Neuromodulation and Homeostasis: Complementary Mechanisms in Ion Channel Expression Adaptation for Robust Neural Function

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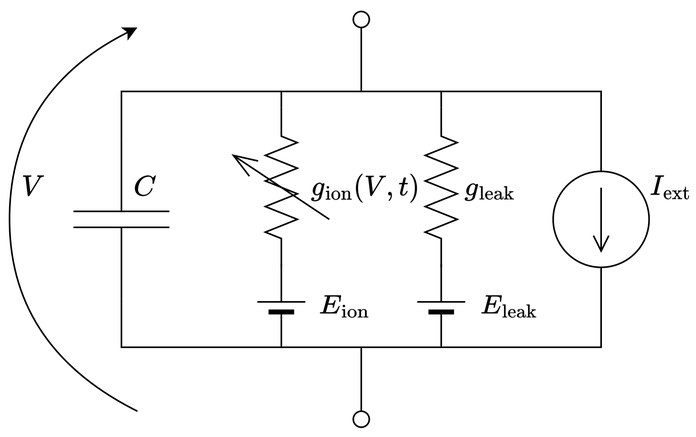
Introduction and context

Neurons and circuits:

- undergo significant changes in their firing patterns and responsiveness to external stimuli through the process of **neuromodulation**.
- possess an extraordinary ability to regulate and sustain their electrical signaling properties in the face of various disruptions through the mechanism of **homeostatic regulation**.

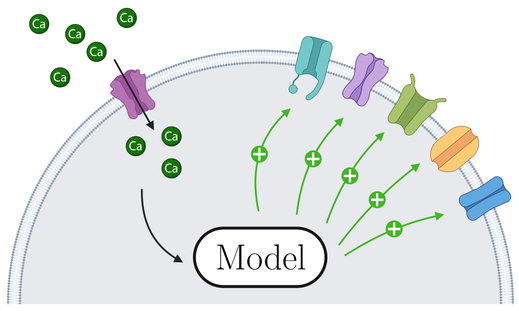
This study seeks to understand the mechanisms behind the robust interaction between neuromodulation and homeostasis in a computational framework.
$\longrightarrow$ realized on stomatogastric conductance based model: $\dot{V} = (1/C) \cdot (-\sum_{\text{ion}} g_{\text{ion}}(V,t)(V - E_{\text{ion}}) + I_{\text{ext}})$.



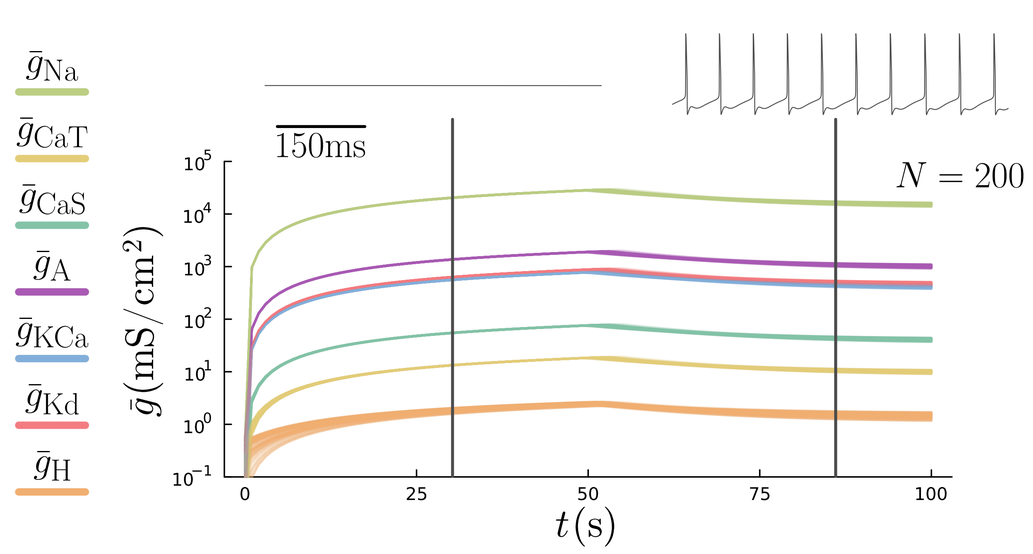
Homeostatic controller

Homeostatic controller:

