150

# A COMPUTER-SIMULATED MODEL FOR THE NEURONAL CIRCUIT MEDIATING THE TAIL-FLIP ESCAPE RESPONSE IN CRAYFISH

by

PRAMATHESH KUMAR

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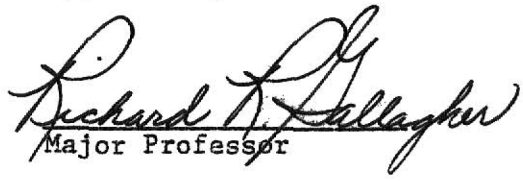

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TABLE OF CONTENTS


| Chapter | | Page |
|---|---|---|
| I. | INTRODUCTION AND PROBLEM STATEMENT..... | 1 |
| II. | NEURONAL MODELING: A PERSPECTIVE..... | 3 |
| | 2.1. Mathematical Models..... | 3 |
| | 2.2. Electronic Models..... | 4 |
| | 2.3. Computer-simulated Models..... | 5 |
| III. | DESCRIPTION OF THE NEURONAL CIRCUIT..... | 7 |
| IV. | DESCRIPTION OF THE MODEL..... | 10 |
| | 4.1. Synaptic Variables..... | 10 |
| | 4.2. Neuronal Variables..... | 16 |
| | 4.3. Sensory Neurons..... | 20 |
| | 4.4. Description of the Computer Programs..... | 22 |
| V. | SIMULATION OF THE NEURONAL CIRCUIT..... | 23 |
| | 5.1. Simulated Neuronal Circuit..... | 23 |
| | 5.2. Simulation Runs..... | 28 |
| VI. | SIMULATION RESULTS..... | 30 |
| | 6.1. Circuit Response to a Single Stimulus..... | 30 |
| | 6.1.1. Generated Action Potentials..... | 30 |
| | 6.1.2. Effect of Feedback Inhibition on the Lateral Giant Membrane Potential..... | 32 |
| | 6.2. Circuit Response to Stimulation at 100 Hz..... | 32 |
| | 6.2.1. Generated Action Potentials..... | 32 |
| | 6.2.2. Effect of Presynaptic Inhibition on Antifacilitation..... | 35 |
| | 6.2.3. Effect of Feedback Inhibition on the Response of Interneurons 1 and 2..... | 37 |
| | 6.2.3.1. Interneuron 1 Membrane Potential..... | 37 |
| | 6.2.3.2. Generated Action Potentials..... | 39 |
| | 6.2.4. Lateral Giant Membrane Potential..... | 43 |
| | 6.2.5. Circuit Response with All the Sensory Interneurons Subject to Feedback Inhibition..... | 43 |
| | 6.2.5.1. Generated Action Potentials..... | 43 |
| | 6.2.5.2. Lateral Giant Membrane Potential..... | 43 |

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CONTAINS
NUMEROUS PAGES
WITH ILLEGIBLE
PAGE NUMBERS
THAT ARE CUT OFF,
MISSING OR OF POOR
QUALITY TEXT.

THIS IS AS RECEIVED
FROM THE
CUSTOMER.

| Chapter | | Page |
|---|---|---|
| | 6.3. Circuit Response to Stimulation at 66.7 Hz..... | 46 |
| VII. | DISCUSSION OF RESULTS..... | 48 |
| | 7.1. Observations on the Neuronal Circuit..... | 48 |
| | 7.2. Observations on the Model..... | 49 |
| VIII. | RECOMMENDATIONS FOR FUTURE WORK..... | 51 |
| IX. | BIBLIOGRAPHY..... | 53 |
| | ACKNOWLEDGEMENTS..... | 57 |
| | APPENDIX I. DETERMINATION OF FACILITATION PARAMETERS... | A1.1 |
| | APPENDIX II. COMPUTER PROGRAMS FOR THE MODEL..... | A2.1 |

# LIST OF FIGURES


| Figure | | Page |
|---|---|---|
| 3.1. | Neuronal Circuit Mediating the Tail-flip Escape Response in the Crayfish..... | 8 |
| 4.1. | Diagram of a Typical Postsynaptic Potential Showing the Quantities Associated with Its Modeling..... | 12 |
| 4.2. | An Actual and a Modeled Postsynaptic Potential..... | 13 |
| 5.1. | Basic Neuronal Circuit Used in the Simulation of the Crayfish Tail-flip Escape Response..... | 24 |
| 6.1. | Action Potentials Generated in the Circuit Due to a Single Input Stimulus to the Circuit..... | 31 |
| 6.2. | Lateral Giant Response to a Single Input Stimulus to the Circuit..... | 33 |
| 6.3. | Action Potentials Generated in the Circuit Due to Stimulation of the Circuit at 100 Hz..... | 34 |
| 6.4. | Effect of Presynaptic Inhibition on the Time Course of the Facilitation, F(t), of the Excitatory Synapse from the Tactile Afferents to Interneuron 1..... | 36 |
| 6.5. | Effect of Feedback Presynaptic Inhibition on the Membrane Potential in Interneuron 1..... | 38 |
| 6.6. | Effect of Feedback Postsynaptic Inhibition on the Membrane Potential in Interneuron 1..... | 40 |
| 6.7. | Combined Effect of Feedback Presynaptic and Postsynaptic Inhibition on the Membrane Potential in Interneuron 1..... | 41 |
| 6.8. | Separate and Combined Effects of Feedback Presynaptic and Postsynaptic Inhibition on the Action Potentials Generated in Interneurons 1 and 2..... | 42 |
| 6.9. | Lateral Giant Response to Stimulation of the Circuit at 100 Hz..... | 44 |
| 6.10. | Action Potentials Generated in the Circuit with All the Sensory Interneurons Subject to Feedback Presynaptic and Postsynaptic Inhibition..... | 45 |

Figure Page

6.11. Action Potentials Generated in the Circuit Due to Stimulation of the Circuit at 66.7 Hz (1 in 15 msec)..... 47

A1.1. Increase in the Fractional Transmitter Loss, L(t), Due to Stimulation of a Synapse at 1 Hz..... A1.2

A2.1. Flowchart of the Main Program..... A2.2

# LIST OF TABLES

Table Page

5.1. Synaptic Parameters Used in the Simulation..... 26

5.2. Neuronal Parameters Used in the Simulation..... 27

# I. INTRODUCTION AND PROBLEM STATEMENT

An important reason for making neuronal models is to develop a system for which all the variables of interest can be monitored continuously, and for which the parameters can be varied as desired. Computer models best achieve these objectives. Also, if small neuronal networks are chosen, it is possible to study the behavior of individual neurons. For this reason, the well-identified neuronal circuit mediating the tail-flip escape response of the crayfish (Procambarus clarkii) has been chosen for this study. A computer model which is physiologically accurate and which satisfies the objectives stated above has been built for this circuit. This model functions in discrete time steps, and is based on an earlier model [1-5].

The tail-flip response can be evoked by strong tactile stimulation of the abdomen of the crayfish. This response, lasting between 70 to 150 msec, consists of a rapid abdominal flexion followed by rapid reextension [6]. As a result, the animal is thrust backwards or upwards. This stimulus-response behavior is of particular interest to psychologists and neurophysiologists because of the strong habituating property of the response, which could serve as a basis for understanding biological memory. The habituation lasts several hours after the first few stimulus-response sequences [7,8]. An explanation for the habituation could come from the strong antifacilitation observed in the chemical synapses to the sensory interneurons in the circuit. However, this antifacilitation lasts for a few minutes at most [9-11]. A complete explanation for the behavioral habituation has not yet been found.

Of interest is the presynaptic inhibition of the sensory interneurons. By preventing transmitter loss, presynaptic inhibition

diminishes the antifacilitation caused by incoming stimuli during the period it is effective [10,12-14]. In this study, emphasis has been placed on providing a better understanding of this phenomenon and its effects.

The specific objectives of this research can be listed as follows:

1. To build a physiologically accurate "general-purpose" neuronal model that provides for control of its parameters and the continuous monitoring of its variables.
2. To apply this model to simulate the neuronal circuit for the crayfish tail-flip escape response, and verify the results of the simulation by comparison with published experimental results.
3. To use the simulation to better understand the circuit; for example, to study the effect of presynaptic inhibition on antifacilitation, the response of the circuit to a different frequency of input stimuli, and the effect of subjecting all the sensory interneurons to feedback inhibition.

## II. NEURONAL MODELING: A PERSPECTIVE

In this section, the different techniques of neuronal modeling are briefly described, and the status of the model presented in these studies vis-a-vis other neuronal models is delineated.

Neuronal models can be classified into three broad categories: (1) Mathematical, (2) Electronic, and (3) Computer-simulated. Within these three classes, a remarkable variety of models can be found in the literature [1-5,15-35].

### 2.1. Mathematical Models

Mathematical models fall into two classes:

(a) Models which attempt to quantify accurately the biophysical and biochemical events occurring at specific locations in a neuron [15,16]. These models take into account the geometrical properties of the region under consideration. Examples include: (i) Hodgkin-Huxley's ionic model for the nerve membrane [17], (ii) Rall's distributed parameter model for passive conduction in the dendritic tree [18,19], (iii) the model by Magleby and Stevens for the flow of end-plate currents upon synaptic excitation [20-22].

(b) Models which attempt to characterize the input-output relationships in single neurons or neuronal networks, with the objective of providing a better understanding of the signal processing performed. However, most of these models serve at present only as academic exercises. In addition to being mathematically onerous, they introduce a number of physiological over-simplifications. These models can be deterministic or stochastic. Deterministic models have been built for small neuronal networks as well as for large aggregates of neurons [16,23]. Practical models using this

technique have been built for the visual signal processing in the retina of the horseshoe crab, Limulus [24]. Stochastic techniques have been used to model random behavior in neurons. Examples of this behavior are: random synaptic excitation, random fluctuations in the membrane potential, random local interconnections in large aggregates of neurons, and spontaneous neuronal firing [25]. A practical model using stochastic techniques has been built by Feldman and Cowan for the brain stem respiratory oscillator in the cat [26,27]. An example of random neuronal firing is the firing in dark of certain neurons in the cat geniculate nucleus [25].

## 2.2. Electronic Models

Electronic models have enjoyed considerable popularity in the past in the simulation of small neuronal networks. An early model of this kind is the one built by Harmon in 1961 [16,28]. This model utilizes only two state variables: membrane potential and threshold. A more sophisticated model has since been built by Lewis [29]. It simulates the postsynaptic ionic conductance changes occurring in a neuron upon excitation and successfully incorporates features such as synaptic excitation, inhibition, facilitation and antifacilitation. Lewis' electronic models have been used by Wilson and Waldron to simulate the rhythmic bursts produced by the central pattern generator (C.P.G.) thought to generate the motor output controlling flight muscles in the locust [30]. They have also been used lately by Friesen to simulate the C.P.G.'s responsible for control of swimming in the leech [31] and control of flight in Drosophila [32].

Electronic models are practical, and accurate to an extent. They have the advantage over computer models in that they work in real time and permit direct visual observation of the generated waveforms [33].

## 2.3. Computer-simulated Models

A variety of digital computer models can be found in the literature [1-5,34,35]. By definition, this category also includes mathematical models that have been implemented on a computer. Computer models have important advantages over electronic models. Neuronal systems exhibit a great diversity in their behavior. Because of their flexibility, computer models can incorporate this diversity. Electronic models, on the other hand, represent "standardized neurons". In addition, certain computer models, such as the one presented in these studies, provide for continuous documentation of all variables of interest in the circuit. Electronic models, by their very nature, permit monitoring of only a restricted range of variables.

A computer model, which has been used with considerable success in the past, is the one presented by Perkel [34,35]. This model does not function in discrete time steps, but jumps from "one interesting event" to another. Such events include the arrival of an action potential at a presynaptic terminal, end of refractory period, spontaneous firing, etc. At each "interesting event", pertinent variables undergo suitable modifications, and if the proper conditions exist, future "interesting events" are generated. An inherent disadvantage of this model is the limited accuracy with which it can incorporate time-dependent variables.

An elaborate computer model, functioning in discrete time steps and incorporating a large range of neuronal and synaptic variables, has been presented by Hartline [1-5]. This modeling technique is well-suited for the simulation of small neuronal networks. The model incorporates variables such as membrane potential, threshold, pacemaker potential, spike and generator adaptation, accommodation, facilitation,

antifacilitation, postinhibitory rebound, etc. It provides for intracellular current injection and antidromic stimulation. This model has been used to simulate pattern generation in the pyloric network in the stomatogastric ganglion of the spiny lobster, Panulirus. The model developed in these studies is patterned after Hartline's model. However, it features a number of modifications.

Features added include:

1. Separation of refractory period into absolute and relative refractory periods.
2. Incorporation of presynaptic inhibition and its effect on antifacilitation.
3. Incorporation of sensory neurons.
4. Non-linear interaction between excitation and inhibition.
5. Automatic curve-fitting for a PSP (postsynaptic potential).
6. Provision for extracellular stimulation.
7. Introduction of a separate variable for accommodation.

Slight changes have been made from Hartline's model in the algorithms for the computation of threshold, spike and generator adaptation. Because they are not needed in this simulation, the following features present in Hartline's model have been omitted: pacemaker and driver potentials, postinhibitory rebound, intracellular current injection, and antidromic stimulation.

## III. DESCRIPTION OF THE NEURONAL CIRCUIT

The tail-flip escape response can be evoked in the crayfish by a single impulse in the lateral giant command neuron (LG) [36]. The neuronal circuit associated with the generation of this "decision" impulse has been studied extensively in the past [10,12,37-45]. It is illustrated in Fig. 3.1 [10]. Tactile stimulation of the crayfish abdomen, in the form of a pinch or a tap, excites a large number of tactile afferents, which innervate the pit receptors located on the surface of the exoskeleton. The tactile afferents, in turn, excite, via strongly antifacilitating chemical synapses, a population of about 40 sensory interneurons. The time constants for this antifacilitation have been calculated using the procedure described in Appendix I, and found to range between 10 to 65 seconds. This antifacilitation probably makes a short-term contribution to the habituation, which has been observed to last for several hours [7,8]. The sensory interneurons have been found to have thresholds ranging between 3 to 7 mv [38]. The action potentials produced by these sensory interneurons converge onto the lateral giant via electrical synapses. The lateral giant has a very high threshold [37,38], and requires a large barrage of excitatory synaptic input to produce the single command impulse that triggers the escape response. The lateral giant receives delayed feedback postsynaptic inhibition from the motor circuits. This inhibition appears in intracellular recordings from the lateral giant as a small-amplitude, slowly-varying, depolarizing potential, which has an equilibrium potential very close to the resting potential [42]. One interneuron, interneuron A, has been demonstrated to receive feedback presynaptic inhibition and postsynaptic excitation-inhibition from the motor circuits [10,12]. The feedback postsynaptic

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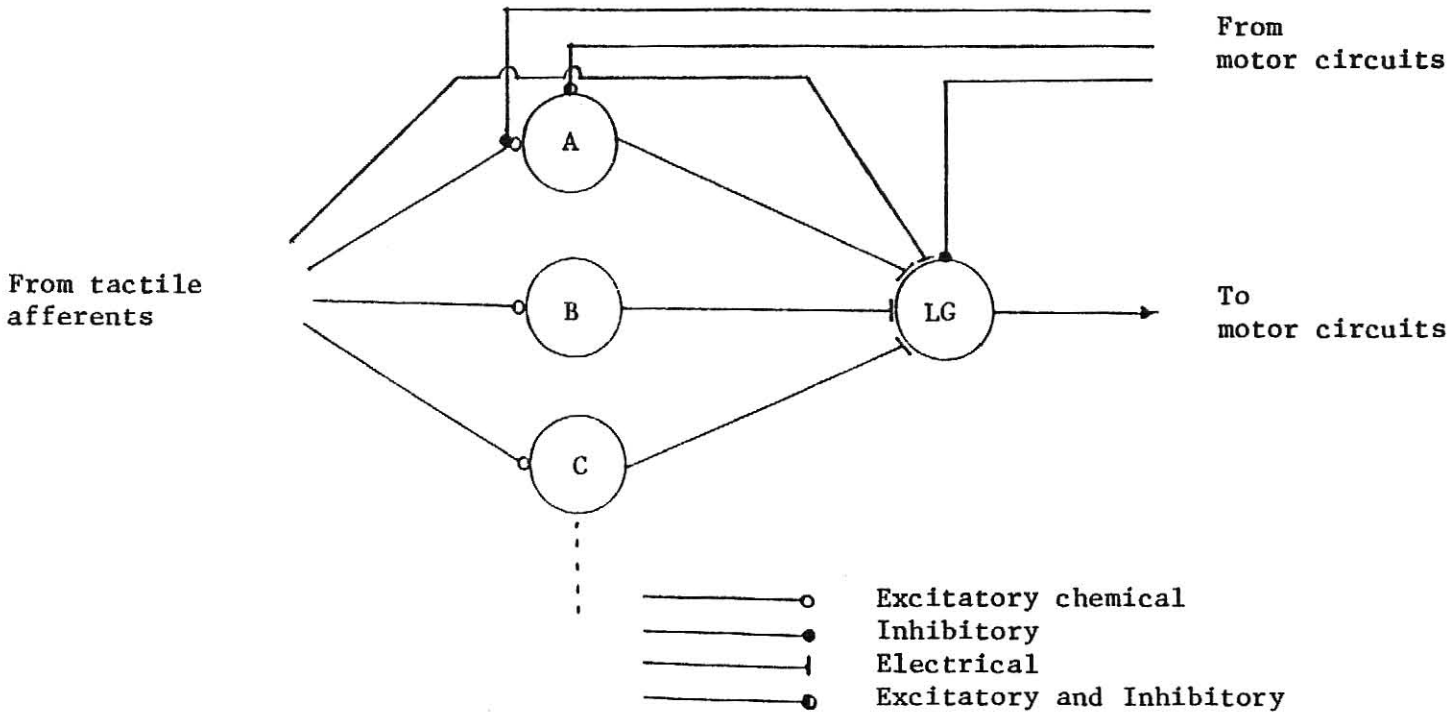


Figure 3.1. Neuronal Circuit Mediating the Tail-flip Escape Response in the Crayfish (Abbreviations: A, B, and C represent sensory interneurons A, B, and C respectively; LG, lateral giant)

response recorded intracellularly from interneuron A appears to be biphasic; a small excitatory phase precedes the inhibitory [10]. The presynaptic inhibition lasts for more than 150 msec, and outlasts the postsynaptic inhibition by 20 to more than 100 msec [10]. Presynaptic inhibition is important; it prevents excessive transmitter loss in the excitatory synapses from the tactile afferents to interneuron A, and thus controls their antifacilitation.

The details of the motor circuitry have been omitted from Fig. 3.1 because they are not relevant to this simulation.

# IV. DESCRIPTION OF THE MODEL

The model incorporates the neuronal properties of refractoriness, accommodation, generator and spike adaptation, perturbation in membrane potential due to a spike, and the synaptic properties of facilitation and antifacilitation. These properties are modeled by time-dependent variables, which undergo an abrupt change in value whenever an action potential is encountered. Except at such points of discontinuities, the time course of a variable is approximated by a first-order linear differential equation, i.e., if the forcing function is constant, the variable rises or decays exponentially to its steady-state value. If the forcing function is not constant, then a "piece-wise constant" approximation is made, i.e., the forcing function is assumed to remain constant during the time interval defined by a time step in the program. These variables, along with synaptic excitation and inhibition, are used to determine the two main variables of interest: membrane potential and threshold. Whenever the membrane potential exceeds the threshold, an action potential is produced.

## 4.1. Synaptic Variables

The following discussion deals with the determination of the postsynaptic potential (PSP) developed in a neuron due to a single impulse to a synapse. The PSP produced when there is no facilitation or antifacilitation in the synapse, and when the postsynaptic neuron is unexcited, i.e., under resting potential conditions, will be referred to as a "standard PSP". As dealt with later, the PSP produced under "non-standard" conditions can be determined by using suitable multiplying factors. Waveforms for the standard PSP are usually readily available

from experimental data. A straight line, an arc of a circle, and an exponential decay can be used to obtain a reasonably accurate curve fit for the rise, inflexion, and decay phases of the standard PSP (Figs. 4.1 and 4.2). The standard PSP is modeled by the following equation:

$$
\begin{aligned}
P'(t) &= g\,t && 0 < t < b_1 \\
&= A - r + \sqrt{r^2 - (T_R - t)^2} && b_1 < t < b_2 \\
&= \left(A - r + \sqrt{r^2 - (T_R - b_2)^2}\right) e^{-(t-b_2)/T_D} \\
& && b_2 < t < T_F \qquad (4.1)
\end{aligned}
$$

where $P'(t)$ = standard PSP at time t,

$g$ = slope of the potential rise,

$b_1$ = starting time of the inflexion phase,

$b_2$ = starting time of the decay phase,

$A$ = peak value of the standard PSP,

$r$ = radius of the inflexion,

$T_R$ = rise time of the standard PSP,

$T_F$ = fall time of the standard PSP, and

$T_D$ = time constant for the decay phase.

The peak amplitude, A, rise time, $T_R$, and fall time, $T_F$, are measured from experimental records. Using these values, the quantities, g, r, $b_1$, $b_2$ and $T_D$, are calculated in such a way that the phase transitions occur smoothly. It should be noted that in Eqn. (4.1), all the quantities are actually treated as being dimensionless.

