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Title: NUMERICAL SOLUTION OF HODGKIN-HUXLEY'S  
PARTIAL DIFFERENTIAL SYSTEM FOR NERVE CONDUCTION

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A numerical solution to Hodgkin and Huxley's partial differential system for the propagated action potential is presented. In addition a three dimensional demonstration of the absolute refractory period is given. Lastly, theoretical evidence supporting Rushton's hypothesis is presented.

Numerical Solution of Hodgkin-Huxley's  
Partial Differential System For  
Nerve Conduction

by

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NUMERICAL SOLUTION OF HODGKIN-HUXLEY'S  
PARTIAL DIFFERENTIAL SYSTEM  
FOR NERVE CONDUCTION

INTRODUCTION

This thesis has been an attempt to integrate two backgrounds-- psychology and applied mathematics (emphasis will be on the latter).

More specifically, this thesis is concerned with mathematics associated with nervous conduction. Although nervous conduction is admittedly not a major subdivision of psychology, some of the basic ideas associated with neurology and nervous conduction are touched upon in courses in general psychology.

A brief outline of the basic neurology pertinent to this thesis will now be reviewed.

The Neuron

The basic unit of the nervous system is the nerve cell or neuron. All of the individual neurons have a cell body and processes, but they vary considerably in shape, size, number of processes, and manner of branching. For example, cell bodies may vary in diameter from four to five microns up to 50 to 100 microns; their processes vary from a few microns to several feet in length (41, p. 65-66).

The neuron is a specialized cell in that it exhibits to a

comparatively great degree the phenomena of irritability and conductivity, and it is capable of initiating and transmitting impulses. Structurally, the neuron is similar to other cells.

The cell processes protrude from the cell body. There are two basic types--dendrites and axons. Typically, each nerve cell has many dendrites; usually a neuron has only one axon. In general the dendrites conduct impulses toward their respective cell bodies and exhibit a local graded potential. Although some neurons have two axons and can deliver two nonidentical pulse-coded outputs at the same time in different directions (21), in general the axon carries impulses away from the cell body. The axon exhibits an all-or-nothing "spike" potential termed the action potential.<sup>1</sup> Axons may or may not be covered by a myelin sheath. Typically, axons of vertebrates have a myelin sheath, whereas axons of invertebrates do not. Axons end by forming synapses with other neurons or by forming motor endings with non-nervous tissue.

The interior of the cell is electrically negative to the exterior, and in resting or nonconducting nerve cells this potential difference (termed the steady or resting potential) may amount to 50 to 90 millivolts (mv.), depending upon the method of recording (41, p. 90).

It is most widely accepted that the resting potential is the

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<sup>1</sup>See Ochs (70), page 71.

result of differences in the concentration of ions in the cell and in the extracellular fluid, differences which are attributable to properties inherent in the cell membrane (41, p. 90). When a sufficiently strong stimulus, either physiological or artificial, is applied, the membrane potential undergoes a unique sequence of changes which constitutes the action potential. The action potential consists of the "spike," the negative after-potential and the positive after-potential. Compared to the spike, the negative and positive after-potentials are of considerably lower magnitude. The negative after-potential is a relatively prolonged negative electrical charge which may last 15 milliseconds (41, p. 96); the positive after-potential is of even longer duration.

These after-potentials are probably associated with processes of recovery following the passage of nerve impulses. The total time of all the changes produced by a stimulus may amount to as much as 80 milliseconds. The potential accounts for less than 1 millisecond (41, p. 97).

Two important properties of the action potential are the threshold phenomena and the all-or-nothing phenomena (74, p. 29). Associated with a single nerve fiber is a minimal strength of stimulus, the threshold, which is required to evoke an action potential. An insufficient stimulus evokes no response, whereas a stimulus equal to or greater than the threshold evokes a stereotyped response which for a given temperature is fixed in size, shape, duration, and



conduction speed. This is termed all-or-nothing behavior.

Following an action potential, there is a brief period of time in which the neuron cannot produce another action potential. This absolute refractory period lasts about one one-thousandth of a second or more (20, p. 29); during this period, a stimulus, no matter how large, will not initiate another action potential. The relative refractory period follows the absolute refractory period. During this period of time an action potential will be initiated only if the stimulus is greater than normal threshold strength.

The time relations of these excitability changes show the period of absolute refractoriness to coincide approximately with the rise of the spike potential and with its decline to the point where the negative after-potential distorts its falling curve. At this point the nerve again becomes excitable but has a high threshold, and so needs a more intense stimulus before it will respond (20, p. 34).

Although a subthreshold stimulus may not set-off an action potential, it is possible for a subthreshold stimulus to initiate an action potential if it is applied for a sufficiently long time. In addition, large above-threshold shocks may fail to excite if applied for sufficiently brief periods of time. The relationship between the strength of stimulus to excite and the duration of the current applied is described by a strength-duration curve.

### The Sodium Hypothesis

The remainder of this thesis will be concerned with aspects of the "modern ionic" basis of nervous conduction.

During the past two decades a technique, commonly called the voltage clamp, has provided a considerable amount of quantitative information regarding electrical and chemical properties of the nerve cell. During a voltage clamp the membrane potential is displaced to a new value and held there by electronic feedback. The effects of the impressed voltage are at the same time measured with a separate amplifier (47). Following extensive research with the voltage clamp technique, A. L. Hodgkin and A. F. Huxley formulated what is sometimes termed the "sodium hypothesis." The hypothesis states that when an above-threshold stimulus is applied, the low permeability of the nerve cell membrane to  $\text{Na}^+$  changes to a higher permeability. Since the interior of the cell is electrically negative to the exterior,  $\text{Na}^+$  ions move into the cell, and the cell interior becomes positive relative to the exterior of the cell. After a few milliseconds the membrane permeability to  $\text{Na}^+$  decreases and the membrane permeability to  $\text{K}^+$  increases. The  $\text{K}^+$  are now driven out of the cell to return the potential to its original level (70, p. 72-73).

Hodgkin and Huxley concluded their series of papers (49, 50, 51, 52, 53) with an electrochemical-mathematical model of the

nerve fiber.

The results described... [in the papers of Hodgkin and Huxley referred to above]... suggest that the behavior of the membrane may be represented by the network in Fig. 1 [Figure 1 of this paper also]. Current can be carried through the membrane either by charging the membrane capacity or by movement of ions through the resistances in parallel with the capacity. The ionic current is divided into components carried by sodium and potassium ions ( $I_{Na}$  and  $I_K$ ), and a small 'leakage current' ( $I_l$ ) made up by chloride and other ions (53, p. 500).

