

# MODELLING PHYSIOLOGICAL DATA FROM THE SCIATIC NERVE OF THE TOAD *XENOPUS LAEVIS*: INTEGRATE-AND-FIRE AND BEYOND

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## ABSTRACT

Since its introduction by Lapicque in 1907 [3], the integrate-and-fire model has become one of the standard models of neuronal activity. We studied firing rates from the sciatic nerve of the toad *Xenopus laevis*, which acts as a physiological model of the mammalian cochlear nerve [4], using a leaky integrate-and-fire (LIF) model (see eg. [5]). A modified version of this model was used to successfully predict responses to sinusoidal stimulation, and we seek an extension to complex stimuli. For this, we find that accommodation is an important factor.

To the basic LIF model we added two refractory periods. These are the absolute refractory period (ARP), immediately after the action potential (AP), during which the neurone cannot produce another AP, and the relative refractory period, during which the neurone's ability to discharge is reduced. The relative refractory period represents a gradual recovery of the probability of firing (in our case by using two time constants).

This model contained 8 parameters, and we performed parameter fitting of the data using a genetic algorithm (see eg. [1]) minimising relative errors between the model and the data. The results of modelling a series of experiments on a single sciatic nerve fibre are shown in Figure 1(a). These experiments consisted of various amplitudes of stimulation of the fibre at each given frequency. Clearly, the firing rates are too high at low frequencies and much too low at high frequencies. This is due to the ARP, which takes as its upper bound the reciprocal of the maximum firing rate across all frequencies. In this example, the nerve fibre fires at a rate in excess of 1 kHz when stimulated at 2 kHz, showing that the maximum ARP should be less than 1 ms. If this value is used to model low-frequency stimulation, the model exhibits very high firing rates. Instead, here, the fitting process has converged on a large value for the ARP, suppressing firing at high frequencies.

Following these results, we expanded the model, allowing the ARP and the threshold to vary independently across frequencies. This allowed the low-frequency stimulation to produce low firing rates in the model, since the ARP could be set to limit the maximum rate of firing for each frequency. These results are shown in Figure 1(b).

This model (which has 6 parameters plus 2 for each frequency being examined (a maximum of 18 for our data)) succeeds in modelling the firing rate of the sciatic nerve for sinusoidal stimulation. In order to model more complex stimuli (in the first instance, correlated Gaussian noise), we need to remove our dependence on frequency as a determining factor for the ARP.

The model described above fails to work (with a single ARP) for a broad range of frequencies because it contains no description of accommodation, a general term used to describe the fact that the neurone adapts to the stimulus, with long, constant amplitude stimuli producing APs at a

declining rate. Allowing the ARP to vary over different frequencies mimics this behaviour, but if we wanted to model a complex stimulus, we have no way of choosing the ARP.

Computations performed using Frankenhaeuser and Huxley's reduced ion channel model (FH model) [2] showed that the ARP of the nerve fibre was altered by the presence of a stimulus between one AP and the next. Figure 2 shows this effect for a simulation using three monophasic pulses. It was found that the value of  $h$ , the sodium inactivation variable, seemed to act as a threshold indicator for the model; the system only produced an AP once  $h$  had recovered to a certain value which depended only on the amplitude of the third pulse (the one causing the AP). This threshold value of  $h$  was independent of the inter-AP stimulus. The dependance of  $h$  on the stimulus provides the accommodation effect which we seek, allowing the threshold to vary according to the past history of the stimulus.

In light of this, we are examining a new model which contains no explicit refractory periods, simply a threshold defined as the reciprocal of  $h$ . The differential equation for  $h$  as given in [2] contains 6 parameters, giving us a total of 9 in our new model. Preliminary results are shown in Figure 1(c). The model captures the onset correctly at most frequencies, and the maximum firing rates are well-constrained except at the very highest frequency. Encouraged by these results, we are now investigating just what relationship the threshold should have to  $h$  (reciprocal, scaled reciprocal, etc.).

