(iv) $f(V)$ is infinite when $V = V_2 = -C/B$. Thus V_1 and V_2 have the same sign. Usually $A/B < 1$ so $|V_1| > |V_2|$.

(v) If $C > 0$, then $f(V)$ is increasing through $V = V_2$, whereas if $C < 0$, then $f(V)$ is decreasing through $V = V_2$.

In Figure 2.17 we show graphically that if $C > 0$, a hyperpolarization relative to the Goldman formula without active transport occurs. Here the intersection of e^V with the ordinate A/B gives the value of γV_m in the absence of active transport, $C = 0$ (labeled γV_G). When active transport is included, the intersection of e^V with $f(V)$ occurs at a smaller value (labeled γV_m). Thus a hyperpolarization relative to γV_G occurs.

Assuming only positive ions (e.g., K^+ and Na^+) are being pumped, a value of $C > 0$ implies an excess of positive ions are being pumped out of the cell. This would be the case when there is an excess of sodium over potassium pumping. Indeed, excessive loading of the intracellular compartment, which occurs due to the injection of sodium ions or by repetitive firing at a rapid rate (called *tetanus*), often leads to a hyperpolarization. In the latter case it is referred to as *posttetanic hyperpolarization* (Holmes 1962; Phillis and Wu 1981). If $C < 0$, a depolarization, relative to the Goldman potential, occurs. Proof of this is left as an exercise.

3

The Lapicque model of the nerve cell

3.1 Introduction

One fundamental principle in neural modeling is that one should use the simplest model that is capable of predicting the experimental phenomena of interest. A nerve-cell model must necessarily contain parameters that admit of physical interpretation and measurement, so that it is capable of predicting the different quantitative behaviors of different cells.

The model we will consider in this chapter is very simple and leads only to first-order linear differential equations for the voltage. However, when we employ the model in many situations of neurophysiological interest, we find that the mathematical analysis becomes quite difficult, due mainly to the nonlinearities introduced by the imposition of a firing threshold. This will become even more apparent in Chapter 9, where we consider stochastic versions of this model.

The model will be called the *Lapicque model* after the neurophysiologist who first employed it in the calculation of firing times (Lapicque 1907). Other names for this model, which have recently appeared in the literature are *the leaky integrator* or the *forgetful integrate and fire model.*

According to Eccles (1957) the resting motoneuron membrane can be represented by the circuit shown in Figure 3.1A. A battery with a potential difference equal to that of the resting membrane potential maintains that potential across the membrane circuit elements consisting of a resistor and capacitor in parallel. We call this a *lumped model* or a *point model* to indicate that the whole cell (with attention focused on the soma and dendrites) is lumped together into one representative circuit. Hence with this model we cannot address questions concerning the effects of input position or concerning the interaction between inputs at various locations on the soma–dendritic surface.

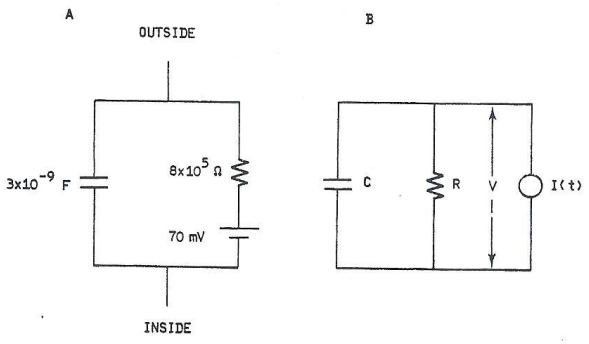

Figure 3.1. A–Electrical circuit employed to represent the resting nerve cell. Values of the resistance, capacitance, and resting potential are average values from Eccles (1957). B–Electrical circuit employed in the Lapicque model for subthreshold depolarizations.

