NEURAL PROSTHESES

Fundamental Studies

EDITORS

WILLIAM F. AGNEW

DOUGLAS B. MCCREERY

Prentice Hall

Englewood Cliffs, New Jersey 07632

Library of Congress Cataloging-in-Publication Data

Neural prostheses.

(Prentice Hall biophysics and bioengineering)
(Prentice Hall advanced reference series)
Includes bibliographies and index.
1. Neural stimulation. I. Agnew, William F.,
II. McCreery, Douglas B. III. Series.
IV. Series: Prentice Hall advanced reference series.
[DNLM: 1. Electric Stimulation. 2. Neurophysiology.
3. Prosthesis Design. WL 102 N4935]
RC350.N48N47 1990 616.8'04645 89-8592
ISBN 0-13-615444-1

Editorial/production supervision
and interior design: Karen Bernhaut
Cover design: Ben Santora
Manufacturing buyer: Mary Ann Gloriande

Prentice Hall Advanced Reference Series

Prentice Hall Biophysics and Bioengineering Series

Printed in the United States of America
10 9 8 7 6 5 4 3 2 1

ISBN 0-13-615444-1

Prentice-Hall International (UK) Limited, *London*
Prentice-Hall of Australia Pty. Limited, *Sydney*
Prentice-Hall Canada Inc., *Toronto*
Prentice-Hall Hispanoamericana, S.A., *Mexico*
Prentice-Hall of India Private Limited, *New Delhi*
Prentice-Hall of Japan, Inc., *Tokyo*
Simon & Schuster Asia Pte. Ltd., *Singapore*
Editora Prentice-Hall do Brasil, Ltda., *Rio de Janeiro*

3

Electrical Excitation of Nerve

J. THOMAS MORTIMER

INTRODUCTION

The electrical excitability phenomenon of nerve, through which propagated action potentials can be initiated, is understandable and can be used in many ways to restore function to people with neurological handicaps. However, for many practitioners, the phenomenon is more like a mystery, involving the application of two electrodes to a region on or within the body and connecting the electrodes to a source of electrical energy and observing an evoked physiological response. In this chapter I hope to remove some of the mystery that is associated with the phenomenon and to make it more comprehendible. I will develop an analytical model of the nerve membrane, use it to simulate the electrical excitation process, and plot the calculated membrane response. Through the latter, the rich variations of the phenomenon will become apparent.

Analytical models for the giant axon of the squid [2, 3], the amphibian myelinated nerve [1, 6], and the mammalian myelinated nerve [10] have been developed. In the material that follows, the focus will be on the Hodgkin and Huxley model of the squid axon; it formed the basis of the higher level models and it embodies the essence of the membrane excitability phenomenon that is shared by the other models.

ANALYTICAL MODEL OF THE NERVE MEMBRANE

The electrical excitability phenomenon is a by-product of the action potential propagation phenomenon, the mechanism by which information is passed from one end of a nerve cell to the other end. Information, in the form of action potentials, is carried along the nerve as a propagated transient change in the resting transmembrane potential. The resting transmembrane potential arises because of an ionic concentration difference between the inside and the outside of the cell body or axon. The concentration of sodium ions [Na^+] is higher outside the axon than inside, and the concentration of potassium ions [K^+] is higher inside than outside. The flow of ions across the membrane can be represented as an electrical current that obeys Ohm's law:

$$I_{\text{ion}} = g_{\text{ion}}(V_m - E_{ion}) \tag{3.1}$$

where g_{ion} is the membrane conductance (related to the ionic permeability) and V_m is the membrane potential. E_{ion} is the equilibrium potential for a particular ion and is given by the Nernst equation:

$$E_{\text{ion}} = (RT/zF)log_e C_o\backslash C_i) \tag{3.2}$$

where R is the gas constant, T is the absolute temperature, z is the valence of the ion, F is the Faraday constant, C_o is the concentration of the ion on the outside of the axon, and C_i is the concentration of the ion on the inside of the axon. Under resting conditions, the inward sodium current is equal and opposite to the outward potassium current. Therefore, there is no net current across the membrane:

$$I_{\text{Na}} = -I_{\text{K}} \tag{3.3}$$

Using Eq. (3.1), Eq. (3.3) can be written as

$$g_{Na}(V_m - E_{Na}) = -g_K(V_m - E_K) \tag{3.4}$$

This equation can be solved for V_m:

$$V_m = \frac{(g_{Na}\backslash g_K)(E_{Na}) + E_K}{(g_{Na}\backslash g_K) + 1} \tag{3.5}$$

This expression shows that the membrane potential is regulated by the relative ion conductances (permeability of the membrane to sodium and potassium). If the sodium conductance is very small, the membrane potential approaches E_k ($\approx -60\ mV$), as is the case at rest. If the sodium conductance becomes large, the membrane potential approaches the sodium potential, E_{Na} ($\approx +55\ mV$), as is the case during an action potential.

An electrical circuit model, used to describe the behavior of a nerve membrane, is shown in Fig. 3.1. The membrane is modeled as a parallel network composed of a capacitor and conductances that represent the membrane permeability to sodium, potassium, and a class of ions that do not exhibit a variable permeability. The chloride ion is included in the latter group. The capacitor, C_m, accounts for the charge storage capacity of the membrane.