**Keywords:** Integrate-and-fire, cochlear nerve, accommodation.

## References

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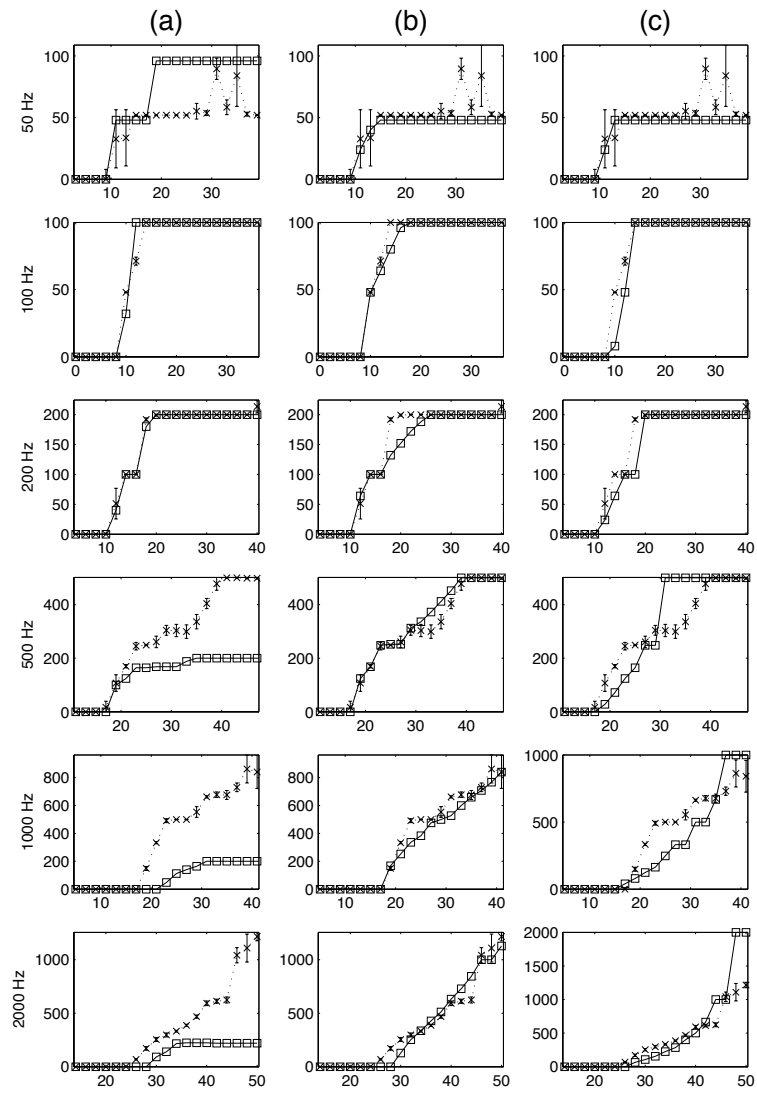


Figure 1: Firing rate curves from a single fibre of a sciatic nerve. Lines are the experimental data, squares the results from the model. (a) basic LIF model; (b) relaxed LIF model; (c) accommodative model.

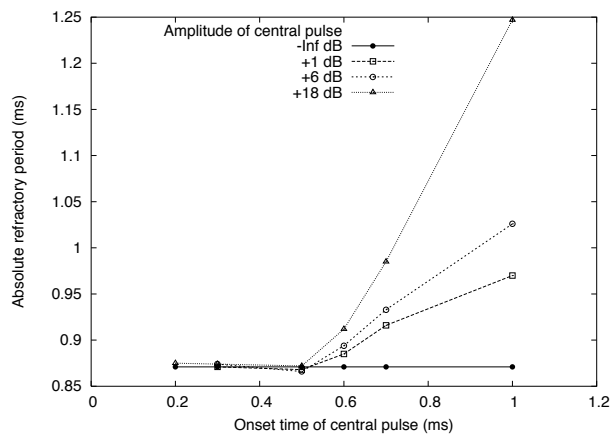


Figure 2: Absolute refractory period changes with the amplitude and width of the central monophasic pulse when three such pulses are applied to the Frankenhaeuser Huxley ion channel model.