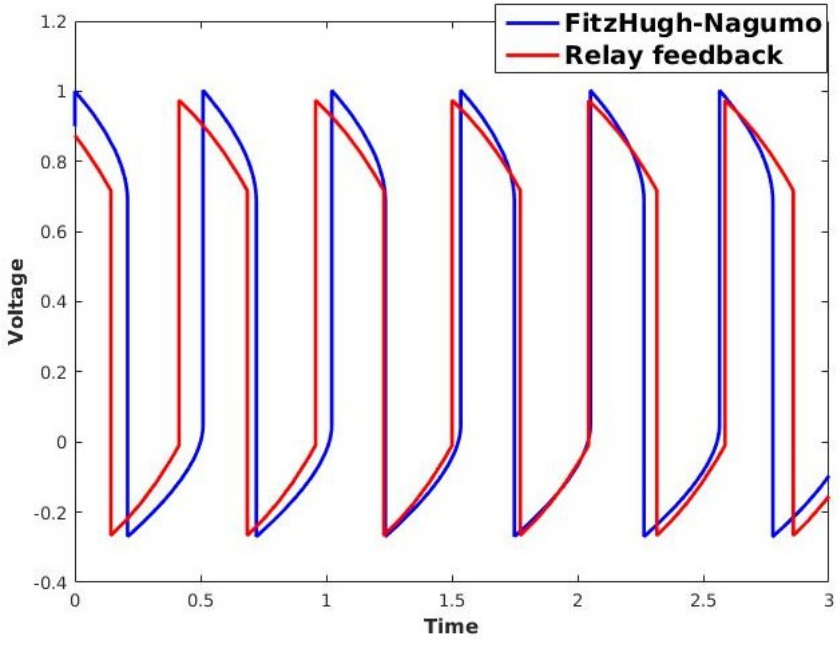
Separation of timescales



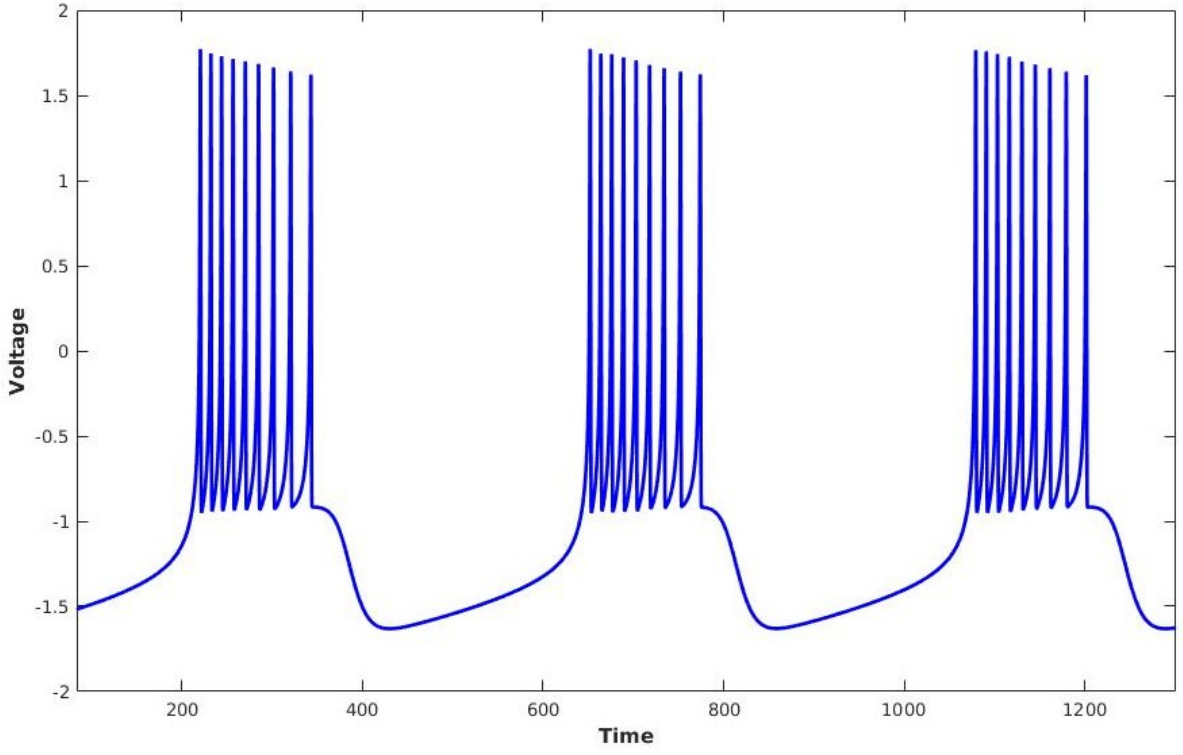


FitzHugh-Nagumo and Relay feedback



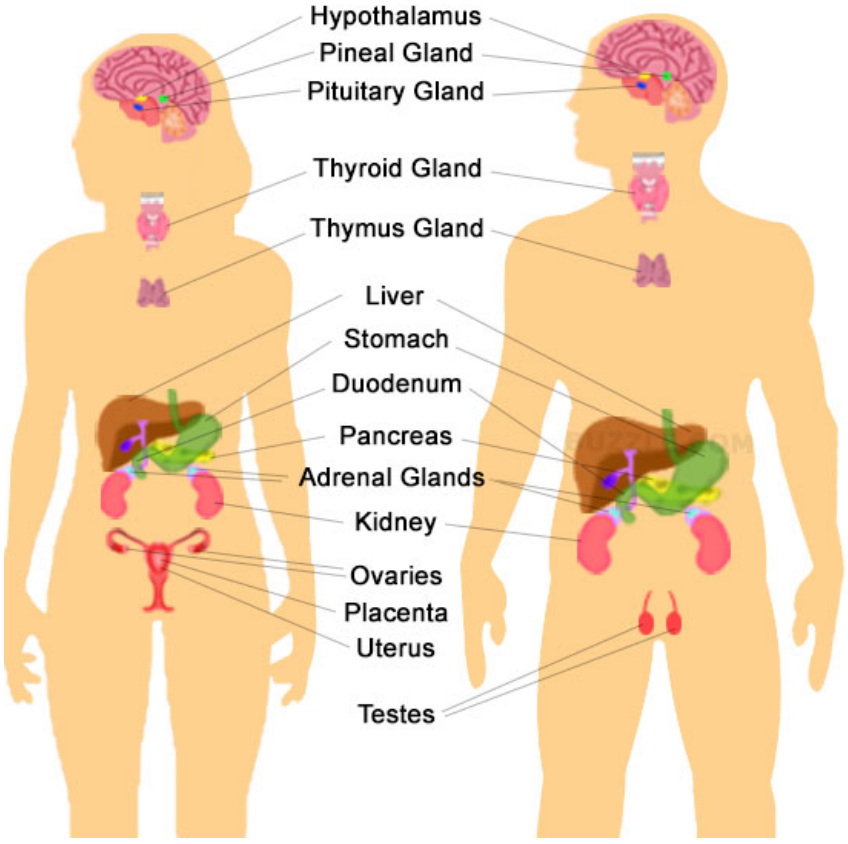