The variable conductances g_{Na} and g_K, which control the membrane potential, were found experimentally to be a function of time and transmembrane potential. For the squid axon, their behavior can be described quantitatively by the following equations:

$$g_{Na} = \hat{g}_{Na} m^3 h \tag{3.6}$$

$$g_K = \hat{g}_K n^4 \tag{3.7}$$

where $\hat{g}_{Na}$ and $\hat{g}_K$ are the maximum conductances, and

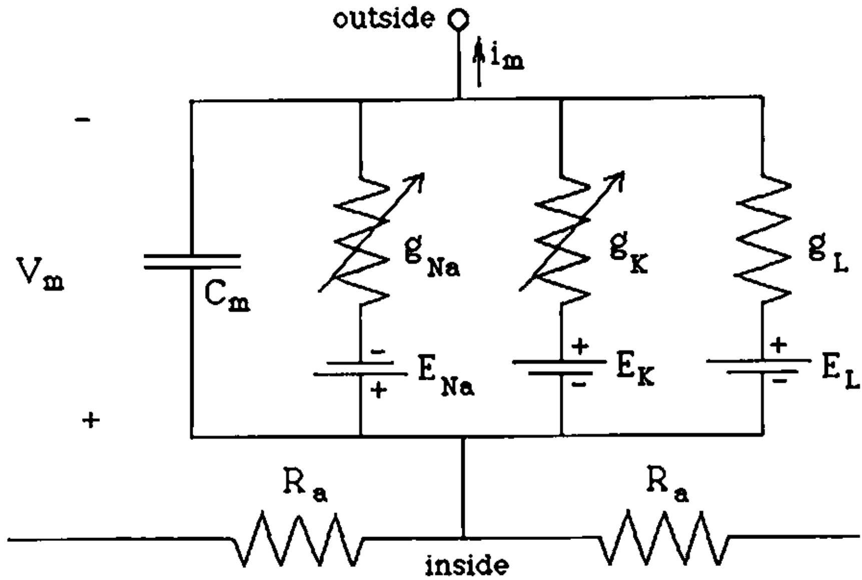

Figure 3.1 The capacitor C_m is the membrane capacitance ($\approx 1 uF/cm^2$). E_K and E_{Na} are the driving potentials for the potassium and sodium currents and are given by the Nernst potential. The membrane conductances, g_K and g_{Na}, are variable, while g_L, the leakage conductance, is the constant. The transmembrane potential is V_m. The internal resistance of the axon is given by R_a.

$$dm/dt = \alpha_m(1 - m) - \beta_m m \tag{3.8}$$

The expressions relating the parameters h and n to the parameters α and β are similar in form to Eq. (3.8). The parameters h, m, and n are functions of membrane potential and time. The equations are mathematical constructs that describe the behavior of the sodium and potassium conductances. They take on values between zero and one. The parameters α and β may be viewed as rate constants for processes that regulate the activation and inactivation of the ion channels that control the membrane permeability. The parameters, α and β, are dependent only on the membrane potential, V_m. For the sodium activation parameter, m

$$\alpha_m = \frac{-0.1(V_m + 35)}{\exp[(-V_m - 35)/10] - 1} \tag{3.9}$$

$$\beta_m = 4 \exp[(-V_m - 60)/18] \tag{3.10}$$

where V_m is the transmembrane potential in millivolts. Similar expressions describe the behavior of α and β for the h and n parameters. A solution for Eq. (3.8) is

$$m(t) = m_\infty - (m_\infty - m_o)\exp[-1/\tau_m] \tag{3.11}$$

where $$m_\infty = \alpha_m(\alpha_m + \beta_m) \tag{3.12}$$

and $$\tau_m = 1/(\alpha_m + \beta_m) \tag{3.13}$$

At the normal resting membrane potential and under resting conditions m_∞ and n_∞ have values near zero, and h_∞ has an approximate value of 0.6. As the membrane potential, as measured inside to outside, is made more negative (hyperpolarized), m_∞ and n_∞ become even smaller while h_∞ becomes larger, approaching a value of one for large values of hyperpolarization. As the membrane potential is made more positive (depolarization), m_∞ and n_∞ become larger and h_∞ becomes smaller. Thus, m represents the tendency for the Na^+ conductance to increase when the membrane is depolarized, and to decrease when hyperpolarized. The h parameter expresses an opposing process that develops more slowly and thus later in the action potential: hyperpolarization causes the Na^+ conductance to increase, and depolarization causes it to decrease. The rate constants τ_h, τ_m, and τ_n also are dependent upon the membrane potential. τ_m is an order of magnitude smaller than τ_h and τ_n. This means that the m parameter will respond rapidly to changes in membrane potential while h and n will be, comparatively, more sluggish. As will become apparent later, this property will explain some of the electrical excitability phenomenon and it may offer opportunities to manipulate membrane excitability.