The postsynaptic response depends on: (a) the facilitation of the synapse, and (b) the excitation and inhibition already present in the postsynaptic neuron. For an EPSP,

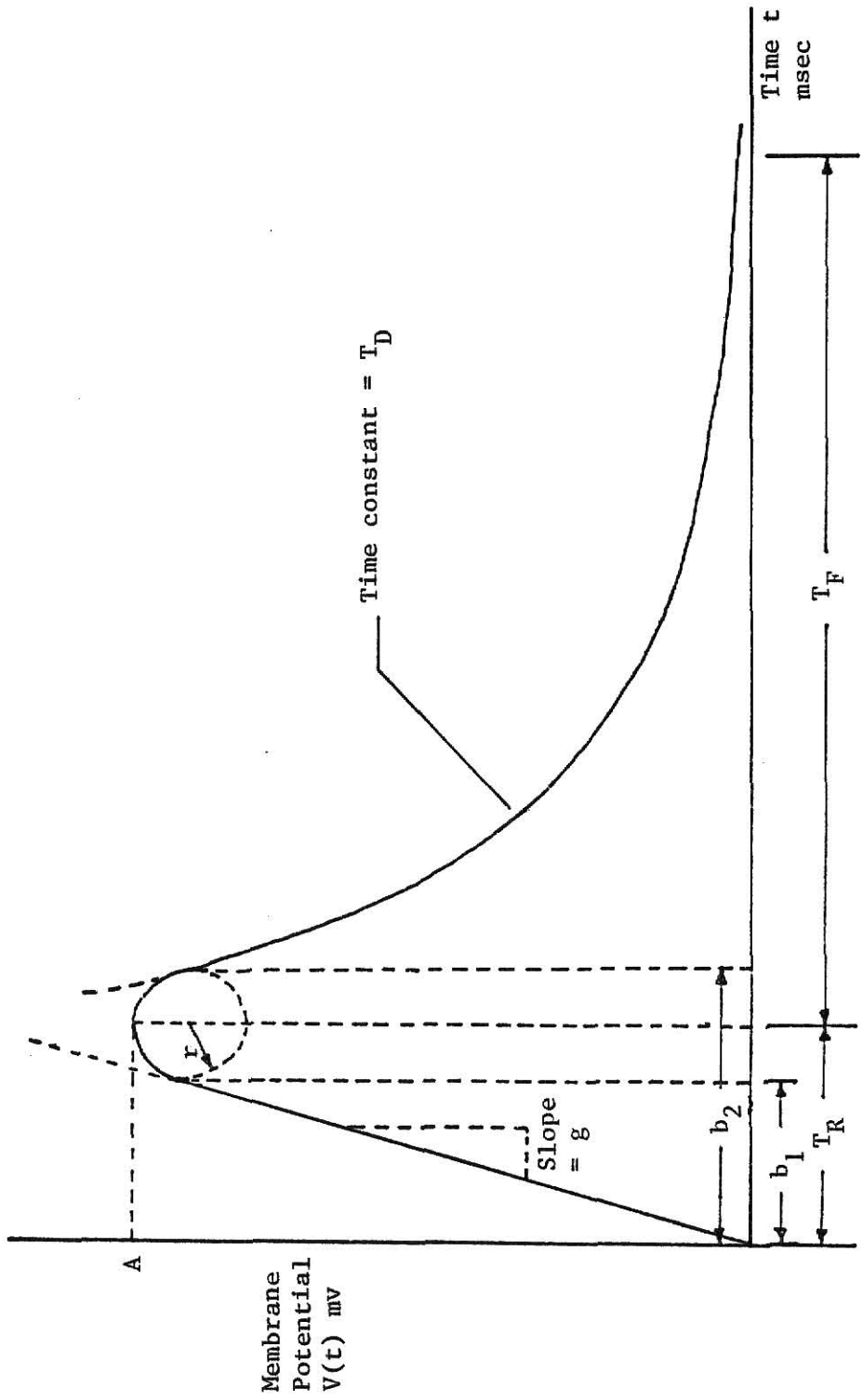


Figure 4.1. Diagram of a Typical Postsynaptic Potential Showing the Quantities Associated with Its Modeling

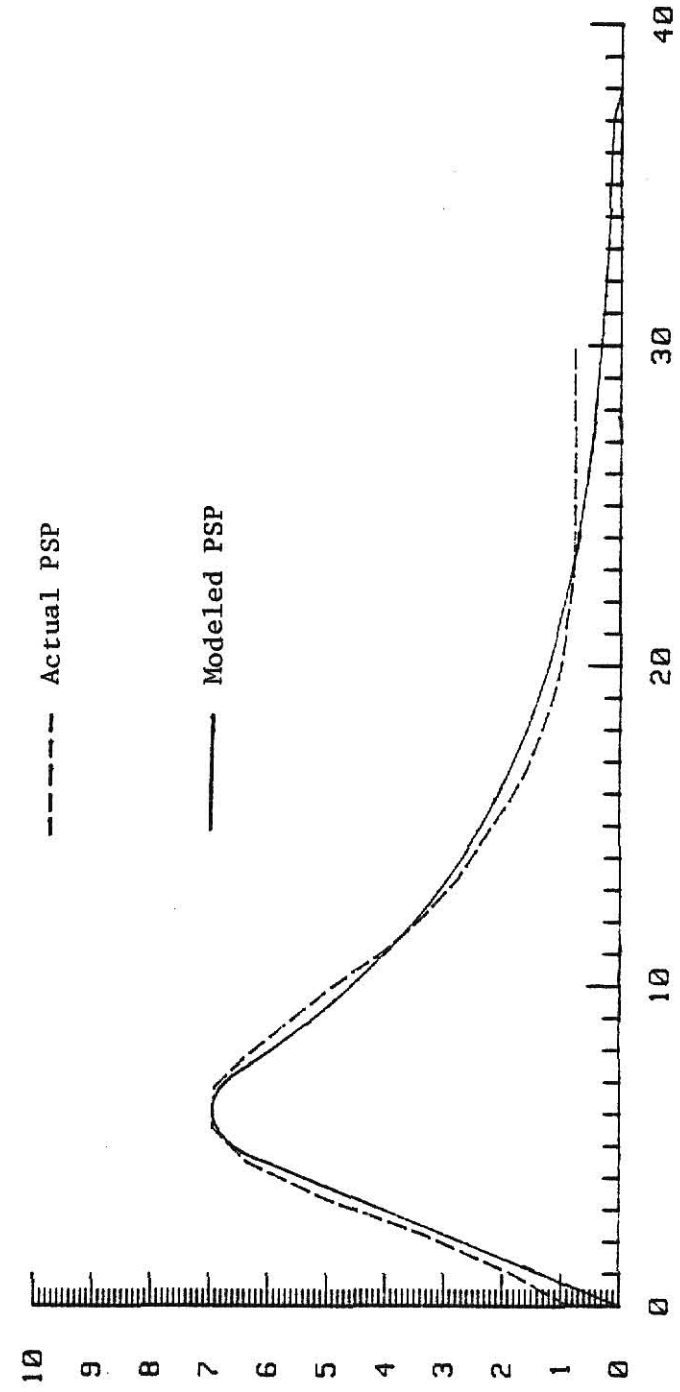


Figure 4.2. An Actual and a Modeled Postsynaptic Potential (For the actual PSP, A = 6.95 mv, $T_R$ = 6.1 msec, $T_F$ = 31.6 msec; for the modeled PSP, g = 1.34 mv/msec, r = 1.89 msec, $b_1$ = 4.59 msec, $b_2$ = 7.32 msec, $T_D$ = 7.6 msec; data for the actual PSP obtained from Fig. $6A_3$, Ref. 40)

$$P(t) = F(t_1-)\ C_{VREV}(t_1)\ P'(t) \tag{4.2}$$

where $P(t)$ = postsynaptic potential,

$t_1$ = instant of arrival of the action potential at the synapse, and

$F(t_1-)$ = facilitation of the synapse (discussed later) just before the arrival of the action potential.

$C_{VREV}(t_1)$ is defined as follows:

$$C_{VREV}(t_1) = \frac{P_1(t_1) - (V_{REV}-V_0)}{V_0 - V_{REV}} \tag{4.3}$$

where $P_1(t_1)$ = total excitation present in the postsynaptic neuron at time $t_1$,

$V_{REV}$ = reversal potential for the EPSP, and

$V_0$ = resting potential.

For an IPSP, similar equations apply:

$$P(t) = F(t_1-)\ C'_{VREV}(t_1)\ P'(t) \tag{4.4}$$

$$C'_{VREV}(t_1) = \frac{P_2(t_1) - (V'_{REV}-V_0)}{V_0 - V'_{REV}} \tag{4.5}$$

where $P_2(t_1)$ = total inhibition present in the postsynaptic neuron at time $t_1$, and

$V'_{REV}$ = reversal potential for the IPSP.

The postsynaptic response is reduced by an amount proportional to the nearness of the total excitation or inhibition already present in the neuron to the reversal potential of the PSP.

For a neuron that is presynaptically inhibited [46,47], the EPSP is given by the following equation:

$$P(t) = F(t_1-)\ C_{VREV}(t_1)\ I(t_1)\ P'(t) \tag{4.6}$$

$$I(t_1) = 1 - I'(t_1) \tag{4.7}$$

where $I'(t_1)$ = normalized value of the presynaptic inhibition at time $t_1$.

The quantity, F(t), represents the facilitation of a synapse. The following discussion applies only to the case when $0 \leq F(t) \leq 1$ (antifacilitation). In this case, F(t) also represents, on a normalized scale, the amount of transmitter substance present in the presynaptic terminal at time t. Using first-order approximation, the time variation of F(t) can be written as:

$$F(t) = 1 - e^{-t/T_{Fc}} \tag{4.8}$$

where $T_{Fc}$ = time constant for recovery from antifacilitation.

When an action potential arrives at the presynaptic terminal, an abrupt loss of a fixed fraction, c, of the total transmitter substance present in the presynaptic terminal is assumed.

$$F(t+) = F(t-)\ (1-c) \tag{4.9}$$

where F(t+) = facilitation just after the arrival of an action potential, and

F(t-) = facilitation just before the arrival of the action potential.

If presynaptic inhibition is present,

$$F(t+) = F(t-)\ (1 - c\ I(t)) \tag{4.10}$$

In this case, the transmitter loss is decreased in direct proportion to

the amount of presynaptic inhibition. Thus, presynaptic inhibition, by preventing transmitter loss, protects the synapse from too much antifacilitation.

The quantities, c and $T_{Fc}$, are determined from experimental data using suitable equations and a least-squares method to fit the data. A detailed description and a computer program for determining c and $T_{Fc}$ are included in Appendix I.

It should be noted that the model does not distinguish between electrical and chemical synapses. For electrical synapses, F(t) is always equal to 1, the electrotonic propagation of the PSPs between neurons is neglected, and an action potential in the presynaptic neuron causes a short-latency, fast-rising EPSP in the postsynaptic neuron. The last two conditions may not be applicable to all systems; but they are valid for the circuit simulated here.

## 4.2. Neuronal Variables

In the following discussion, equations for the membrane potential and threshold are developed.

In the neuronal circuit simulated here, the inhibitory equilibrium potential is very close to the resting potential. As a result, the IPSPs are very small depolarizing or hyperpolarizing potentials. However, when present in a neuron, the IPSPs tend to bring the membrane potential closer to the inhibitory equilibrium potential, and reduce the effect of the excitation. Therefore, the following equation is obtained for the membrane potential:

$$V(t) = V_0 + P_1(t)\ C'_{VREV}(t) + P_2(t) + W(t) \qquad (4.11)$$

where $V_0$ = resting potential,

$P_1(t)$ = total excitation present in the neuron,

$P_2(t)$ = total inhibition present in the neuron,

$W(t)$ = perturbation in membrane potential due to a spike (explained later), and

$$C'_{VREV}(t) = \frac{P_2(t) - (V'_{REV} - V_0)}{V_0 - V'_{REV}} \tag{4.5}$$

By multiplying $P_1(t)$ by $C'_{VREV}(t)$, the contribution of the excitation to the membrane potential is reduced in direct proportion to the nearness of the total inhibition to the inhibitory equilibrium potential, $V'_{REV}$.

An action potential is assumed to cause a small perturbation, $W_R$, in the membrane potential. The parameter $W_R$, and other similar parameters used in the equations that follow, are determined from experimental records.

$$W(t_2+T_{ARP}+) = W_R \tag{4.12}$$

where $t_2$ = starting time of the generation of the action potential (this notation used throughout),

$T_{ARP}$ = absolute refractory period, and

$W(t_2+T_{ARP}+)$ = perturbation in membrane potential just at the end of the absolute refractory period.

After the absolute refractory period, the time course of the perturbation follows the following equation:

$$W(t) = W_R\, e^{-(t-t_2-T_{ARP})/T_M} \tag{4.13}$$

where $T_M$ = membrane time constant.

The threshold, H(t), is represented by the following equation:

$$H(t) = R(t) + Ac(t) + A_S(t) + V_0 \tag{4.14}$$

where R(t) = refractoriness of the neuron,

Ac(t) = accommodation of the neuron, and

$A_S(t)$ = spike adaptation of the neuron.

R(t) is arbitrarily large during the absolute refractory period. During the relative refractory period,

$$R(t) = C_R R_0 \, e^{-(t-t_2-T_{ARP})/T_R} + R_0(1-e^{-(t-t_2-T_{ARP})/T_R}) \tag{4.15}$$

where $C_R$ = reset constant for the refractoriness,

$R_0$ = steady state value of the refractoriness (value of the threshold depolarization under resting potential conditions), and

$T_R$ = time constant for the refractoriness.

It should be noted that $C_R R_0$ is the value of refractoriness just after the end of the absolute refractory period.

Between action potentials, the accommodation, Ac(t), can be represented by the following equation:

$$Ac(t+1) = Ac(t) \, e^{-1/T_{Ac}} + C_{Ac}(V(t) - V_0) \, x \, (1 - e^{-1/T_{Ac}}) \tag{4.16}$$

where $T_{Ac}$ = time constant for accommodation, and

$C_{Ac}$ = constant of proportionality.

In Eqn. (4.16), the steady-state value of the accommodation, $C_{Ac}(V(t) - V_0)$, is directly proportional to the deviation of the membrane potential from the resting potential. Since accommodation is a process dependent on a subthreshold depolarization [47], an action potential resets it to 0.

The spike adaptation, $A_S(t)$, is responsible for the gradual decline observed in the output spike frequency of a neuron as a result of a prolonged depolarization, with the amount of depolarization held constant [46-48]. Between action potentials, $A_S(t)$ is described by the following equation:

$$A_S(t+1) = A_S(t)\, e^{-1/T_{AS}} \tag{4.17}$$

where $T_{AS}$ = time constant for spike adaptation.

The effect of the generation of an action potential on $A_S(t)$ is assumed to be an abrupt increase in its value. This increment is decreased in direct proportion to the nearness of $A_S(t)$ to a maximum value of spike adaptation, $A_{SM}$. As a result, the following equation is obtained:

$$A_S(t_2+T_{ARP}^+) = A_S(t_2+T_{ARP}^-) + \frac{A_{SM} - A_S(t_2+T_{ARP}^-)}{A_{SM}} A_{SR} \tag{4.18}$$

where $A_S(t_2+T_{ARP}^-)$ = spike adaptation just before the end of the absolute refractory period,

$A_S(t_2+T_{ARP}^+)$ = spike adaptation just after the end of the absolute refractory period,

$A_{SM}$ = maximum spike adaptation, and

$A_{SR}$ = maximum spike adaptation increment.

Eqns. (4.11) and (4.14) for the membrane potential and threshold are the key equations in the model. At each iteration, the two values are compared. If the membrane potential exceeds the threshold, an action potential is produced. The action potential then reaches a synapse after the associated conduction delay.

## 4.3. Sensory Neurons

The membrane potential of a tactile sensory neuron is expressed by the following equation:

$$V(t) = V_0 + S(t)\, C'_{VREV}(t) + P_2(t) + W(t) - A_G(t) \qquad (4.19)$$

where $S(t)$ = generator potential, and

$A_G(t)$ = generator adaptation of the neuron (explained later).

The following equation is used for determining the generator potential:

$$S(t+1) = S(t)\, e^{-1/T_{Sen}} + (k_1 S_{In}(t) + k'_1) \times (1 - e^{-1/T_{Sen}}) + V_0 \qquad (4.20)$$

where $T_{Sen}$ = time constant associated with the generation of the generator potential,

$S_{In}$ = sensory input in units of force or pressure, and

$k_1$, $k'_1$ = constants of proportionality.

In Eqn. (4.20), a linear relation is assumed between the steady-state generator potential, $k_1 S_{In}(t) + k'_1$, and the sensory input, $S_{In}(t)$.

The generator adaptation, $A_G(t)$, is responsible for the gradual drop in membrane potential observed in a sensory neuron due to a prolonged sensory input, with the magnitude of the sensory input held constant [48,49]. The generator adaptation is given by the following equation:

$$A_G(t+1) = A_G(t)\, e^{-1/T_{AG}} + C_{AG}(V(t) - V_0) \times (1 - e^{-1/T_{AG}}) \qquad (4.21)$$

where $T_{AG}$ = time constant for generator adaptation, and

$C_{AG}$ = constant of proportionality.

An action potential at time $t_2$ is assumed to cause a small abrupt change, $A_{GR}$, in the generator adaptation, as represented by the following equation:

$$A_G(t_2+T_{ARP}^+) = A_G(t_2+T_{ARP}^-) + A_{GR} \qquad (4.22)$$

where $A_G(t_2+T_{ARP}^+)$ = generator adaptation just after the end of the absolute refractory period, and

$A_G(t_2+T_{ARP}^-)$ = generator adaptation just before the end of the absolute refractory period.

In Eqn. (4.22), the steady-state value of the generator adaptation, $C_{AG}(V(t) - V_0)$, is directly proportional to the deviation of the membrane potential from the resting potential.

The model has provision for extracellular stimulation of any desired number of neurons in the circuit. The stimulation frequency, and the starting time of stimulation (the time of delivery of the first stimulus) can be varied as desired, and they can be chosen differently for each synapse.

## 4.4. Description of the Computer Programs

The main computer program is written in FORTRAN IV. It incorporates the mathematical model described in this chapter. It provides, as output, the values of all variables of interest at desired intervals of time, for any neuron or synapse in the circuit. The program also lists, in chronological order, the instants at which action potentials are generated by each neuron in the circuit.

Two BASIC programs, run on an HP9835A desk-top computer, are used to store the results of the simulation run on an HP9134A hard disk. One of the programs, DATA, is used to store the values of a neuronal or synaptic variable. The other program, DAP, is used for storing the times at which action potentials are generated by a neuron.

Two other BASIC programs, PLOT and PAP, are used to plot the data stored by the programs, DATA and DAP respectively. An HP9872 plotter is used.

The listings for all the programs described above are included in Appendix II.

# V. SIMULATION OF THE NEURONAL CIRCUIT

## 5.1. Simulated Neuronal Circuit

The generalized neuronal model described in Chap. IV is used to simulate the crayfish tail-flip circuit. The basic neuronal circuit used in the simulation is illustrated in Fig. 5.1.

In the animal, each sensory interneuron, in a population of 30 to 50 sensory interneurons, receives excitatory input from a number of tactile afferents [36,39]. In the model, 7 representative interneurons are chosen, each receiving input from a single tactile afferent. Obviously, these assumptions make the model a "lumped" representation of the real system. The frequency of the spike train impinging on the sensory interneurons is assumed to be 100 Hz (1 in 10 msec), which is the typical high frequency discharge of a phasic tactile afferent [39]. Each incoming action potential creates a compound EPSP in the sensory interneuron. This compound EPSP is chosen to have an amplitude, rise time, and fall time greater than those of a unitary EPSP, and is really a lumped representation for the excitation from a number of tactile afferents. Two out of the seven sensory interneurons are assumed to receive feedback presynaptic inhibition and postsynaptic excitation-inhibition from the motor circuit. This assumption follows from the fact that although all the sensory interneurons have been "predicted" to receive feedback inhibition, it has been successfully demonstrated in only one interneuron, interneuron A [50]. The biphasic postsynaptic response is modeled by an EPSP followed by an IPSP. Consequently, the excitatory-inhibitory synapse has to be represented by two synapses, one excitatory, and the other inhibitory. The pathway for the feedback inhibition is assumed to be disynaptic from the lateral

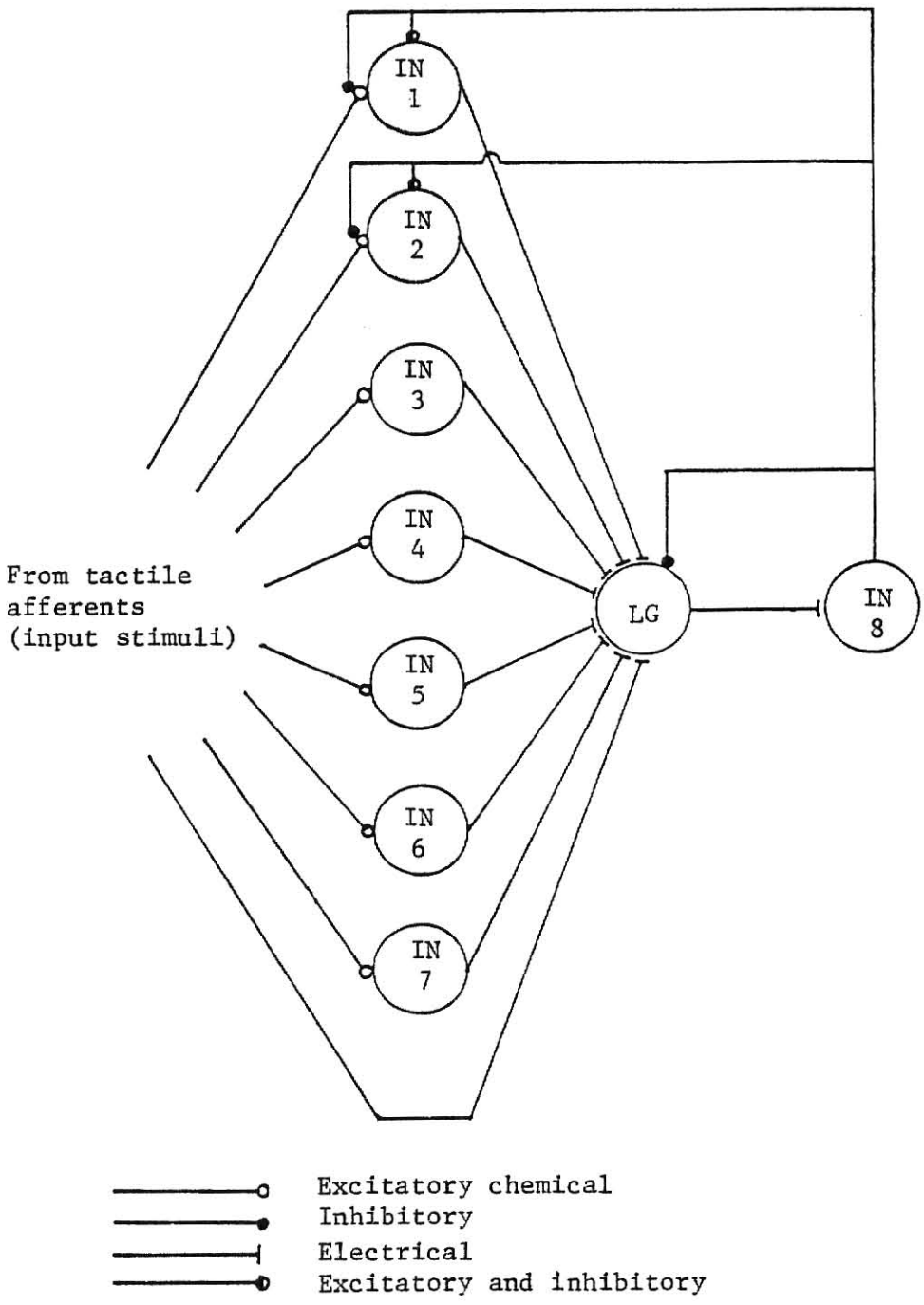


Figure 5.1. Basic Neuronal Circuit Used in the Simulation of the Crayfish Tail-flip Escape Response

giant. This assumption results in a delay of about 7 msec between the generation of the LG impulse and the onset of inhibition. Such a situation is justified on the basis that the inhibition has to occur rapidly enough to prevent the lateral giant from firing more than once during the tail-flip [42].