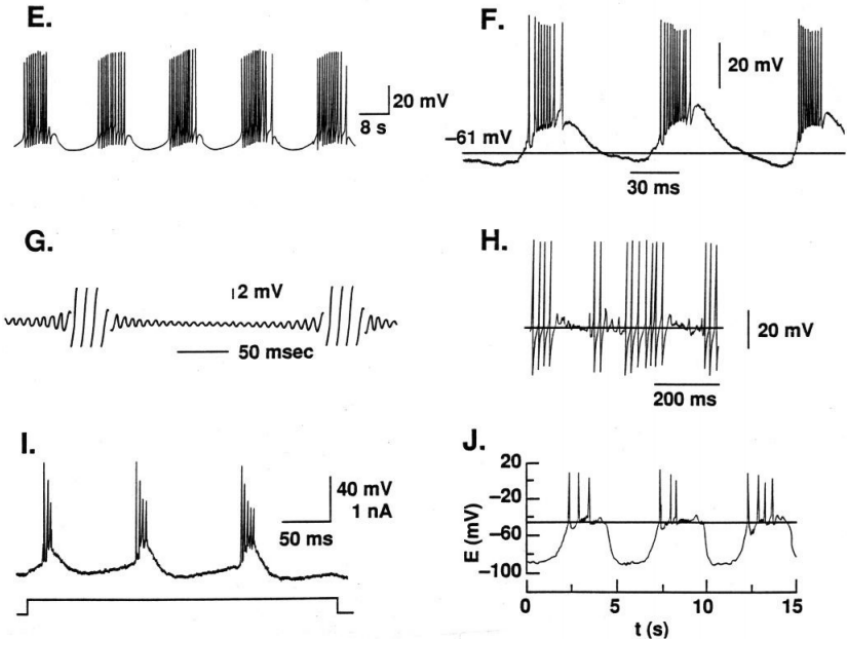
Bursting



Bursting

- Important role in signalling mechanisms
- Neuroendocrine cells and nerve cells
- Very few tools to analyse bursting