RECONSTRUCTION OF THE ACTION POTENTIAL

The numerical expressions that were presented in the previous section can be utilized in the model shown in Fig. 3.1 to simulate the behavior of a nerve membrane. In the simulation that follows, it will be assumed that the transmembrane current density and potential are uniform along the entire length of the axon under study. The arrangement is similar to the physical experiment where the membrane is "space clamped" to eliminate current flowing along the axis of the axon. Under these conditions, we can describe the membrane current for the model in Fig. 3.1 as the sum of the branch currents:

$$I_m = i_c + \Sigma i_{ion} \tag{3.14}$$

where

$$i_c = C_m[dV_m/dt] \tag{3.15}$$

and i_{ion} is given by Eq. (3.1).

Under space clamped conditions, the membrane current is controlled and I_m can be replaced by I_s, the stimulus current. Equation (3.14) can be rewritten using Eqs. (3.1) and (3.15) to yield

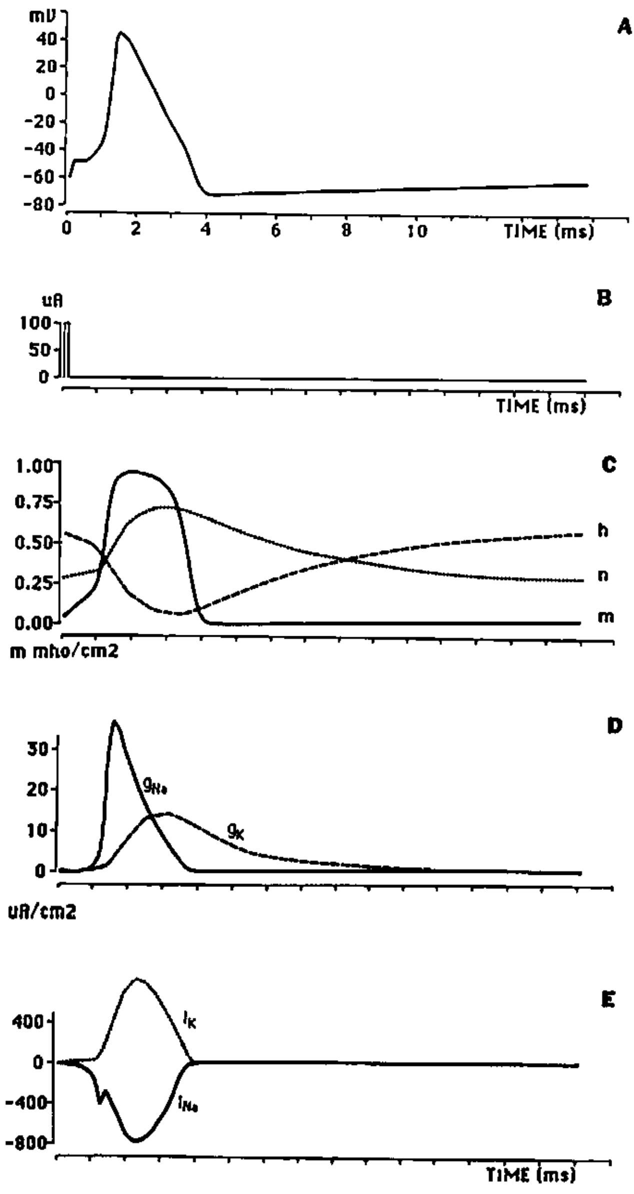

Figure 3.2 (Response to suprathreshold stimulation.) (A) The simulated membrane potential resulting from (B), a 100 μs monophasic cathodic stimulus. (C) The behavior of the parameters that control the membrane conductances. (D) The behavior of g_{Na} and g_K. (E) The behavior of the ionic currents, i_{Na} and i_K.

$$dV_m/dt = (1/C_m)[I_s - \bar{g}_{Na}m^3h(V_m - E_{Na}) - \bar{g}_K n^4(V_m - E_K) - \bar{g}_L(V_m - E_L)] \tag{3.16}$$

The behavior of the membrane potential, $V_m(t)$, in response to various stimuli, I_s, can be evaluated by solving Eq. (3.16).

Figure 3.2 shows the results of a simulation [7] for a depolarizing stimulus of 100 $\mu A/cm^2$ and 100 μs in duration. (This is a suprathreshold stimulus. Threshold excitation will be discussed below.) The transmembrane potential is shown in Fig. 3.2A. The rapid depolarization phase begins about 1 ms after the stimulus, and the duration of the action potential is about 3 ms. Figure 3.2C shows $h(t)$, $m(t)$, and $n(t)$, the parameters that regulate the ionic conductances of the membrane. At the peak of the action potential, $m(t)$ is very close to 1 and $h(t)$ has decreased only slightly. The m parameter follows closely the time course of the membrane potential, while h and n lag. Thus, $m(t)$ has almost fully recovered to its initial value (the value at $t = 0$) at the end of the action potential, but $h(t)$ and $n(t)$ do not recover to their initial values until about 10 ms have elapsed. Since $h(t)$ is less than its initial value for a period of time after the action potential has terminated, the sodium conductance (g_{Na}) will be lower than its resting value during that time. Further, since $n(t)$ is higher than the resting value during this same period, the potassium conductance (g_K) will be abnormally high for a period of time following the termination of the action potential. The combination of the lowered sodium conductance and the elevated potassium conductance will render the membrane less excitable; it will require a greater stimulus to initiate an action potential during this transient recovery period. This is called the refractory period and is divided into two parts, the absolute and the relative refractory period. The absolute refractory period is the phase immediately following the action potential when the membrane is not excitable even with very high stimulus amplitudes, due to the near complete inactivation of the Na^+ conductance. The relative refractory period follows the absolute refractory period; during this time the membrane can again be depolarized but stimulus amplitudes for action potential initiation are elevated above normal values.