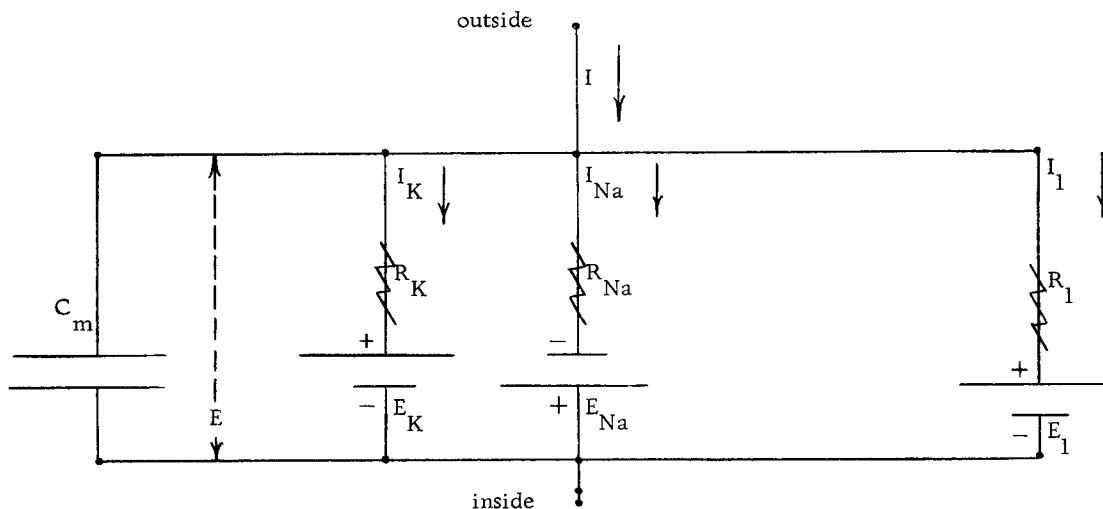


Figure 1. Hodgkin and Huxley's electrical model of the nerve fiber.

The equation describing this electrical network would be

$$I = C_m \frac{dV}{dt} + I_K + I_{Na} + I_l,$$

where  $C_m \frac{dV}{dt}$  is the capacitance current;  $I_K$ ,  $I_{Na}$ , and  $I_l$  are the ionic currents associated respectively with potassium, sodium,

and leakage. This is equivalent to

$$I = C_m \frac{dV}{dt} + g_K(V - V_K) + g_{Na}(V - V_{Na}) + \bar{g}_l(V - V_l),$$

where  $g_K$ ,  $g_{Na}$ ,  $\bar{g}_l$  are conductances associated respectively with potassium, sodium, and leakage, and  $V_K$ ,  $V_{Na}$ ,  $V_l$  are the magnitudes of the resting or nonconduction potentials associated with the same (53).

When one is concerned with propagated nerve impulses, the cable properties of the axon must be included in the analysis. However, the voltage clamp technique simplifies the situation in two ways.

First, all parts of the inside of the axon are connected together by a metal wire so that there are, at any rate in principle, no complications from current spreading along the fibre. In effect, instead of having to deal with a cable, the nerve can be treated as an isolated patch of membrane. The second simplification is that the experimenter controls the voltage across the membrane and so can make it do what he wants (47, p. 56-57).

During a voltage clamp, a typical action potential can be obtained by passing a brief pulse of current through the membrane. Since the membrane potential is uniform throughout the length of the fibre, this action potential must be distinguished from the propagated action potential in which the cable properties of the axon must be considered. The action potential obtained during a voltage clamp is termed the membrane action potential.

The two components of the current,  $I_K$  and  $I_{Na}$ , vary with the concentrations of  $K^+$  and  $Na^+$  in the surrounding fluid of the clamped axon; by changing these concentrations, the ionic current can be separated into its two components. The conductivity of the membrane to each ion can then be calculated (47, p. 57-59).

After sufficient data had been obtained on the time course of the potassium and sodium conductance for different clamping depolarizations, Hodgkin and Huxley proceeded

... to find equations which describe the conductances with reasonable accuracy and are sufficiently simple for theoretical calculation of the action potential and refractory period (53, p. 506).

The potassium conductance,  $g_K$ , was assumed to be proportional to  $n^4$  where  $n$  is a dimensionless variable which can vary between zero and one; it is assumed to satisfy the differential equation

$$\frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n,$$

where  $\alpha_n$  and  $\beta_n$  have been fitted to data derived from voltage clamp experiments (53).<sup>2</sup>

These equations may be given a physical basis if we assume that potassium ions can only cross the membrane when four similar particles occupy a certain region of the membrane.  $n$  represents the proportion of the particles in a certain position (for example at the inside of the membrane) and  $1-n$  represents the proportion

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<sup>2</sup>See Figure 4, page 511, of Hodgkin and Huxley (53).

that are somewhere else (for example at the outside of the membrane).  $\alpha_n$  determines the rate of transfer from outside to inside, while  $\beta_n$  determines the transfer in the opposite direction (53, p. 507).

The sodium conductance was described by the following:

$$g_{\text{Na}} = m^3 u \bar{g}_{\text{Na}},$$

$$\frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m,$$

$$\frac{du}{dt} = \alpha_u (1 - u) - \beta_u u,$$

where  $\bar{g}_{\text{Na}}$  is a constant and  $\alpha_m$ ,  $\beta_m$ ,  $\alpha_u$ , and  $\beta_u$  are fitted curves<sup>3</sup> which are functions of  $V$  but not of  $t$  (53). A physical basis for the equations describing the sodium conductance was likewise described by Hodgkin and Huxley (53).

The complete Hodgkin-Huxley equations are now listed (33).

$$I = C \frac{dV}{dt} + \bar{g}_K n^4 (V - V_K) + \bar{g}_{\text{Na}} m^3 u (V - V_{\text{Na}}) + \bar{g}_l (V - V_l), \quad (\text{A})$$

$$\frac{dn}{dt} = \phi[(1 - n)\alpha_n(V) - n\beta_n(V)], \quad (\text{B})$$

$$\frac{dm}{dt} = \phi[(1 - m)\alpha_m(V) - m\beta_m(V)], \quad (\text{C})$$

$$\frac{du}{dt} = \phi[(1 - u)\alpha_u(V) - u\beta_u(V)], \quad (\text{D})$$

where

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<sup>3</sup>See Figures 7 and 9, pages 515 and 516-517 respectively of Hodgkin and Huxley (53).