We let $V(t)$ be the potential difference across the cell membrane, minus the resting potential at time t. That is, $V(t)$ is the *depolarization* and in the resting state $V = 0$. We remove the battery from the circuit as in Figure 3.1B, where a resistance R and capacitance C are in parallel. The depolarization varies according to the effects of the input current $I(t)$, which may come from activation of synaptic inputs or other natural means (e.g., due to a sensory input in a receptor) or from current injection. In Chapter 7 a more realistic model for the effects of synaptic inputs will be employed.

Subthreshold behavior

Assume for now that the membrane resistance R does not depend on the voltage and is, in fact, constant. The current through it is, by Ohm's law, V/R. The current through the capacitance is $C\,dV/dt$ so we must have, by conservation of current,

$$C\frac{dV}{dt} + \frac{V}{R} = I(t), \qquad t > 0. \tag{3.1}$$

The solution of this differential equation, given an initial value $V(0)$, will give the time course of the depolarization for subthreshold voltages.

Threshold

Equation (3.1) is only appropriate for subthreshold responses. If the nerve cell under consideration is capable of generating action

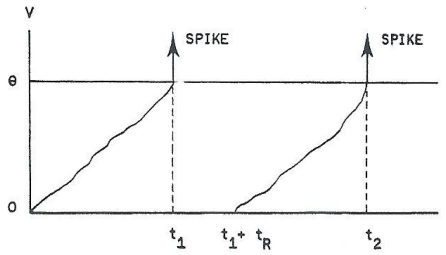

Figure 3.2. Spike generation in the Lapicque model. Whenever $V(t)$ reaches $\theta(t)$, the threshold, an action potential is generated. The threshold function depicted here is the constant threshold (3.2).

potentials, a threshold condition must be superimposed, because (3.1) has no *natural* threshold properties (see Chapter 8). Let the threshold depolarization for action-potential generation be $\theta(t)$, $t \geq 0$. The model nerve cell is completed by imposing the condition that when $V(t)$ reaches $\theta(t)$, an action potential is generated. Following the action potential the depolarization and the threshold are reset, usually to their initial values.

A simple choice for the threshold, which is appropriate for a cell that is not firing rapidly, is to assume that it is *constant* at θ until the generation of a spike, after which it becomes infinite for the duration of an *absolute refractory period* of length t_R. Let the sequence of times at which action potentials occur be $\{t_i,\ i = 1, 2, \ldots\}$ as depicted in Figure 3.2. Then

$$\theta(t) = \begin{cases} \infty, & t_i < t < t_i + t_R, \\ \theta, & \text{otherwise.} \end{cases} \tag{3.2}$$

Note that the spikes have no structure in this model. The output train is completely described by the sequence of t_i's. Other threshold functions commonly employed are given in Table 3.1. In the next three sections we study the subthreshold responses of a Lapicque model neuron and then consider the problem of determining the sequence of times of occurrence of spikes.

3.2 Subthreshold response to current steps

By means of intracellular current injection a neuron may be either depolarized or hyperpolarized. The results of applying constant depolarizing and hyperpolarizing currents for a certain length of time are shown in Figure 3.3. Figure 3.3A shows a depolarization reaching

Table 3.1. *Some commonly employed threshold functions*[a]

Threshold	Name of proposer
$k\tau/t$	Buller
$k(1-\tau t)$	Calvin and Stevens
$k/(e^{\tau t}-1)$	Geisler and Goldberg
$ke^{\tau/t}$	Hagiwara
$ke^{-\tau t}$	Weiss

[a]From Holden (1976).

a final value of about 8 mV in response to a current step of 3 nA (1 nA) = 10^{-9} A), whereas Figure 3.3B shows an earlier recording of the response of a cat spinal motoneuron to a depolarizing and hyperpolarizing current step. Indeed, the Lapicque model predicts these responses.