PROPERTIES OF ELECTRICALLY ACTIVATED NERVE

Threshold Activation

The threshold for activation is most commonly defined as the minimum stimulus amplitude (or duration) required to initiate an action potential. This definition, associated with the "all or none" concept of the action potential, may suggest that once the membrane reaches a certain potential, a trigger mechanism is released and the action potential results. This would suggest that at potentials below the "trigger level" nothing happens. In practice, the "trigger level" is difficult to define since the membrane does not behave exactly like an on–off switch with a well-defined threshold value for the transmembrane potential. Figure 3.2A indicates that V_m actually decreases for a period of time, following the increase induced by the stimulus, before the clear signs of the regenerative process take hold to give rise to the action potential. This means that it may not be possible to predict if an action potential will be initiated by observing the membrane potential shortly after the application of the stimulus. The behavior of $V_m(t)$ in Fig. 3.2A, in response to what is actually a "suprathreshold" stimulus, suggests an alternative definition of threshold. The alternative definition considers competing processes to be operating that are dependent upon the potential at that moment of time and the history of the potential.

This definition of "threshold" takes into account an unstable equilibrium state for the transmembrane current. In the first equilibrium state, small transient changes in membrane potential produce a net membrane current that will tend to force the membrane potential back to the resting state. This is a locally stable state. In contrast, at the threshold of excitation, where the net ionic currents are also in equilibrium, the state of the membrane is unstable; any further *increase* in the inward flow of positive charge will initiate a self-sustaining increase in Na^+ current (that is, inducing more depolarization which causes more inward current flow which in turn causes more depolarization, a positive regenerative process that proceeds until maximum depolarization is achieved). On the other hand, if the membrane is in the unstable equilibrium state and the membrane potential was made more negative (hyperpolarization), the membrane potential will return to the resting potential, the equilibrium state. It is possible for the membrane to "hang" with the ionic currents in balance at the boundary between the stable and unstable state for a long time between the application of the stimulus and when the regenerative process takes hold to produce the action potential.

Figure 3.3 shows the behavior of the membrane potential V_m and the conductance parameters h, m, and n for I_s just above threshold (50.229 $\mu A/cm^2$) and just below threshold (50.228 $\mu A/cm^2$). The prolonged onset of the action potential is evident, particularly when compared to the time of onset when the stimulus is suprathreshold (Fig. 3.2A).

Virtual Cathode and Anodic Break Response

The effect of an anodic stimulus pulse is to move the membrane potential in the opposite direction as when a cathodic pulse is applied. However, it is possible to generate an action potential using only anodic

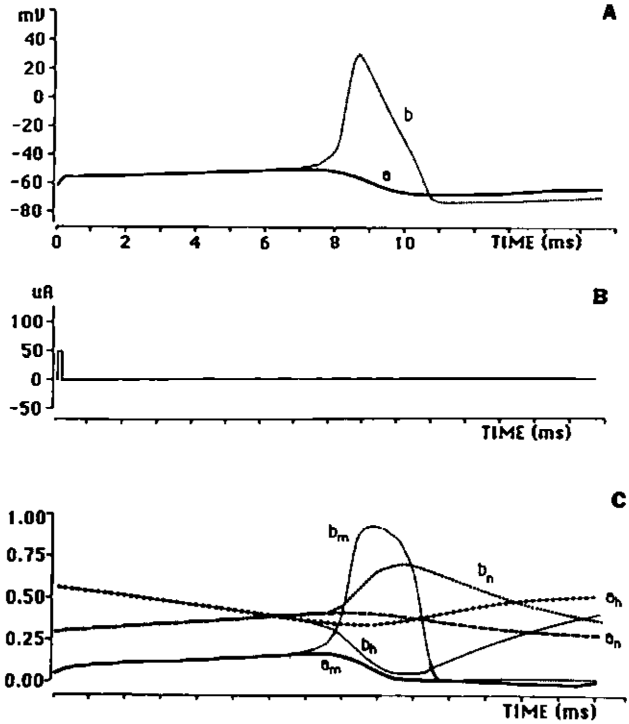

Figure 3.3 (Simulated membrane response near threshold.) (A) Curve (a) shows the membrane potential to a subthreshold (50.228 $\mu A/cm^2$) stimulus pulse shown in (B). Curve (b) shows the threshold response to 50.229 $\mu A/cm^2$. (C) The behavior of the membrane parameters. The subthreshold responses are labeled a, with the parameter as a subscript. Threshold responses are labeled b.

pulses. There are two mechanisms by which an anodic pulse can effect an action potential; one is by a depolarizing current exiting the membrane, and the other is by positive current entering the membrane.