$$\alpha_n = \frac{.01(V + 10)}{\exp[(V + 10)/10] - 1},$$

$$\beta_n = .125 \exp(V/80),$$

$$\alpha_m = \frac{.1(V + 25)}{\exp[(V + 25)/10] - 1},$$

$$\beta_m = 4 \exp(V/18),$$

$$\alpha_u = .07 \exp(V/20),$$

$$\beta_u = \frac{1}{\exp[(V + 30)/10] + 1},$$

$$C_m = 1 \mu\text{f}/\text{cm.}^2,$$

$$\phi = 3^{(T - 6.3)/10},$$

$$T = \text{temperature } (^{\circ}\text{C}),$$

$$\bar{g}_K = 36, \quad \bar{g}_{Na} = 120, \quad \bar{g}_l = 0.3 \quad (\text{all in mmho}/\text{cm.}^2),$$

$$V_K = 12, \quad V_{Na} = -115, \quad V_l = -10.5989 \quad (\text{all in mv.}).$$

Under a variety of conditions, Hodgkin and Huxley compared the behavior of their nerve model as predicted by the above equations to the experimentally observed phenomena. Good agreement was obtained with respect to the following phenomena:

- 1) the form, amplitude and threshold of a membrane action potential;
- 2) the form, amplitude and velocity of a propagated action potential;

- 3) the form and amplitude of the impedance changes associated with an action potential;
- 4) the total inward movement of sodium ions and the total outward movement of potassium ions associated with an impulse;
- 5) the threshold and response during the refractory period;
- 6) the existence and form of subthreshold responses;
- 7) the existence and form of an anode break response;
- 8) the properties of the subthreshold oscillations seen in cephalopod axons (53).

Since their introduction in 1952, the Hodgkin-Huxley equations have stood up well under 14 years of investigation. Following their classic series of papers, the equations have been investigated by various researchers (22, 23, 24, 25, 27, 29, 30, 31, 33, 34, 43, 44, 54, 66). The range of application of these empirical equations has been extended considerably without uncovering any serious or fundamental defects (23).

#### Statement of Problem

During a membrane action potential the membrane potential is uniform throughout the length of the clamped fibre. That is, there is no longitudinal current. Thus, when solving the Hodgkin-Huxley equations for a membrane action potential,  $I$  equals zero in



equation A, page 9, and the system of differential equations is greatly simplified (53).

The situation is more complicated in a propagated action potential. The fact that the local circuit currents have to be provided by the net membrane current leads to the well-known relation

$$i = \frac{1}{r_1 + r_2} \frac{\partial^2 V}{\partial x^2},$$

where  $i$  is the membrane current per unit length,  $r_1$  and  $r_2$  are the external and internal resistances per unit length, and  $x$  is distance along the fibre. For an axon surrounded by a large volume of conducting fluid,  $r_1$  is negligible compared with  $r_2$ . Hence

$$i = \frac{1}{r_2} \frac{\partial^2 V}{\partial x^2},$$

or

$$I = \frac{a}{2R_2} \frac{\partial^2 V}{\partial x^2},$$

where  $I$  is the membrane current density,  $a$  is the radius of the fibre and  $R_2$  is the specific resistance of the axoplasm. Inserting this relation in eqn. (26) [same as equation A of this paper] we have

$$\begin{aligned} \frac{a}{2R_2} \frac{\partial^2 V}{\partial x^2} = C_m \frac{\partial V}{\partial t} + \bar{g}_K n^4 (V - V_K) + \bar{g}_{Na} m^3 u (V - V_{Na}) \\ + \bar{g}_l (V - V_l), \end{aligned} \quad (E)$$

the subsidiary equations being unchanged (53, p. 522).

Hodgkin and Huxley felt it impracticable to solve their system of partial differential equations for the propagated action potential. Assuming that the propagated action potential is a fixed wave

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<sup>4</sup>In the following, this equation will be referred to as equation E.

traveling at constant velocity, Hodgkin and Huxley reasoned that

$$\frac{\partial^2 V}{\partial x^2} = \frac{1}{\theta^2} \frac{\partial^2 V}{\partial t^2},$$

where  $\theta$  is the velocity of conduction. This assumption enabled Hodgkin and Huxley to describe the propagated action potential by a system of ordinary differential equations, which has been solved numerically (25, 27, 34, 53).

This thesis presents a numerical solution to the more complicated partial differential system for the propagated action potential. The work was intended as a check on the above assumption and as an interesting problem in its own right. In addition several interesting related problems have been investigated.

## NUMERICAL METHODS

In the classroom situation numerical techniques for solving differential or partial differential equations are learned by numerically solving equations with known analytic solutions. The numerical solution obtained and the analytic solution are compared, and when the numerical solution is the same as (or sufficiently close to) the analytic solution, it is generally assumed that the mathematics and coding associated with the numerical technique are correct. In a like manner, one procedure when attempting to numerically solve a complicated system of differential or partial differential equations with unknown analytic solution is to find another system which is similar in form to the given system and whose analytic solution is known. The system with known analytic solution is then solved numerically, and when the numerical solution coincides with (or is sufficiently close to) the analytic solution, the analyst is fairly certain that the mistakes in the mathematics and the mistakes in the computer coding associated with the mathematics have been eliminated. The next step is to modify the computer program to correspond to the system with unknown analytic solution. This system is then solved.

Due to lack of success in finding a system similar in form to the Hodgkin-Huxley partial differential system (with known analytic

solution), it was decided to use two independent methods of solution. The obvious advantage of using two methods is that one can be reasonably certain that the solution obtained is correct if the solutions obtained by the two methods are the same. The less obvious advantage is that the mathematics associated with each method can be mastered and the respective coding can be debugged while using short computer runs. The importance of this advantage is realized when one considers the large amounts of computer time necessary to solve such a system and the expense of using a large computer.

#### An Explicit Method

The first method utilized a formula which expresses one unknown pivotal value in terms of other known pivotal values. A method such as this is called an explicit method.

Using conventional notation,<sup>5</sup> the second derivative with respect to distance in equation E, page 12, was approximated by formula

$$\frac{\partial^2 V}{\partial x^2} = \left( \frac{\partial^2 V}{\partial x^2} \right)_{i,j} = \frac{1}{h^2} (V_{i+1,j} - 2V_{i,j} + V_{i-1,j}) ,$$

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<sup>5</sup> Assuming  $V$  is a function of independent variables  $x$  and  $t$ , assuming the  $x-t$  plane has been subdivided into sets of equal rectangles of sides  $\Delta x = h$  and  $\Delta t = k$ , and letting the coordinates  $(x, t)$  of the pivot point  $P$  be  $x = ih$  and  $t = jk$ , where  $i$  and  $j$  are integers, then the value of  $V$  at  $P$  is denoted  $V_P = V(ih, jk) = V_{i,j}$  (15, p. 7).

where the right-hand side has a leading error of order  $h^2$ .

