A cellular mechanism makes switches in brain states compatible with synaptic plasticity

Kathleen Coutisse, Guillaume Drion

Department of Electrical Engineering and Computer Science, University of Liege, Liege, Belgium

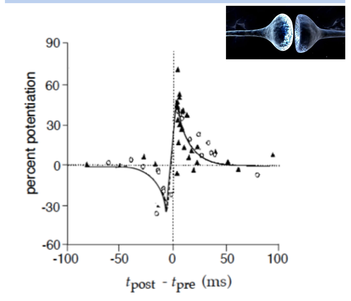
III-9

Contacts

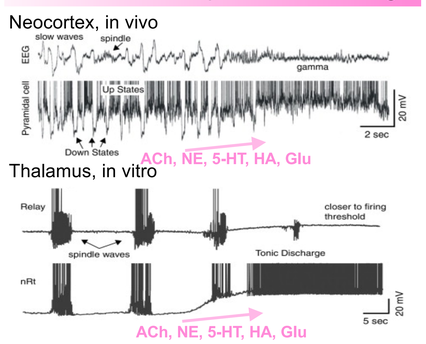
kathleen.coutisse@uliege.be

gdrion@uliege.be

Synaptic plasticity



Slow-wave sleep Waking



How can switches in brain states be compatible with synaptic plasticity?

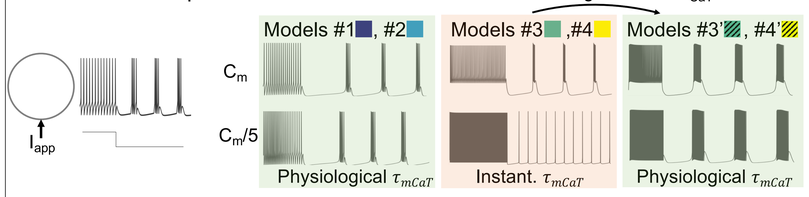
We compare 4 different conductance-based models of thalamic neurons composed of a similar number of ionic currents but with a different T-type calcium channel activation (m_{CaT}) : $C_m \dot{V}_m = - I_{Na} - I_K - \boxed{I_{CaT}} - I_{others}$

Slow activation CaT channels (m_{CaT})
Model #1 Drion et al.2018
Model #2 Destexhe et al.1996
Model #3' Rush + slow mCaT
Model #4' Wang + slow mCaT

Instant. activation CaT channels
Model #3 Rush 1994
Model #4 Wang 1994

CELLULAR LEVEL

Models with slow activation of T-type calcium channels are robust to change in the membrane capacitance.

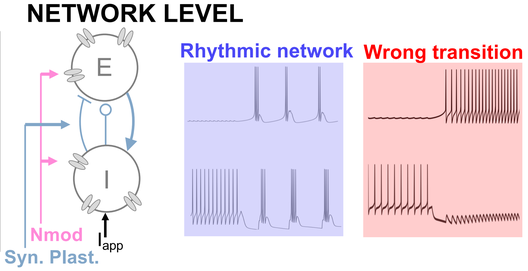


NETWORK LEVEL

Intrinsic conductances
g_{Na}, g_K, g_{CaT}, g_{others}

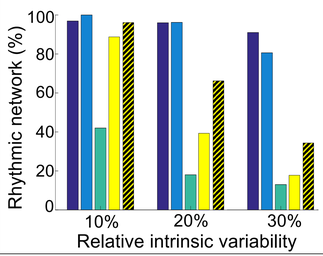
Synaptic conductances
g_{AMPA} g_{GABAa} g_{GABAb}

Relative intrinsic variability
$\tilde{g} \in [(1-\gamma)g; (1+\gamma)g]$

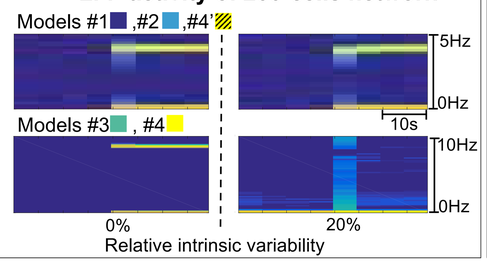


For an increasing variability, models with a slow activation of T-type calcium channels are robust to change in neuron intrinsic properties (max. conductances), mimicking the effect of neuromodulation, and changes in synaptic weights, mimicking the effect of synaptic plasticity. While, models with an instantaneous activation are no more able to systematically reproduce a rhythmic network.