We introduce the unit (Heaviside) step function,

$$H(t)=\begin{cases}0, & t<0,\\ 1, & t\geq 0.\end{cases} \tag{3.3}$$

Then with a maintained current of magnitude I = constant,

$$I(t)=IH(t). \tag{3.4}$$

Equation (3.1) for subthreshold voltages is a first-order linear differential equation with integrating factor $\exp(t/RC)$. Thus (see Section 2.4) its general solution is

$$V(t)=\exp\left(-\frac{t}{RC}\right)\left[\int^{t}\frac{I(t')}{C}\exp\left(\frac{t'}{RC}\right)dt'+k\right], \tag{3.5}$$

where k is a constant to be determined by the initial value of V. If we take the cell to be initially at rest, then $V(0)=0$, and

$$V(t)=\exp\left(\frac{-t}{RC}\right)\int_{0}^{t}\frac{I(t')}{C}\exp\left(\frac{t'}{RC}\right)dt'. \tag{3.6}$$

For a constant current we insert (3.4) in (3.6) to get

$$V(t)=IR(1-e^{-t/RC}), \qquad t\geq 0. \tag{3.7}$$

If the current were maintained *indefinitely*, then as $t\to\infty$, the depolarization would approach the *steady-state value* IR. However, if the current is switched off at $t=t_1$ so that

$$I(t)=I[H(t)-H(t-t_1)], \tag{3.8}$$

then the depolarization will decay exponentially according to

$$\frac{dV}{dt}=-\frac{V}{RC}, \qquad t\geq t_1, \tag{3.9}$$

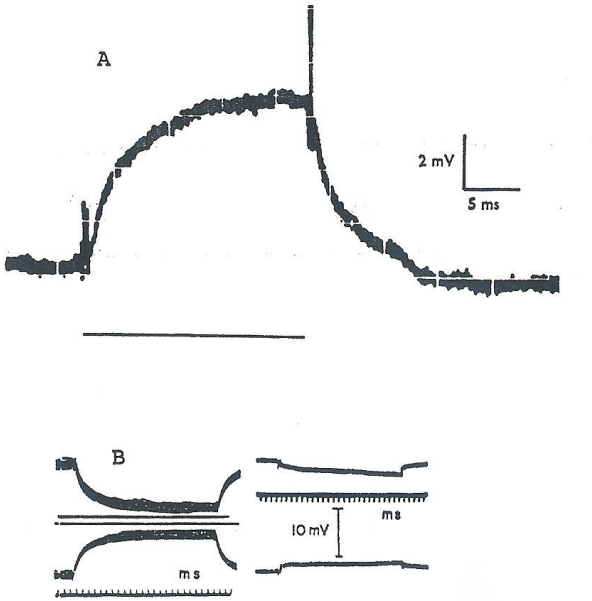

Figure 3.3. Time course of the membrane potential of a cat spinal motoneuron under current steps. A–Response of a cell to a 3-nA current step of duration about 25 ms. [From Barrett and Crill (1974). Reproduced with the permission of The Physiological Society and the authors.] B–*Left column*. Intracellular potential as a result of an 8.5-nA current step that depolarized the cell (lower figure) and another that hyperpolarized the cell (upper figure). *Right column*. Corresponding extracellular potentials illustrating difficulty in measurement techniques. [From Eccles (1957). Reproduced with the permission of Johns Hopkins University Press and the author.]

with "initial" value equal to $V(t_1)$. Thus the results shown in Figure 3.3 will be described by

$$V(t)=\begin{cases}IR(1-e^{-t/RC}), & 0\leq t\leq t_1,\\ IR(1-e^{-t_1/RC})e^{-(t-t_1)/RC}, & t>t_1.\end{cases} \tag{3.10}$$

This solution is sketched in Figure 3.4 for the case $I>0$. The simple model performs reasonably well. Furthermore, the results of the current-step experiment enable the parameters R and C to be estimated. The quantity RC has the dimensions of time and is called the

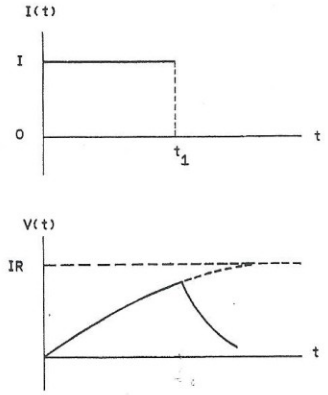

Figure 3.4. Subthreshold response of the Lapicque model neuron to a constant current step, switched on at $t = 0$ and off at $t = t_1$.

time constant τ of the membrane because in time RC the depolarization drops to e^{-1} of its initial (nonzero) value.