The first derivative with respect to time in equation E was approximated by the forward-difference formula

$$\frac{\partial V}{\partial t} = \left( \frac{\partial V}{\partial t} \right)_{i,j} = \frac{1}{k} (V_{i,j+1} - V_{i,j}).$$

Here the right-hand side has a leading error of order  $k$  (15, p. 7).

Substituting these approximations into equation E and manipulating terms, the following recursive relation can be obtained.

$$\begin{aligned} V_{i,j+1} = & V_{i,j} + C_1 (V_{i+1,j} - 2V_{i,j} + V_{i-1,j}) \\ & - C_2^{n_{i,j}^4} (V_{i,j} - V_K) - C_3^{m_{i,j}^3} u_{i,j} (V_{i,j} - V_{Na}) \\ & - \frac{k\bar{g}_1}{C_m} (V_{i,j} - V_1), \end{aligned} \quad (F)$$

where

$$C_1 = \frac{ak}{2C_m R_2 h^2}, \quad C_2 = \frac{k\bar{g}_K}{C_m}, \quad \text{and} \quad C_3 = \frac{k\bar{g}_{Na}}{C_m}.$$

Noting that  $V$ ,  $n$ ,  $m$ , and  $u$  are the dependent variables of the system, it is seen that the system has many nonlinearities. Due to the fact that questions of stability and convergence for complicated nonlinear systems are largely unsolved (6, p. 250), as a first cut, it was assumed that conditions insuring convergence and stability of equation F would be similar to conditions insuring convergence and stability of the corresponding finite-difference representation of the

one-dimensional diffusion equation--

$$\frac{\partial^2 V}{\partial x^2} = \sigma \frac{\partial V}{\partial t} .$$

The corresponding finite-difference representation of the above equation can be shown to be convergent and stable if and only if  $\frac{k}{\sigma h^2} \leq .5$ . (11, p. 1-10; 5, p. 92; 15, p. 58-60).

In the present problem  $\frac{k}{\sigma h^2}$  corresponds to  $C_1$  where

$$C_1 = \frac{ak}{2C_m R h^2} = .336 \frac{k}{h^2} .$$

Thus, choosing  $\Delta x = h = .1$ , for example;  $\Delta t = k$  must be less than or equal to .0149 if  $C_1$  is to be less than or equal to .5. It is seen that this situation forces one to choose a relatively small time increment. With this in mind and noting that equations B, C, and D (page 9) contain only derivatives with respect to time, it was found that the modified Euler method (4, p. 12-14; 8, p. 201) for "predicting" and "correcting" the values of the dependent variables  $n$ ,  $m$ , and  $u$  at the pivot points is well suited to the problem. The major advantage here is that for a small time increment the calculated values of  $n$ ,  $m$ , and  $u$  are reasonably accurate, while at the same time the simplicity of the method saves an enormous amount of computer time. With a partial differential system such as this, computer time is a major practical consideration.

With respect to this problem the modified Euler method uses the following approximation to start the solution,

$$n_{i,1} = n_{i,0} + \left(\frac{\partial n}{\partial t}\right)_{i,0} k, \quad (\text{G})$$

and similar equations for  $m$  and  $u$ . This has been derived from a Taylor's series expansion whose terms of order  $k^2$  and higher have been truncated.

Once the solution has been started, the values of the dependent variable  $n$  on the  $(j+1)$ th time row can be "predicted" by the formula

$$n_{i,j+1} = n_{i,j-1} + 2\left(\frac{\partial n}{\partial t}\right)_{i,j} k \quad (\text{H})$$

(and similarly for dependent variables  $m$  and  $u$ ). Here the truncation error is  $O(k^3)$  where  $O(k^3)$  denotes terms containing third and higher powers of  $k$ .

Using the equation (called the "corrector")

$$n_{i,j+1} = n_{i,j} + .5 \left[ \left(\frac{\partial n}{\partial t}\right)_{i,j} + \left(\frac{\partial n}{\partial t}\right)_{i,j+1} \right] k, \quad (\text{J})$$

where  $\left(\frac{\partial n}{\partial t}\right)_{i,j+1}$  is evaluated using the value of  $n_{i,j+1}$  found previously by equation G or equation H, the accuracy of the numerical solution is improved and a computational check is performed (similar equations for  $m$  and  $u$ ). In addition, an idea of the accuracy of the solution is obtained by finding the difference between

predicted and corrected values.

Neglecting the boundary conditions for the time being, the numerical solution proceeds as follows. Given starting conditions at  $t = 0$  (i. e.  $V_{i,0}$ ,  $n_{i,0}$ ,  $m_{i,0}$ , and  $u_{i,0}$  for  $i = 0, \dots, p$ ),  $V_{i,1}$  is calculated using equation F ( $i = 1, \dots, p - 1$ ). Equations G and J are then used to calculate  $n_{i,1}$ ,  $m_{i,1}$ , and  $u_{i,1}$  ( $i = 1, \dots, p - 1$ ).  $V_{i,2}$  is now calculated from time row one ( $i = 1, \dots, p - 1$ ), and equations H and J are used to calculate  $n_{i,2}$ ,  $m_{i,2}$ , and  $u_{i,2}$  ( $i = 1, \dots, p - 1$ ) from time rows zero and one. And so on.

Thus the solution proceeds one time row at a time. To calculate the  $(j+1)$ th time row, the previous time row  $j$  is used to calculate the  $V_{i,j+1}$ 's. The previous two time rows (assuming the solution has gotten past the first calculated time row) and the  $V_{i,j+1}$ 's just calculated are then used to calculate the  $n_{i,j+1}$ 's, the  $m_{i,j+1}$ 's, and the  $u_{i,j+1}$ 's.<sup>6</sup>

#### Crank-Nicolson Method

The second method of solution (used only as a check on the first method) utilizes for calculating the values of  $V$  what is called the Crank-Nicolson method. J. Crank and P. Nicolson (3) developed a method with certain advantages--better stability properties and smaller truncation error. In addition, this method reduces the total volume of calculations. The numerical procedures are more

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<sup>6</sup>See flow diagrams, Appendices 1 and 2.



complicated however (15, p. 17).