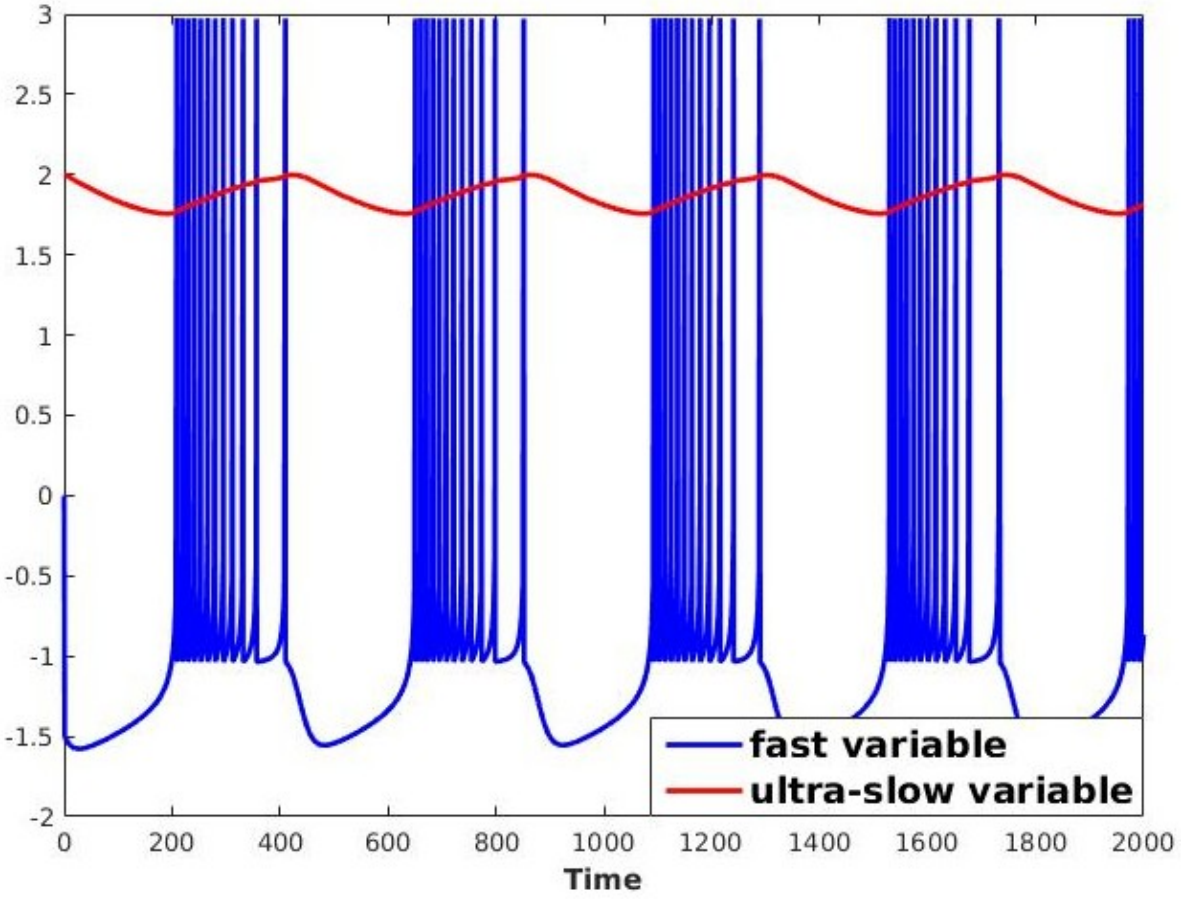




Bursting

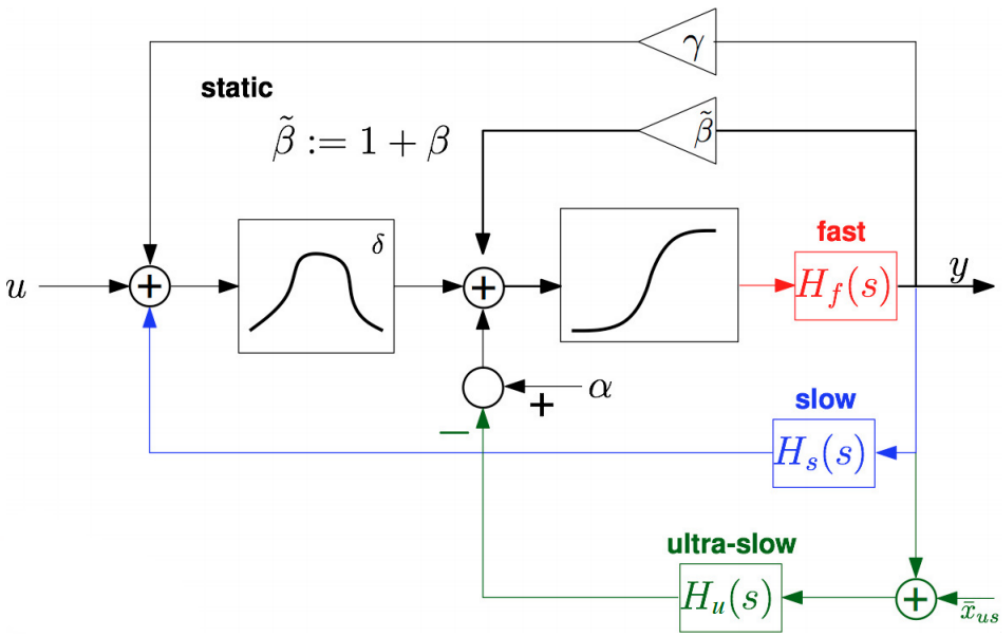
Three variables and three time-scales

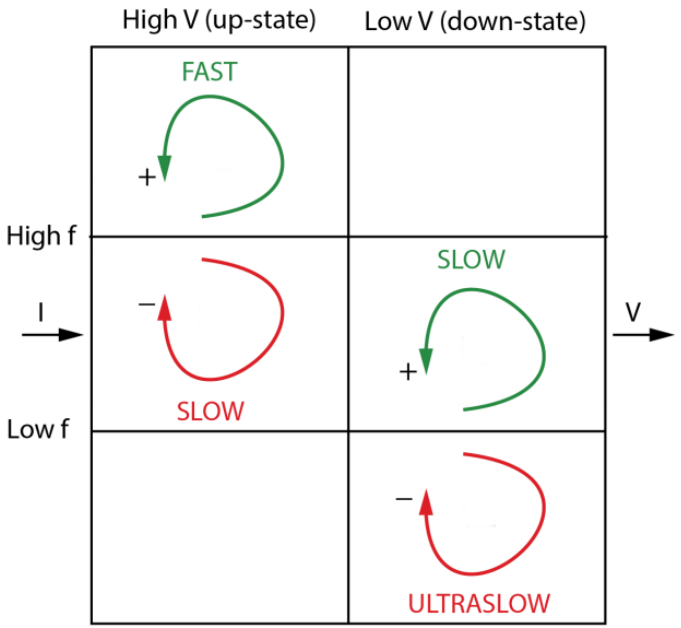
- Like FitzHugh-Nagumo, but with third (ultra-slow) state
- Ultra slow process modulates the fast processes



A bursting normal form

Franci and Sepulchre. *Realization of nonlinear behaviours from organizing centers.* (2014)
Drion et al. *Neuoronal behaviors: a control perspective.* (2015)