3.3 Impulse response (Green's function): EPSP and IPSP

The response of a linear system to an impulsive input is called the *impulse response* or *Green's function* (a term we will come across frequently in the chapters ahead). Suppose a charge C is delivered instantaneously at $t = 0$ to the resting nerve cell. Then, using the delta function introduced in Section 2.16.1, the input current is

$$I(t) = C\delta(t). \tag{3.11}$$

The solution of (3.1) with this input current is defined as the Green's function $G(t)$. Thus G satisfies

$$\frac{dG}{dt} + \frac{G}{\tau} = \delta(t), \qquad G(t) = 0, \quad t < 0. \tag{3.12}$$

Inserting $I(t)$ given by (3.11) in (3.6) gives

$$G(t) = \begin{cases} 0, & t < 0, \\ e^{-t/\tau}, & t \geq 0, \end{cases} \tag{3.13}$$

or

$$G(t) = H(t)e^{-t/\tau}. \tag{3.14}$$

The Green's function is useful to have because the response to an arbitrary input can be expressed in terms of it by means of the integral equation,

$$V(t) = \frac{1}{C}\int_0^t G(t - t')I(t')\,dt', \qquad V(0) = 0. \tag{3.15}$$

The proof of this is left as an exercise.

If Q units of charge are delivered to the nerve cell at $t = 0$, the response is $QG(t)/C$. Thus the voltage has a discontinuity of magnitude Q/C at $t = 0$. If $Q > 0$, an abrupt depolarization occurs at $t = 0$, followed by an exponential decay of the potential towards zero (resting level) with time constant τ. This response can be employed as an approximation to an EPSP. Similarly, if $Q < 0$, an abrupt hyperpolarization occurs corresponding to an IPSP. Such theoretical EPSPs and IPSPs are sketched in Figure 3.5.

Using the results so far, we can make a rough estimate of the *charge delivered* to a motoneuron during the generation of an EPSP. From Figure 1.13 we see that some EPSPs have amplitudes of about 10 mV. Using the above standard value, $C = 3 \times 10^{-9}$ F, the charge delivered during this EPSP is about 3×10^{-11} C.

The equation satisfied by $V(t)$ can be rearranged to give

$$I(t) = C\left[\frac{dV}{dt} + \frac{V}{\tau}\right]. \tag{3.16}$$

Hence if $V(t)$ and dV/dt are known, we can obtain the input current, within the framework of the present model. Experimentalists can, in fact, find dV/dt directly with electronic circuitry. This was utilized by

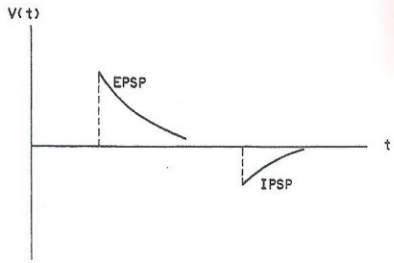

Figure 3.5. Approximations to EPSP and IPSP in the Lapicque model when impulsive currents are applied.