Crank and Nicolson replaced  $\frac{\partial^2 V}{\partial x^2}$  by the mean of its finite-difference representation on the  $(j+1)$ th and  $j$ th time rows, i. e.

$$\begin{aligned} \frac{\partial^2 V}{\partial x^2} &= \frac{1}{2h^2} (V_{i+1, j+1} - 2V_{i, j+1} + V_{i-1, j+1}) \\ &+ \frac{1}{2h^2} (V_{i+1, j} - 2V_{i, j} + V_{i-1, j}). \end{aligned}$$

Substituting the above approximation into equation E (page 12), the following equation can be obtained.

$$\begin{aligned} -K_1 V_{i-1, j+1} + (2K_1 + 1)V_{i, j+1} - K_1 V_{i+1, j+1} &= V_{i, j} \\ + K_1 (V_{i-1, j} - 2V_{i, j} + V_{i+1, j}) \\ - K_2 n_{i, j}^4 (V_{i, j} - V_K) - K_3 m_{i, j}^3 u_{i, j} (V_{i, j} - V_{Na}) \\ - \frac{k\bar{g}_1}{C_m} (V_{i, j} - V_1), \end{aligned} \quad (L)$$

where

$$K_1 = \frac{ak}{4R_2 C_m h^2}, \quad K_2 = \frac{k\bar{g}_K}{C_m}, \quad \text{and} \quad K_3 = \frac{k\bar{g}_{Na}}{C_m}.$$

The quantities on the right-hand side of equation L are known, and the quantities on the left-hand side are unknown. Let us assume that there are  $N$  pivot points on the  $j$ th and the  $(j+1)$ th time rows

(i. e.  $i = 1, \dots, N$ ). Given the values of the dependent variables at the pivot points on the  $j$ th time row, equation L gives  $N$  linear equations with  $N$  unknowns. This necessitates solving a set of simultaneous linear equations to determine the values of  $V$  at the pivot points on the  $(j+1)$ th time row.

It may be noted that each equation of the system of  $N$  linear equations contains only three unknowns. A method which is especially adaptable for solving a linear system such as this is the Gauss elimination method (15, p. 20-23; 16, p. 13-21); accordingly, this method was the method used in the problem for solving the systems of linear equations.

At the same time, the previously mentioned modified Euler method was used to calculate the values of  $n$ ,  $m$ , and  $u$  at the pivot points.

The solution to Hodgkin-Huxley's system proceeded as before. After the solution had been started,<sup>7</sup> the values of  $V$  at the pivot points of the  $(j+1)$ th time row were calculated by the Crank-Nicolson procedure. The previous two time rows and the  $V_{i, j+1}$ 's just calculated were then used to calculate  $n$ ,  $m$ , and  $u$  at the pivot points of the  $(j+1)$ th time row. And the solution proceeded from one time row to the next (see flow diagram, Appendix 3).

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<sup>7</sup>The explicit method was used to start the solution. See Appendix 1.

### Boundary and Initial Conditions

First let us review what the Hodgkin-Huxley partial differential equations describe. Suppose an axon of the type studied (49, 50, 51, 52) is stimulated by an electric shock applied on a finite length of the axon. With initial conditions expressing the shock and with appropriate boundary conditions, the Hodgkin-Huxley partial differential equations describe the voltage ( $V$ ), potassium conductance ( $\bar{g}_K n^4$ ), and sodium conductance ( $\bar{g}_{Na} m^3 u$ ) changes with respect to distance ( $x$ ) along the axon and with respect to time ( $t$ ).

As was previously mentioned, although antidromic conduction in the axon may occur, in general the nerve impulse travels along the axon in the direction away from the neuron soma. It was thus assumed that if a shock applied on a finite length of the axon beginning at  $x = h$ , the boundary condition at  $x = 0$  would be the resting values of the dependent variables. That is, it is assumed that a shock at  $x = h$  leaves the portion of the axon between the cell soma and a small distance from the starting point of the shock in the resting state. This gives the following boundary condition

$$V(0, t) = V_0 = 0,$$

$$n(0, t) = n_0 = \frac{4}{5e - 1},$$

$$m(0, t) = m_0 = \frac{5}{8e^{2.5} - 3},$$

$$u(0, t) = u_0 = \frac{7(e^3 + 1)}{7e^3 + 107} \cdot 8$$

These have been derived from equations A, B, C and D (page 9).

For example in the resting state  $V = 0$  and  $\frac{dn}{dt} = 0$ ; therefore

$$\frac{dn}{dt} = 0 = \phi \left[ (1 - n) \frac{.01(V + 10)}{\exp[(V + 10)/10] - 1} - .125 \exp(V/80)n \right] .$$

From this relation  $n_0 = \frac{4}{5e - 1}$  follows.

To start the solution a shock is applied at  $t = 0$ . More explicitly,

$$V(ih, 0) = V_{\text{Shock}} = V_S \quad (i = 1, 2, \dots, p),$$

$$V(x, 0) = 0 \quad \text{for } x \leq 0; x > ph,$$

$$n(x, 0) = n_0,$$

$$m(x, 0) = m_0,$$

$$u(x, 0) = u_0 .$$

Let us for definitiveness assume for the time being that the shock,  $V_S$ , is at one pivot point only. That is, in the above  $p$  is equal to one. With this in mind the boundary condition and initial conditions are illustrated in Figure 2, where  $R$  will denote not only the resting value of  $V$  at the designated pivot point but also the

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<sup>8</sup>We draw attention to the error for the resting value of  $u$  in reference 27.

resting values of the other dependent variables  $n$ ,  $m$ , and  $u$  ( $\bar{R}$  will be defined on page 25).

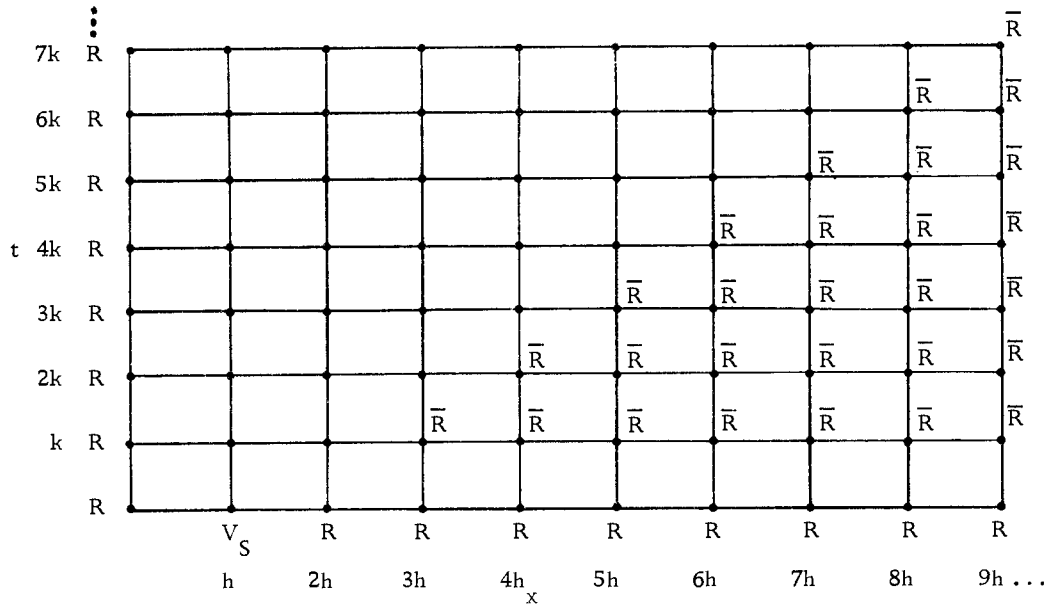


Figure 2.

