Principles of Pharmacodynamics & Pharmacokinetics

Understanding general anaesthesia using electrophysiology

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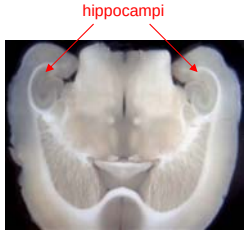
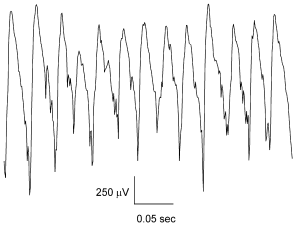
Effects of anaesthetics on γ oscillations in brain slices

1



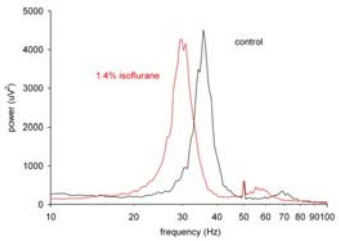
Thin slices of brain tissue maintained *in vitro* preserve many of the properties of the intact brain. One of the most remarkable of these is the occurrence of spontaneous oscillations in the gamma frequency band (~40Hz) observed in the hippocampus. Gamma oscillations are believed to underlie consciousness.

2



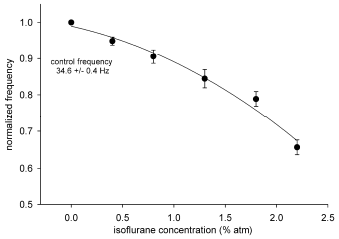
Extracellular voltage recordings showing typical gamma oscillations recorded in the CA1 region of the hippocampus. The oscillations persist for hours in hippocampal slices maintained in an interfacial perfusion chamber.

3



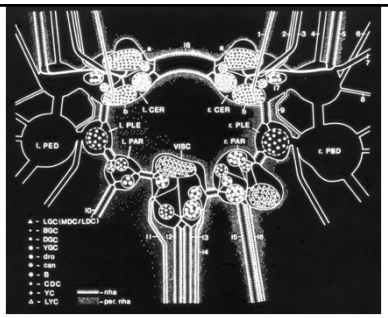
The frequency distribution is illustrated in the power spectrum (a Fourier transform) of the oscillations. The control trace shows a sharp peak in the gamma band. In the presence of the volatile general anaesthetic isoflurane the peak frequency is reversibly shifted to a lower value.

4



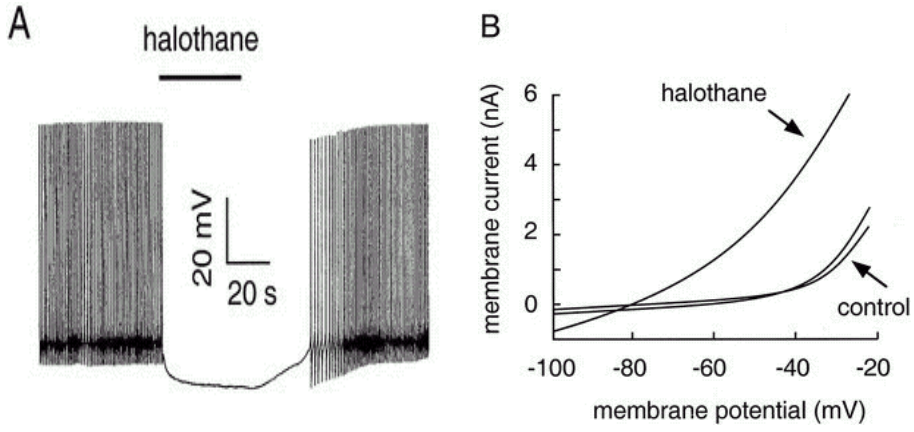
The graph above shows the shift in frequency as a function of isoflurane concentration. The data are pooled from 6 different slices and the control frequency has been normalized to be 1.


Lymnaea stagnalis




Right parietal ganglion

Anaesthetic actions on neuronal properties.