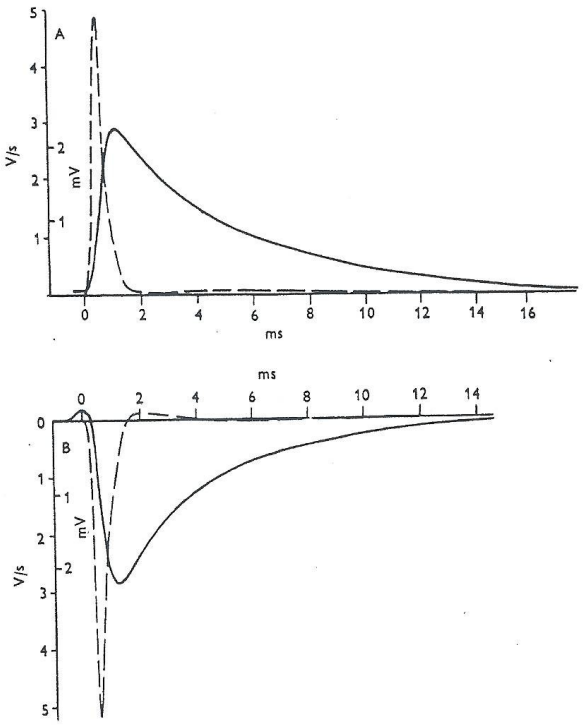

Figure 3.6. Computed current flow during the EPSP and IPSP of a cat spinal motoneuron. The dashed lines are the currents deduced from the Lapicque model via Equation (3.16). The solid lines are the observed postsynaptic potentials. Note the scales for voltage and current. [From Curtis and Eccles (1959). Reproduced with the permission of The Physiological Society and the authors.]

Curtis and Eccles (1959) and the results they obtained for the current that flows during an EPSP and an IPSP are shown in Figure 3.6.

According to these results, the currents that flow, while synaptic inputs occur, rise quickly to their maximum values and decline more slowly. For the current generating the EPSP there is a small residual depolarizing current and for that generating the IPSP there is an overshoot past zero. It was further noted by Curtis and Eccles (1959) that the time constant of decay of the EPSP, the time constant of decay of the IPSP, and the time constant of decay after a current step is terminated were all different. Such discrepancies are accounted for in a natural way with models that incorporate the spatial extent of the nerve cell (see Chapter 5).

Impulsive currents lead to discontinuous voltage trajectories, whereas the EPSPs and IPSPs of the motoneuron (Figures 1.13 and 1.15) rise smoothly from zero to achieve their maxima and minima. The chief components of the current pulses in Figure 3.6 can be approximated using various mathematical expressions. One approximation is a triangular pulse, which is studied in the next section on repetitive stimulation. However, a commonly employed approximation is a function that has been called an *alpha function* by Jack et al. (1985) and is proportional to a gamma density. For this approximation to a synaptic input current, we put

$$I(t) = kte^{-\alpha t}, \qquad \alpha > 0, \tag{3.17}$$

which corresponds to delivering a total charge of k/α^2 to the cell, as the reader may verify.

Assuming $V(0) = 0$, we find that the response of the Lapicque model neuron to such a current pulse is, from (3.6),

$$V(t) = \frac{k}{C} e^{-t/\tau} \int_0^t t' e^{(1/\tau - \alpha)t'}\, dt'. \tag{3.18}$$

Now put

$$\beta = 1/\tau - \alpha. \tag{3.19}$$

Using the rule for *integration by parts*

$$\int_0^t u'v\, dt' = [uv]_0^t - \int_0^t uv'\, dt', \tag{3.20}$$

we finally obtain

$$V(t) = \frac{ke^{-t/\tau}}{\beta C}\left[te^{\beta t} - \frac{(e^{\beta t} - 1)}{\beta}\right], \qquad \beta \neq 0. \tag{3.21}$$

If $\alpha = 1/\tau$, then $\beta = 0$ and the following result is obtained:

$$V(t) = \frac{kt^2}{2C} e^{-t/\tau}, \qquad \beta = 0. \tag{3.22}$$

Notice that if $\alpha \to \infty$ and $k = \alpha^2$, the pulse given by (3.17) approaches a delta function. Thus the rise time becomes smaller as $\alpha \to \infty$. EPSPs in response to inputs of the form of (3.17) for various α are drawn in Figure 3.7.