Referring to equation E (page 12), when the nerve fiber is at rest,  $V = 0$ ,  $\frac{\partial^2 V}{\partial x^2} = 0$ , and  $\frac{\partial V}{\partial t} = 0$ . This implies that

$$\bar{g}_K n_0^4 (-V_K) + \bar{g}_{Na} m_0^3 u_0 (-V_{Na}) + \bar{g}_l (-V_l) = 0$$

Rewriting equation F (page 16) in an equivalent form, we have

$$V_{i,j+1} = V_{i,j} + C_l (V_{i+1,j} - 2V_{i,j} + V_{i-1,j}) - \frac{k}{C_m} \left[ \bar{g}_K n_{i,j}^4 (V_{i,j} - V_K) + \bar{g}_{Na} m_{i,j}^3 u_{i,j} (V_{i,j} - V_{Na}) + \bar{g}_l (V_{i,j} - V_l) \right],$$

where

$$C_1 = \frac{ak}{2C_m R_2 h^2} .$$

Let us consider the value of  $V$  at the pivot point  $(3, 1)$ .

$$\begin{aligned} V_{3,1} &= V_{3,0} + C_1(V_{4,0} - 2V_{3,0} + V_{2,0}) \\ &\quad - \frac{k}{C_m} \left[ \bar{g}_K n_{3,0}^4 (V_{3,0} - V_K) + \bar{g}_{Na} m_{3,0}^3 u_{3,0} (V_{3,0} \right. \\ &\quad \left. - V_{Na}) + \bar{g}_1 (V_{3,0} - V_1) \right] \\ &= 0 + C_1(0 - 0 + 0) - \frac{k}{C_m}(0) \\ &= 0 . \end{aligned}$$

In a like manner an application of the modified Euler method yields

$$n_{3,1} = n_0, \quad m_{3,1} = m_0, \quad \text{and} \quad u_{3,1} = u_0.$$

Repeating the above, one is lead to the conclusion that given the above mentioned boundary and initial conditions, if  $i + 2 \geq j$ , then  $V_{i,j} = 0$ ,  $n_{i,j} = n_0$ ,  $m_{i,j} = m_0$ , and  $u_{i,j} = u_0$ . The situation is illustrated in Figure 2 where to avoid confusion with the boundary and initial conditions,  $\bar{R}$  now denotes the resting values of the dependent variables.

This has important implications with regard to the numerical solution. Suppose we are given the same boundary and initial

conditions that are illustrated in Figure 2. Suppose further we have a rough idea of what the solution is supposed to look like. That is, suppose we know that the impulse has an approximate velocity of

$$\frac{dx}{dt} = 20\text{m./sec.} = 2\text{cm./msec.}$$

Choosing a time increment of  $k = .01$  msec. and a space increment of  $h = .02$  cm., after 100 steps of the solution we would be at  $t = 1$  msec. However, from what was shown above the dependent variables assume their resting values for  $t = 1$  and  $x \geq 2.04$ .

Assuming that  $x$  is in units of centimeters, we see that the impulse has at most a velocity of

$$\frac{dx}{dt} = 2.04 \text{ cm./msec.}$$

This only tells us what we already know from the mathematics involved in numerically solving parabolic type partial differential equations--that  $k$  must be small compared to  $h$ .

As a first cut, it was decided to choose a time increment of  $k = .005$  for the explicit method of solution and a time increment of  $k = .01$  for the implicit method; the space increment of  $h = .1$  was chosen for both methods.

After relatively short trial runs of the programs coded for the two methods, it was seen that the pivot points corresponding to a sufficient distance ahead of the traveling nerve impulse were relatively

unaffected. That is, the calculated values of the dependent variables for those pivot points were essentially the respective resting values.

For example, the following values of  $V(V_0 = 0)$  were obtained for the indicated pivot points.

$$V_{8,13} = -.2,$$

$$V_{9,13} = -.04,$$

$$V_{10,13} = -.007,$$

$$V_{11,13} = -.0007,$$

$$V_{12,13} = -.00005,$$

$$V_{13,13} = -.000002,$$

$$V_{14,13} = -.00000001.$$

Let us assume that the solution has proceeded to time row  $j$ , and  $i$  pivot points have been calculated on this time row. Before proceeding to the next time row, the last three pivot points ( $(i, j)$ ,  $(i - 1, j)$ , and  $(i - 2, j)$ ) were checked to see whether or not they were sufficiently close to their resting values to warrant the assumption that the nerve impulse had not traveled to the distance corresponding to the last three pivot points. If the values at the last three pivot points were sufficiently close to resting, the next time row would also have  $i$  pivot points; otherwise, the next time row would have  $i + 1$  pivot points.

Consequently, the numerical solution "traveled" in the positive



x direction at the same average velocity as the calculated nerve impulse. This saved a considerable amount of computer time.

### Computer Programs

Three CDC 3300 computer programs evolved from the above mathematics. The first program (Appendix 1) was used exclusively for starting the solution. It contains the explicit approximation for equation E (page 12).

The second program (Appendix 2) used the same explicit approximation for equation E as did the first program. At the same time however, it has more flexibility. Once the solution has been started by the first program, data can be read in and the solution carried to any number of steps. The data derived from this run can then be read in and the solution can be carried to any additional number of steps. Long runs can then be subdivided into several short runs. This was a precaution taken to avoid wasting computer time due to the possibility of unforeseen problems arising in the coding or in the mathematics.

Although the third program (Appendix 3) was used sparingly and only as a check on program two, it has the same flexibility as the second program. Once the solution has been started, data can be read in and the solution carried to any number of steps. As with the second program, long programs may be subdivided into several

shorter programs.

With respect to these programs several points merit attention.