- maintains a basal **intracellular calcium** level.
- tunes conductances of all ion channels, either up or down, while **preserving** predetermined **correlations** between each conductance.



$$\begin{cases} \tau_{\text{ion}} \dot{m}_{\text{ion}} & = Ca_{\text{target}} - [Ca^{+2}] \\ \tau_g \dot{\bar{g}}_{\text{ion}} & = m_{\text{ion}} - \bar{g}_{\text{ion}} \end{cases}$$

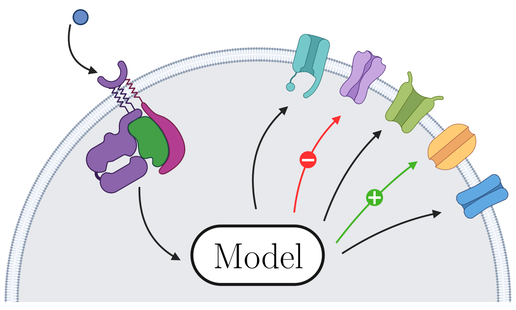


$\longrightarrow$ In response to some disturbances, such as **channel deletion**, **homeostatic compensation** might be **pathological**.

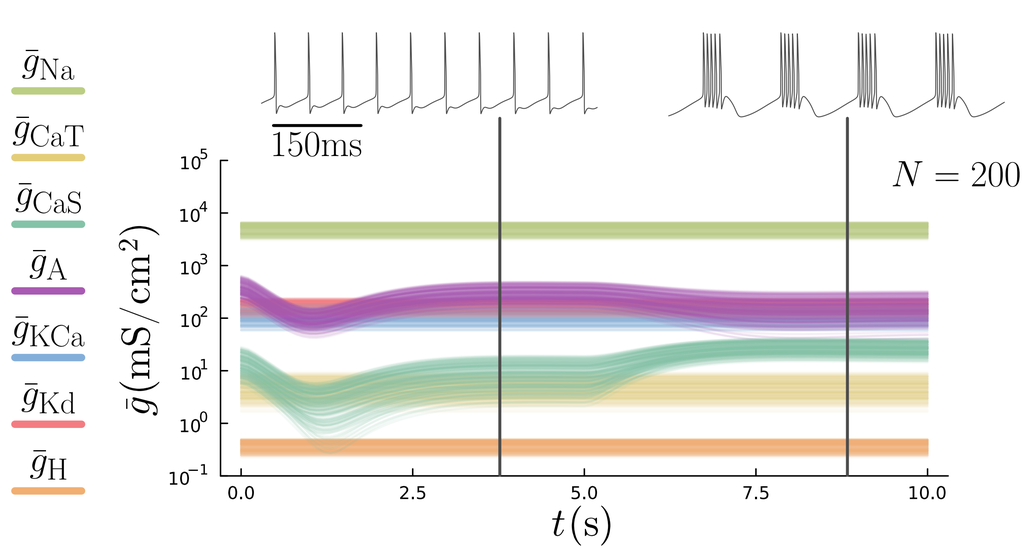
Neuromodulation controller

Neuromodulation controller:

- robustly modifies the **firing pattern** and responsiveness to external stimuli.
- tunes a subset of ion channel conductances by **modifying correlations** between those conductances.