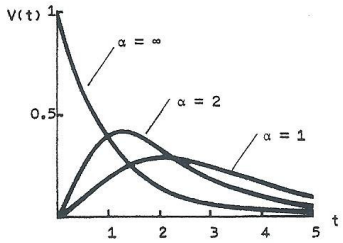

Figure 3.7. EPSP's in the Lapicque model neuron for input currents of the form of an alpha function (3.17) with $k = C$, $\tau = 1$.

3.4 Subthreshold repetitive excitation

Delta-function input currents

We start with a simple situation – a train of impulse currents at regular intervals. If these occur a time interval T apart, we have

$$I(t) = kC \sum_{n=1}^{\infty} \delta(t - nT), \tag{3.23}$$

where k is a constant and C is the membrane capacitance. After the first input event, $V(t)$ will jump from zero to k, then decay exponentially to $k \exp[-T/\tau]$ and the second input event takes $V(t)$ to $k \exp[-T/\tau] + k$, then $V(t)$ decays to $(k \exp[-T/\tau] + k)\exp[-T/\tau]$, and so forth (see Figure 3.8).

We see that the values of $V(t)$, just before and after the nth impulse current is delivered, are

$$V(nT^-) = ke^{-T/\tau}[1 + e^{-T/\tau} + \cdots + e^{-(n-2)T/\tau}], \qquad n \geq 2, \tag{3.24}$$

and

$$V(nT^+) = V(nT^-) + k. \tag{3.25}$$

These geometric series may be summed but it is immediate that if a steady state prevails and we denote the *maxima and minima in the steady state* by $V_{\max}$ and $V_{\min}$, then we must have

$$V_{\max} e^{-T/\tau} = V_{\min}, \tag{3.26}$$

and

$$V_{\max} = V_{\min} + k. \tag{3.27}$$

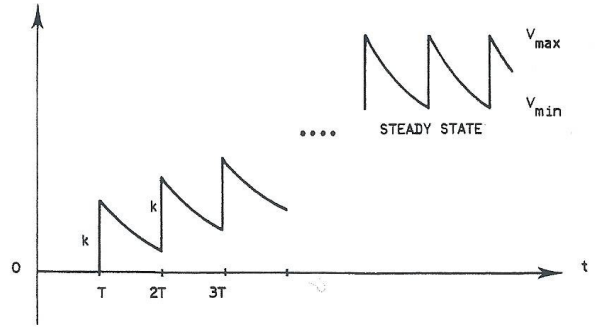

Figure 3.8. Response of the Lapicque model to a repetitive train of impulse currents each of which causes $V(t)$ to jump by k. It is assumed that the steady-state maxima and minima are below threshold for action-potential generation.

Solving these, we get

$$V_{\max} = \frac{k}{1 - e^{-T/\tau}}, \tag{3.28A}$$

$$V_{\min} = \frac{ke^{-T/\tau}}{1 - e^{-T/\tau}}. \tag{3.28B}$$

If the maxima in the steady state do not rise above a threshold level θ (assumed constant), then the neuron will never fire. Hence a *necessary condition for firing* is

$$\frac{k}{1 - e^{-T/\tau}} \geq \theta. \tag{3.29}$$

If we rearrange this expression, we get a value (the reciprocal of the T value) for the *critical frequency* of inputs that is necessary to make the cell fire

$$f_{\text{crit}} = \frac{1}{\tau \ln\left(\dfrac{1}{1 - k/\theta}\right)}. \tag{3.30}$$

Suppose the neuron receives *multiple inputs* each of which is periodic and with constant magnitude. Then the input current has the form

$$I(t) = C \sum_{j=1}^{m} k_j \sum_{n=1}^{\infty} \delta(t - nT_j), \tag{3.31}$$

where there are m inputs. k_j is the strength of the jth input and $1/T_j$ is its frequency. The subthreshold equation is linear so the response is just the sum of the responses to the individual inputs. The determination of the steady-state response, however, is difficult unless simplifying assumptions are made about the frequencies of the inputs. For example, suppose the cell receives excitation as before, but now there is also an inhibitory input with half the strength and half the frequency. That is,

$$I(t) = kC \sum_{n=1}^{\infty} \left(\delta(t-nT) - \tfrac{1}{2}\delta(t-2nT)\right). \tag{3.32}$$