The first mechanism is similar to that by which a cathodic stimulus causes an action potential. It can be visualized by considering that when positive current enters the membrane under the anode it must also exit the membrane. At the exit point(s) the membrane is depolarized as it would be beneath the cathode. The exit points are referred to as virtual cathodes and they are usually distributed over several nodes or patches of membrane as opposed to being localized to the immediate vicinity of the electrode. The threshold for depolarization by this mechanism, as defined by the electrode current, is higher than for cathodic excitation, since the depolarizing current is more diffuse.

The second mechanism by which an anodic stimulus can effect an action potential is a consequence of the different time constants governing the behavior of the membrane conductivity parameters h, m, and n. The effect of an anodic pulse (a hyperpolarizing stimulus) is to cause m to become smaller (approaching zero), h to become larger, and n to become smaller. For an anodic pulse of approximately the same magnitude, the membrane is transiently hyperpolarized. However, for a much larger anodic stimulus, the relative rates of recovery of the membrane conductivity parameters become important. Recall that τ_m is much smaller than τ_h and τ_n. This means that m can recover much sooner than either h or n after the end of the anodic stimulus. When this occurs, the sodium conductance is higher than at resting levels, the potassium conductance is lower than resting value and there is a net flow of positive ions into the axoplasm. The net flow of inward current causes the membrane to further depolarize and the process can become regenerative to produce an action potential. This response is termed the anodic break response. Although it occurs after the end of a large anodic pulse, it is not a result of the lagging edge of the pulse, as its name might suggest, but rather it arises from an imbalance in I_K and I_{Na} brought about by the fact that τ_m is faster than both τ_h and τ_n.

The anodic break response is illustrated in Fig. 3.4. The curve labeled as a, in the upper panel, is the membrane potential in response to a 100 $\mu A/\text{cm}^2$, 100 μs, anodic stimulus (recall from Fig. 3.2 that the cathodic threshold is about 50 $\mu A/\text{cm}^2$). For a stimulus of this magnitude, the membrane is hyperpolarized transiently and no action potential occurs; the behavior of h, m, and n are shown in Fig. 3.4C. Increasing the magnitude of the stimulus to 200 $\mu A/\text{cm}^2$ results in an action potential, the membrane response, labeled as b, is shown in the upper panel of Fig. 3.4C. Approximately 9 ms after the stimulus an action potential occurs. Notice in Fig. 3.4C that after 4 ms have elapsed, m has recovered to the resting value, and h (labeled b_h) is elevated above the resting value, and n (labeled b_n) is below resting value. Therefore, from Eqs. (3.6) and (3.7), g_K is lower than at rest and g_{Na} is higher than the normal resting value. There is a net positive ion current into the axon. Since the outward potassium current is suppressed, it cannot counter the inward sodium current and the membrane continues to depolarize until eventually an action potential occurs. Were τ_h *or* τ_n faster, the action potential might not have occurred.

The anodic break response is not usually encountered in the implementation of most neural prostheses because the magnitude of the stimulus required to cause the response is well above threshold values for cathodic stimuli. However, collision block is an application where the anodic break response is encountered and is a problem [12]. This neural prosthesis causes unidirectionally propagating action potentials to be effected by blocking, at an anode electrode, the propagation in one direction of a cathodically initiated action potential. The block can only be

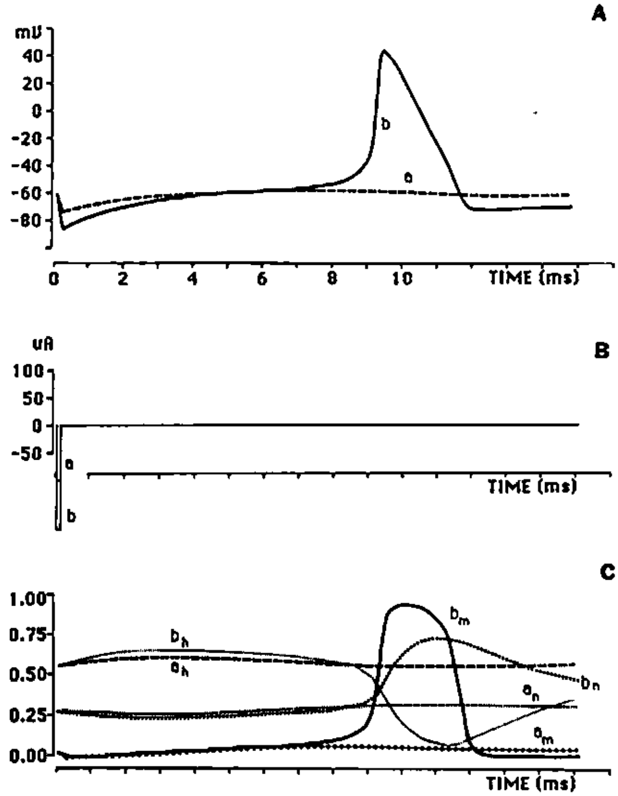

Figure 3.4 (Anodic Break Response.) (A) The simulated membrane response to an anodic stimulus of two amplitudes. The response labeled *a* corresponds to a stimulus of 100 $\mu A/cm^2$, 100 μs in duration. Curve *b* is the response to 200 $\mu A/cm^2$, 100 μs. (B) The stimulus pulses. (C) The behavior of the membrane parameters (labeled as in Fig. 3.3).

effected by the application of anodic stimuli that are much greater in amplitude and duration than are required to initiate action potentials. The anodic break response can be eliminated by terminating the stimulus with an exponentially decaying edge rather than an abrupt change. The slowly decaying edge of the anodic pulse presumably falls at a rate that is similar to τ_h, which keeps m suppressed as h recovers.

