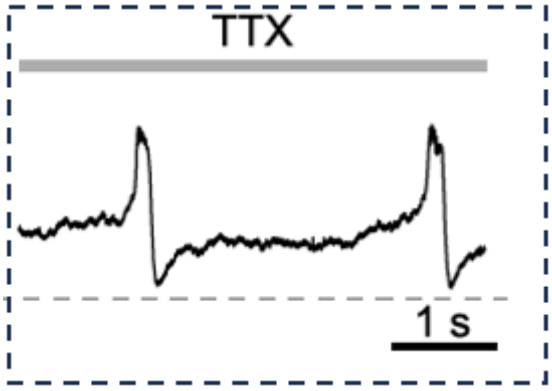
1 Modelling LTS: Control TTX

What do we know?

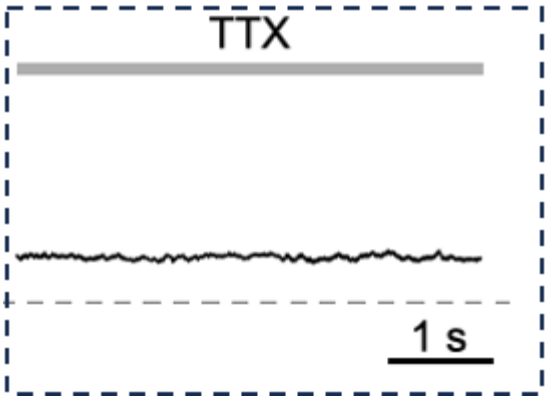
$$\min_{\mathbf{x}_0, T} \quad J(\mathbf{x}_0, T) \tag{1}$$

$$\text{with,} \quad J = \|\mathbf{x}(T; \mathbf{x}_0, \boldsymbol{\theta}) - \mathbf{x}_0\| \tag{2}$$

- The initial uprize is potentially caused by T-type Ca current, as no activity is found in the T-Type Ca channel KD scenario (Figure 1b)
- Fast hyperpolarizing current when the membrane potential reaches specific value (Figure 1a) By rough approximation, the timescale of the strong hyperpolarization is around 100ms
- Slightly reduced bursting frequency in T-type KD neurons, as well as increased resting membrane potential (by approximately 5 mV)



(a) Recording of membrane potential after application of TTX in control flies

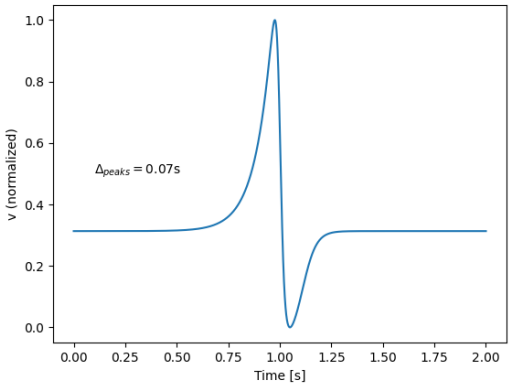


(b) Recording of membrane potential after application of TTX in T-type Ca channel KD flies

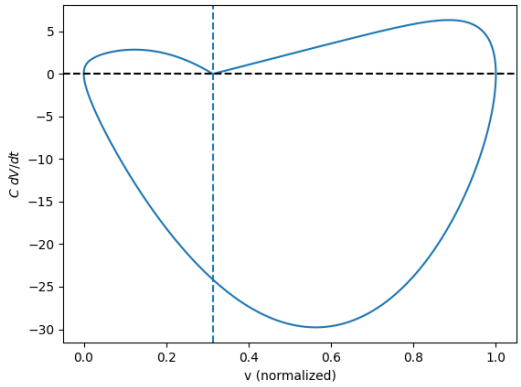
Figure 1

Generally, subthreshold oscillations might have various different origins. Minimal models can be constructed with

- T-Type and Leak channels
- T-Type and Noninactivating hyperpolarizing channels
- T-Type and Inactivating hyperpolarizing channels
- T-Type and hyperpolarizing Ca gated channels



(a) Rough estimate (a guessed function) for the observed LTS after TTX



(b) Membrane potential versus its rate of change for the guessed function

Figure 2

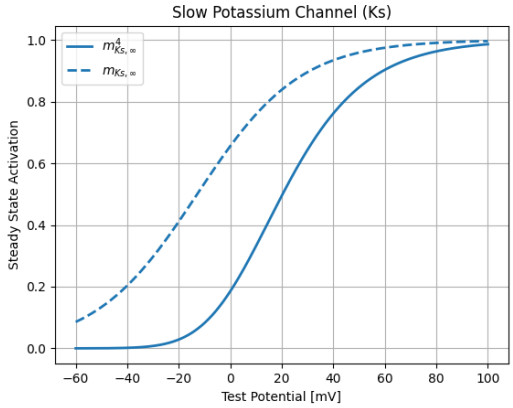
- What can cause the strong hyperpolarization?
  - **(X) Noninactivating channel (e.g. Slow K current (Ks))**

    No, because the current is very strong. The time constant of the activation variable is still quite fast (Figre 3b).