Interneurons 1-7 in the model have a wide range of thresholds. The high-threshold interneurons fire only a few times, and are assumed to deliver the large-amplitude components of the postsynaptic excitation observed in the lateral giant. The low-threshold interneurons fire repeatedly, and their action potentials are assumed to generate small-amplitude EPSPs in the lateral giant, and to cause the observed dispersal of the excitation in the lateral giant.

As discussed in Chp. IV, the electrical synapses are treated in the same way as chemical synapses, except that for the former, the conduction delays are smaller, and there is no facilitation or antifacilitation.

The input stimulation is assumed to be strong, and the first stimulus is sufficient in itself to elicit an impulse in the lateral giant. This stimulation corresponds to a very strong tactile stimulus delivered to the abdomen of a crayfish, whose tail-flip response shows no previous habituation.

The important simulation parameters are listed in Tables 5.1 and 5.2. Most of these values have been obtained using experimental records in previously published papers [9-11,37-42]. Suitable values have been assumed for unavailable data. As discussed earlier in this chapter, the experimental data for the amplitudes, and rise and fall times of certain EPSPs were intentionally modified to compensate for the lumped representation of the real system by the model.

| No. | From | To | Syn. Type | $T_{CD}$ msec | A mv | $T_R$ msec | $T_F$ msec | c | $T_{Fc}$ sec |
|---|---|---|---|---|---|---|---|---|---|
| 1 | TA | IN 1 | A | 2 | 7 | 5 | 30 | 0.2 | 13 |
| 2 | TA | IN 2 | A | 2 | 7 | 5 | 30 | 0.16 | 10 |
| 3 | TA | IN 3 | A | 2 | 7 | 5 | 30 | 0.25 | 10 |
| 4 | TA | IN 4 | A | 2 | 7 | 2 | 15 | 0.19 | 63 |
| 5 | TA | IN 5 | A | 2 | 8 | 6 | 40 | 0.18 | 30 |
| 6 | TA | IN 6 | A | 2 | 8 | 5 | 40 | 0.2 | 10 |
| 7 | TA | IN 7 | A | 2 | 7 | 3 | 20 | 0.19 | 63 |
| 8 | TA | LG | A | 1.5 | 6 | 1 | 5 | - | - |
| 9 | IN 1 | LG | A | 0.5 | 7 | 1.5 | 24 | - | - |
| 10 | IN 2 | LG | A | 0.5 | 4 | 1.5 | 24 | - | - |
| 11 | IN 3 | LG | A | 0.5 | 2 | 1.5 | 24 | - | - |
| 12 | IN 4 | LG | A | 0.5 | 2 | 1.5 | 24 | - | - |
| 13 | IN 5 | LG | A | 0.5 | 2 | 1.5 | 24 | - | - |
| 14 | IN 6 | LG | A | 0.5 | 3 | 1.5 | 24 | - | - |
| 15 | IN 7 | LG | A | 0.5 | 2 | 1.5 | 24 | - | - |
| 16 | LG | IN 8 | A | 0.5 | 4 | 3.5 | 12 | - | - |
| 17 | IN 8 | LG | B | 1 | 2 | 10 | 160 | - | - |
| 18 | IN 8 | IN 1 | A | 1 | 0.86 | 6 | 15 | - | - |
| 19 | IN 8 | IN 1 | B | 11 | -0.6 | 5 | 80 | - | - |
| 20 | IN 8 | IN 1 | C | 1 | 1 | 20 | 180 | - | - |
| 21 | IN 8 | IN 2 | A | 1 | 0.86 | 6 | 15 | - | - |
| 22 | IN 8 | IN 2 | B | 11 | -0.6 | 5 | 80 | - | - |
| 23 | IN 8 | IN 2 | C | 1 | 1 | 20 | 180 | - | - |

Table 5.1. Synaptic Parameters Used in the Simulation.

Synapse types: A = postsynaptic excitatory.

B = postsynaptic inhibitory, and

C = presynaptic inhibitory.

$T_{CD}$ = conduction delay,

A = amplitude of response (normalized for presynaptic inhibition),

$T_R$ = rise time of response,

$T_F$ = fall time of response,

c = transmitter loss constant, and

$T_{Fc}$ = time constant for recovery from antifacilitation.

| No. | Neuron | $V_0$ mv | $V_{REV}$ mv | $V'_{REV}$ mv | $R_0$ mv | $T_{ARP}$ msec | $T_R$ msec | $C_R$ | $C_{Ac}$ | $T_{Ac}$ msec |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | IN 1 | -36 | 0 | -36.6 | 6 | 2 | 1.4 | 2 | 0.8 | 70 |
| 2 | IN 2 | -36 | 0 | -36.6 | 5 | 1.5 | 1.4 | 2 | 0.8 | 70 |
| 3 | IN 3 | -36 | 0 | -36.6 | 4 | 1.5 | 1.4 | 2 | 0.8 | 70 |
| 4 | IN 4 | -36 | 0 | -36.6 | 3 | 1.5 | 1.4 | 2 | 0.8 | 70 |
| 5 | IN 5 | -36 | 0 | -36.6 | 3 | 1.5 | 1.4 | 2 | 0.8 | 70 |
| 6 | IN 6 | -36 | 0 | -36.6 | 4 | 1.5 | 1.4 | 2 | 0.8 | 70 |
| 7 | IN 7 | -36 | 0 | -36.6 | 3 | 1.5 | 1.4 | 2 | 0.8 | 70 |
| 8 | LG | -90 | 0 | -87.9 | 20 | 2.5 | 3.5 | 3 | 0.8 | 70 |
| 9 | IN 8 | -70 | 0 | -71 | 3.9 | 1.5 | 1.4 | 2 | 0.8 | 70 |

Table 5.2. Neuronal Parameters Used in the Simulation.

$V_0$ = resting potential of the neuron,

$V_{REV}$ = reversal potential for the EPSP,

$V'_{REV}$ = reversal potential for the IPSP,

$R_0$ = threshold depolarization under resting potential conditions,

$T_{ARP}$ = absolute refractory period,

$T_R$ = time constant for decay of refractoriness,

$C_R$ = reset constant for refractoriness,

$C_{Ac}$ = constant for accommodation, and

$T_{Ac}$ = time constant for accommodation.

## 5.2. Simulation Runs

Eight simulation runs are performed. The nature and purpose of each simulation are as follows:

Runs 1 and 2 (single stimulus to the circuit with and without feedback inhibition to the lateral giant). The purpose is to observe the excitation in the lateral giant and the effect of feedback inhibition on its time course.

Runs 3-6 (ten stimuli delivered to the circuit at 100 Hz with interneurons 1 and 2 subject to different conditions):

Run 3. Without feedback presynaptic inhibition and postsynaptic excitation-inhibition.

Run 4. With presynaptic inhibition, but without postsynaptic excitation-inhibition.

Run 5. Without presynaptic inhibition, but with postsynaptic excitation-inhibition.

Run 6. With both presynaptic inhibition and postsynaptic excitation-inhibition.

The purpose of simulation runs 3-6 is (a) to study the effect of presynaptic inhibition on the time course of antifacilitation in the excitatory synapse from the tactile afferents, and (b) to study the separate and combined effects of presynaptic and postsynaptic inhibition on the membrane potential of interneurons 1 and 2.

Run 7 (Seven input stimuli delivered to the circuit at 66.7 Hz (1 in 15 msec)). This is done to observe the response of the circuit to stimulation at a different frequency.

Run 8 (Ten input stimuli delivered at 100 Hz with all 7 sensory interneurons subject to feedback presynaptic inhibition and

postsynaptic excitation-inhibition). As stated earlier, feedback presynaptic and postsynaptic inhibition has been hypothesized for all the sensory interneurons [10,13]. The purpose of this simulation run is to study the behavior of the circuit with the assumption that the above hypothesis is true.

It should be noted that simulation runs 3 through 8 are designed to reflect the behavior of the circuit in response to a fairly massive tactile stimulus (lasting for about 90 msec) delivered to a real animal with no previously existing habituation of its tail-flip response.

# VI. SIMULATION RESULTS

The results of the simulation are presented in Figs. 6.1-6.11. Two types of plots are made, one showing the membrane potential, V(t), or facilitation, F(t), with respect to time and the other illustrating the train of action potentials developed in a set of neurons. It should be noted that the plots of the membrane potential do not show the generated action potentials. These plots represent only the total excitation and inhibition present in a neuron at any time, t, during the course of the response.

## 6.1. Circuit Response to a Single Stimulus

### 6.1.1. Generated Action Potentials

Fig. 6.1 shows the action potentials generated in the neuronal circuit in response to a single input stimulus to the circuit. The sensory interneurons 1-7 produce a variety of spike outputs. Interneurons 1 and 2 have relatively high thresholds (6 and 5 mv respectively), and produce one action potential each. These action potentials produce the large-amplitude components in the lateral giant response. Interneurons 5 and 6 have lower thresholds (3 and 4 mv respectively), and receive slightly stronger excitation (8 mv amplitude rather than 7). As a result, they produce a larger number of action potentials. These action potentials create the observed dispersed excitation in the lateral giant. The lateral giant always produces a single command impulse. Interneuron 8, which lies in the feedback inhibitory pathway also produces a single impulse.

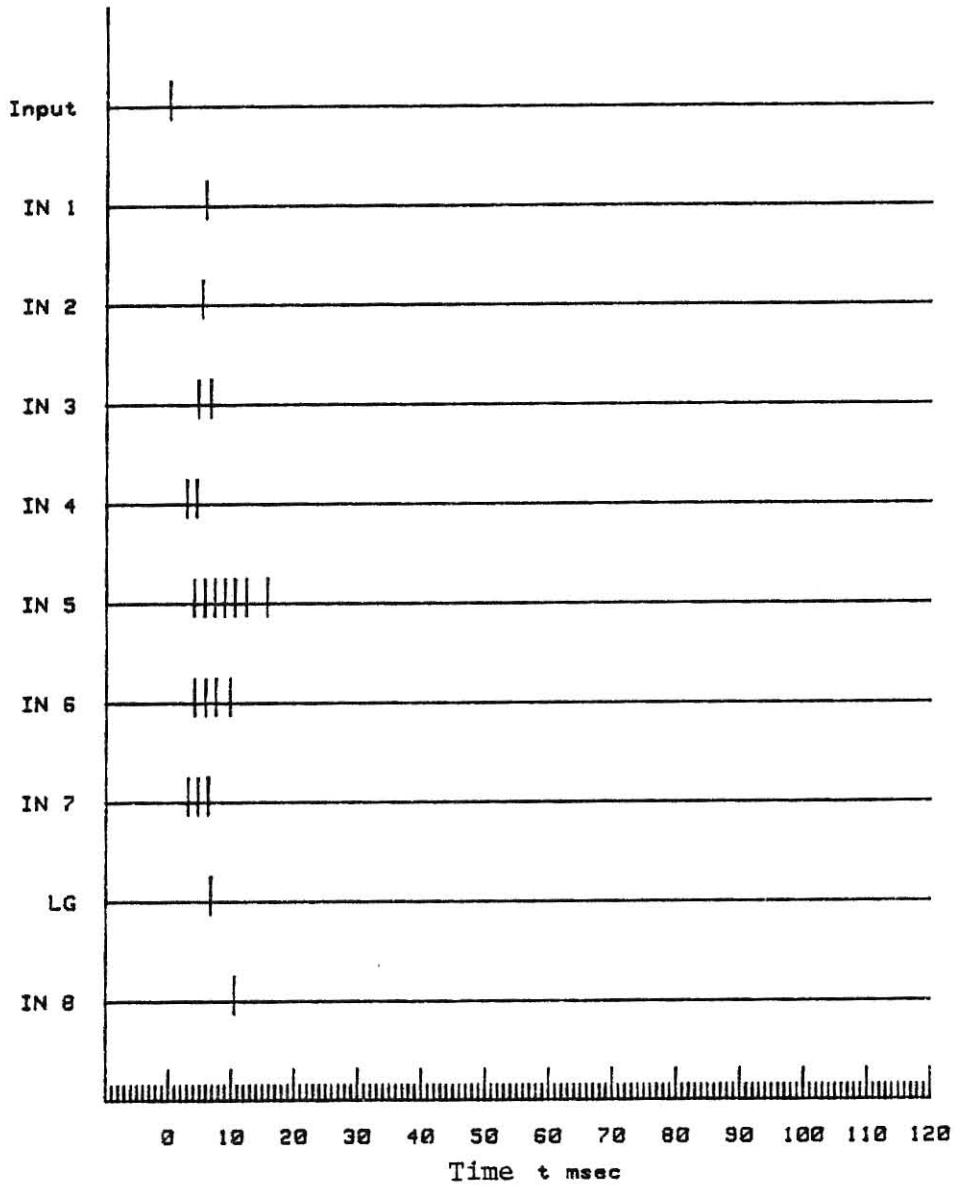


Figure 6.1. Action Potentials Generated in the Circuit Due to a Single Input Stimulus to the Circuit

### 6.1.2. Effect of Feedback Inhibition on the Lateral Giant Membrane Potential

The membrane potential produced in the lateral giant with and without feedback inhibition, in response to a single-input stimulus to the circuit, is illustrated in Fig. 6.2. The early short-latency component, "m", is the so-called alpha component of the lateral giant response, and corresponds to the direct electrical excitation of the lateral giant by the tactile afferents. The lateral giant produces its command impulse at 6.7 msec. The inhibition begins at 11.5 msec and peaks at 21.5 msec. The effect of inhibition is clearly illustrated; it causes a rapid repolarization of the LG response. Without inhibition, the excitation lasts for about 30 msec. This is close to the values obtained from experimental data (25-35 msec) [9,38]. The later component, "n", observed in the response with inhibition is the slow depolarizing IPSP.

## 6.2. Circuit Response to Stimulation at 100 Hz

### 6.2.1. Generated Action Potentials

Fig. 6.3 illustrates the response of the circuit to an input train of stimuli at 100 Hz. Interneurons 1 and 2 fire only a few times before habituation and feedback inhibition set in. The other interneurons (interneurons 3-7) do not receive any feedback inhibition, and their firing is more prolonged. The effect of antifacilitation is clearly noticeable in the output spike patterns of interneurons 3-7. The number of action potentials produced by each successive input stimulus decreases with time and the interspike intervals become longer. Interneuron 6 illustrates this effect well. For each neuron, the frequency of firing varies directly as the magnitude of excitation and inversely as the value

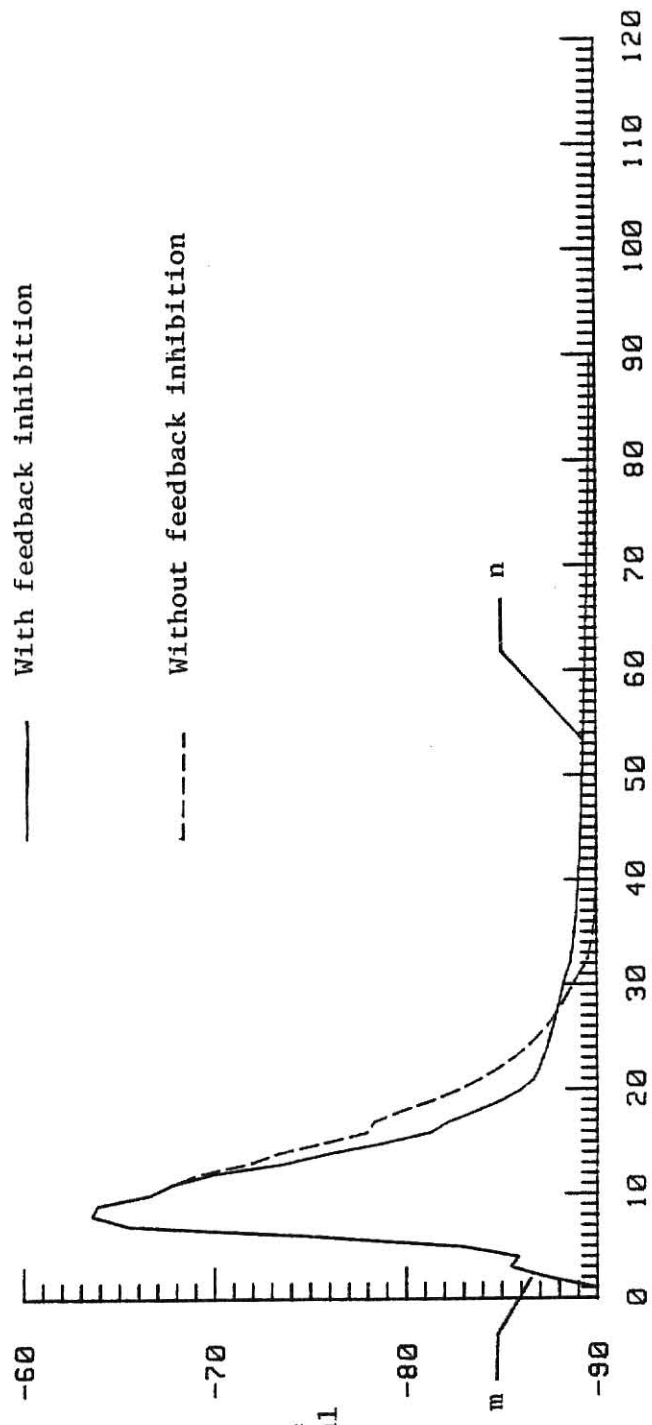


Figure 6.2. Lateral Giant Response to a Single Input Stimulus to the Circuit (LG impulse at 6.7 msec)

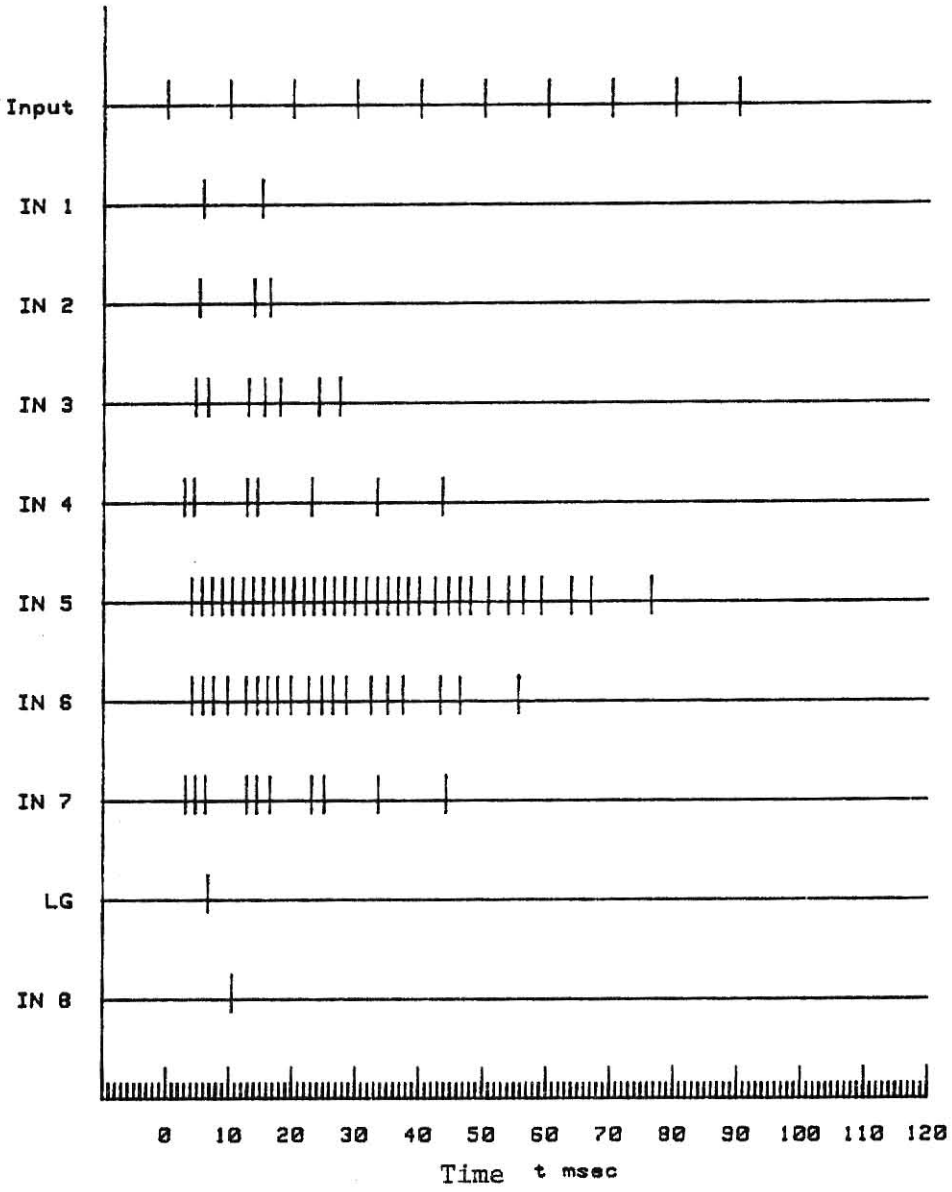


Figure 6.3. Action Potentials Generated in the Circuit Due to Stimulation of the Circuit at 100 Hz

of the threshold. The lateral giant goes into a prolonged inhibitory phase lasting for more than 100 msec, after producing its command impulse. This prevents the lateral giant from firing again during the tail-flip.

