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Investigating the effects of propofol-induced tonic inhibition on rhythmic neural activity in a hippocampal interneuron network

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Motivation

- Propofol-induced sedation is achieved by positively modulating GABAergic inhibitory activity [1]
- Synaptic and extrasynaptic GABA_A receptors are ubiquitous in the brain [2]
- GABAergic hippocampal interneurons have been shown capable of generating γ-band (20 – 80) Hz rhythmic neural activity [3]
- γ-band oscillations are thought to underlie long-term memory consolidation [4]
- We study the effect of the propofol-induced extrasynaptic GABAergic modulation [5] on such self-emerging synchronous activity

Neuron Model

- Neuron Model:
  \[ C_{m} \frac{dV}{dt} = -I_L - I_K - I_A - I_{synaptic} + I_{ion} \]
- Hodgkin-Huxley Currents and Stimulation:
  \[ I_{ion} = f(V_{syn}) \]
  \[ I_{synaptic} = f(V_{syn}, m^4, h) \]
  \[ I_{ion} = 0.4 mA \]

Synapses and Propofol

Schematic of GABA (in orange) binding on synaptic and extrasynaptic receptors causing Cl⁻ ion influx in the postsynaptic neuron. Extrasynaptic GABA receptors mediate tonic inhibition, and are potentiated by extrasynaptic propofol (red). Propofol also binds on synaptic GABA receptors (not modelled in the present work, thus not shown).

Results – Increasing Anaesthetic Dosage

- Increasing the dosage of propofol to \( g_t = 18 \) nS causes stronger synchrony amongst the neurons in the network \( \kappa(t) = 0.8 \), while slowing down the oscillatory activity to a frequency of \( f_{osc} \approx 0.8 \) Hz.

Results – γ-band Synchronisation

- Increasing the dosage of propofol to \( g_t \geq 21 \) nS weakens the synchrony amongst the neurons in the network \( \kappa(t) = 0.2 \), and slows down the oscillatory activity to a frequency of \( f_{osc} \approx 10 \) Hz.

Conclusion

- Anaesthetics target both synaptic and extrasynaptic GABA_A receptors
- Increasing the dosage of anaesthetic agents can strengthen synchronous activity in networks of hippocampal neurons
- Paradoxical excitation behaviours might be mediated by the effects of anaesthetics on extrasynaptic GABA_A receptors

References