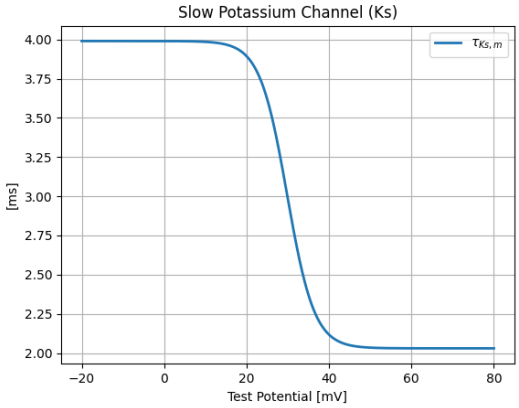
    1. If the activation threshold is lower than the peak, it would have affected the phase of the oscillation, when T-Type channels are activated;
    2. If the activation threshold is around the peak, it would have deinactivated fast and would not have caused the membrane potential to reach its trough.

    (✔) However, it can still cause the small drop seen on top of the peak in Figure 1a (see also Fig. for the simulation results.)
  - **(?): Inactivating channel (e.g. Fast K current (Kf))**
  - **(?): Ligand gated hyperpolarizing currents (e.g. Ca activated K channel)**

    As the uprize of the membrane potential is potentially mediated through influx of calcium, the negative feedback in the modulation of the membrane potential can be cased by Ca activated hyperpolarizing channels, such as Ca gated K channels.

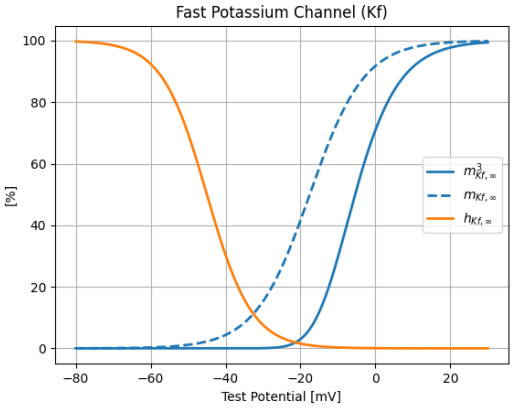


(a) Steady state activation

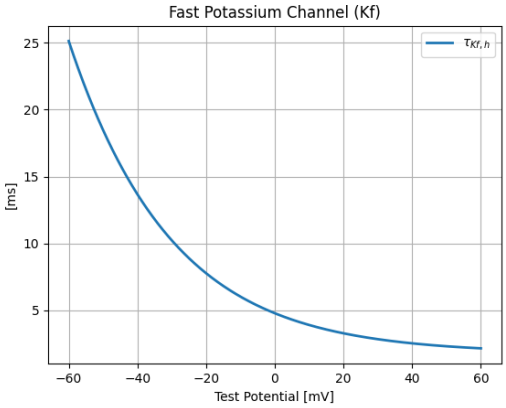


(b) Activation time constant

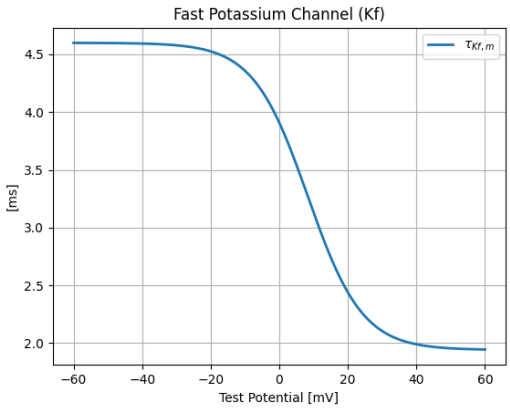
Figure 3: Kinetiks of Ks channel (parameters taken from [1])



(a) Steady state activation



(b) Inactivation time constant



(c) Activation time constant

Figure 4: Kinetiks of Kf channel (parameters taken from [1])

References

1. Günay, C. *et al.* Distal Spike Initiation Zone Location Estimation by Morphological Simulation of Ionic Current Filtering Demonstrated in a Novel Model of an Identified Drosophila Motoneuron. *PLOS Computational Biology* **11** (ed Blackwell, K. T.) e1004189. ISSN: 1553-7358. https://dx.plos.org/10.1371/journal.pcbi.1004189 (2025) (May 15, 2015).