

INVESTIGATING THE EFFECTS OF PROPOFOL-INDUCED TONIC INHIBITION ON RHYTHMIC NEURAL ACTIVITY IN A HIPPOCAMPAL INTERNEURON NETWORK

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Propofol is an anaesthetic agent commonly used in surgical operations for the induction and maintenance of general anaesthesia. Propofol-induced sedation is achieved by positively modulating GABAergic inhibitory activity, as the drug binds on $GABA_A$ receptors enhancing their activation [1]. $GABA_A$ receptors are ubiquitous in the brain [2], and can be present both within synaptic clefts, as well as on extrasynaptic locations along the dendrites where they mediate tonic inhibitory currents. Synaptic GABAergic interactions between sparsely connected interneurons are thought to play an important role in the generation and maintenance of rhythmic neural activity, in particular in the γ -band (20 – 80) Hz [3]. This oscillatory frequency range is often recorded in functionally-coupled brain regions for cooperation during memory tasks. One such example is cortico-hippocampal synchronisation during long-term memory consolidation [4].

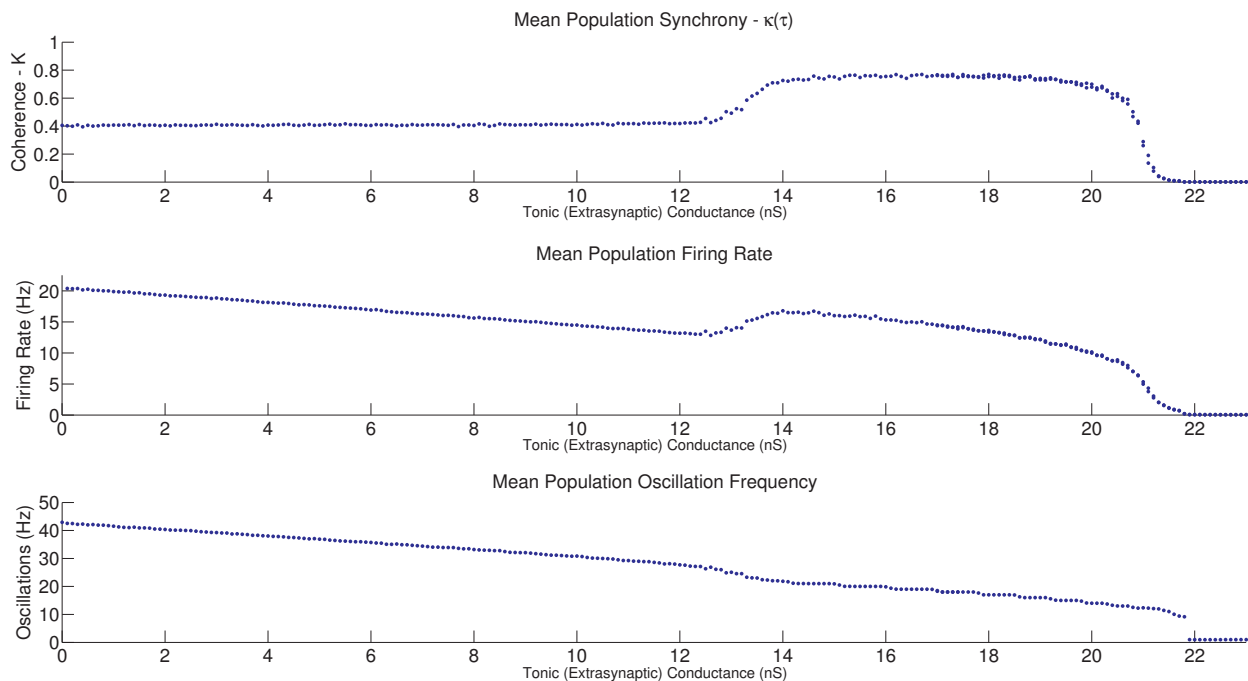


Figure 1: Increasing the tonic conductance causes the overall activity of the network to decrease, until a critical value of $g = 14 \text{ nS}$ at which both the network synchronisation and firing rate increase until $g = 21 \text{ nS}$ value at which the activity fades out.

This work studies the effect of propofol-induced tonic inhibition on the oscillations elicited in a network of hippocampal Hodgkin-Huxley *GABA* interneurons [3]. The action of propofol on extrasynaptic GABAergic receptors was modelled by varying the conductance g of a tonic current in the form $I_{ton} = g(V - E_{ton})$ as described in [5]. To measure the synchronisation of the neural activity in the network we used the coherence metric K defined in [3], where a value of 1 indicates global synchrony across all neurons. In the absence of tonic inhibition $g = 0nS$, the network synchronises its activity with $K = 0.4$ at an oscillatory frequency of $\sim 43 Hz$. Increasing doses of propofol reduce the overall network activity and slow down its oscillations until a critical value of $g = 14nS$ at which the synchronisation increases abruptly reaching a plateau at $K = 0.8$, and the mean firing rate increases. These results point towards a possible mechanism for the emergence of paradoxical excitation under general anaesthesia.

References

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