6.2.2. Effect of Presynaptic Inhibition on Antifacilitation

In Fig. 6.4, F(t) is the facilitation of the excitatory synapse from the tactile afferents to interneuron 1. As stated earlier, F(t) (for antifacilitation only, i.e., $0 \leq F(t) \leq 1$) is a normalized representation of the amount of transmitter substance present in the presynaptic terminal at time t. Without presynaptic inhibition, the loss of transmitter substance due to each stimulus is directly proportional to the amount of transmitter substance present in the presynaptic terminal at that instant. As a result, the incremental step decreases in F(t) due to successive stimuli approach 0 asymptotically. The size of each step decrease represents the amount of transmitter substance lost from the presynaptic terminal due to an input stimulus. Therefore, the step decrease is also in direct proportion to the amplitude of the EPSP generated in the postsynaptic neuron due to that stimulus. It should be noted that, on the time scale of Fig. 6.4, the time constants for recovery from antifacilitation are very large (10 to 65 seconds). Hence, negligible recovery occurs. Presynaptic inhibition is maximal at 31.5 msec, and at 32 msec, the $4^{th}$ input stimulus arrives at the presynaptic terminal. As a result, virtually no transmitter is lost due to the $4^{th}$ stimulus, and negligible change in F(t) occurs. Therefore, the size of the EPSP produced in interneuron 1, in response to the $4^{th}$ stimulus, would be close to 0. Presynaptic inhibition has noticeable effects on

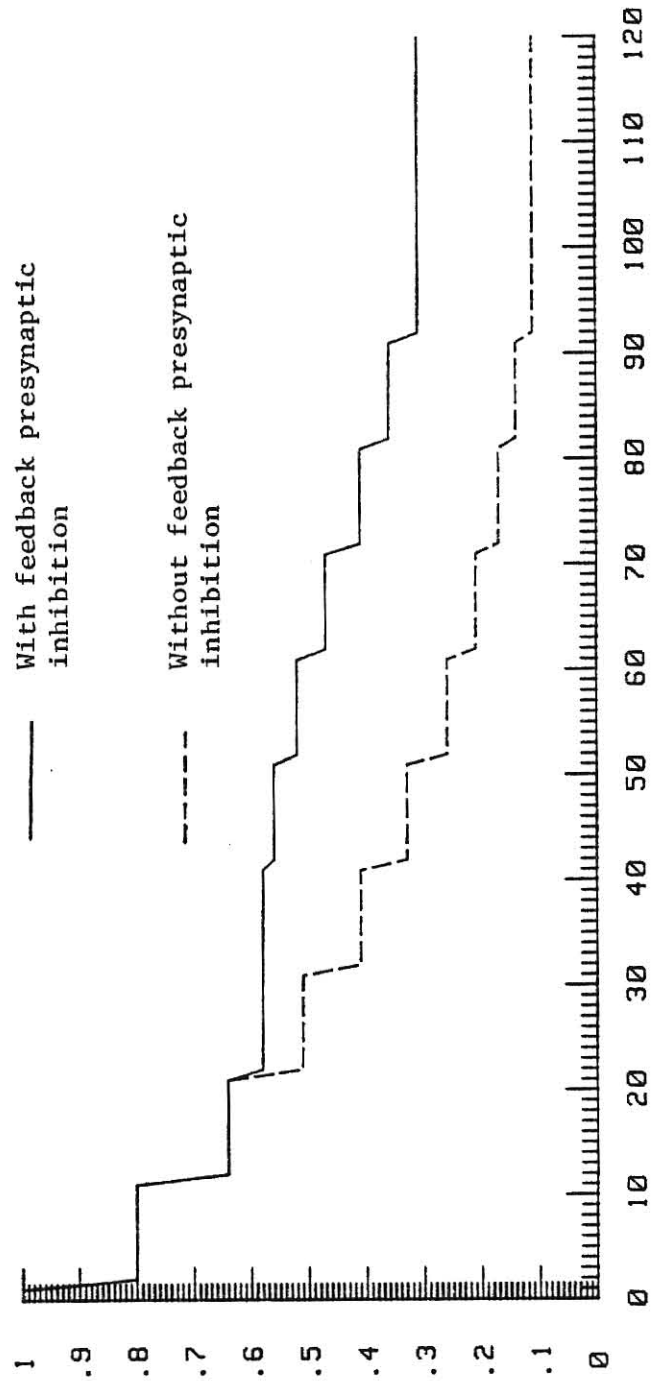


Figure 6.4. Effect of Presynaptic Inhibition on the Time Course of the Facilitation, F(t), of the Excitatory Synapse from the Tactile Afferents to Interneuron 1 (Input stimulation at 100 Hz)

the step decreases in F(t) when the $3^{rd}$, $5^{th}$ and $6^{th}$ stimuli arrive at 22, 42 and 52 msec respectively. At 72 msec, the step decrease in F(t) is actually larger with presynaptic inhibition than without it. This is due to not only the dimunition of the presynaptic inhibition, but also the fact that the amount of transmitter substance present at that instant is more than two times that present without presynaptic inhibition. The same effect is observed for the $9^{th}$ and $10^{th}$ stimuli arriving at the presynaptic terminal at 82 and 92 msec respectively. It should be noted that the difference at any time, t, between the two waveforms is a measure of the transmitter substance conserved by presynaptic inhibition.

### 6.2.3. Effect of Feedback Inhibition on the Response of Interneurons 1 and 2

#### 6.2.3.1. Interneuron 1 Membrane Potential

Figs. 6.5-6.7 illustrate the effect of feedback presynaptic and postsynaptic inhibition on the membrane potential in interneuron 1.

In Fig. 6.5, the effect of presynaptic inhibition on the membrane potential can be observed. When presynaptic inhibition is at its peak (at 31.5 msec), it virtually eliminates the EPSP due to the $4^{th}$ stimulus (beginning at 32 msec). As the presynaptic inhibition wanes, the later components become bigger, and then as the antifacilitation becomes stronger, they decrease in amplitude once again. The EPSPs beginning at 72, 82 and 92 msec have a larger amplitude with presynaptic inhibition than without it. By conserving the transmitter during a certain period (roughly between 20 and 62 msec), presynaptic inhibition results in larger EPSPs during the later period. Thus, presynaptic inhibition protects the synapse from too much antifacilitation.

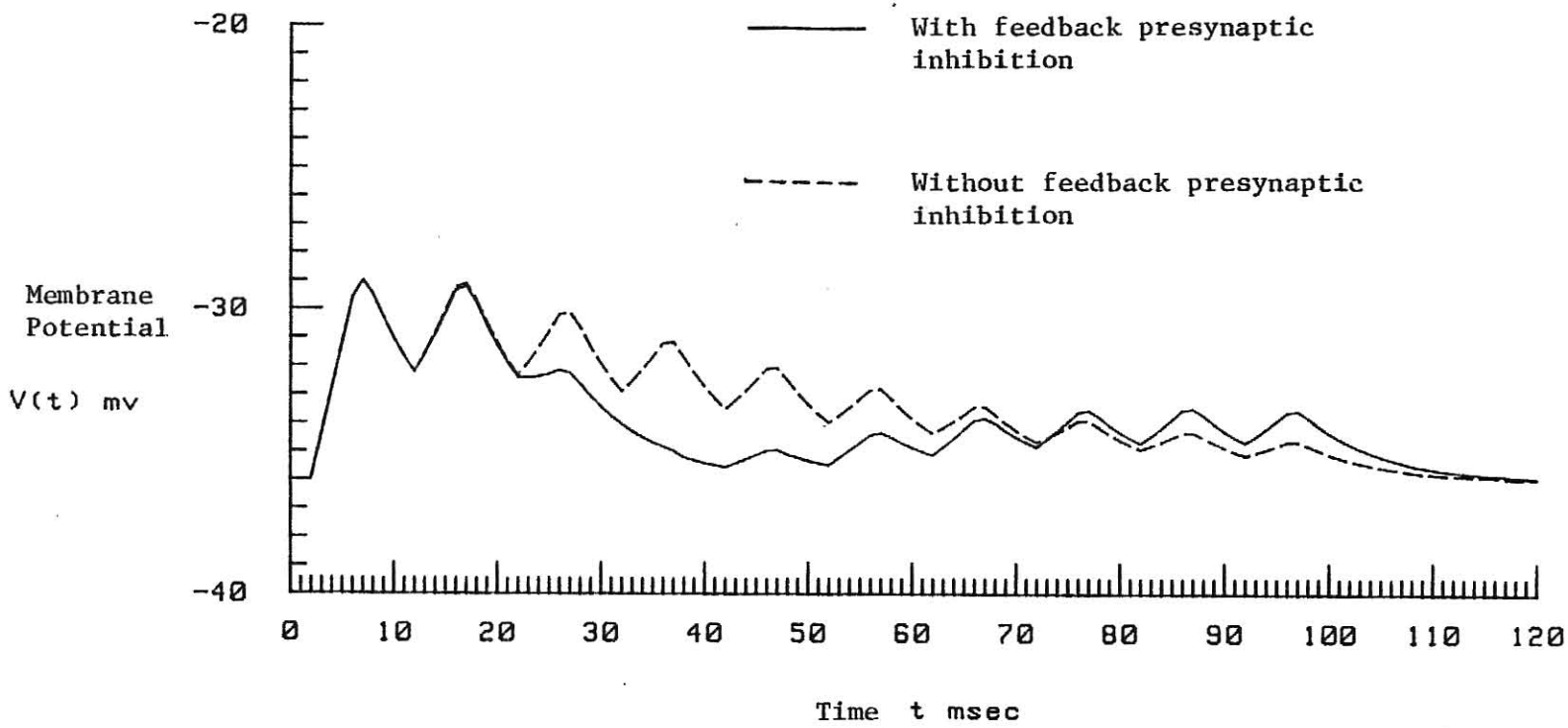


Figure 6.5. Effect of Feedback Presynaptic Inhibition on the Membrane Potential in Interneuron 1 (Input stimulation at 100 Hz)

The effect of feedback postsynaptic inhibition is illustrated in Fig. 6.6. Postsynaptic inhibition is maximal at 26.5 msec, when a slight hyperpolarization is observed. Postsynaptic inhibition almost completely suppresses the EPSP due to the $3^{rd}$ stimulus. As the postsynaptic inhibition diminishes (fall time, $T_F$ = 80 msec), its effect on the membrane potential decreases. It has negligible effect after 90 msec. As expected, no protection from antifacilitation is observed, as is indicated by the components of the response with postsynaptic inhibition after 80 msec.

The combined effect of presynaptic and postsynaptic inhibition is much stronger than the effect of each acting alone (Fig. 6.7). The EPSPs due to the $3^{rd}$ and $4^{th}$ stimuli are suppressed almost completely, and the EPSP due the $5^{th}$ stimuli is severely attenuated. The protective effect of the presynaptic inhibition is clearly observable in the components of the response with feedback inhibition after 70 msec.

6.2.3.2. Generated Action Potentials

The effect of feedback presynaptic and postsynaptic inhibition on the output spike patterns of interneurons 1 and 2 can be seen in Fig. 6.8. For interneuron 1, antifacilitation alone seems to be sufficient in determining the nature of its output spike pattern. However, for interneuron 2, due to a lower threshold, stronger excitation, and weaker antifacilitation, both presynaptic and postsynaptic inhibition have noticeable effects; either of the two acting alone suppresses the generation of the $4^{th}$ and $5^{th}$ spikes. It is interesting to note that the feedback postsynaptic excitation-inhibition causes a slight advance of the $2^{nd}$ spike in interneuron 1 and the $2^{nd}$ and

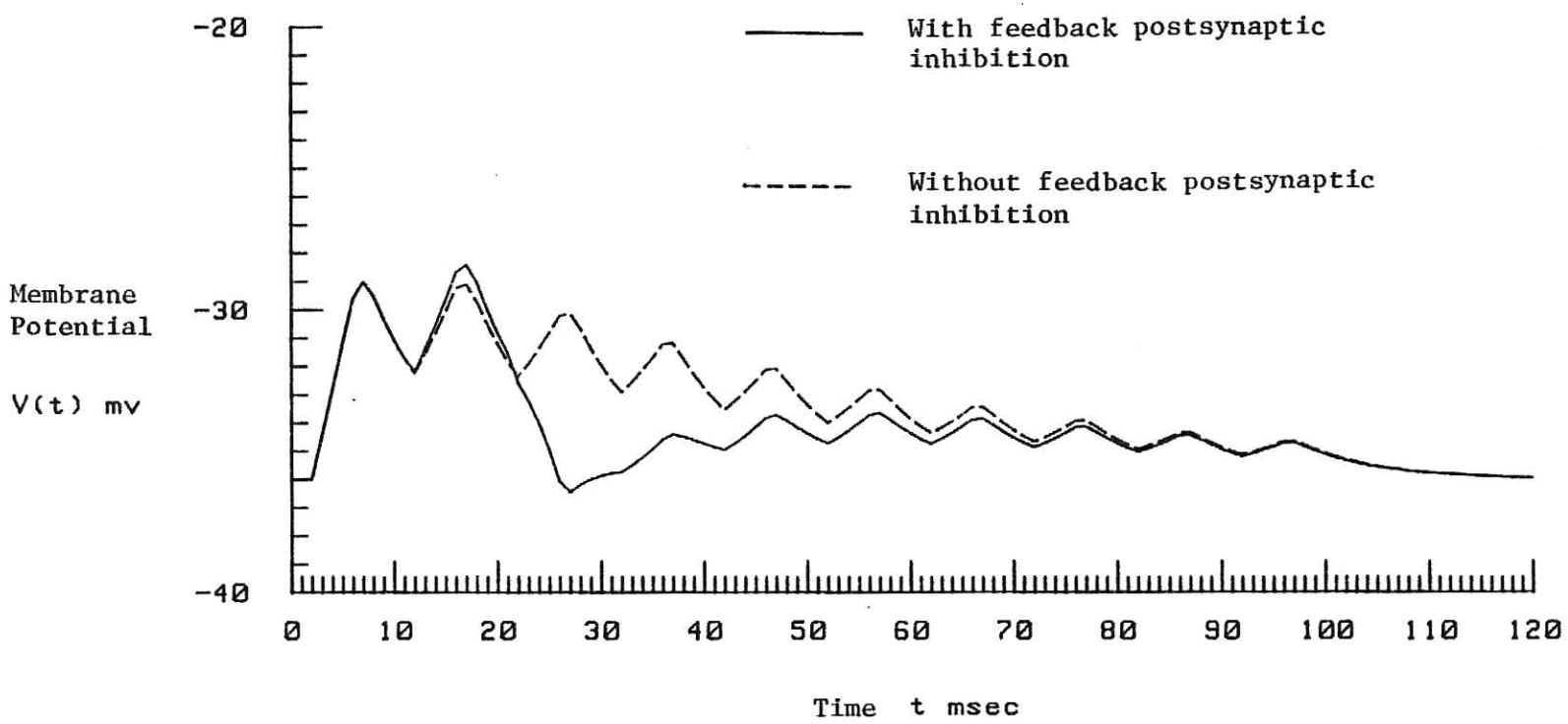


Figure 6.6. Effect of Feedback Postsynaptic Inhibition on the Membrane Potential in Interneuron 1 (Input stimulation at 100 Hz)

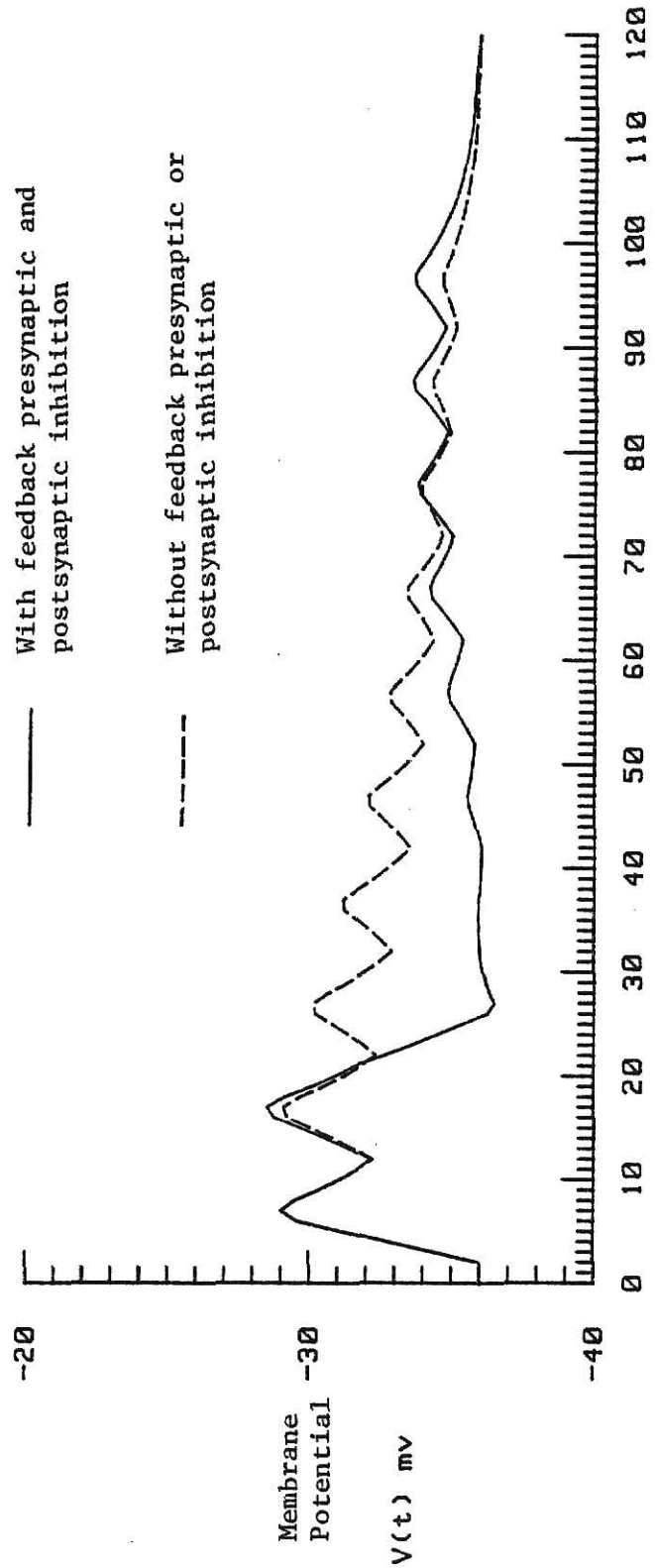


Figure 6.7. Combined Effect of Feedback Presynaptic and Postsynaptic Inhibition on the Membrane Potential in Interneuron 1 (Input stimulation at 100 Hz)

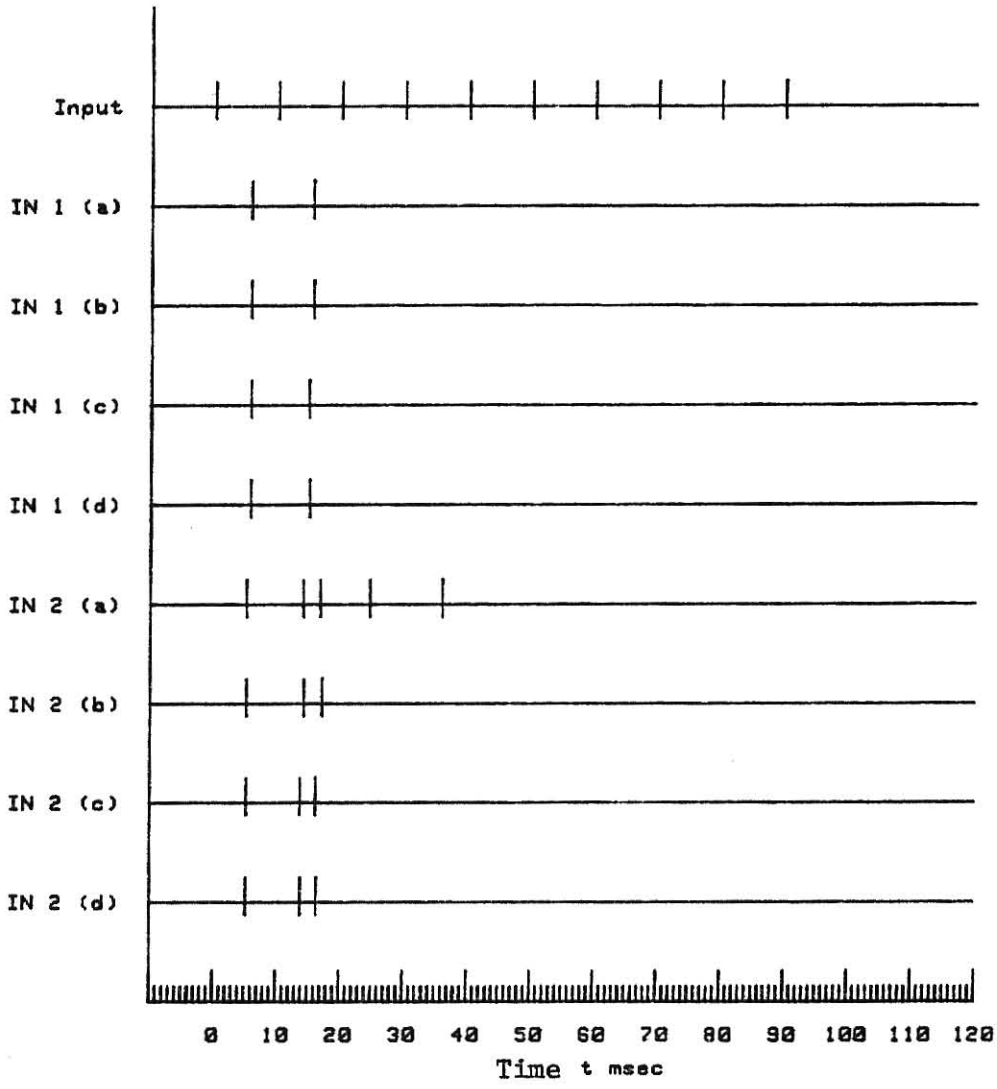


Figure 6.8. Separate and Combined Effects of Feedback Presynaptic and Postsynaptic Inhibition on the Action Potentials Generated in Interñeurons 1 and 2

a: Without feedback presynaptic or postsynaptic inhibition
b: With presynaptic inhibition, without postsynaptic inhibition
c: Without presynaptic inhibition, with postsynaptic inhibition
d: With both presynaptic and postsynaptic inhibition

$3^{rd}$ spikes in interneuron 2 (compare a and c in Fig. 6.8). This is due to the small excitatory phase which precedes the inhibitory phase in the feedback postsynaptic response.

