Temperature dependent depolarization blocking in neurons

Wolfram Höps

Supervisors: Jan-Hendrik Schleimer, Prof. Dr. Susanne Schreiber

February 13, 2017

Abstract

Cooling is a way to reversibly silence neurons. Although the effect is thought to be related to a temperature induced shift of the so-called *excitation block*, the overall mechanism is not yet well understood. In the proposed short study, we will try to analytically examine which ion channel properties contribute to the addressed phenomenon and how the onset of the exciation block is shifted by temperature in different channel configurations. The study will mostly rely on the Wang-Buzsaki neuron model and the method of numerical continuation for bifurcation analyses.

1 Introduction

Cooling is a way to reversibly deactivate brain areas *in vitro* and *in vivo* [1]. At the same time, studies have shown that mild hypothermia can even enhance neuronal excitability, before neurons are silenced upon further cooling below 10 to 15 °C. The effect has been observed in CA3 pyramidal cells of guinea pigs [2], cat spinal motoneurones [3,4] and slices of rat visual cortex [5]. Volgushev et al. [5] have argued that silencing was likely caused by a cold-induced shift in the total K^+/Na^+ conductance ratio, leading cells from a hyperexcitable state in a depolarization block. Although this block is a well-known phenomenon (see e.g. [6]), its temperature dependence has not been studied extensively before. It remains unclear how exactly the excitation block relates to temperature and what the implications for temperature dependence on the level of ion channels are.

The aim of the proposed study is to analytically describe the effect of temperature changes on the excitation block and to help a better understanding of neuronal behaviour in a hypothermic environment in general.

1

2 Work of this study

The project will rely on the Wang-Buzsaki neuron model [7] and the software *AUTO* [8] for numerical continuation of bifurcation problems. We will use different implementations of temperature dependency to investigate how the excitation block evolves over a range of channel configurations. A spike-blocking Hopf bifurcation [9] will serve as a marker for the event.

For a first approximation, we will use the membrane capacity as a basic indicator of temperature and see how it affects the boundary of excitation blocking. Afterwards, the neuron model will be carefully extended to account for temperature in a more realistic way, considering temperature dependence of peak channel conductances, changes in the equilibrium potential and, as needed, modifications in the channel opening and closing rates. It will be of particluar interest if the shift in the ratio of sodium and potassium conductance, as observed by Volgushev et al. [5], can indeed explain hypothermic inactivation.

References

[1] Stephen G. Lomber, Bertram R. Payne, and James A. Horel. The cryoloop: An adaptable reversible cooling deactivation method for behavioral or electrophysiological assessment of neural function, 1999.

[2] Hideo Aihara, Yasuhiro Okada, and Norihiko Tamaki. The effects of cooling and rewarming on the neuronal activity of pyramidal neurons in guinea pig hippocampal slices. *Brain Research*, 893(1):36–45, 2001.

[3] M R Klee, F K Pierau, and D S Faber. Temperature effects on resting potential and spike parameters of cat motoneurons. *Experimental brain research*, 19(5):478–492, mar 1974.

[4] A Michalski, B M Wimborne, and G H Henry. The effect of reversible cooling of cat's primary visual cortex on the responses of area 21a neurons. *J Physiol*, 466:133–56., 1993.

[5] M Volgushev, T R Vidyasagar, M Chistiakova, T Yousef, and U T Eysel. Membrane properties and spike generation in rat visual cortical cells during reversible cooling. *The Journal of physiology*, 522 Pt 1:59–76, 2000.

[6] Daniela Bianchi, Addolorata Marasco, Alessandro Limongiello, Cristina Marchetti, Helene Marie, Brunello Tirozzi, and Michele Migliore. On the mechanisms underlying the depolarization block in the spiking dynamics of CA1 pyramidal neurons. *Journal of computational neuroscience*, 33(2):207–225, oct 2012.

[7] Xiao-Jing Wang and György Buzsáki. Gamma Oscillation by Synaptic Inhibition in a Hippocampal Interneuronal Network Model. *Journal of Neuroscience*, 16(20):6402–6413, 1996.

[8] Eusebius J Doedel. AUTO: A program for the automatic bifurcation analysis of autonomous systems, 1981.

[9] Janina Hesse, Jan-Hendrik Schleimer, and Susanne Schreiber. Saddle-node loop bifurcations ubiquitously occur in conductance-based model neurons and promote spike-based coding and synchronization. *arXiv*, 2016.