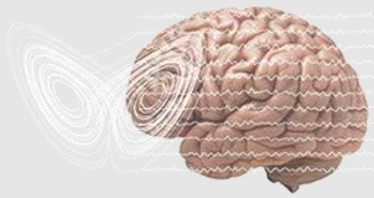
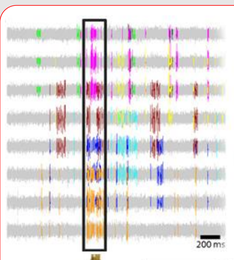
Investigating the mechanisms underlying synchronization in sensory neural populations during burst firing

Amin Akhshi[1], Anmar Khadra[1], Maurice Chacron[1]

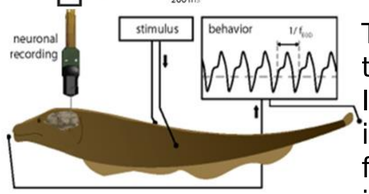
[1]Department of Physiology, McGill University



INTRODUCTION



Electrophysiological recording from Pyramidal cells in electorsensory lateral line lobe of weakly electric fish shows they can be synchronized through **burst firing.**

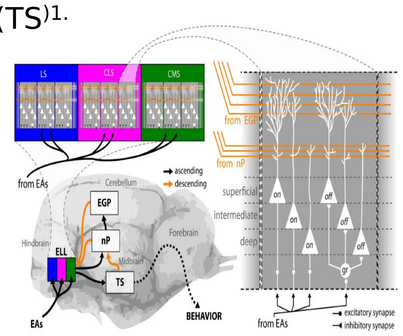


There are two (ON/OFF) types of PCs in the ELL. In ON (OFF) type PCs, by increasing the stimulus firing rate will be increased (decreased).

Anatomy of electrosensory pathway:

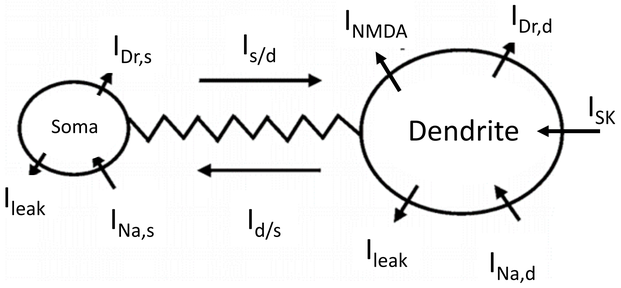
Electroreceptor afferents (EA) synapse onto PCs in the ELL. PCs project to the midbrain torus semicircularis (TS)[1].

Previous studies show that the intrinsic bursting mechanism of ELL PCs relies on somato-dendritic interactions within the cell[2,3].



METHODS

We used mathematical modeling to investigate how such synchronization is affected by neural intrinsic dynamics of individual cells.



Two – compartmental Hodgkin – Huxley model with Ca^{2+}

$$C_m \frac{dV_S}{dt} = I_{Na,S} + I_{Dr,S} + I_{leak} + I_{D\to S} + I_{stim}$$

$$C_m \frac{dV_D}{dt} = I_{Na,D} + I_{Dr,D} + I_{leak} + I_{S\to D} + I_{SK} + I_{NMDA}$$

$$\frac{dx}{dt} = \frac{x_\infty(V) - x}{\tau_x(V)}$$

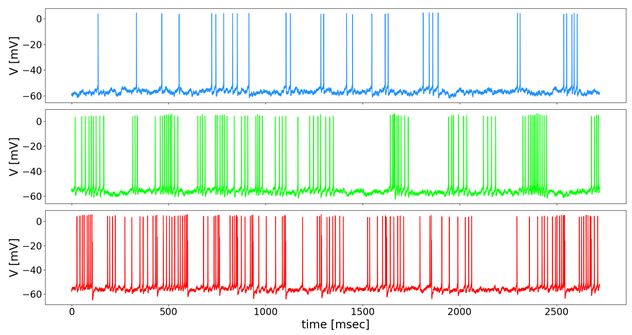
$$\frac{dCa_c^{2+}}{dt} = f_{Ca^{2+}}(\alpha I_{NMDA} + J_{Serca} + J_{PMCA} - J_{IP3} + J_{leak})$$

$$\frac{dCa_{ER}^{2+}}{dt} = f_{ER}\gamma(J_{IP3} + J_{leak} + J_{Serca} + J_{PMCA})$$

$$x_\infty(V) = {1}\Big/{1 + exp\left(\frac{V_x - V}{S_x}\right)}$$

Note: x denotes activation/inactivation gating variables

RESULTS

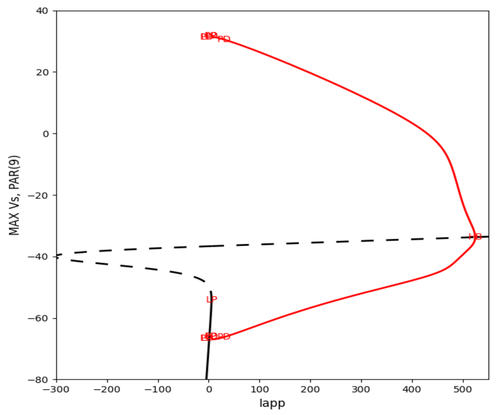


Simulation of the model for $g_{SK} = 2.0\ \mu S$ (blue), $g_{SK} = 1.0\ \mu S$ (green), and $g_{SK} = 0.0\ \mu S$ (red) using Euler – Maruyama integration with noise intensity $\sigma = \sqrt{2d\tau}$. The results show burst firing has increased by blocking of the SK channel.