### 6.2.4. Lateral Giant Membrane Potential

The membrane potential in the lateral giant is clearly seen to be the result of a wide variety of inputs (Fig. 6.9, solid curve). The feedback postsynaptic inhibition in the lateral giant peaks at 21.5 msec and has a significant effect up to about 60 to 80 msec. It suppresses the excitation strongly enough to prevent the lateral giant from firing more than once during the tail-flip (LG fires only once at 6.7 msec).

### 6.2.5. Circuit Response with All the Sensory Interneurons Subject to Feedback Inhibition

#### 6.2.5.1. Generated Action Potentials

Fig. 6.10 illustrates the response of the circuit when all the sensory interneurons are subject to feedback presynaptic or postsynaptic inhibition. It is interesting to note that no action potential is generated in any sensory interneuron after 21 msec. Presynaptic inhibition, by its protective effect, results in larger EPSPs during the later period of the response (as seen earlier in Fig. 6.5). However, as revealed by Fig. 6.10, this protection is insufficient for any of the sensory interneurons to generate an action potential during the later period (after about 80 msec).

#### 6.2.5.2. Lateral Giant Membrane Potential

With all the sensory interneurons subject to feedback inhibition, all the components of the lateral giant membrane potential after 21 msec

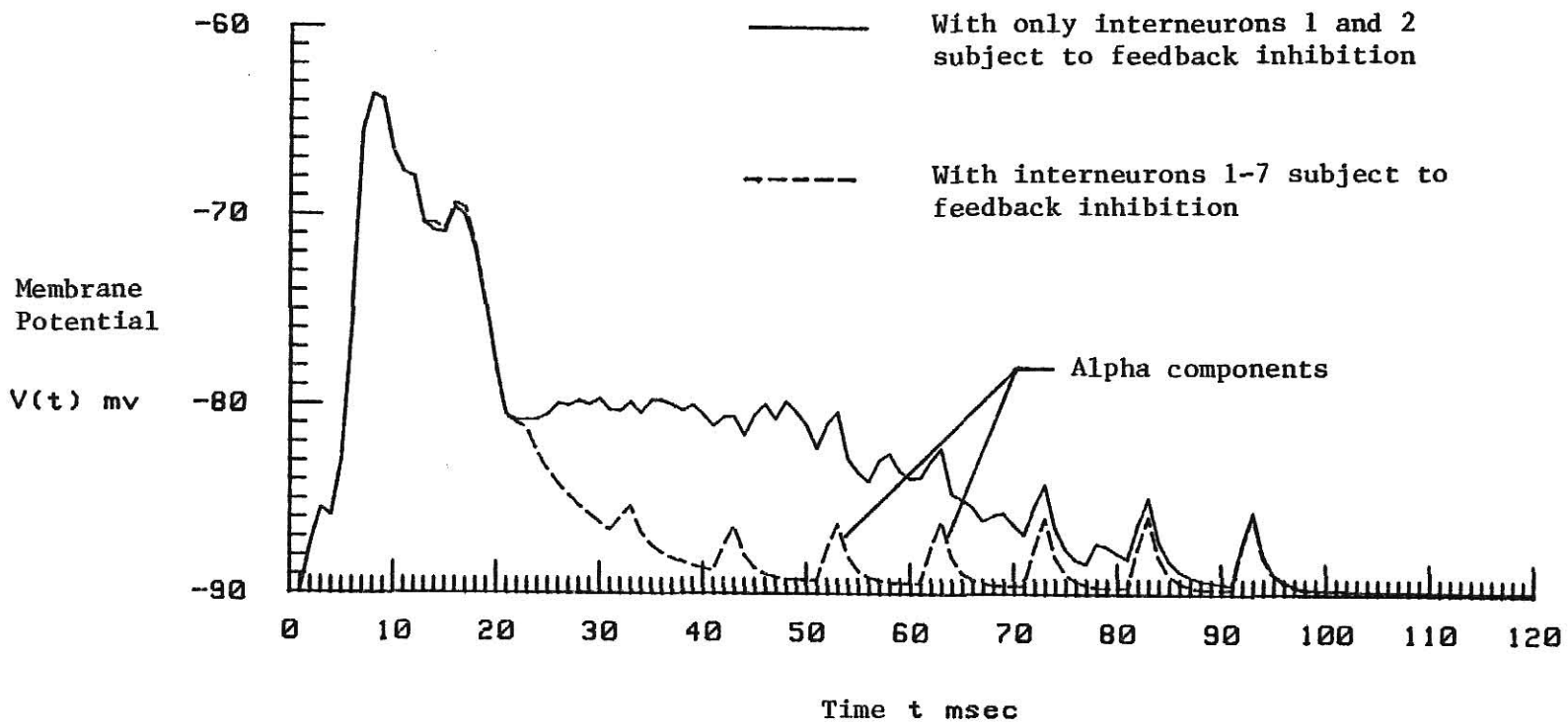


Figure 6.9. Lateral Giant Response to Stimulation of the Circuit at 100 Hz (LG impulse at 6.7 sec)

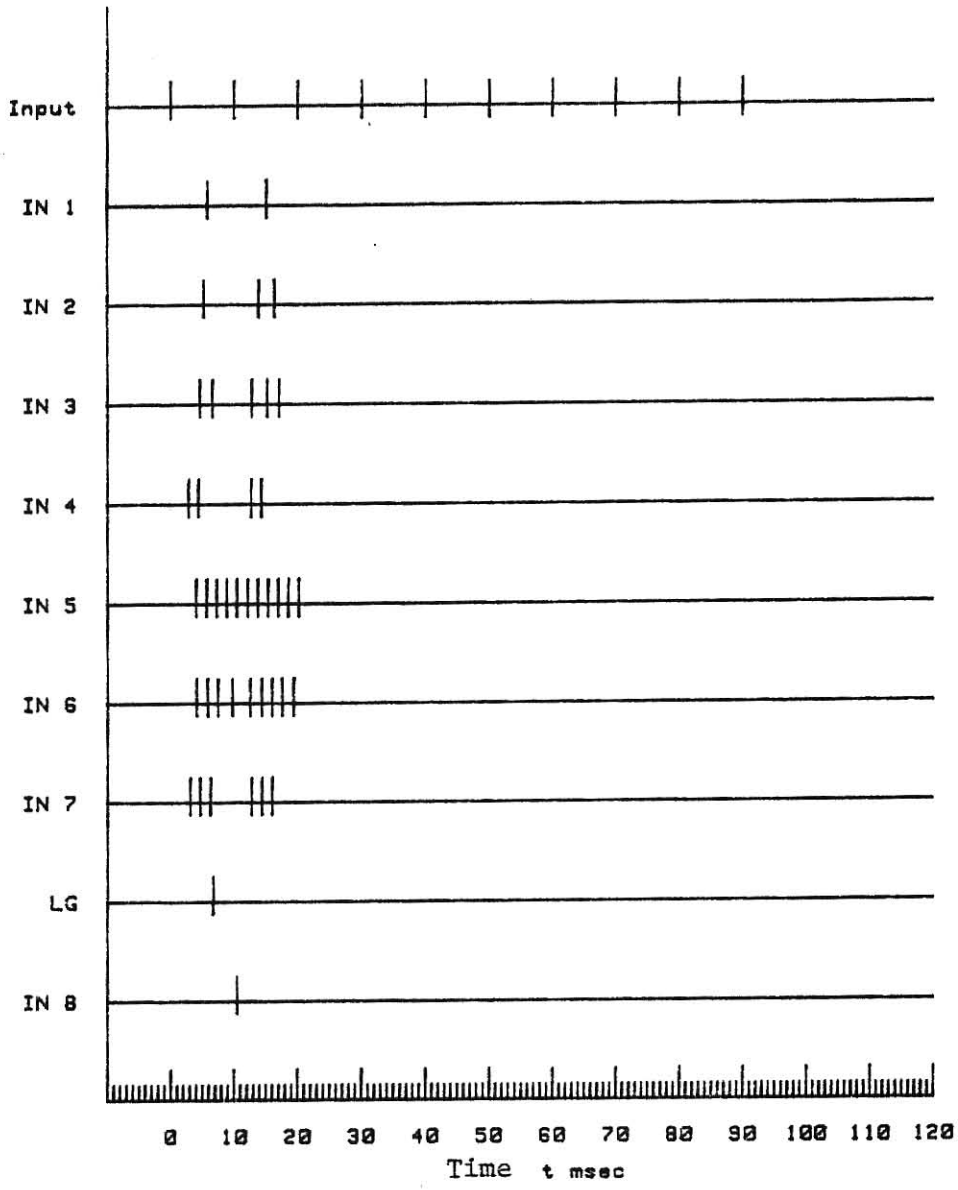


Figure 6.10. Action Potentials Generated in the Circuit with All the Sensory Interneurons Subject to Feedback Presynaptic and Postsynaptic Inhibition (Input stimulation at 100 Hz)

drop off, except for the alpha components which are due to the direct electrical synapse between the tactile afferents and the lateral giant (Fig. 6.9, dashed curve).

## 6.3. Circuit Response to Stimulation at 66.7 Hz

If the frequency of the input stimulation is reduced to 66.7 Hz (1 in 15 msec), the number of action potentials produced by the sensory interneurons decreases (Fig. 6.11). For instance, interneurons 2 and 5 produce 3 and 34 action potentials respectively when stimulated at 100 Hz. On stimulation at 66.7 Hz, the number of action potentials produced decreases to 1 and 27 for interneurons 1 and 2 respectively. Since in this simulation only a single stimulus was necessary to produce the lateral giant impulse, and since this impulse is generated at only 6.7 msec, neither stimulation at 100 Hz (1 in 10 msec) nor 66.7 Hz (1 in 15 msec) has any effect on the time at which this impulse is generated.

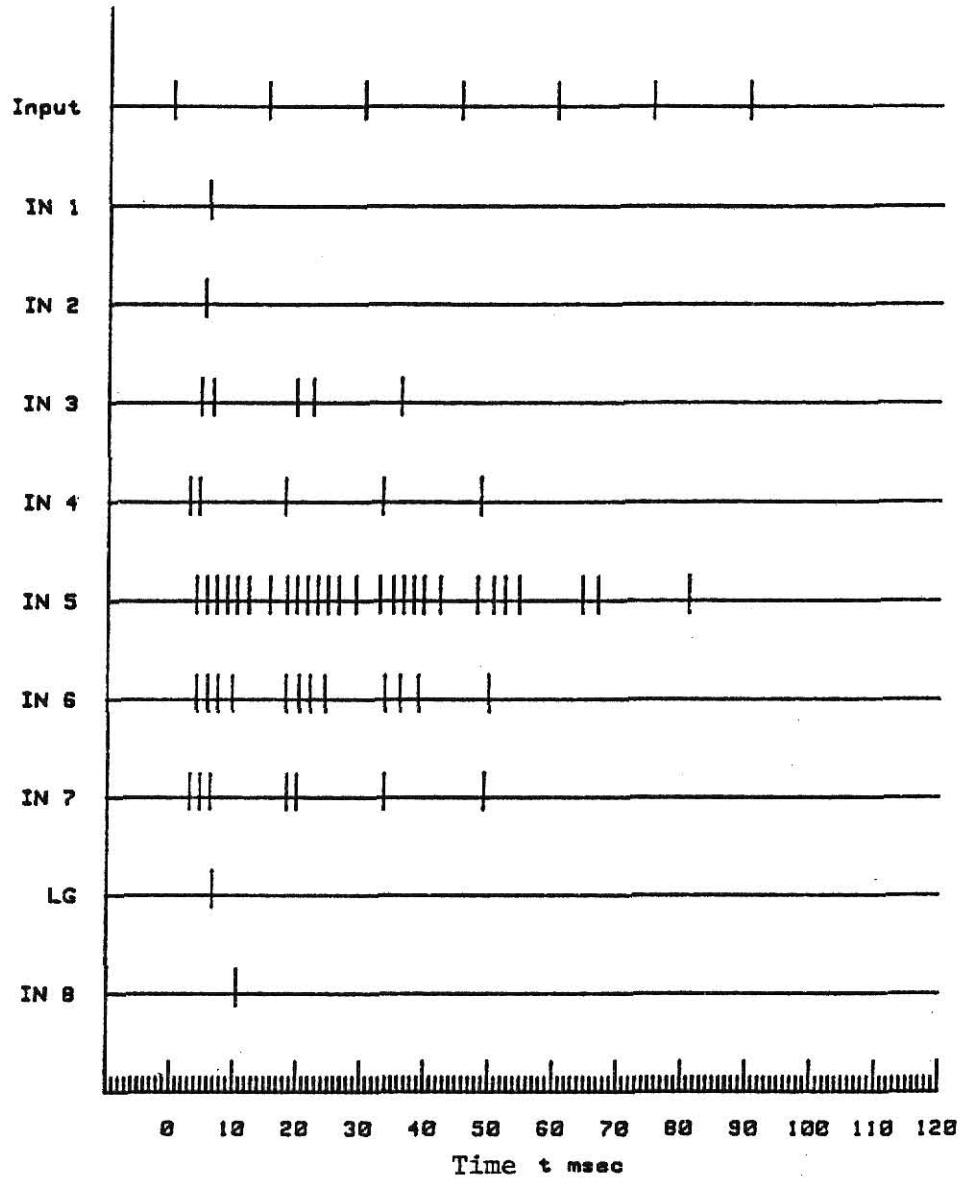


Figure 6.11. Action Potentials Generated in the Circuit Due to Stimulation of the Circuit at 66.7 Hz (1 in 15 msec)

# VII. DISCUSSION OF RESULTS

## 7.1. Observations on the Neuronal Circuit

From the results of the simulation, three interesting observations can be made:

1. Due to its very high threshold, the lateral giant needs a very strong excitatory input to produce its command impulse (Figs. 6.1 and 6.2). Weak tactile stimulation is always present due to the animal's own movements, water currents, etc. The high threshold of the lateral giant ensures that only a sufficiently strong tactile stimulus produces the escape response.
2. A possible significance of the protection from antifacilitation (habituation) has been presented in the literature [10,13]. When the animal makes a tail-flip during normal swimming movements (which it occasionally does), the motor circuits cause strong presynaptic and postsynaptic inhibition in some sensory interneurons. This tail-flip is not an escape response, but it could excite a number of tactile afferents which innervate the pit cells on the animal's exoskeleton. The resulting excitation of the sensory interneurons cannot cause unwanted habituation of the escape response, because of the protection provided by the presynaptic inhibition. As can be inferred from the results of the simulation, such a protection is needed only for those sensory interneurons which contribute to the important large-amplitude components of the lateral giant postsynaptic response. The animal's movement, due to a tail-flip response not related to escape, would be expected to induce excitation in only a relatively small number of tactile afferents.

Therefore, as long as the excitatory synapses to the important sensory interneurons (those which contribute to the large-amplitude components of the lateral giant response) are protected from antifacilitation, the animal would still be able to generate its escape response when needed.

3. The generation of the lateral giant impulse is followed by strong feedback postsynaptic inhibition in the lateral giant and presynaptic and postsynaptic inhibition in interneuron A. If all these inhibitory pathways were absent, the lateral giant would possibly have fired more than once during the course of a tail-flip. Therefore, this three-way feedback inhibition is present to ensure that the lateral giant fires only once during a tail-flip response.

## 7.2. Observations on the Model

1. As illustrated in this simulation, one of the most important advantages of building a model is the ability of the model to enable the researcher to conveniently "dissect" the simulated neuronal circuit. This can be used to study the effect of each synapse separately on the membrane potential of the postsynaptic neuron. Such a model can also be used to test different hypothetical circuit configurations, or to observe the response of a given circuit to varying input stimuli.
2. One of the biggest limitations of the model presented in these studies is the loss of accuracy which results when a large population of neurons is simulated by a few representative neurons. Such an approximation is justified when the properties

of individual neurons are of interest, as is true in this case. It should be noted that this model can be used for any number of neurons; however, for a very large number of neurons, the simulation process would be forbiddingly cumbersome. Where the properties of individual neurons are not significant, statistical techniques may provide a better simulation. However, if large neuronal aggregates can be conveniently represented by a small network of neurons, the model presented in these studies could be used to obtain a simple deterministic analysis of the system.

3. The most important observation is that the resultant membrane potential cannot always be regarded as a simple algebraic summation of EPSPs and IPSPs. If the inhibitory equilibrium potential is close to the resting potential, the IPSPs are small in amplitude, and can be either depolarizing or hyperpolarizing. Both excitation and inhibition tend to "pull" the membrane potential towards their respective equilibrium potentials. The ideal way to simulate this would be to calculate the membrane potential using the conductance changes that occur in the postsynaptic membrane due to excitation and/or inhibition, and the passive R-C properties of the membrane. However, since the postsynaptic events that occur upon stimulation of an excitatory or inhibitory synapse are still relatively obscure, such an approach cannot, at present, yield a wholly accurate model. In the model presented in these studies, a non-linear interaction between excitation and inhibition has been assumed, as described earlier. This approach has provided reasonably accurate results in this simulation.

# VIII. RECOMMENDATIONS FOR FUTURE WORK

A tremendous scope for future work is available in the area related to these studies. A few suggestions are as follows:

1. Although the tail-flip escape circuit of the crayfish is one of the best-understood neuronal systems, quantitative data related to a number of aspects of the circuit are still unavailable. These data are very essential in order to build a truly accurate simulation. A number of experiments can be designed to obtain data pertaining to the following aspects of the circuit: (a) the exact nature of excitation of the identified sensory interneurons A, B, and C from the tactile afferents, (b) the exact contributions of the interneurons A, B, and C to the membrane potential of the lateral giant, (c) the nature of feedback inhibition from the motor circuits, and (d) the exact conduction delays between the neurons of the circuit. More challenging areas of research are: (a) identification of the feedback inhibitory pathways, (b) determination of the exact cause of habituation, and (c) incorporation of the motor portion of the circuit in the simulation. While the physiological experiments associated with the above research are very difficult to perform, working with the model, on the other hand, is much easier. Therefore, one use of the model could be to better interpret indirect evidence obtained from physiological experiments. Once an accurate model has been built, it can be used in lieu of the real system. It can then be used for a number of purposes, e.g., to simultaneously observe the response of all the neurons of the circuit to any desired type of

stimuli, a feat that is virtually impossible to accomplish using real systems. The computer model presented in these studies can also be used, with suitable modifications, to simulate other neuronal systems, e.g., the leech's neuronal circuit which is responsible for the control of swimming.

2. Another goal for continued research is that of building an accurate "general-purpose" neuronal model. Although the tail-flip escape circuit of the crayfish is well-suited for a better understanding of a number of neuronal properties, other systems can be chosen to achieve the same advantage. Experiments can be done, to better incorporate into the model properties such as spike and generator adaptation, facilitation and antifacilitation, accommodation, interaction between excitation and inhibition, etc. A number of features can be added to the model, e.g., incorporation of spiking and non-spiking muscles, pacemaker neurons, postinhibitory rebound, etc. An important aspect of this suggested research would be the development of equations that attempt to accurately describe the biophysical and biochemical events responsible for a particular property, instead of merely "curve-fitting" the time variation of the property.
3. A BASIC version of the model, to be run on the HP9826 or HP9835A desk-top computer, may be developed. This would permit direct storage and plotting of the results.

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# APPENDIX I. DETERMINATION OF FACILITATION PARAMETERS

In the following derivation, three important assumptions have been made:

1. A stimulus causes an abrupt decrease in the amount of transmitter substance present in the presynaptic terminal.
2. Each stimulus causes the loss of a fixed fraction, c, of the total transmitter substance present in the presynaptic terminal at that instant.
3. The recovery from antifacilitation can be modeled by a single exponentially rising waveform with time constant, $T_{Fc}$.

When an antifacilitating chemical synapse is stimulated repeatedly at a fixed frequency, the amplitudes of the successive EPSPs decline with respect to the stimulus number. Plots showing this decline can be used to determine the transmitter loss constant, c, and the time constant, $T_{Fc}$ associated with the recovery from antifacilitation.

The fractional transmitter loss, L(t), from a presynaptic terminal, due to stimulation of the synapse at a fixed frequency, is illustrated in Fig. A1.1. It should be noted that

$$F(t) = 1 - L(t) \tag{A1.1}$$

where F(t) = facilitation of the synapse.