A close look at the factor

$$a_n = \frac{.01(V + 10)}{\exp[(V + 10)/10] - 1}$$

in equation B (page 9) reveals that when  $V = -10$ , we have the indeterminate form  $0/0$ . The limit as  $V$  goes to  $-10$  can be shown via l'Hospital's rule to be  $.1$ . Realizing that the computer is ignorant of infinite processes, it was decided to set this factor equal to  $.1$  whenever  $V$  was in the closed interval  $-10 \pm \epsilon$ , where  $\epsilon = 10^{-5}$ .

Similarly, the factor

$$a_m = \frac{.1(V + 25)}{\exp[(V + 25)/10] - 1}$$

in equation C (page 9) was set equal to one whenever  $V$  was in the closed interval  $-25 \pm \epsilon$ , where as before  $\epsilon = 10^{-5}$ .

It may be noticed that  $V_1$  in equation A (page 9) has been changed from Hodgkin-Huxley's  $-10.5989$  to  $-10.598921$ . As was previously mentioned, when the dependent variables assume their resting state values, the quantity

$$\bar{g}_K n_0^4(-V_K) + \bar{g}_{Na} m_0^3 u_0(-V_{Na}) + \bar{g}_l(-V_1)$$

is equal to zero. However, using  $V_1 = -10.5989$  and substituting in the resting values of  $n$ ,  $m$ , and  $u$ , one arrives at the quantity

$-6. \times 10^{-6}$ . Although the change of  $V_1$  to  $-10.598921$  was actually unnecessary, the effect of the change is that the above quantity is now  $+9. \times 10^{-9}$ .

## RESULTS

The original numerical work on the Hodgkin-Huxley equations was done before the advent of the high-speed computer. There can be little doubt that Hodgkin and Huxley considered a numerical solution to their partial differential system out of the question. More recently (1962), R. Fitzhugh stated (30, p. 12),

The estimated time required to solve the HH partial differential equation with an IBM 704 digital computer was too high to make such solutions practical, because for each instant of time the HH ordinary equations must be solved at a large number of points along the fiber (using the usual difference equation approximation to the differential equation, with small enough distance increments for reasonable accuracy).

Nevertheless, using on a newer digital computer the techniques outlined above, we are enabled to avoid the difficulties anticipated by Fitzhugh and make an actual determination of the solution of the Hodgkin-Huxley partial differential system.

### The Propagated Action Potential

Using a time increment of  $k = .005$  and a space increment of  $h = .1$ , reasonably good results were obtained. The solution for the propagated action potential is summarized<sup>9</sup> in Figure 3, page 32

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<sup>9</sup>Actually, a closer look was taken by graphing the curves corresponding to the following fixed  $x$ 's:  $x = .1, .2, .3, .4, .5, .6, .7, .8, .9, 1.0, 1.1, 1.2, 1.3, 1.6, 1.8, 2.0, 2.4, 2.8, 3.2, 3.6,$  and  $4.0$ .

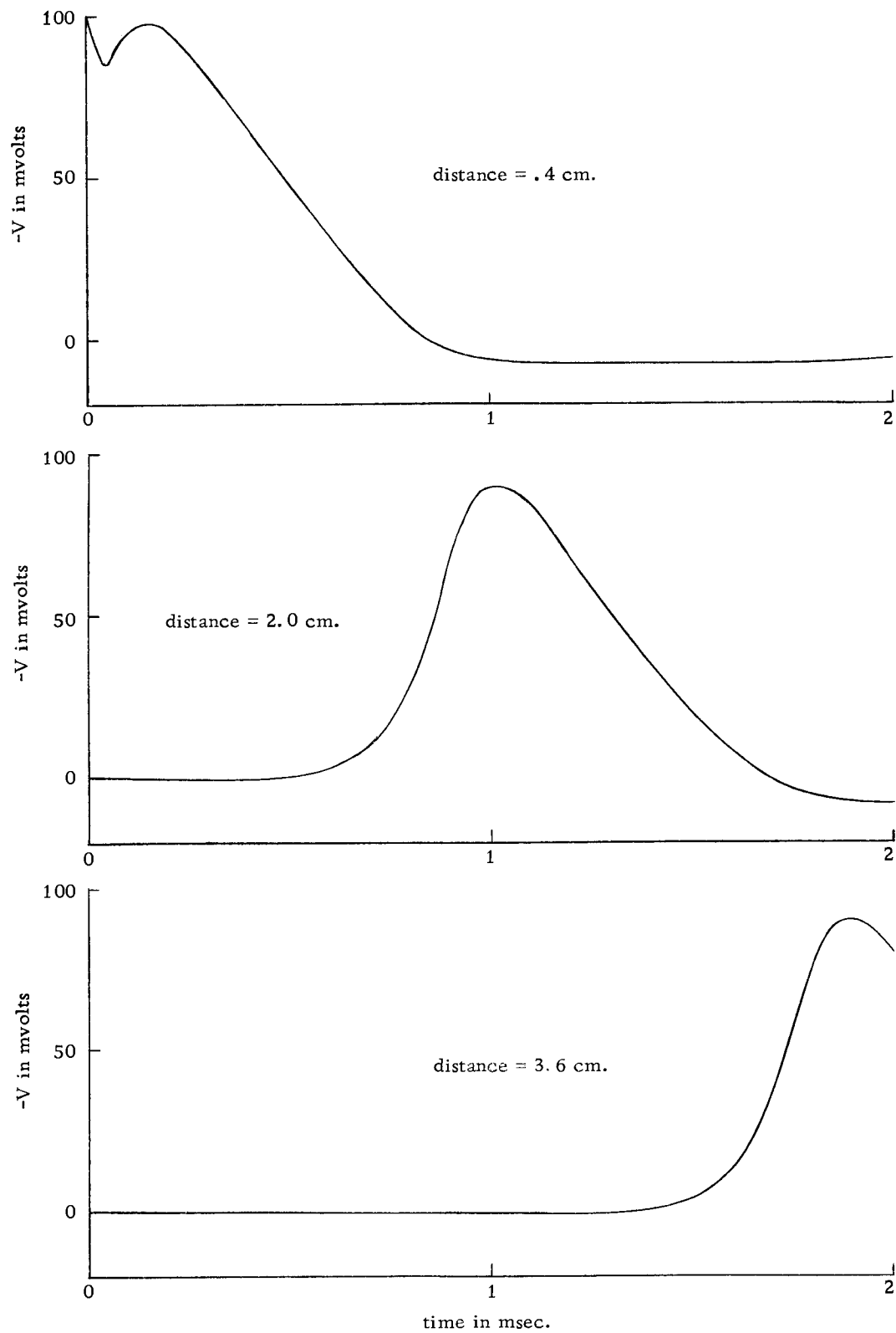


Figure 3. Numerical solution of Hodgkin-Huxley's partial differential system for the propagated action potential. Temperature  $18.5^{\circ}\text{C}$ .

