Channel density regulation of neuronal firing patterns: Modelling cortical neurons

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Background: The electrical activity of the brain is characterized by dynamically interacting impulse patterns. The molecular basis of this activity is formed by a class of membrane bound proteins, voltage-gated ion channels. The density and distribution vary continuously during normal activity to maintain or modify ongoing firing patterns [1]. Drugs, such as general anaesthetics and antiepileptics, modify interacting patterns by similar mechanisms. Our aim is to analyse how the density of voltage-gated channels in a model neuron determines the firing patterns.

Methods: The model neuron was constructed from an experimental analysis of hippocampal interneurons, using the Frankenhaeuser-Huxley equations [2]. The analysis comprised numerical solutions of differential equations and a stability analysis.

Results: The oscillatory activity of the model neuron shows distinct density-dependent patterns. For a high Na and K channel density neuron (Fig. 1, region B) the onset of firing is characterised by a discontinuous jump from no repetitive firing to high frequency firing at increased stimulation (Hopf bifurcation). A lower K channel density (region C1) leads to a continuously increasing firing rate at increased stimulation (saddle node bifurcation). The latter region coincides with the region for an all-or-nothing behaviour. A survey of our own and others experimental recordings shows that hippocampal interneurons can be both graded non-oscillators [2] and saddle-node oscillators [3], and that dorsal horn neurons can be Hopf oscillators [4].

Conclusions: The results suggest that a neuron can switch between Hopf bifurcation firing and saddle node firing, and between graded and all-or-nothing impulses by regulating ion channel densities. This suggests that certain general anaesthetics might function by inducing a switch from frequencies associated with conscious states, to frequencies associated with sleep or unconscious states, and that up and down regulation of channels might switch the information processing in parts of the brain from rate coding to amplitude coding.

References:

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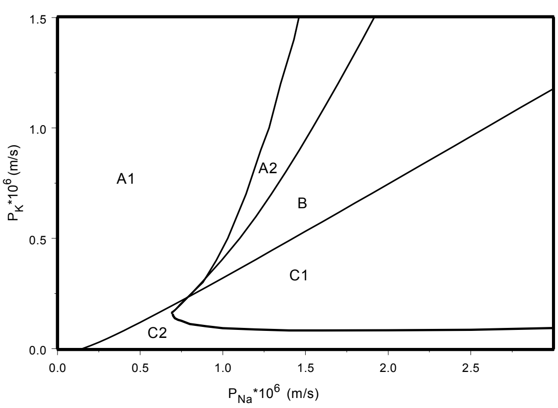

Fig. 1. Regions with different oscillatory behaviour. The axes show Na and K permeabilities, proportional to the channel densities. There is always a stable stationary situation in regions A1, A2, but while stimulation always leads to that state in A1, it can lead to oscillations around a stable state in A2. Region B yields oscillations of Hopf-bifurcation type and C1 of a saddle-node bifurcation type.