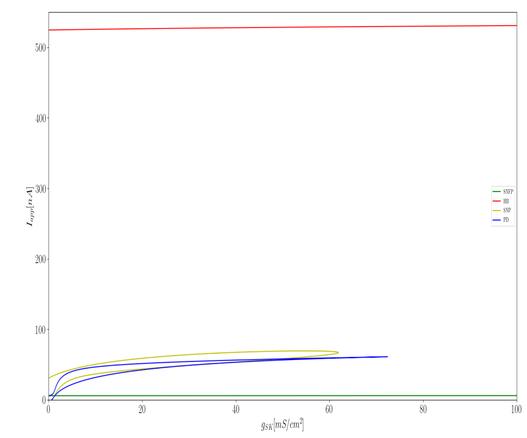
The result shows that decreasing the SK conductance will promote the increase cytosolic calcium concentration during burst synchronization.

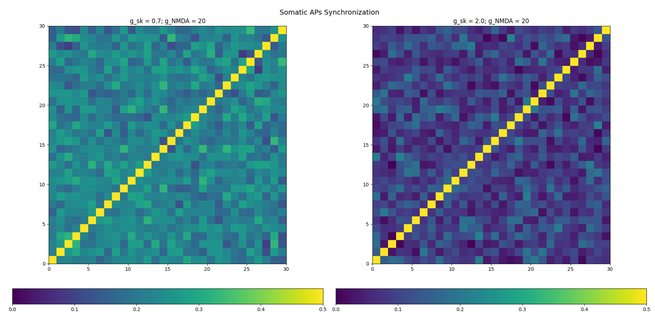
The model also characterize how calcium release (influx) from (into) the ER via IP3R (SERCA) pumps affects burst synchrony by controlling the cytosolic calcium concentration.

Changes in the dynamical behavior of the model with respect to changes in the stimulus current. The results shows the neuron starts firing action potential at $I_{stim} = 5.76\ nA$. The red curve shows the regime for which neurons tend to fire train of APs. The curves partition related to burst firing (i.e., period doubling bifurcation) is denoted as PD.



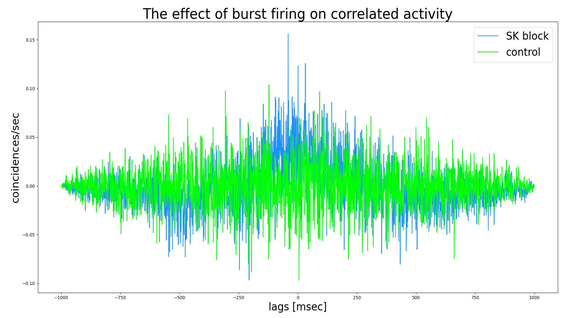
Two-parameter bifurcation set. Both the saddle-node bifurcations of fixed points (green) and limit cycles (yellow) bifurcations are tracked, using AUTO in the (I_{stim}, g_{SK}) subspace of parameter space. The curves partition the space into quiescence, tonic firing, and chaotic bursting regimes.[4]





Mean phase coherence of somatic APs for $N = 30$ neurons for $g_{SK} = 0.7\ \mu S$ (green) and $g_{SK} = 2.0\ \mu S$ (dark blue). The result shows that by increasing the g_{SK} in the model, synchronous behaviour of neurons is decreased.

Cross-correlogram (CCG) of dendritic spike trains for $N = 1000$ neurons for $g_{SK} = 1.0\ \mu S$ (green) and $g_{SK} = 0.0\ \mu S$ (blue). The result shows that the correlated activity of neurons is decreased by increase in g_{SK}.



DISCUSSION

- We studied the characteristics of burst firing in ELL PCs using our model and showed that Ca^{2+} dynamics plays an important role in synchronous activity of neural population.
- By adding the Ca^{2+} to our model, we were able to generate similar behaviour of ELL PCs compared to in vivo recordings where the SK current counteracts depolarization afterpotential (DAP) and does not lead to dendritic failure in the dendritic membrane potential.
- Experimental results have shown that neuromodulatory serotonergic input can strongly enhance burst firing in pyramidal neurons by downregulating SK channels.
- Our model shows that how the SK channel can be activated by feedback input through calcium influx by N-methyl-D-aspartate (NMDA) receptors.
- Moreover, by the this model we show how the SK channel can alter dynamics and promote burst synchronization when it's decreased.

REFERENCES

1. Hofmann, V., & Chacron, M. J. (2018). Population coding and correlated variability in electrosensory pathways. *Frontiers in integrative neuroscience*, *12*, 56.
2. Doiron, B., Laing, C., Longtin, A., & Maler, L. (2002). Ghostbursting: a novel neuronal burst mechanism. *Journal of computational neuroscience*, *12*(1), 5-25.
3. Toporikova, N., & Chacron, M. J. (2009). SK channels gate information processing in vivo by regulating an intrinsic bursting mechanism seen in vitro. *Journal of Neurophysiology*, *102*(4), 2273-2287.
4. Doedel E (1981) A program for the automatic bifurcation analysis of autonomous systems. Congr. Nemer. 30: 265–484.

ACKNOWLEDGEMENTS

The study was designed by A.K., M. C. A. A, gratefully acknowledge the support of the National Science and Engineering Research Council of Canada (NSERC) for the NSERC-CREATE in Complex Dynamics program grant. A. A. would also like to thank A. K., M. C., for their helpful discussions.