Biphasic Pulses

Two closely spaced pulses can interact to alter the effect of a single pulse applied to the nerve membrane. A common example of two closely spaced pulses is the charge-balanced, biphasic pulse, consisting of a closely spaced pair of pulses, each of equal charge but opposite polarity. This is the stimulus waveform recommended for neural prostheses, in order to avoid tissue damage. The concept behind the balanced-charge biphasic pulse waveform is that the electrochemical reactions occurring during the first pulse are reversed by the following pulse of opposite polarity. For the purposes of the discussion that follows, the cathodic pulse will be assumed to be the pulse responsible for the nerve excitation and the anodic pulse is the charge-balancing phase of the stimulus.

Biphasic pulses (cathodic phase first). For the most common form of balanced-charge biphasic stimulation, the cathodic pulse occurs first. The discussion in the previous sections of this chapter suggests that the anodic pulse will turn off the regenerative depolarization processes that were initiated by the cathodic phase; the membrane response is illustrated in the simulation shown in Fig. 3.5.

The effect of three stimulus waveforms on the membrane potential are shown in Fig. 3.5A. The stimulus wave forms are:

1. a monophasic cathodic stimulus applied at $t = 3$ ms (unlabeled curve)
2. a biphasic stimulus with the cathodic phase applied at $t = 3$ ms and the anodic phase applied 0.5 ms after the cathodic phase (curve labeled a)
3. a biphasic stimulus with the anodic phase applied 0.75 ms after the cathodic pulse (curve labeled b).

If the anodic pulse occurs within 0.5 ms after the cathodic pulse, the effect is to turn off the regenerative processes that would have otherwise produced the action potential. However, if the anodic pulse is delayed by 0.75 ms after the cathodic pulse, the regenerative processes are sufficiently well developed, and the anodic pulse cannot suppress but only delay the development of the action potential. The suppressive effect of the second anodic pulse was mentioned by Lilly [5] and later studied in a nerve-muscle preparation (motor prosthesis) by van den Honert and Mortimer [11]. In the latter study, a delay of 100 μs between the termination of the cathodic pulse and the onset of the anodic pulse was recommended, to avoid the suppressive effect of the anodic pulse.

The suppressive effect of the anodic pulse is manifested as an increased threshold for biphasic stimulation, as compared to monophasic stimulation. Therefore, in an application such as a motor prosthesis, the muscle force-stimulus (recruitment) curve for the biphasic stimulus is shifted to the right of the recruitment curve generated using a monophasic stimulus. The shift is minimal when the delay between the two pulses is 100 μs or more.

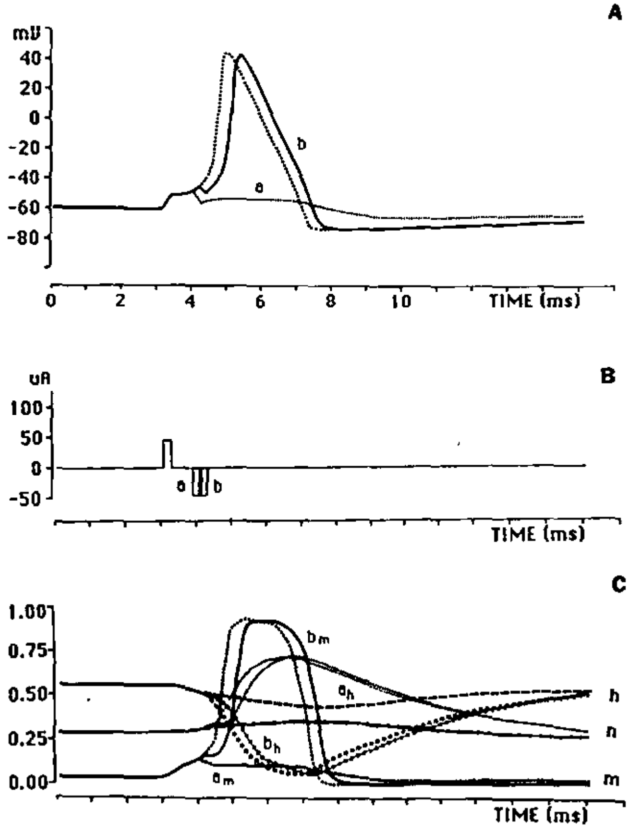

Figure 3.5 (Response to biphasic stimulus, cathodic phase first.) (A) The response of the membrane potential to three stimulus waveforms. The unlabeled curve is response to a monophasic cathodic stimulus applied at $t = 3\ \mu s$. Curve (a) is response to a cathodic phase applied at $t = 3\ \mu s$ and the anodic phase applied 0.5 ms after the cathodic phase. Curve (b) is response when the anodic phase is applied 0.75 ms after the cathodic pulse. (B) The three stimulus waveforms. The shaded area shown on the anodic phases of the stimuli represents overlap of the two pulses. (C) The response of the membrane parameters, m, n, and h, to the three types of stimuli. Curves labeled a are the response with the anodic pulse a, b with anodic pulse b. Unlabled curves are the response to the monophasic cathodic pulse alone.