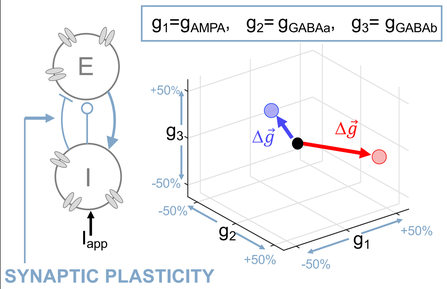
2-cell network

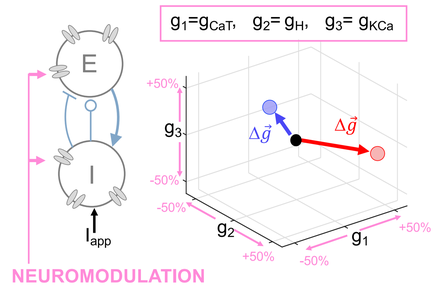


LFP activity of 200-cells network

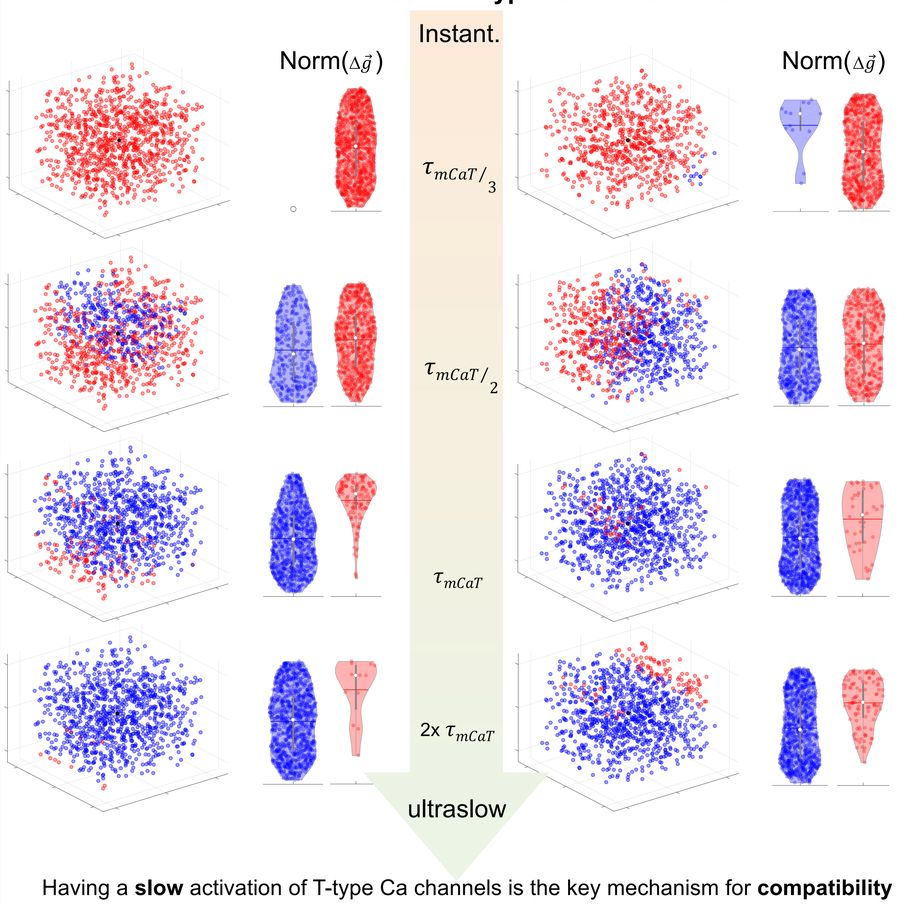


In **Model #1**, we study the influence of the **kinetics** of T-type calcium channel activation on the model robustness when it is subjected either to synaptic plasticity or to neuromodulation. A 2-cell network is simulated for 1000 different triplets of conductances either synaptic conductances (g_{AMPA}, g_{GABAa}, g_{GABAb}) to test to the synaptic plasticity or maximum conductances to test the neuromodulation (g_{CaT}, g_H, g_{KCa})