From Fig. A1.1, the following equations can be readily inferred:

$$L(0-) = 0 \tag{A1.2a}$$

$$L(0+) = c \tag{A1.2b}$$

For the succeeding stimuli,

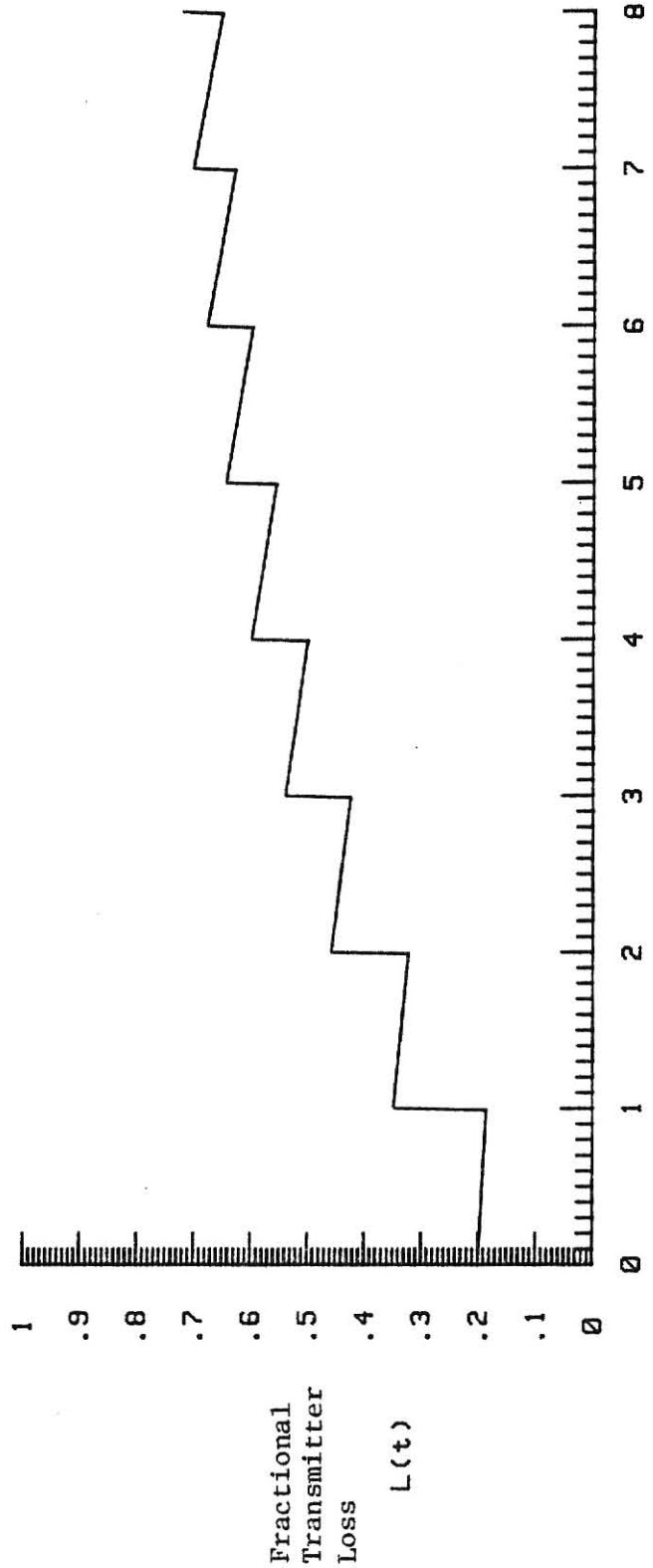


Figure A1.1. Increase in the Fractional Transmitter Loss, L(t), Due to Stimulation of a Synapse at 1 Hz ($c = 0.2$, $T_{Fc} = 13$ sec)

$$L(T-) = c\, e^{-T/T_{Fc}}$$

$$= L(0+)\, e^{-T/T_{Fc}} \qquad \text{(A1.3a)}$$

$$L(T+) = L(T-) + c\,[1 - L(T-)]$$

$$= c + L(T-)\,(1-c) \qquad \text{(A1.3b)}$$

$$L(2T-) = L(T+)\, e^{-T/T_{Fc}}$$

$$= [c + L(T-)\,(1-c)]\, e^{-T/T_{Fc}} \qquad \text{(A1.4a)}$$

$$L(2T+) = L(2T- + c\,[1 - L(2T-)]$$

$$= c + L(2T-)\,(1-c) \qquad \text{(A1.4b)}$$

$$L(3T-) = L(2T+)\, e^{-T/T_{Fc}}$$

$$= [c + L(2T-)\,(1-c)]\, e^{-T/T_{Fc}} \qquad \text{(A1.5)}$$

By induction,

$$L(nT-) = [c + L((n-1)T-)\,(1-c)]\, e^{-T/T_{Fc}}$$

$$n > 0 \qquad \text{(A1.6)}$$

From Eqn. (A1.1),

$$F(nT-) = 1 - L(nT-) \qquad \text{(A1.7)}$$

It should be noted that F(nT-) is the synaptic facilitation just before the $n+1^{st}$ stimulus.

Following the above procedure, the quantities, c and $T_{Fc}$, are determined using a BASIC program run on an HP9835A desk-top computer. The experimental values of L(nT-) are entered as data into the program.

Using Eqns. (A1.2) and (A1.5), the theoretical values of L(nT-) are calculated for each value of n using assumed values of c and $T_{Fc}$. The quantities, c and $T_{Fc}$, are then changed in steps, and the final values of c and $T_{Fc}$ chosen correspond to a least-squares fit for the data [51].

The BASIC program, FP, for determining c and $T_{Fc}$ is included in the following pages of this appendix.

```
10   ! ************************************************************************
20   !
30   ! PROGRAM NAME: FP
40   ! THIS PROGRAM IS USED TO DETERMINE THE TRANSMITTER LOSS CONSTANT, C, AND
50   ! THE TIME CONSTANT OF FACILITATION, TFC, USING A LEAST-SQUARES FIT FOR
60   ! THE DATA.
70   !
80   ! ************************************************************************
90   !
100  DIM Lm(10),Lt(10),S(10)
110  PRINTER IS 11
120  INPUT "REMARKS",Rem$
130  PRINT Rem$
140  !
150  ! Lm(I) AND Lt(I) ARE THE EXPERIMENTALLY MEASURED AND THEORETICALLY
160  ! CALCULATED VALUES, RESPECTIVELY, FOR THE FRACTIONAL TRANSMITTER LOSS,
170  ! L(N*T), FOR THE ITH DATA POINT.  S(I) IS THE STIMULUS NUMBER FOR THE
180  ! ITH DATA POINT.
190  !
200  ! ************************************************************************
210  !
220  ! DATA ENTRY
230  !
240  !
250  ! ************************************************************************
260  !
270  PRINTER IS 16
280  INPUT "ENTER THE NUMBER OF DATA POINTS,N",N
290  INPUT "ENTER THE PERIOD OF THE INPUT STIMULI (secs),Per",Per
300  INPUT "ENTER THE ESTIMATED MAXIMUM VALUE OF TFC (secs),Tmax",Tmax
310  FOR I=1 TO N
320  PRINT I
330  INPUT "ENTER S(I),Lm(I)",S(I),Lm(I)
340  NEXT I
350  PRINTER IS 11
360  PRINT "S(I)                Lm(I)"
370  FOR I=1 TO N
380  PRINT S(I),Lm(I)
390  NEXT I
400  PAUSE
410  !
420  ! ************************************************************************
430  !
440  ! CALCULATION OF C AND TFC
450  !
460  ! ************************************************************************
470  !
480  PRINTER IS 16
490  Mn=100000
500  FOR Cd=0 TO 1 STEP .01
510  FOR T=.1 TO Tmax STEP .1
520  Ls=0
530  FOR I=1 TO N
540  Z=0
550  Lt(I)=0
560  IF S(I)=1 THEN 610
570  FOR J=2 TO S(I)
580  Z=(Cd+Z*(1-Cd))*EXP(-Per/T)
590  NEXT J
600  Lt(I)=Z
610  Ls=Ls+(Lt(I)-Lm(I))^2
620  NEXT I
630  K=K+1
640  PRINT K
```

```
650  IF Ls>=Mn THEN 690
660  Mn=Ls
670  Tfc=T
680  C=Cd
690  NEXT T
700  NEXT Cd
710  PRINTER IS 11
720  PRINT "C = ",C
730  PRINT "TFC = ",Tfc,"secs"
740  PRINTER IS 16
750  END
```

# APPENDIX II. COMPUTER PROGRAMS FOR THE MODEL

This appendix includes a flow chart of the main program (Fig. A2.1), and a description of the variables used in the main program. The listings for the main program, and for the programs for storage and plotting of the results have also been included.

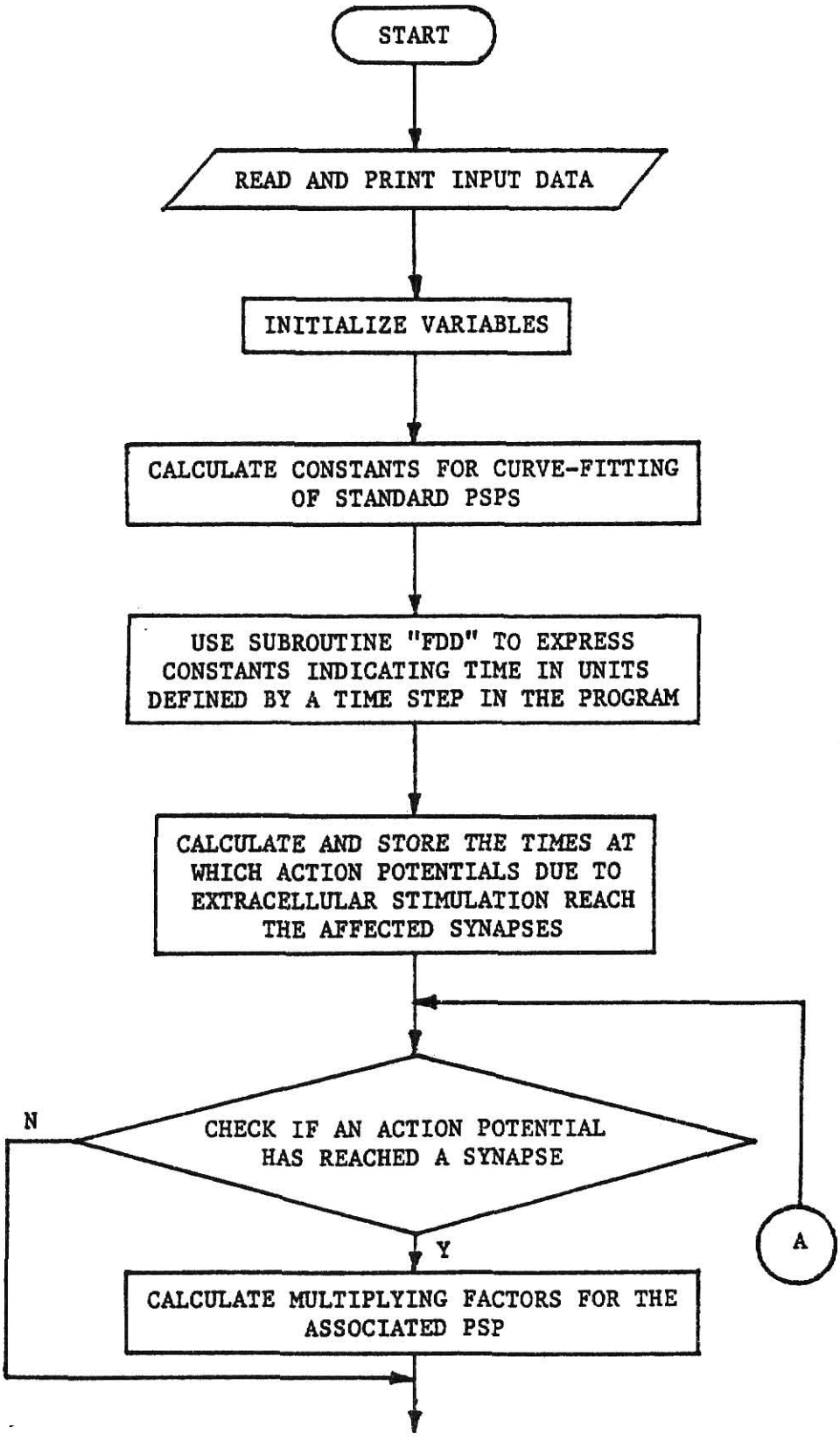


Figure A2.1. Flowchart of the Main Program

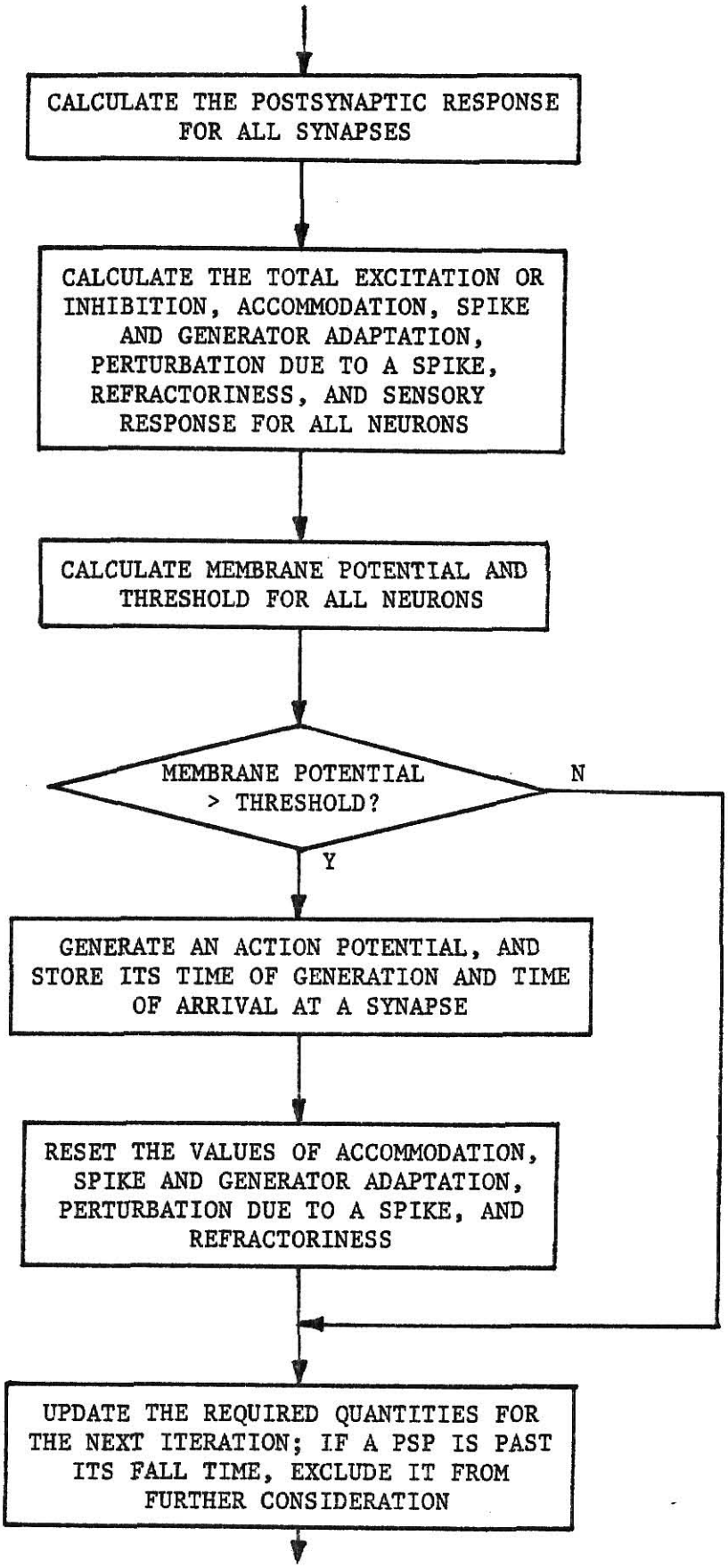


Figure A2.1. (cont.)

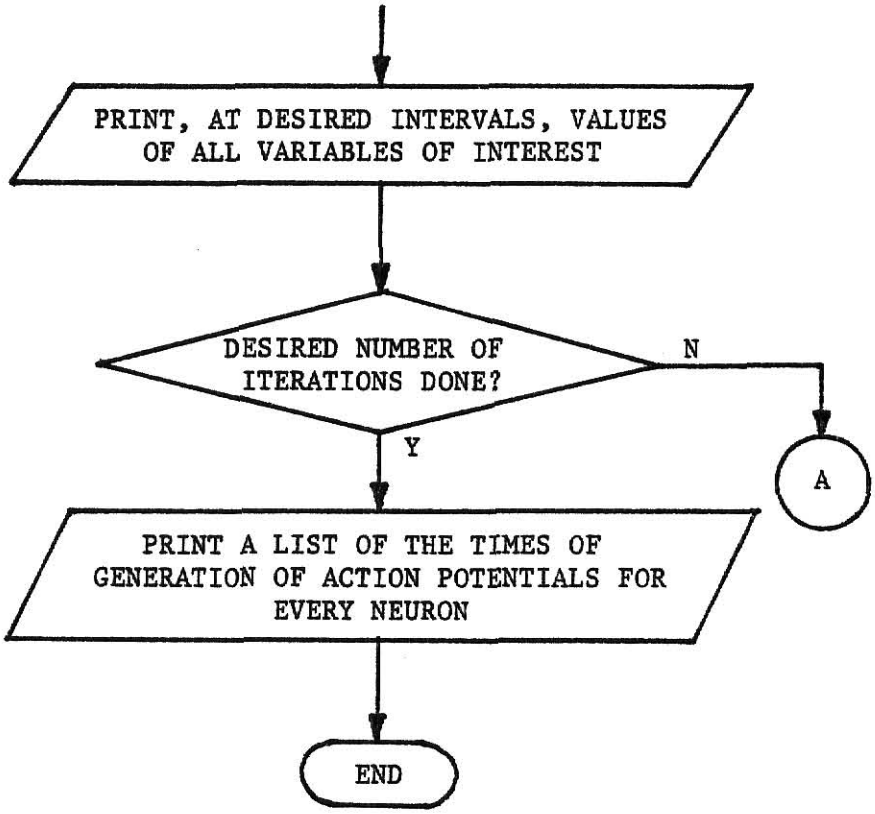


Figure A2.1. (cont.)

## Description of the Variables Used in the Main Program

| Notation in Main Program | Notation in Thesis | Description |
|---|---|---|
| M | | Number of neurons. |
| N | | Number of synapses. |
| KLIM | | Duration of simulation (msec). |
| LS | | Number of tactile sensory neurons. |
| LIMS | | Duration of tactile sensory input (msec). |
| AS | | Amplitude of tactile sensory input (pulse shape assumed; force or pressure units). |
| INT | | Duration of time intervals at which the values of desired variables are outputted (msec). |
| FD | | Value of the time steps of the model (msec). |
| IES | | Number of synapses that are extracellularly stimulated. |
| CLOCK | $t$ | Denotes time (msec). |
| KLOCK | | Denotes (iteration number - 1). |
| I | | Denotes the $i^{th}$ neuron. |
| J | | Denotes the $j^{th}$ synapse. |
| VO(I) | $V_0$ | Resting potential (mv). |
| VREV(I) | $V_{REV}$ | Reversal potential for the EPSP (mv). |
| VDREV(I) | $V'_{REV}$ | Reversal potential for the IPSP (mv). |
| CARAS(I) | $C_{AG}$ | Constant of proportionality for generator adaptation. |
| TAUAS(I) | $T_{AG}$ | Time constant for generator adaptation (msec). |

| Notation in Main Program | Notation in Thesis | Description |
|---|---|---|
| ARASR(I) | $A_{GR}$ | Abrupt change in generator adaptation due to a spike (mv). |
| ARAFM(I) | $A_{SR}$ | Maximum increment in spike adaptation due to a spike (mv). |
| TAUAF(I) | $T_{AS}$ | Time constant for spike adaptation (sec). |
| ARAFMX(I) | $A_{SM}$ | Maximum spike adaptation (mv). |
| THDO(I) | $R_0$ | Threshold depolarization under resting potential conditions (mv). |
| ARP(I) | $T_{ARP}$ | Absolute refractory period (mv). |
| TAUTH(I) | $T_R$ | Time constant for decay of refractoriness (msec). |
| CTHR(I) | $C_R$ | Reset constant for refractoriness. |
| TAUM(I) | $T_M$ | Membrane time constant (msec). |
| WR(I) | $W_R$ | Abrupt change in membrane potential due to a spike (mv). |
| CACCOM(I) | $C_{Ac}$ | Constant of proportionality for accommodation. |
| TAUACC(I) | $T_{Ac}$ | Time constant for decay of accommodation (msec). |
| V(I) | V(t) | Membrane potential (mv). |
| ARAS(I) | $A_G(t)$ | Generator adaptation (mv). |
| ARAF(I) | $A_S(t)$ | Spike adaptation (mv). |
| THD(I) | H(t) | Threshold (mv). |
| RF(I) | R(t) | Refractoriness (mv). |
| W(I) | W(t) | Perturbation in membrane potential due to a spike (mv). |
| RSEN(I) | S(t) | Generator potential in a sensory neuron (mv). |

| Notation in Main Program | Notation in Thesis | Description |
|---|---|---|
| ACCOM(I) | $Ac(t)$ | Accommodation (mv). |
| P1(I) | $P_1(t)$ | Total excitation present in a neuron (mv). |
| P2(I) | $P_2(t)$ | Total inhibition present in a neuron (mv). |
| CIN(I) | $C'_{VREV}(t)$ | Multiplying factor for the excitation, takes care of the effect of inhibition on excitation. |
| KK(I) | | Number of action potentials generated in a neuron. |
| S(I,J) | | Time of generation of the $j^{th}$ action potential in a neuron (msec). |
| NAP(I) | | Time elapsed since the generation of the last action potential (in units of time defined by a time step in the program). |
| NFROM(J) | | Denotes the presynaptic neuron. |
| NTO(J) | | Denotes the postsynaptic neuron. |
| DE(J) | $T_{CD}$ | Conduction delay (msec). |
| KSTY(J) | | Synapse type; equals 1 for a simple synapse, 2 for a synapse to a presynaptic terminal, and 3 for a synapse that is presynaptically inhibited. |
| NSTY(J) | | Synapse type; equals +1 for an excitatory synapse, -1 for an inhibitory synapse. |
| A(J) | A | Amplitude of standard PSP (mv). |
| RT(J) | $T_R$ | Rise time of standard PSP (msec). |
| FT(J) | $T_F$ | Fall time of standard PSP (msec). |

| Notation in Main Program | Notation in Thesis | Description |
|---|---|---|
| FCMX(J) | c | Transmitter loss constant. |
| TAUF(J) | $T_{Fc}$ | Time constant for recovery from antifacilitation (sec). |
| FCD(J) | F(t) | Synaptic facilitation. |
| FPD(J) | I(t) | The expression, 1 - I(t), equals the normalized value of presynaptic inhibition. |
| FC(J,L) | $F(t_1)$ | Multiplying factor for the $1^{th}$ PSP, denotes the same quantity as FCD(J). |
| FP(J,L) | $I(t_1)$ | Multiplying factor for the $1^{th}$ PSP, denotes the same quantity as FPD(J). |
| CVREV(J,L) | $C_{VREV}(t_1)$ | Multiplying factor for the $1^{th}$ EPSP, takes care of the effect of excitation already present in the postsynaptic neuron on the EPSP. |
| CDVREV(J,L) | $C'_{VREV}(t_1)$ | Multiplying factor for the $1^{th}$ IPSP, takes care of the effect of inhibition already present in the postsynaptic neuron on the IPSP. |
| P(J) | P(t) | Magnitude of the postsynaptic response due to a single synapse (mv). |
| G1(J) | g | Slope of the rise phase of a standard PSP (mv/msec). |
| B1(J) | $b_1$ | Starting time of the inflexion phase of the standard PSP (msec). |
| R(J) | r | Radius of the inflexion phase of the standard PSP (mv or msec). |
| B2(J) | $b_2$ | Starting time of the decay phase of the standard PSP (msec). |
| TAUD(J) | $T_D$ | Time constant for the decay phase of the standard PSP (msec). |

| Notation in Main Program | Notation in Thesis | Description |
|---|---|---|
| MC(J) | | Number of action potentials that are on their way to, but have not yet reached a synapse. |
| IC(J,L) | | Time still needed by the $l^{th}$ action potential, on its way to a synapse, to reach that synapse (in units of time defined by a time step in the program). |
| MD(J) | | Number of PSPs present in a neuron due to the $j^{th}$ synapse. |
| TO(J,L) | | Time elapsed since the start of the $l^{th}$ PSP in a neuron due to the $j^{th}$ synapse (in units of time defined by a time step in the program). |
| ITO(J) | | Denotes the postsynaptic neuron for the $j^{th}$ extracellularly stimulated synapse. |
| T(J) | | Period (reciprocal of frequency) of extracellular stimulation (msec). |
| TS(J) | | Starting time of extracellular stimulation (msec). |
| NS(J) | | Number of stimuli to be delivered to a synapse by extracellular stimulation. |
| CSEN(I) | $k_1$ | Constant of proportionality for the response of a tactile sensory neuron (mv/force or pressure units). |
| CDSEN(I) | $k_1'$ | Constant of proportionality for the response of a tactile sensory neuron (mv). |
| TAUSEN(I) | $T_{Sen}$ | Time constant associated with the generator potential in a sensory neuron (msec). |

| Notation in Main Program | Notation in Thesis | Description |
|---|---|---|
| SENIN(I,L) | $S_{In}(t)$ | Sensory input at the $1^{th}$ iteration, with the present iteration always defined as the $1^{st}$ iteration (force or pressure units). |
| NSTO(J) | | Denotes the sensory neuron to which the sensory input is applied. |