Biphasic pulses (anodic phase first). It may be desirable to operate some electrode materials with the anodic pulse preceding the cathodic pulse (for example, Ta-Ta_2O_5 [8] and iridium oxide [9]). The discussion of anodic break excitation suggests that if the cathodic phase follows the anodic phase after a sufficient delay, the biphasic threshold value would

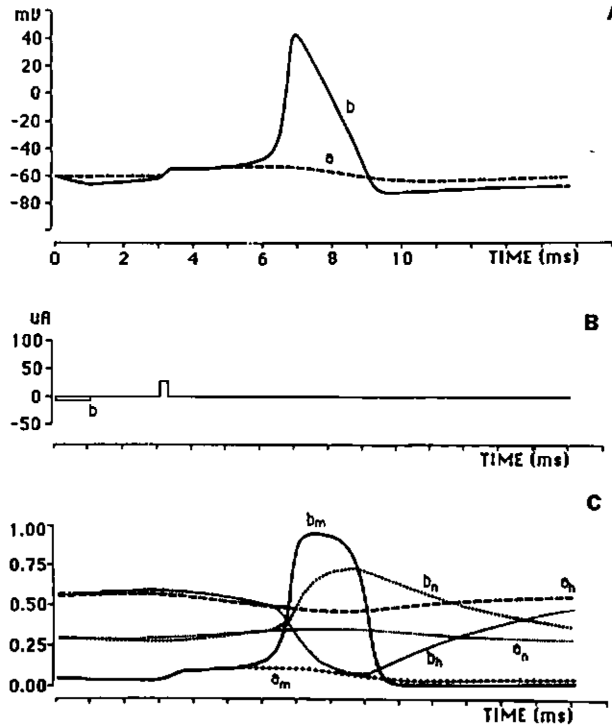

Figure 3.6 (Response to biphasic stimulus, anodic phase first.) (A) The curve labeled (*a*) is the membrane response to a subthreshold monophasic stimulus. Curve (*b*) is the response to the biphasic stimulus shown in (B). The stimulus is charge balanced but the first phase is of longer duration and lower amplitude than the second, cathodic, phase. (C) The response of the membrane parameters.

be lower than the monophasic threshold. This is illustrated in the simulation shown in Fig. 3.6.

Two membrane voltage waveforms are shown in the upper panel of Fig. 3.6. The curve labeled *a* is the response to a subthreshold monophasic cathodic stimulus. The second waveform, labeled *b*, is the response to the biphasic stimulus shown in the center panel. The biphasic stimulus is charge-balanced, but the first phase is of longer duration and lower amplitude than is the second (cathodic) phase. The combined effect of the anodic pulse and the delay is to increase the sodium conductance and decrease the potassium conductance at the time the cathodic phase is applied. The apparent effect of the anodic first pulse is then to lower the threshold of the nerve to the cathodic pulse. However, if the delay is not interposed between the two phases, the biphasic threshold current will be elevated relative to the monophasic cathodic stimulus.

Strength-Duration Relationship

The amplitude of the stimulus required to initiate an action potential is greater for pulses of shorter duration than for longer pulses. The relationship between stimulus amplitude and the duration of the pulse has been studied extensively. The experimentally derived data can be fitted to a mathematical expression of the following form [4]

$$I_{th} = \frac{I_R}{1 - \exp[-PD/\tau]} \tag{3.17}$$

I_R is the rheobase current, PD is the pulse duration, and τ is a time constant of the excited neuron or axon. A curve having this form is graphed in Fig. 3.7. (Additional discussion of this relationship is presented in Chapters 7 and 11.) Equation 3.17 can provide assistance in choosing a particular stimulus amplitude or pulse duration. If current is to be minimized, then one should employ long duration pulses. However, under some conditions, it may be desirable to minimize charge per phase. The relationship between stimulus charge per phase and pulse duration can be studied by converting Eq. (3.17) to charge: multiplying the current by the pulse duration (for rectangular current stimuli) to yield the following expression:

$$Q_{th} = \frac{(PD)I_R}{1 - \exp[-PD/\tau]} \tag{3.18}$$

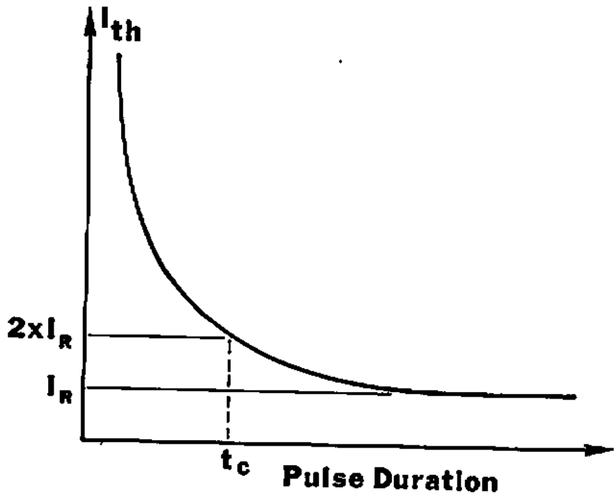

Figure 3.7 (Strength-Duration Curve.) The amplitude I_{th} of the stimulus required to initiate an action potential. The chronaxie, tc, is defined as the pulse duration at a stimulus amplitude that is twice the rheobase current, I_R.