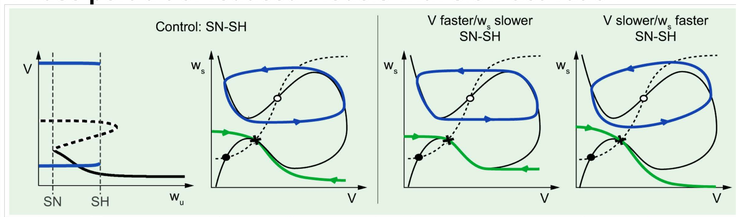
Activation kinetics of T-type calcium channels



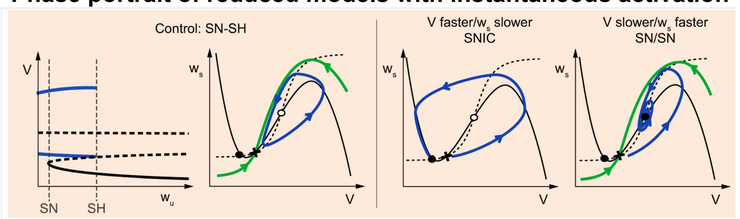
Having a **slow** activation of T-type Ca channels is the key mechanism for **compatibility** between **brain states**, **synaptic plasticity** and **neuromodulation**.

The phase portrait of reduced models with slow activation of T-type calcium channels (top) exhibits a lower branch inexistent in classical phase portrait. This characteristics ensures the model robustness across a broad range of variations.

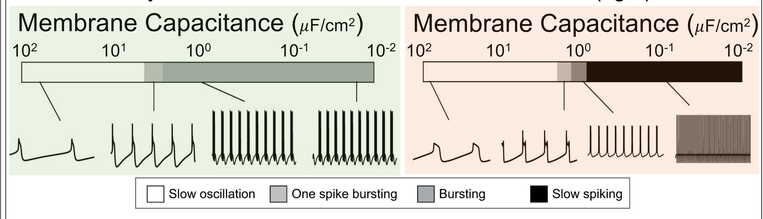
Phase portrait of reduced models with slow activation



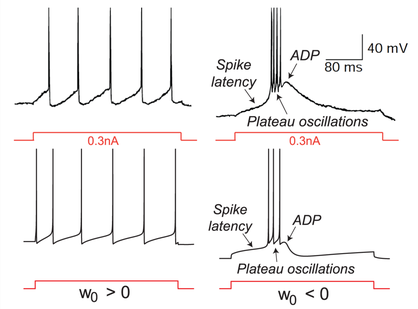
Phase portrait of reduced models with instantaneous activation



Bursting only persists in a tiny window around the nominal published value for model with instantaneous activation (left) while the capacitance can reach arbitrary small values for models with slow activation (right).



Hybrid model responding to phase portrait including slow activation of CaT channels, called **transcritical hybrid model**, can be used to **model thalamic neuron.** (top) Experimental trace of thalamic neuron in vitro and (bottom) hybrid mode reproducing spiking and bursting



Classical hybrid model

$\dot{V} = V^2 - w + I$

Transcritical hybrid model

$\dot{V} = V^2 - w^2 + I$

$\dot{w} = \varepsilon(aV - w + w_0)$

SUMMARY

- ✓ **Modeling switches in brain states compatible with synaptic plasticity and neuromodulation relies on the presence of a slow calcium current activation.**
- ✓ **Models without this cellular property are fragile to change in parameters.**
- ✓ **This key mechanism can be embedded in hybrid neuron model without increasing the model complexity.**

REFERENCES

Abbott LF, Nelson SB. Synaptic plasticity: taming the beast. Nature neuroscience, 2000.

Zagha E, McCormick DA. Neural control of brain state. Curr Opin Neurobiol, 2014.

G. Drion, A. Franci, R. Sepulchre. Cellular switches orchestrate rhythmic circuits. Biol Cybernetics, 2018.

Destexhe A, Contreras D, Steriade M, Sejnowski TJ, Huguenard JR. In vivo, in vitro and computational analysis of dendritic calcium currents in thalamic reticular neurons.J Neurosci, 1996

Wang XJ. Multiple dynamical modes of thalamic relay neurons: rhythmic bursting and intermittent phase-locking. Neuroscience, 1994.

Rush M., Rinzel J. Analysis of bursting in a thalamic neuron model. Biological Cybernetics, 1994.

Franci A., Drion G., Sepulchre R. Robust and tunable bursting requires slow positive feedback. J Neurophysiol, 2018.

Drion G., Franci A., Seutin V., Sepulchre, R. A novel phase portrait for neuronal excitability. Plos one,2012.