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FORTRAN IV G LEVEL  21                MAIN                DATE = 83180          20/08/47

              C     ******************************************************************
              C     ******************************************************************
              C
              C     MAIN COMPUTER PROGRAM FOR THE MODEL OF A NEURONAL NETWORK
              C
              C     ******************************************************************
              C     ******************************************************************
              C
              C
0001                 DIMENSION V(9),VO(9),VREV(9),VDREV(9),NSTO(3),RSEN(9),CSEN(3),
                    1SENIN(3,1200),CDSEN(3),TAUSEN(3),MC(38),IC(38,99),MD(38),
                    2TO(38,99),NFROM(38),NTO(38),CVREV(38,99),FCO(38),FCMX(38),
                    3TAUF(38),FC(38,99),KSTY(38),NSTY(38),FPO(38),FP(38,99),P(38),
                    4A(38),RT(38),FT(38),R(38),B1(38),B2(38),TAUD(38),G1(38),DE(38),
                    5ARAS(9),CARAS(9),TAUAS(9),ARASR(9),ARAF(9),ARAFM(9),ARAFMX(9),
                    6TAUAF(9),THO(9),ARP(9),TAUTH(9),THDO(9),CTHR(9),W(9),
                    7TAUM(9),WR(9),S(9,99),KK(9),NAP(9),ACCOM(9),CACCOM(9),TAUACC(9),
                    8CIN(9),T(9),TS(9),NS(9),ITO(9),P1(9),P2(9),RF(9)
              C
              C     ******************************************************************
              C
              C     READING IN AND PRINTING OUT OF INPUT DATA
              C
              C     ******************************************************************
              C
0002                 READ 1,M,N,KLIM,LS,LIMS,INT,AS,FO,IES
0003          1      FORMAT(I2,1X,I2,1X,I4,1X,I1,1X,I4,1X,I3,1X,F8.4,1X,F4.2,1X,I1)
0004                 PRINT 2,M,N,KLIM,LS,LIMS,INT,AS,FO,IES
0005          2      FORMAT(' ',1X,'M',2X,'N',1X,'KLIM',1X,'LS',1X,'LIMS',1X,'INT',
                    13X,'AS',4X,'FO',1X,'IES'/' ',I2,1X,I2,1X,I4,2X,I1,1X,I4,1X,I3,1X,
                    2F9.4,1X,F5.2,3X,I1)
0006                 DO 3 I=1,M
0007                 READ 4,VO(I),VREV(I),VDREV(I),ARASR(I),TAUAS(I),CARAS(I),ARAFM(I),
                    1TAUAF(I),ARAFMX(I),THDO(I),ARP(I),TAUTH(I),CTHR(I),TAUM(I),WR(I),
                    2CACCOM(I),TAUACC(I)
0008          4      FORMAT(3(F8.4,1X)/3(F8.4,1X)/3(F8.4,1X)/4(F8.4,1X)/2(F8.4,1X)/
                    12(F8.4,1X))
0009          3      CONTINUE
0010                 PRINT 7
0011          7      FORMAT('0',1X,'I'/' ',4X,'VO(I)',6X,'VREV(I)',5X,'VDREV(I)'/' ',
                    11X,'ARASR(I)',5X,'TAUAS(I)',5X,'CARAS(I)'/' ',1X,'ARAFM(I)',5X,
                    2'TAUAF(I)',4X,'ARAFMX(I)'/' ',2X,'THDO(I)',7X,'ARP(I)',5X,
                    3'TAUTH(I)',6X,'CTHR(I)'/' ',2X,'TAUM(I)',8X,'WR(I)'/' ',
                    4'CACCOM(I)',4X,'TAUACC(I)')
0012                 DO 6 I=1,M
0013                 PRINT 5,I,VO(I),VREV(I),VDREV(I),ARASR(I),TAUAS(I),CARAS(I),
                    1ARAFM(I),TAUAF(I),ARAFMX(I),THDO(I),ARP(I),TAUTH(I),CTHR(I),
                    2TAUM(I),WR(I),CACCOM(I),TAUACC(I)
0014          5      FORMAT('0',I2/' ',3(F9.4,4X)/' ',3(F9.4,4X)/' ',3(F9.4,4X)/' ',
                    14(F9.4,4X)/' ',2(F9.4,4X)/' ',2(F9.4,4X))
0015          6      CONTINUE
0016                 DO 106 J=1,N
0017                 READ 8,NFROM(J),NTO(J),DE(J),KSTY(J),NSTY(J),A(J),RT(J),FT(J),
                    1FCMX(J),TAUF(J)
0018          8      FORMAT(2(I2,1X),F8.4,1X,I1,1X,I2,5(1X,F8.4))
0019          106    CONTINUE
0020                 PRINT 55
0021          55     FORMAT('0',1X,'NFROM(J)',1X,'NTO(J)',5X,'DE(J)',4X,'KSTY(J)',
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FORTRAN IV G LEVEL  21                  MAIN                DATE = 83180          20/08/47

                     14X,'NSTY(J)',9X,'A(J)',8X,'RT(J)',8X,'FT(J)',6X,'FCMX(J)',6X,
                     2'TAUF(J)')
0022                  DO 57 J=1,N
0023                  PRINT 56,NFROM(J),NTO(J),DE(J),KSTY(J),NSTY(J),A(J),RT(J),FT(J),
                     1FCMX(J),TAUF(J)
0024          56      FORMAT(' ',7X,I2,5X,I2,1X,F9.4,10X,I1,9X,I2,5(4X,F9.4))
0025          57      CONTINUE
0026                  IF(LS.EQ.0) GOTO 655
0027                  DO 58 I=1,LS
0028                  READ 59,NSTO(I),CSEN(I),CDSEN(I),TAUSEN(I)
0029          59      FORMAT(I1,1X,3(F8.4,1X))
0030          58      CONTINUE
0031                  PRINT 60
0032          60      FORMAT(' ',2X,'NSTO(I)',6X,'CSEN(I)',5X,'CDSEN(I)',4X,
                     1'TAUSEN(I)')
0033                  DO 61 I=1,LS
0034                  PRINT 62,NSTO(I),CSEN(I),CDSEN(I),TAUSEN(I)
0035          62      FORMAT(' ', 6X,I1,3(4X,F9.4))
0036          61      CONTINUE
0037          655     DO 680 J=1,IES
0038                  READ 650,ITO(J),T(J),TS(J),NS(J)
0039          650     FORMAT(I1,1X,2(F6.3,1X),I3)
0040          680     CONTINUE
0041                  PRINT 651
0042          651     FORMAT('0',2X,'J',1X,'ITO(J)',7X,'T(J)',6X,'TS(J)',4X,'NS(J)')
0043                  DO 652 J=1,IES
0044                  PRINT 653,J,ITO(J),T(J),TS(J),NS(J)
0045          653     FORMAT(' ',I3,6X,I1,2(4X,F7.3),6X,I3)
0046          652     CONTINUE
                      C
                      C     ***************************************************************
                      C
                      C     INITIALIZATION OF VARIABLES
                      C
                      C     ***************************************************************
                      C
0047                  KLOCK=-1
0048                  INTD=IFIX(FLOAT(INT)/FD)-1
                      C     INITIALIZE NEURONAL VARIABLES
0049                  DO 63 I=1,M
0050                  V(I)=VO(I)
0051                  P1(I)=0.
0052                  P2(I)=0.
0053                  THD(I)=VO(I)+THDO(I)
0054                  RF(I)=THDO(I)
0055                  ARAS(I)=0.
0056                  ARAF(I)=0.
0057                  ACCOM(I)=0.
0058                  W(I)=0.
0059                  RSEN(I)=0.
0060                  KK(I)=0
0061                  NAP(I)=10./FD
0062                  TAUAF(I)=TAUAF(I)*1000.
0063                  DO 63 J=1,99
0064                  S(I,J)=0.
0065          63      CONTINUE
                      C     INITIALIZE SYNAPTIC VARIABLES
0066                  DO 64 J=1,N
```

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FORTRAN IV G LEVEL  21                  MAIN                DATE = 83180          20/08/47

0067                TAUF(J)=TAUF(J)*1000.
0068                MD(J)=0
0069                MC(J)=0
0070                P(J)=0.
0071                FPD(J)=1.
0072                FCD(J)=1.
0073                R(J)=0.
0074                B1(J)=RT(J)
0075                B2(J)=RT(J)
0076                TAUD(J)=FT(J)/4.
0077                G1(J)=ABS(A(J))/RT(J)
0078                DO 66 K=1,99
0079                IC(J,K)=10000
0080                TO(J,K)=1.0E5
0081                CVREV(J,K)=1.
0082                FP(J,K)=0.
0083                FC(J,K)=1.
0084          66    CONTINUE
0085          64    CONTINUE
0086                IF(LS.EQ.0) GOTO 656
0087                DO 67 I=1,LS
0088                DO 67 J=1,4000
0089                SENIN(I,J)=0.
0090          67    CONTINUE
                    C
                    C     ***************************************************************
                    C
                    C     CALCULATION OF CONSTANTS FOR THE CURVE-FITTING OF THE STANDARD
                    C     PSPS
                    C
                    C     ***************************************************************
                    C
0091          656   DO 300 J=1,N
0092                R(J)=(RT(J)+FT(J))/0.3
                    C     CALCULATE B1(J), G1(J)
0093                K1=RT(J)*100.-R(J)
0094                K2=RT(J)*100.-1.
0095                ABA=ABS(A(J))*100.
0096                L=K2-K1
0097                DO 301 KD=1,L
0098                K=K2-KD+1
0099                H=(PT(J)*100.-FLOAT(K))/SQRT(R(J)**2-(RT(J)*100.-FLOAT(K))**2)
0100                G=(SQRT(R(J)**2-(RT(J)*100.-FLOAT(K))**2)+ABA -R(J))/FLOAT(K)
0101                IF((G-H).LT.0.) GOTO 302
0102                B1(J)=(FLOAT(K))/100.
0103                G1(J)=(G+H)/2.0
0104          301   CONTINUE
                    C     CALCULATE B2(J), TAUD(J)
0105          302   K1=RT(J)*100.+1.
0106                K2=RT(J)*100.+R(J)-1
0107                DIF=4.*ABA/(FT(J)*100.)
0108                DO 303 K=K1,K2
0109                G=4.*(ABA -R(J)+SQRT(R(J)**2-(FLOAT(K)-RT(J)*100.)**2))/
                   1((FT(J)+RT(J))*100.-FLOAT(K))
0110                H=(FLOAT(K)-RT(J)*100.)/(SQRT(R(J)**2-(FLOAT(K)-RT(J)*100.)**2))
0111                IF((G-H).LT.0.) GOTO 715
0112                B2(J)=FLOAT(K)/100.
0113                TAUD(J)=(RT(J)+FT(J)-B2(J))/4.
```

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FORTRAN IV G LEVEL  21                  MAIN                DATE = 83180          20/08/47

0114          303   CONTINUE
0115          715   R(J)=R(J)/100.
0116          300   CONTINUE
0117                PRINT 702
0118          702   FORMAT('0',5X,'R(J)',8X,'G1(J)',8X,'B1(J)',8X,'B2(J)',6X,
                   1'TAUD(J)')
0119                DO 700 J=1,N
0120                PRINT 701,R(J),G1(J),B1(J),B2(J),TAUD(J)
0121          701   FORMAT(' ',5(F9.4,4X))
0122          700   CONTINUE
                    C
                    C     ***************************************************************
                    C
                    C     USE OF SUBROUTINE "FDD" TO EXPRESS THE CONSTANTS INDICATING TIME
                    C     IN THE UNITS DEFINED BY A TIME STEP IN THE PROGRAM
                    C
                    C     ***************************************************************
                    C
0123                CALL FDD(FD,M,N,LS,KLIM,LIMS,INT,TAUSEN,TAUF,TAUD,DE,TAUAS,TAUAF,
                   1TAUTH,T,TS,A,B1,B2,R,RT,IES,ARP,TAUACC)
                    C
                    C     ***************************************************************
                    C
                    C     CALCULATION AND STORAGE OF THE TIMES AT WHICH THE ACTION
                    C     POTENTIALS DUE TO EXTRACELLULAR STIMULATION REACH THE AFFECTED
                    C     SYNAPSES
                    C
                    C     ***************************************************************
                    C
0124                DO 654 JO=1,IES
0125                J=ITO(JO)
0126                IF(NS(JO).EQ.0) GOTO 654
0127                MC(J)=NS(JO)
0128                NSD=NS(JO)
0129                DO 654 K=1,NSD
0130                IC(J,K)=FLOAT(K-1)*T(JO)+TS(JO)+DE(J)
0131          654   CONTINUE
                    C
                    C     ***************************************************************
                    C
                    C     CALCULATION OF SENSORY INPUT
                    C
                    C     ***************************************************************
                    C
0132                IF(LS.EQ.0) GOTO 657
0133                DO 68 I=1,LS
0134                DO 68 J=1,LIMS
0135                SENIN(I,J)=AS
0136          68    CONTINUE
                    C
0137          657   PRINT 47
0138          47    FORMAT('1',2X,'CLOCK',5X,'I',9X,'V(I)',6X,'ARAS(I)',6X,'ARAF(I)',
                   17X,'THD(I)',9X,'W(I)',6X,'RSEN(I)',5X,'ACCOM(I)')
0139                PRINT 103
0140          103   FORMAT(' ',2X,'CLOCK',5X,'J',7X,'FCD(J)',7X,'FPD(J)')
                    C
                    C
                    C
```

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FORTRAN IV G LEVEL  21                  MAIN                DATE = 83180          20/08/47

              C     ***************************************************************
              C
              C     START OF THE MAIN LOOP; CALCULATION OF THE MULTIPLYING FACTORS FOR
              C     A NEW PSP (IF AN ACTION POTENTIAL HAS REACHED A SYNAPSE)
              C
              C     ***************************************************************
              C
 0141         42    KLOCK=KLOCK+1
 0142               INTD=INTD+1
 0143               DO 11 J=1,N
              C     CHECK IF AN ACTION POTENTIAL HAS REACHED A SYNAPSE
 0144               IF(IC(J,1).NE.0) GOTO 52
 0145               MD(J)=MD(J)+1
 0146               MDD=MD(J)
 0147               TO(J,MDD)=0.
 0148               MG=NTO(J)
 0149               IF(KSTY(J).EQ.2) GOTO 933
 0150               IF(NSTY(J).EQ.-1) GOTO 930
 0151               CVREV(J,MDD)=(P1(MG)+VO(MG)-VREV(MG))/(VO(MG)-VREV(MG))
 0152               GOTO 52
 0153         930   CVREV(J,MDD)=(P2(MG)+VC(MG)-VOREV(MG))/(VC(MG)-VOREV(MG))
 0154               GOTO 52
 0155         933   CVREV(J,MDD)=1.-P(J)
 0156         52    FCD(J)=F(1.,FCD(J),TAUF(J))
 0157               IF(IC(J,1).NE.0) GOTO 11
 0158               FC(J,MDD)=FCD(J)
 0159         11    CONTINUE
              C
 0160         400   DO 9 I=1,M
 0161               NAP(I)=NAP(I)+1
 0162         9     CONTINUE
              C
              C     ***************************************************************
              C
              C     CALCULATION OF THE POSTSYNAPTIC RESPONSE FOR ALL THE SYNAPSES
              C
              C     ***************************************************************
              C
 0163               KSYN=1
 0164         12    DO 13 J=1,N
 0165               IF((KSTY(J).EQ.3).AND.(KSYN.EQ.1)) GOTO 13
 0166               IF(((KSTY(J).EQ.1).OR.(KSTY(J).EQ.2)).AND.(KSYN.EQ.2)) GOTO 13
 0167               IF((KSTY(J).EQ.3).AND.(KSYN.EQ.2)) GO TO 16
              C     CALCULATE THE POSTSYNAPTIC RESPONSE FOR A SYNAPSE OF TYPE 1 OR 2
 0168               P(J)=0.
 0169               IF(MD(J).EQ.0) GOTO 13
 0170               MDD=MD(J)
 0171               IF(A(J).LT.0.) GOTO 320
 0172               DO 17 L=1,MDD
 0173               IF(TO(J,L).GE.B1(J)) GOTO 310
 0174               P(J)=P(J)+FC(J,L)*CVREV(J,L)*G1(J)*TC(J,L)*FD
 0175               GOTO 17
 0176         310   IF(TO(J,L).GE.B2(J)) GOTO 311
 0177               P(J)=P(J)+FC(J,L)*CVREV(J,L)*(A(J)-R(J)+SQRT(R(J)**2-(RT(J)-
                   1TO(J,L))**2))*FD
 0178               GOTO 17
 0179         311   P(J)=P(J)+FC(J,L)*CVREV(J,L)*(A(J)-R(J)+SQRT(R(J)**2-(RT(J)-B2(J))
                   1**2))*EXP(-(TO(J,L)-B2(J))/TAUC(J))*FD
```

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FORTRAN IV G LEVEL  21                MAIN                DATE = 83180          20/08/47

0180          17    CONTINUE
0181                GOTO 13
0182          320   DO 321 L=1,MDD
0183                IF(TO(J,L).GE.B1(J)) GOTO 322
0184                P(J)=P(J)-FC(J,L)*CVREV(J,L)*G1(J)*TO(J,L)*FD
0185                GOTO 321
0186          322   IF(TO(J,L).GE.B2(J)) GOTO 323
0187                P(J)=P(J)+FC(J,L)*CVREV(J,L)*(A(J)+R(J)-SQRT(R(J)**2-(RT(J)-
                   1TO(J,L))**2))*FD
0188                GOTO 321
0189          323   P(J)=P(J)+FC(J,L)*CVREV(J,L)*(A(J)+R(J)-SQRT(R(J)**2-(RT(J)-B2(J))
                   1**2))*EXP(-(TO(J,L)-B2(J))/TAUD(J))*FD
0190          321   CONTINUE
0191                GOTO 13
              C     CALCULATE THE POSTSYNAPTIC RESPONSE FOR A SYNAPSE OF TYPE 3
0192          16    MDD=MD(J)
0193                DO 401 JD=1,N
0194                IF((KSTY(JD).EQ.2).AND.(NTO(JD).EQ.J)) GOTO 402
0195                GO TO 401
0196          402   FPD(J)=1.+P(JD)/NSTY(JD)
0197                IF(IC(J,1).NE.0) GOTO 450
0198                IF(MD(J).EQ.0) GOTO 450
0199                FP(J,MDD)=FPD(J)
0200                GO TO 450
0201          401   CONTINUE
0202          450   P(J)=0.
0203                IF(MD(J).EQ.0) GOTO 13
0204                IF(A(J).LT.0.) GOTO 451
0205                DO 452 L=1,MDD
0206                IF(TO(J,L).GE.B1(J)) GOTO 453
0207                P(J)=P(J)+FP(J,L)*FC(J,L)*CVREV(J,L)*G1(J)*TO(J,L)*FD
0208                GOTO 452
0209          453   IF(TO(J,L).GE.B2(J)) GOTO  454
0210                P(J)=P(J)+FP(J,L)*FC(J,L)*CVREV(J,L)*(A(J)-R(J)+SQRT(R(J)**2-
                   1(RT(J)-TO(J,L))**2))*FD
0211                GOTO 452
0212          454   P(J)=P(J)+FP(J,L)*FC(J,L)*CVREV(J,L)*(A(J)-R(J)+SQRT(R(J)**2-
                   1(RT(J)-B2(J))**2))*EXP(-(TO(J,L)-B2(J))/TAUD(J))*FD
0213          452   CONTINUE
0214                GOTO 13
0215          451   DO 455 L=1,MDD
0216                IF(TO(J,L).GE.B1(J)) GOTO 456
0217                P(J)=P(J)-FP(J,L)*FC(J,L)*CVREV(J,L)*G1(J)*TO(J,L)*FD
0218                GOTO 455
0219          456   IF(TO(J,L).GE.B2(J)) GOTO  457
0220                P(J)=P(J)+FP(J,L)*FC(J,L)*CVREV(J,L)*(A(J)+R(J)-SQRT(R(J)**2-
                   1(RT(J)-TO(J,L))**2))*FD
0221                GOTO 455
0222          457   P(J)=P(J)+FP(J,L)*FC(J,L)*CVREV(J,L)*(A(J)+R(J)-SQRT(R(J)**2-
                   1(RT(J)-B2(J))**2))*EXP(-(TO(J,L)-B2(J))/TAUD(J))*FD
0223          455   CONTINUE
0224          13    CONTINUE
0225                IF(KSYN.EQ.2) GO TO 21
0226                KSYN=2
0227                GOTO 12
              C
              C
              C
```