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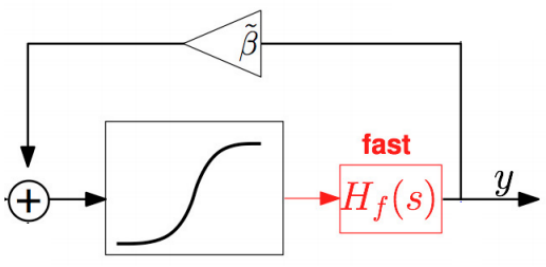

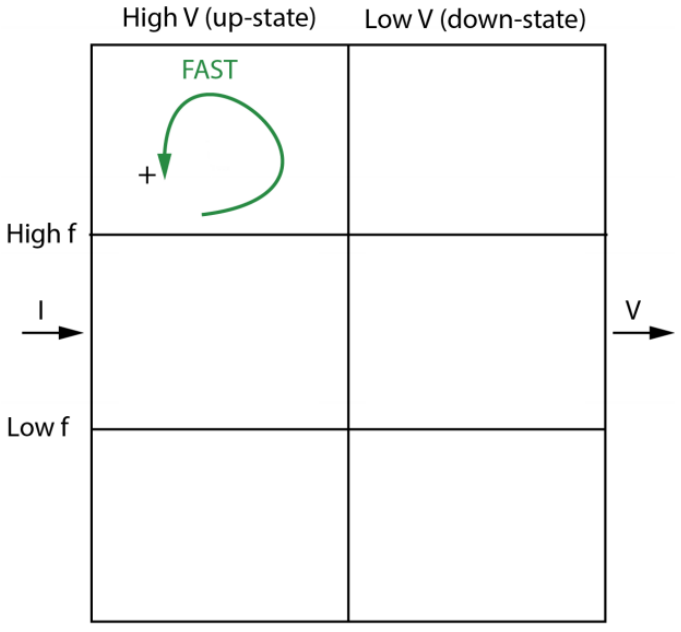

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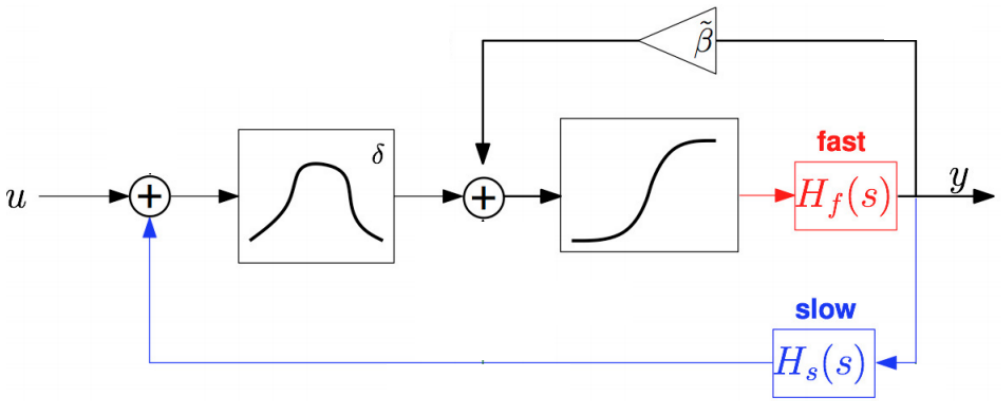