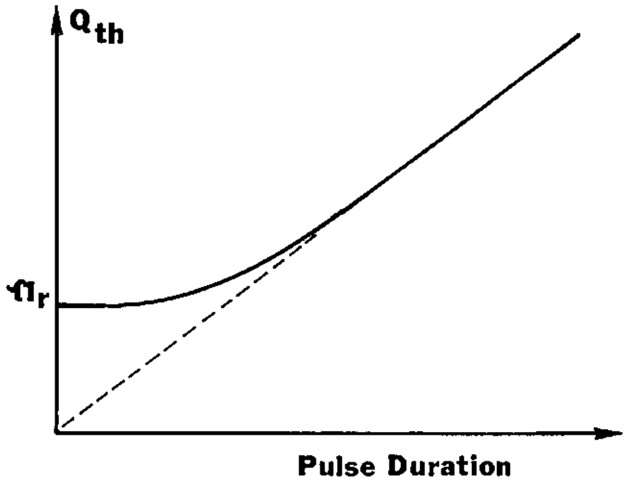

Figure 3.8 (Charge-Duration Curve.) The amount of charge that must be injected to initiate an action potential. Note that for very short pulse widths, Q_{th} approaches an asymptote that has a constant value.

The expression given in Eq. (3.18) is plotted in Fig. 3.8. As PD becomes very large, Q_{th} approaches an asymptote that increases linearly with pulse duration. At very short pulse widths, Q_{th} approaches an asymptote that has a constant value (τI_R). A pulse duration of 50 to 100 μs is appropriate for exciting the myelinated axons encountered in many neuroprosthetic applications.

SUMMARY

The electrical excitability phenomenon of nerve can be characterized analytically. The key to comprehending the phenomenon is to understand the properties of the h, m, and n parameters that control the conductivity of the membrane to the sodium and potassium ions. Through these time- and voltage-dependent parameters, the membrane excitability and the threshold stimulus current can be manipulated. This in turn offers the investigator a degree of control over how and which neurons are excited. Finally, to minimize the charge that must be injected in order to excite axons, short duration pulses are recommended.

REFERENCES

[1] Frankenhauser, B., and A. F. Huxley. 1964. The action potential in the myelinated nerve fiber of *Xenopus Laevis* as computed on the basis of voltage clamp data. *J. Physiol., 171:*302–315.

[2] Hodgkin, A. L., and A. F. Huxley. 1952. Currents carried by sodium and potassium ions through the membrane of the giant axon of *Loligo*. *J. Physiol. 116:*449–472.

[3] Hodgkin, A. L., and A. F. Huxley. 1952. A quantitative description of membrane current and its application to conduction and excitation in nerve. *J. Physiol. 117:*500–544.

[4] Lapicque, L. 1907. Recherches Quantitatives Sur L'excitation Electrique Des Nerfs Traitee Comme Une Polarization. *J. Physiol.* (Paris). *9:*622–635.

[5] Lilly, J. C., J. R. Hughes, E. C. Alvord, and T. W. Galkin. 1955. Brief noninjurious electric waveforms for stimulation of the brain. *Science. 121:*468–469.

[6] McNeal, D. R. 1976. Analysis of a model for electrical excitation of myelinated nerve. *IEEE Trans. on BME. 23:*329–336.

[7] Munir, Z. H., and J. T. Mortimer. 1988. Hodgkin and Huxley space clamped membrane. Simulation for Apple Macintosh. Available from Applied Neural Control Laboratory, Case Western Reserve University, Cleveland OH, 44106.

[8] Rose, T. L., E. M. Kelliher, and L. S. Robblee. 1985. Assessment of capacitor electrodes for intracortical stimulation. *J. Neuroscience Methods. 12:*181–193

[9] Robblee, L. S., M. J. Mangudis, E. D. Lasinsky, A. G. Kimball, and S. B. Brummer. 1986. Charge injection properties of thermally prepared Iridium Oxide films. *Materials Res. Soc. Symp. Proc. 55:*303–310.

[10] Sweeney, J. D., D. Durand, and J. T. Mortimer. 1987. Modeling of mammalian myelinated nerve for functional neuromuscular stimulation. *IEEE-EMBS Conference, Boston.* 1577.

[11] van den Honert, C., and J. T. Mortimer. 1979. Response of the myelinated nerve fiber to short duration biphasic stimulating currents. *Annals of Biomed. Eng. 7:*117–125.

[12] van den Honert, C., and J. T. Mortimer. 1981. A technique for collision block of peripheral nerve: single stimulus analysis. *IEEE Trans. on BME. 28:*373–378.