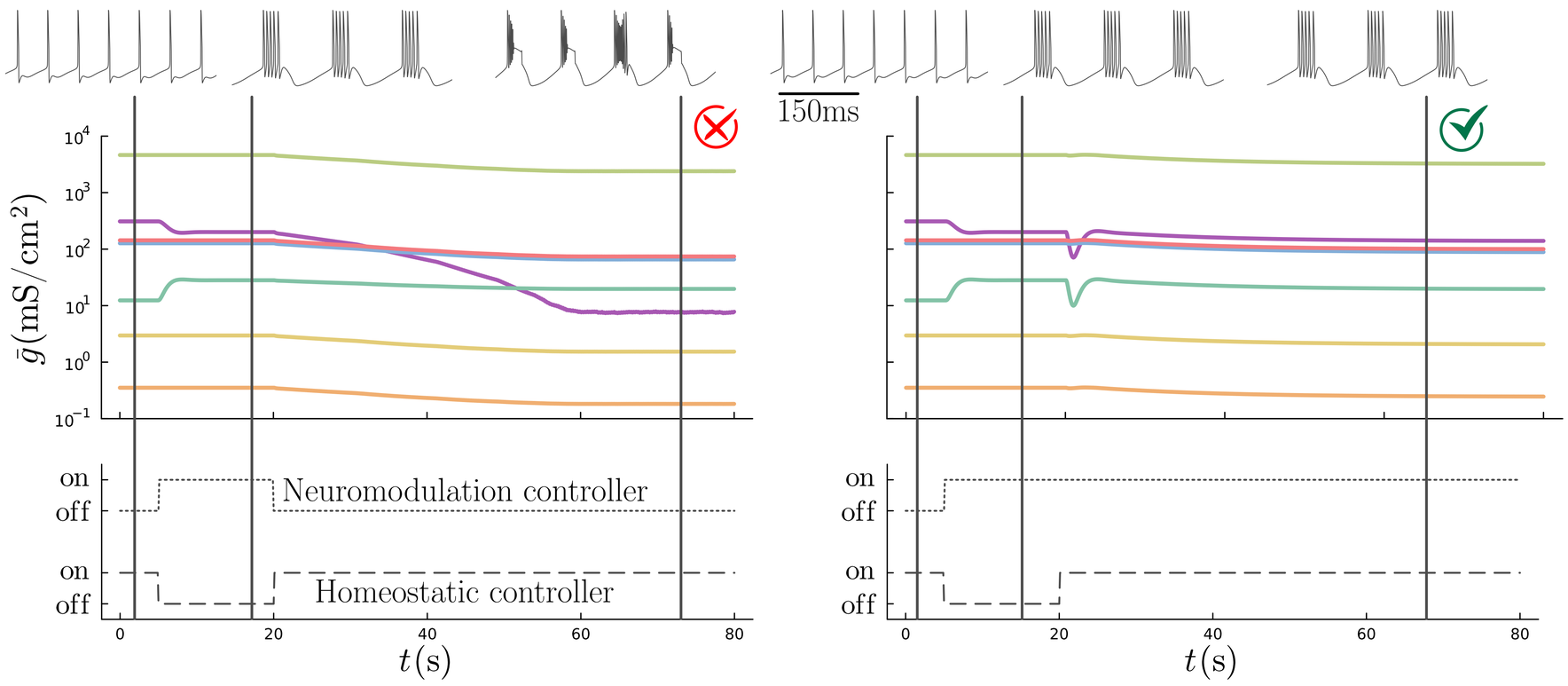
$$\begin{cases} e_{\text{mod}} & = \bar{g}_0\left([\text{nmod}]\right) - \bar{g}_{\text{mod}} \\ \dot{\bar{g}}_{\text{mod}} & = f\left(K_p \cdot e + K_i \cdot \int e\right) \end{cases}$$



$\longrightarrow$ In response to high neuromodulator concentration, **calcium level** might **raise up** drastically, eventually leading to **apoptosis**.

Both controllers complement each other to achieve robust neural function

- Both mechanisms present **contrasting perspectives**, yet they are essential to the **survival** and **neural functions** of biological neurons. How do these two mechanisms work in tandem?
- Even a biological disturbance (here neuromodulation) leads to **pathological** behavior of the **homeostatic controller** (left).
- However, by **maintaining neuromodulation** alongside **homeostasis**, bursting is **sustained** (right).



Conclusions and perspectives

This work demonstrates that our neuromodulation controller model perfectly complements previous homeostatic models by introducing activity adaptation and robustness against pathological behaviors. It could greatly benefit neuromorphic systems by providing robust activity modulation.

Acknowledgements

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