Franks & Lieb (1988) Nature 333, p662

Determinants of the Anesthetic Sensitivity of Two-pore Domain Acid-sensitive Potassium Channels

*MOLECULAR CLONING OF AN ANESTHETIC-ACTIVATED POTASSIUM CHANNEL FROM LYMNAEA STAGNALIS**

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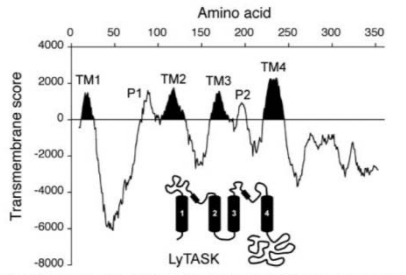


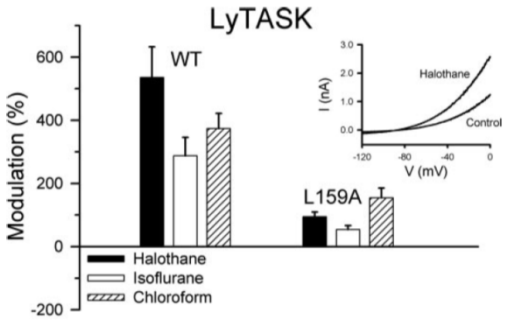
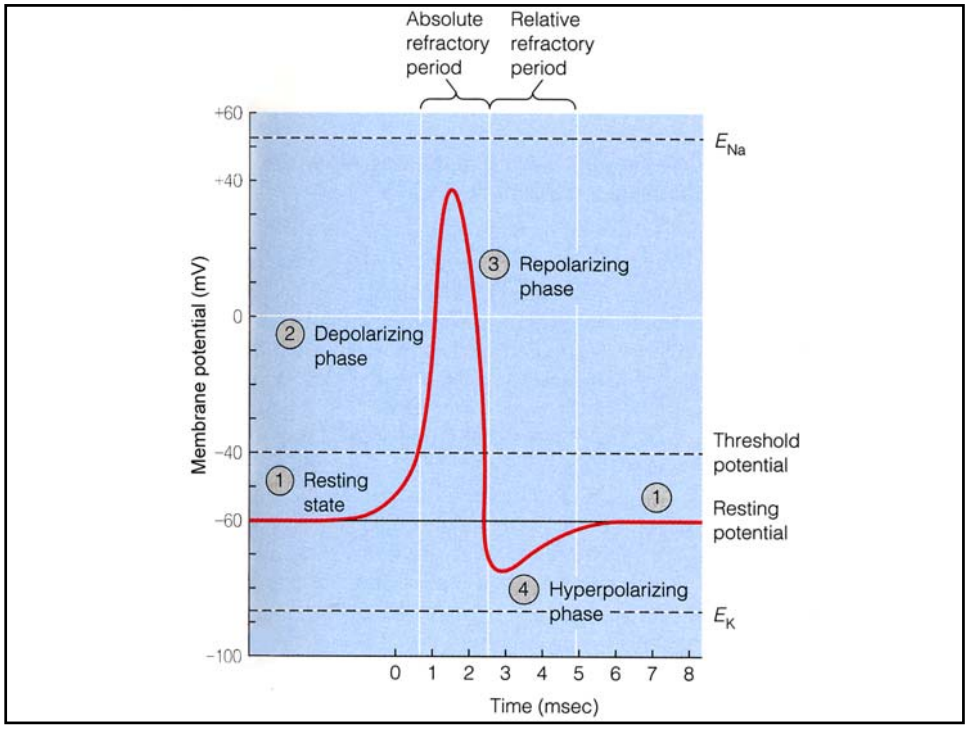


FIGURE 1. **Sequence analysis of LyTASK and predicted membrane topology.** *A*, nucleotide and deduced amino acid sequences of *L. stagnalis* TASK (LyTASK GenBank™; accession number EF640973). The positions of the

Lymnaea – the movie


Absolute refractory period
Relative refractory period
+60
+40
0
−40
−60
−100
Membrane potential (mV)
E_{Na}
3 Repolarizing phase
2 Depolarizing phase
Threshold potential
1 Resting state
1
Resting potential
4 Hyperpolarizing phase
E_K
0 1 2 3 4 5 6 7 8
Time (msec)