```
FORTRAN IV G LEVEL  21                MAIN                DATE = 83180          20/08/47

                C     ***************************************************************
                C
                C     CALCULATION OF FACILITATION FOR EVERY SYNAPSE
                C
                C     ***************************************************************
                C
0228            21    DO 360 J=1,N
0229                  IF(IC(J,1).NE.0) GOTO 360
0230                  IF(KSTY(J).EQ.3) GOTO 361
0231                  FCD(J)=FCD(J)*(1.-FCMX(J))
0232                  GOTO 360
0233            361   FCD(J)=FCD(J)*(1.-FCMX(J)*FPD(J))
0234            360   CONTINUE
                C
                C     ***************************************************************
                C
                C     CALCULATION OF THE TOTAL EXCITATION OR INHIBITION, ACCOMMODATION,
                C     SPIKE AND GENERATOR ADAPTATION, PERTURBATION DUE TO A SPIKE,
                C     REFRACTORINESS, AND SENSORY RESPONSE FOR EVERY NEURON
                C
                C     ***************************************************************
                C
0235                  DO 940 I=1,M
0236                  P1(I)=0.
0237                  P2(I)=0.
0238            940   CONTINUE
0239                  DO 22 J=1,N
0240                  NT=NTO(J)
0241                  IF(NSTY(J).EQ.-1) GOTO 22
0242                  IF(KSTY(J).EQ.2) GOTO 22
0243                  P1(NT)=P1(NT)+P(J)
0244            22    CONTINUE
0245                  DO 673 J=1,N
0246                  NT=NTO(J)
0247                  IF(NSTY(J).EQ.1) GOTO 673
0248                  IF(KSTY(J).EQ.2) GOTO 673
0249                  P2(NT)=P2(NT)+P(J)
0250            673   CONTINUE
0251                  DO 674 I=1,M
0252                  ACCOM(I)=F(CACCOM(I)*(V(I)-VC(I)),ACCOM(I),TAUACC(I))
0253                  ARAF(I)=F(0.,ARAF(I),TAUAF(I))
0254                  ARAS(I)=F(CARAS(I)*(V(I)-VO(I)),ARAS(I),TAUAS(I))
0255                  W(I)=F(0.,W(I),TAUM(I))
0256                  IF(NAP(I).LE.IFIX(ARP(I))) GOTO 14
0257                  RF(I)=F(THDO(I),RF(I),TAUTH(I))
0258                  GOTO 674
0259            14    RF(I)=100.
0260            674   CONTINUE
0261                  IF(LS.EQ.0) GOTO 658
0262                  DO 10 I=1,LS
0263                  MS=NSTO(I)
0264                  RSEN(MS)=F(CSEN(MS)*SENIN(MS,1)+CDSEN(MS),RSEN(MS),TAUSEN(MS))
0265            10    CONTINUE
                C
                C
                C
                C
                C
```

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FORTRAN IV G LEVEL  21                MAIN              DATE = 83180          20/08/47

              C     ***************************************************************
              C
              C     CALCULATION OF THE MEMBRANE POTENTIAL AND THRESHOLD FOR EVERY
              C     NEURON
              C
              C     ***************************************************************
              C
 0266         658   DO 23 I=1,M
              C     CALCULATE THE MEMBRANE POTENTIAL OF A NEURON
 0267               CIN(I)=(VOREV(I)-P2(I)-VO(I))/(VOREV(I)-VO(I))
 0268               V(I)=VO(I)+CIN(I)*P1(I)+P2(I)+W(I)-ARAS(I)+RSEN(I)*CIN(I)
              C     CALCULATE THE THRESHOLD OF A NEURON
 0269               IF(NAP(I).LE.IFIX(ARP(I))) GOTO 600
 0270               THD(I)=RF(I)+ARAF(I)+ACCOM(I)+VO(I)
 0271               GOTO 23
 0272         600   THD(I)=RF(I)
 0273         23    CONTINUE
              C
              C     ***************************************************************
              C
              C     STORAGE OF THE TIME OF GENERATION OF AN ACTION POTENTIAL, AND
              C     RESETTING OF THE VALUES OF ACCOMMODATION, SPIKE AND GENERATOR
              C     ADAPTATION, PERTURBATION DUE TO A SPIKE, AND REFRACTORINESS (IF AN
              C     ACTION POTENTIAL IS GENERATED)
              C
              C     ***************************************************************
              C
 0274               DO 26 J=1,N
 0275               IF(NFROM(J).EQ.0) GOTO 26
 0276               I=NFROM(J)
              C     CHECK IF AN ACTION POTENTIAL IS GENERATED
 0277               IF(V(I).LT.THD(I)) GOTO 26
 0278               MC(J)=MC(J)+1
 0279               MCD=MC(J)
 0280               IC(J,MCD)=IFIX(DE(J))
 0281         26    CONTINUE
 0282               DO 24 I=1,M
              C     CHECK IF AN ACTION POTENTIAL IS GENERATED
 0283               IF(V(I).LT.THD(I)) GOTO 601
 0284               NAP(I)=0
 0285               KK(I)=KK(I)+1
 0286               KKD=KK(I)
 0287               S(I,KKD)=FLOAT(KLOCK)*FD
 0288         601   IF(NAP(I).NE.IFIX(ARP(I))) GOTO 24
              C     RESET THE VALUES OF THE REQUIRED QUANTITIES
 0289               ACCOM(I)=0.
 0290               ARAF(I)=ARAF(I)+((ARAFMX(I)-ARAF(I))/ARAFMX(I))*ARAFM(I)
 0291               ARAS(I)=ARAS(I)+ARASR(I)
 0292               W(I)=WR(I)
 0293               RF(I)=CTHR(I)*THDO(I)
 0294         24    CONTINUE
              C
              C     ***************************************************************
              C
              C     UPDATING OF THE REQUIRED QUANTITIES FOR THE NEXT ITERATION
              C
              C     ***************************************************************
              C
```

```
FORTRAN IV G LEVEL  21                    MAIN                    DATE = 83180          20/08/47

0295                IF(LS.EQ.0) GOTO 659
0296                DO 27 I=1,LS
0297                DO 27 K=1,2000
0298                SENIN(I,K)=SENIN(I,K+1)
0299          27    CONTINUE
0300          659   DO 30 J=1,N
0301                IF(MD(J).EQ.0) GOTO 500
              C     CHECK IF A PSP IS PAST ITS FALL TIME
0302                IF((TO(J,1)-B2(J)).LE.(4.*TAUD(J))) GOTO 31
0303                MD(J)=MD(J)-1
0304                MDD1=MC(J)+1
0305                DO 32 L=1,MDD1
0306                FC(J,L)=FC(J,L+1)
0307                TO(J,L)=TO(J,L+1)
0308                FP(J,L)=FP(J,L+1)
0309                CVREV(J,L)=CVREV(J,L+1)
0310          32    CONTINUE
              C     UPDATE TO(J,L)
0311          31    IF(MD(J).EQ.0) GOTO 500
0312                MDD=MD(J)
0313                DO 33 L=1,MDD
0314                TO(J,L)=TO(J,L)+1.
0315          33    CONTINUE
              C     UPDATE IC(J,L)
0316          500   IF(MC(J).EQ.0) GOTO 30
0317                IF(IC(J,1).NE.0) GO TO 38
0318                MC(J)=MC(J)-1
0319                MCD1=MC(J)+1
0320                DO 39 L=1,MCD1
0321                IC(J,L)=IC(J,L+1)
0322          39    CONTINUE
0323          38    IF(MC(J).EQ.0) GOTO 30
0324                MCD=MC(J)
0325                DO 40 L=1,MCD
0326                IC(J,L)=IC(J,L)-1
0327          40    CONTINUE
0328          30    CONTINUE
              C
              C     ***************************************************************
              C
              C     PRINTING OUT OF THE VALUES OF ALL THE VARIABLES OF INTEREST AT
              C     DESIRED INTERVALS
              C
              C     ***************************************************************
              C
0329                IF(INTD.NE.INT) GO TO 43
0330                CLOCK=FLOAT(KLOCK)*FD
0331                DO 45 I=1,M
0332                PRINT 46,CLOCK,I,V(I),ARAS(I),ARAF(I),THD(I),W(I),RSEN(I),ACCUM(I)
0333          46    FORMAT(' ',F7.2,4X,I2,7(4X,F9.4))
0334          45    CONTINUE
0335                DO 104 J=1,N
0336                IF(FCMX(J).EQ.0.) GOTO 104
0337                PRINT 105,CLOCK,J,FCD(J),FPD(J)
0338          105   FORMAT(' ',F7.2,4X,I2,2(4X,F9.4))
0339          104   CONTINUE
0340                INTD=0
0341          43    IF(KLOCK.LE.KLIM) GO TO 42
```

```
FORTRAN IV G LEVEL  21                MAIN              DATE = 83180          20/08/47

                C
                C     ******************************************************************
                C
                C     END OF THE MAIN LOOP; PRINTING OUT OF THE TIMES OF GENERATION OF
                C     ACTION POTENTIALS FOR EVERY NEURON
                C
                C     ******************************************************************
                C
 0342        41     DO 90 I=1,M
 0343               PRINT 48 ,I
 0344        48     FORMAT('1','I=',I2)
 0345               PRINT 101
 0346        101    FORMAT('0',1X,'K',7X,'S(I,K)')
 0347               IF(KK(I).EQ.0)  GOTO 90
 0348               KKD=KK(I)
 0349               DO 90 K=1,KKD
 0350               PRINT 102,K,S(I,K)
 0351        102    FORMAT(' ',I2,6X,F7.2)
 0352        90     CONTINUE
 0353        999    CONTINUE
 0354               STOP
 0355               END
```

```
FORTRAN IV G LEVEL  21                  FDD                 DATE = 83180          20/08/47

0001                  SUBROUTINE FDD(FD,M,N,LS,KLIM,LIMS,INT,TAUSEN,TAUF,TAUD,DE,TAUAS,
                     1TAUAF,TAUTH,T,TS,A,B1,B2,R,RT,IES,ARP,TAUACC)
0002                  DIMENSION TAUSEN(1),TAUF(38),TAUD(38),DE(38),TAUAS(9),TAUAF(9),
                     1TAUTH(9),T(9),TS(9),A(38),B1(38),B2(38),R(38),RT(38),ARP(38),
                     2TAUACC(9)
0003                  DO 1 I=1,LS
0004                  TAUSEN(I)=TAUSEN(I)/FD
0005             1    CONTINUE
0006                  DO 2 J=1,N
0007                  R(J)=R(J)/FD
0008                  RT(J)=RT(J)/FD
0009                  A(J)=A(J)/FD
0010                  B1(J)=B1(J)/FD
0011                  B2(J)=B2(J)/FD
0012                  TAUF(J)=TAUF(J)/FD
0013                  TAUD(J)=TAUD(J)/FD
0014                  DE(J)=DE(J)/FD
0015             2    CONTINUE
0016                  DO 3 I=1,M
0017                  ARP(I)=ARP(I)/FD
0018                  TAUAS(I)=TAUAS(I)/FD
0019                  TAUAF(I)=TAUAF(I)/FD
0020                  TAUTH(I)=TAUTH(I)/FD
0021                  TAUACC(I)=TAUACC(I)/FD
0022             3    CONTINUE
0023                  DO 6 J=1,IES
0024                  T(J)=T(J)/FD
0025                  TS(J)=TS(J)/FD
0026             6    CONTINUE
0027                  KLIM=FLOAT(KLIM)/FD
0028                  INT=INT/FD
0029                  LIMS=FLOAT(LIMS)/FD
0030                  RETURN
0031                  END
```

```
FORTRAN IV G LEVEL  21                  F                       DATE = 83180          20/08/47

 0001               FUNCTION F(SS,YO,TAU)
 0002               IF(YO.LT.1.0E-8)  YO=0.
 0003               F=YO*(EXP((-1.)/TAU))+SS*(1.-EXP((-1.)/TAU))
 0004               RETURN
 0005               END
```

```
10   ! ************************************************************************
20   !
30   ! PROGRAM NAME: DATA
40   ! THIS PROGRAM IS USED TO ENTER DATA INTO A FILE IN  THE FORM OF X-Y
50   ! COORDINATES.  THE FILE CAN THEN BE USED FOR MAKING A X-Y PLOT USING
60   ! THE "PLOT" PROGRAM.
70   !
80   ! ************************************************************************
90   !
100  INPUT "ENTER FILE NAME,NUMBER OF DATA POINTS",A$,N
110  DIM X(500),Y(500)
120  No_of_records=N*2+1
130  Bytes_per_rec=8
140  CREATE A$,No_of_records,Bytes_per_rec
150  ASSIGN #1 TO A$
160  !
170  PRINT #1;N
180  !
190  FOR I=1 TO N
200  INPUT "ENTER X,Y",X(I),Y(I)
210  PRINT I,X(I),Y(I)
220  NEXT I
230  INPUT "DO YOU WANT TO MAKE ANY CORRECTIONS (Y OR N) ?",Y$
240  IF Y$<>"Y" THEN 320
250  INPUT "ENTER THE NUMBER OF CORRECTIONS",C
260  FOR I=1 TO C
270  INPUT "ENTER THE DATA NUMBER ,X COORDINATE,Y COORDINATE",J,X(J),Y(J)
280  PRINT J,X(J),Y(J)
290  NEXT I
300  GOTO 230
310  !
320  FOR I=1 TO N
330  PRINT #1;X(I),Y(I)
340  NEXT I
350  END
```

```
10   ! ************************************************************************
20   !
30   ! PROGRAM NAME: PLOT
40   ! THIS PROGRAM IS USED TO MAKE AN X-Y PLOT OF THE DATA STORED IN A DATA
50   ! FILE USING THE PROGRAM "DATA".
60   !
70   ! ************************************************************************
80   !
90   OPTION BASE 1
100  DIM X(500),Y(500)
110  Count=1
120  !
130  ! ************************************************************************
140  !
150  ! READING IN AND PRINTING OUT OF DATA
160  !
170  ! ************************************************************************
180  !
190  PRINTER IS 16
200  INPUT "ENTER FILE NAME",A$
210  ASSIGN #1 TO A$
220  READ #1;N
230  FOR I=1 TO N
240  READ #1;X(I),Y(I)
250  PRINT X(I),Y(I)
260  NEXT I
270  IF Count>1 THEN 800
280  !
290  ! ************************************************************************
300  !
310  ! DRAWING AND LABELING OF AXES
320  !
330  ! ************************************************************************
340  !
350  PLOTTER IS "9872A"
360  DEG
370  LDIR 0
380  LORG 5
390  OUTPUT 7,5;"VS3,1"
400  INPUT "ENTER X-AXIS LABEL",B$
410  INPUT "ENTER Y-AXIS LABEL",C$
420  LOCATE 29,108,36,72
430  INPUT "ENTER THE SCALE LIMITS: XMIN,XMAX,YMIN,YMAX",Xmin,Xmax,Ymin,Ymax
440  SCALE Xmin,Xmax,Ymin,Ymax
450  INPUT "ENTER THE AXES PARAMETERS: XTIC,YTIC,XINT,YINT,XMAJC,YMAJC,MAJTS",Xt
ic,Ytic,Xint,Yint,Xmajc,Ymajc,Majts
460  AXES Xtic,Ytic,Xint,Yint,Xmajc,Ymajc,Majts
470  CSIZE 2
480  FOR I=Xint TO Xmax STEP Xtic*Xmajc
490  MOVE I,Yint-(Ymax-Ymin)/15
500  LABEL I
510  NEXT I
520  FOR I=Xint-Xtic*Xmajc TO Xmin STEP -Xtic*Xmajc
530  MOVE I,Yint-(Ymax-Ymin)/15
540  LABEL I
550  NEXT I
560  MOVE (Xmax-Xmin)/2+Xmin,Yint-(Ymax-Ymin)/5
570  LORG 2
580  LABEL B$
590  LORG 5
600  FOR I=Yint TO Ymax STEP Ytic*Ymajc
610  MOVE Xint-(Xmax-Xmin)/20,I
620  LABEL I
630  NEXT I
```

```
640  FOR I=Yint-Ytic*Ymajc TO Ymin STEP -Ytic*Ymajc
650  MOVE Xint-(Xmax-Xmin)/20,I
660  LABEL I
670  NEXT I
680  MOVE Xint-(Xmax-Xmin)/8,(Ymax-Ymin)/3+Ymin
690  LORG 8
700  LABEL C$
710  LORG 5
720  !
730  ! ************************************************************************
740  !
750  ! PLOTTING OF DATA
760  !
770  ! ************************************************************************
780  !
790  IF Count=1 THEN LINE TYPE 1
800  IF Count=2 THEN LINE TYPE 5,1
810  IF Count=3 THEN LINE TYPE 6
820  IF Count=4 THEN LINE TYPE 8
830  IF Count=5 THEN LINE TYPE 7
840  FOR I=1 TO N
850  PLOT X(I),Y(I)
860  NEXT I
870  MOVE Xint,Yint
880  !
890  !
900  INPUT "DO YOU WISH TO PLOT MORE PLOTS ON THE SAME PAGE ?",Q$
910  IF Q$<>"Y" THEN 940
920  Count=Count+1
930  GOTO 200
940  PEN 0
950  END
```

```
10   ! ************************************************************************
20   !
30   ! PROGRAM NAME: DAP
40   ! THIS PROGRAM IS USED TO ENTER THE TIMES OF GENERATION OF ACTION
50   ! POTENTIALS IN A NEURON.  THE STORED DATA CAN THEN BE PLOTTED USING THE
60   ! PROGRAM "PAP".
70   !
80   ! ************************************************************************
90   !
100  INPUT "ENTER FILE NAME,NUMBER OF DATA POINTS",A$,N
110  DIM X(100)
120  No_of_records=N+1
130  Bytes_per_rec=8
140  CREATE A$,No_of_records,Bytes_per_rec
150  ASSIGN #1 TO A$
160  PRINT #1;N
170  FOR I=1 TO N
180  INPUT "ENTER X",X(I)
190  PRINT I,X(I)
200  NEXT I
210  INPUT "DO YOU WANT TO MAKE ANY CORRECTIONS (Y OR N) ?",Y$
220  IF Y$<>"Y" THEN 290
230  INPUT "ENTER THE NUMBER OF CORRECTIONS",C
240  FOR I=1 TO C
250  INPUT "ENTER THE DATA NUMBER ,X COORDINATE",J,X(J)
260  PRINT J,X(J)
270  NEXT I
280  GOTO 210
290  FOR I=1 TO N
300  PRINT #1;X(I)
310  NEXT I
320  END
```

```
10   ! ************************************************************************
20   !
30   ! PROGRAM NAME: PAP
40   ! THIS PROGRAM IS USED TO PLOT ACTION POTENTIALS GENERATED IN A SET OF
50   ! NEURONS.  THE DATA NEEDED FOR THIS PROGRAM HAS TO BE STORED USING THE
60   ! PROGRAM "DAP"
70   !
80   ! ************************************************************************
90   !
100  OPTION BASE 1
110  PRINTER IS 16
120  DIM X(100)
130  Count=1
140  INPUT "ENTER THE NUMBER OF ACTION POTENTIAL WAVEFORMS TO BE PLOTTED",M
150  !
160  ! ************************************************************************
170  !
180  ! PLOTTING AND LABELING OF AXES
190  !
200  ! ************************************************************************
210  !
220  PLOTTER IS "9872A"
230  LORG 5
240  OUTPUT 7,5;"VS3,1"
250  LOCATE 26,78,46,115
260  INPUT "ENTER XMAX",Xmax
270  INPUT "ENTER X-AXIS LABEL",B$
280  Ymax=M+1
290  SCALE -10,Xmax,0,Ymax
300  AXES 1,0,-10,0,10,10,4
310  CSIZE 1.5
320  FOR I=0 TO Xmax STEP 10
330  MOVE I,-Ymax/30
340  LABEL I
350  NEXT I
360  MOVE (Xmax+10)/2,-Ymax/15
370  LABEL B$
380  LORG 8
390  FOR I=1 TO M
400  Yc=Ymax-I
410  MOVE -15,Yc
420  INPUT "ENTER LABEL",Z$
430  LABEL Z$
440  NEXT I
450  !
460  ! ************************************************************************
470  !
480  ! READING IN AND PRINTING OUT OF DATA
490  !
500  ! ************************************************************************
510  !
520  INPUT "ENTER FILE NAME",A$
530  ASSIGN #1 TO A$
540  READ #1;N
550  PRINT N
560  FOR I=1 TO N
570  READ #1;X(I)
580  PRINT X(I)
590  NEXT I
600  !
610  ! ************************************************************************
620  !
630  ! PLOTTING OF ACTION POTENTIALS
640  !
650  ! ************************************************************************
```

```
660  !
670  Yd=Ymax-Count
680  MOVE -10,Yd
690  DRAW Xmax,Yd
700  FOR I=1 TO N
710  Down=Yd-.125
720  Up=Yd+.25
730  MOVE X(I),Down
740  DRAW X(I),Up
750  NEXT I
760  !
770  Count=Count+1
780  IF Count<=M THEN 520
790  PEN 0
800  END
```

# A COMPUTER-SIMULATED MODEL FOR THE NEURONAL CIRCUIT MEDIATING THE TAIL-FLIP ESCAPE RESPONSE IN CRAYFISH

by

PRAMATHESH KUMAR

B.E., University of Bombay, 1981

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Kansas State University
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## ABSTRACT

The neuronal circuit mediating the tail-flip escape response of the crayfish (Procambarus clarkii) is simulated using a digital computer model. This model is designed to simulate, with reasonable accuracy, a number of neuronal and synaptic properties, such as membrane potential, refractoriness, adaptation, accommodation, and synaptic facilitation and antifacilitation.

The animal generates its tail-flip escape response when a strong tactile stimulus is applied to its abdomen. This tail-flip response is triggered by a single impulse in the lateral giant command neuron. Following this command impulse, the motor circuits cause strong feedback postsynaptic inhibition in the lateral giant and presynaptic and postsynaptic inhibition in one sensory interneuron. The effect of the feedback inhibition on the membrane potential of a sensory interneuron is studied using the model. The results of the simulation show that feedback presynaptic and postsynaptic inhibition both strongly suppress the excitation in the sensory interneuron. This inhibition, coupled with the postsynaptic inhibition of the lateral giant, serves an important purpose: it prevents the lateral giant from firing more than once during the course of the tail-flip response. The results of the simulation also confirm experimental observations by showing that presynaptic inhibition, by suppressing transmitter loss during a certain period, results in an antifacilitation which is less in amount than that obtained without presynaptic inhibition.

The effects of (1) using a different input stimulation frequency, and (2) subjecting all sensory interneurons are also studied. The results of these simulations confirm the expected results.

The simulations demonstrate the need for using a non-linear interaction between excitation and inhibition; the membrane potential cannot always be represented by a simple algebraic summation of excitation and inhibition.