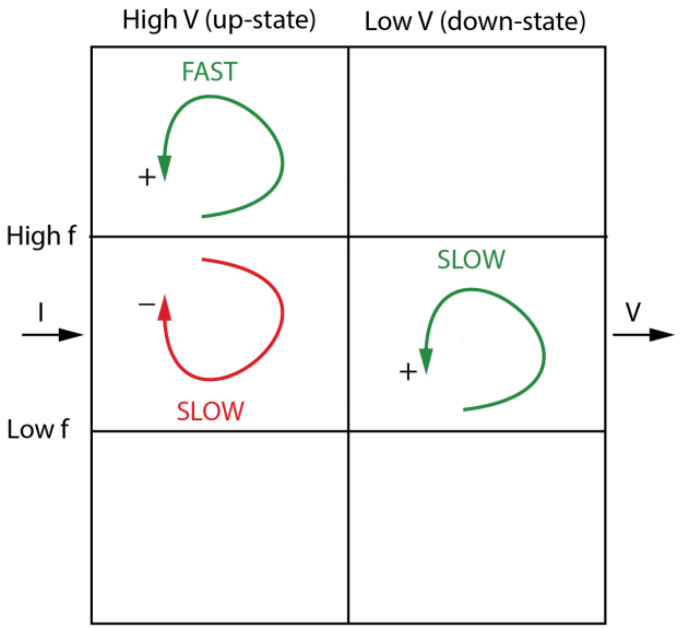

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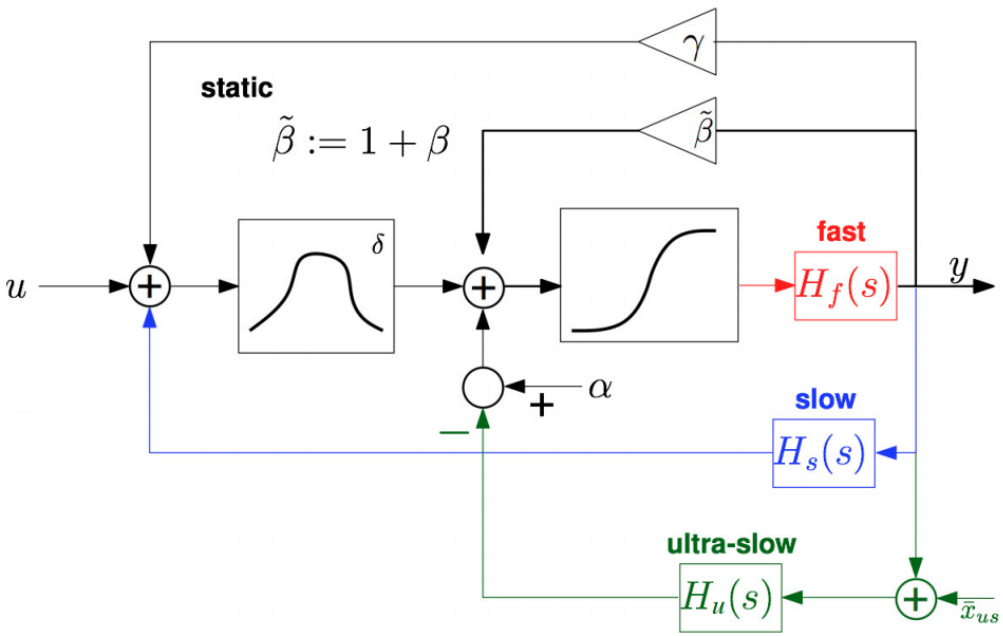
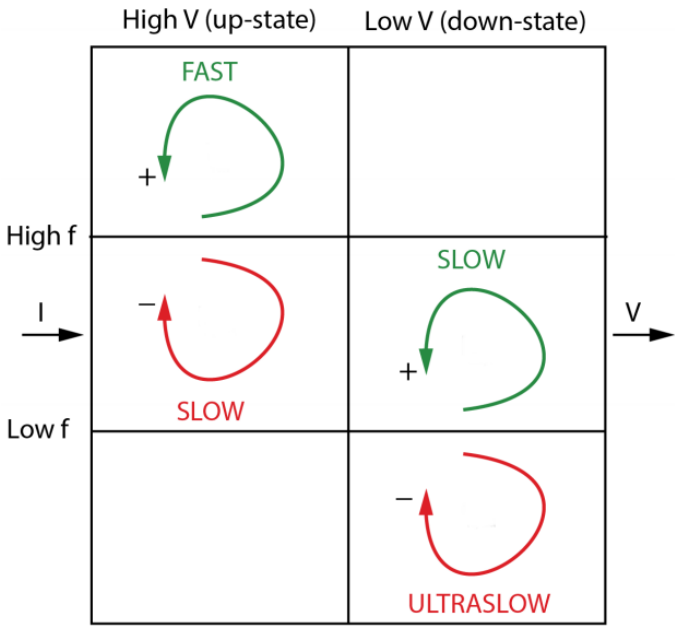
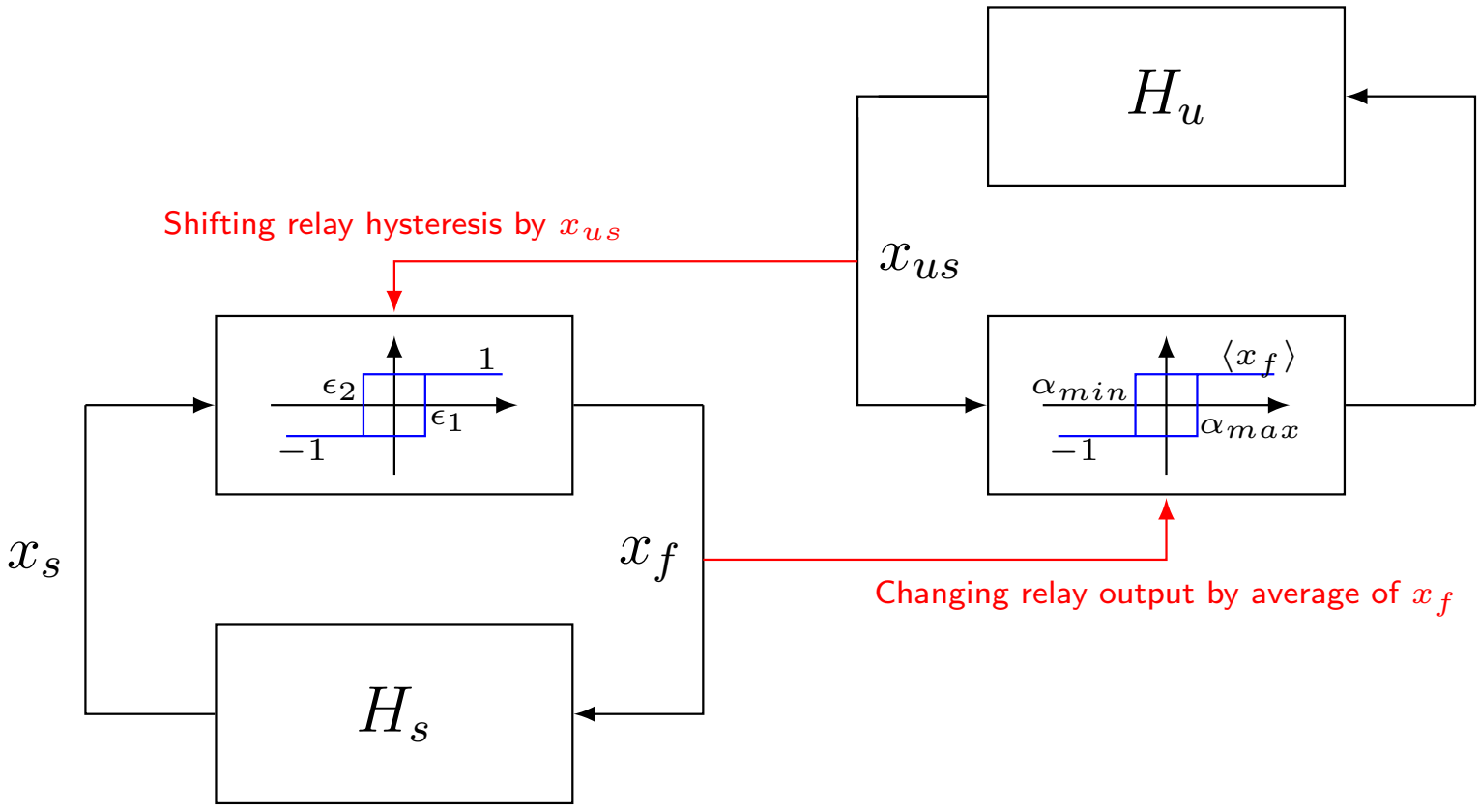




Bursting and Relay feedback



Conclusions

- Modelled simple oscillations using relay feedback
  - Goodwin oscillator model
  - FitzHugh-Nagumo model
- Modelled a complex oscillation using relay feedback
  - Bursting normal form model
  - Hindmarsh-Rose model
- Appealing framework
  - Tractable in high dimensions $\rightarrow$ excitable systems
  - Predict stability, time periods, initial conditions