It is left as an exercise to show that in the steady state the maxima and minima are

$$V_{\max} = \frac{k\left[1+\tfrac{1}{2}e^{-T/\tau}\right]}{\left[1-e^{-2T/\tau}\right]}, \tag{3.33}$$

$$V_{\min} = V_{\max} - k. \tag{3.34}$$

Triangular current pulses

The results obtained by Curtis and Eccles (1959), which are shown in Figure 3.6 for the current that flows during postsynaptic potentials, suggest that a good approximating function for the current would be a triangular one. A particular form for such a current is, for a waveform with period T,

$$I(t) = \begin{cases} Jt/a, & 0 \le t \le a, \\ J - J(t-a)/2a, & a < t \le 3a, \\ 0, & 3a < t \le T, \end{cases} \tag{3.35}$$

with an EPSP occurring if J is positive and an IPSP if J is negative. The train of input pulses and the response $V(t)$ to a single input together with the steady-state response are sketched in Figure 3.9. The calculation of the response is quite involved and provides a good test of manipulative skill with Laplace transforms. The steady-state maxima and minima are

$$V_{\max} = J\tau\left(3 - \frac{t_2}{a}\right)/2C, \tag{3.36}$$

$$V_{\min} = J\tau\frac{t_1}{aC}, \tag{3.37}$$

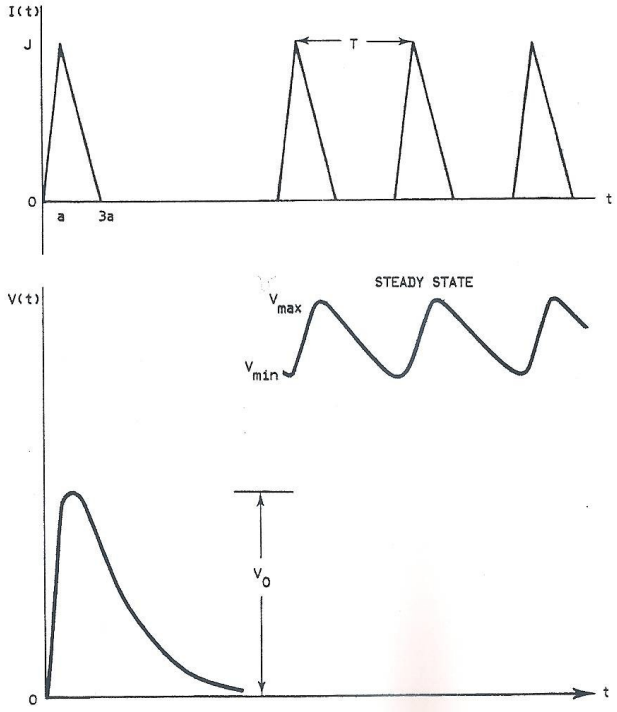

Figure 3.9. The upper graph is the train of triangular current pulses representing repetitive synaptic excitation of the model neuron. The response to the first current pulse has amplitude V_0, and eventually a steady state prevails with maxima $V_{\max}$ and minima $V_{\min}$.

where

$$t_1 = \tau \ln\left[\frac{2e^{T/\tau} - 3e^{a/\tau} + e^{3a/\tau}}{2(e^{T/\tau}-1)}\right], \tag{3.38}$$

$$t_2 = \tau \ln\left[\frac{2 - 3e^{a/\tau} + e^{-T/\tau}e^{3a/\tau}}{e^{-T/\tau}-1}\right]. \tag{3.39}$$

These results turn out to be very useful and provide us with a means of comparing some experimental results on cat spinal motoneurons with those predicted by our simple neuron model.