(this is the three dimensional analogue of Hodgkin and Huxley's Figure 15, page 528 of (53)). The solution was started at  $t = 0$  by giving a shock of -100 mvolts over .5 cm. of axon. Due to the nature of the shock the curves for  $x = .2, .3, .4,$  and .5 cm. resemble membrane action potentials. For  $x$  equal to or greater than 1.2 cm., the nerve impulse assumed a fixed shape and velocity. A transition between a membrane action potential and a propagated action potential was seen for  $x$  between .5 cm. and 1.2 cm.

Although the solution behaved as a membrane action potential for small  $x$  (which was to be expected), for values of  $x$  greater than 1.2 cm. the solution obtained coincided with the solution obtained by Hodgkin and Huxley (53) and others (27, 34) for the simplified system. Basing calculations on the results for  $x$  greater than 1.2 cm., the average velocity obtained was 18.6 mm./msec. This is approximately the same result as Hodgkin-Huxley's 18.8 mm./msec. (53).

The three dimensional analogue of Hodgkin-Huxley's Figure 17, page 530 of (53) showing the components of the membrane conductance during a propagated action potential is seen in Figure 4, page 34.

#### Absolute Refractory Period

By applying at  $t = .97$  msec. the same strong shock which started the solution which is illustrated in Figure 3, a three

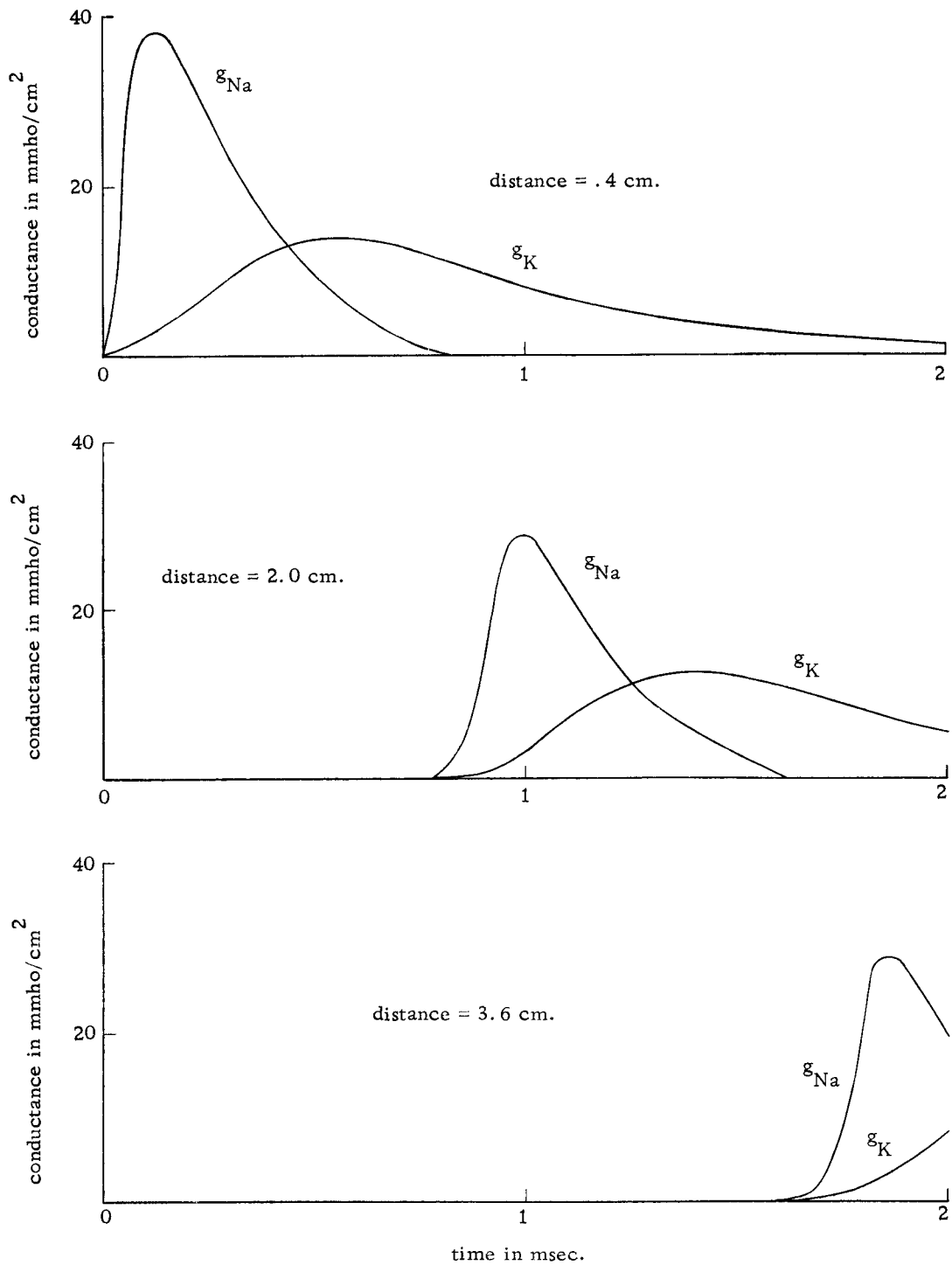


Figure 4. Numerical solution of Hodgkin-Huxley's partial differential system showing components of membrane conductance during propagated action potential. Temperature 18.5°C.

dimensional demonstration of the absolute refractory period is provided. The result is summarized in Figure 5, pages 36 and 37. Curve A in each frame is the same solution as was illustrated in Figure 3. Curve B in each frame is the result of applying the mentioned shock at  $t = .97$  msec. Here the shock fails to set off another nerve impulse, and the membrane is said to be in the absolute refractory period. Figure 5 is the three dimensional analogue of Hodgkin and Huxley's Figure 20, page 534 of (53).

#### On Rushton's Hypothesis

Theoretical evidence supporting Rushton's hypothesis (75) that excitation is inadequate to set off a nerve impulse unless a sufficient length of nerve is stimulated has been established. Starting the solution with a shock of -100 mvolts (the threshold is around -10 mvolts) at the point  $(h, 0)$  and resting values of the dependent variables at the other pivot points along time row zero, the solution summarized in Figure 6 (page 38) was obtained. It is seen that a shock many times the threshold value has failed to set off an action potential. This suggests the three dimensional extension of the strength-duration curve to the strength-duration-spatial surface.

#### Summary and Conclusions

Although as late as 1962 it was stated that a numerical solution



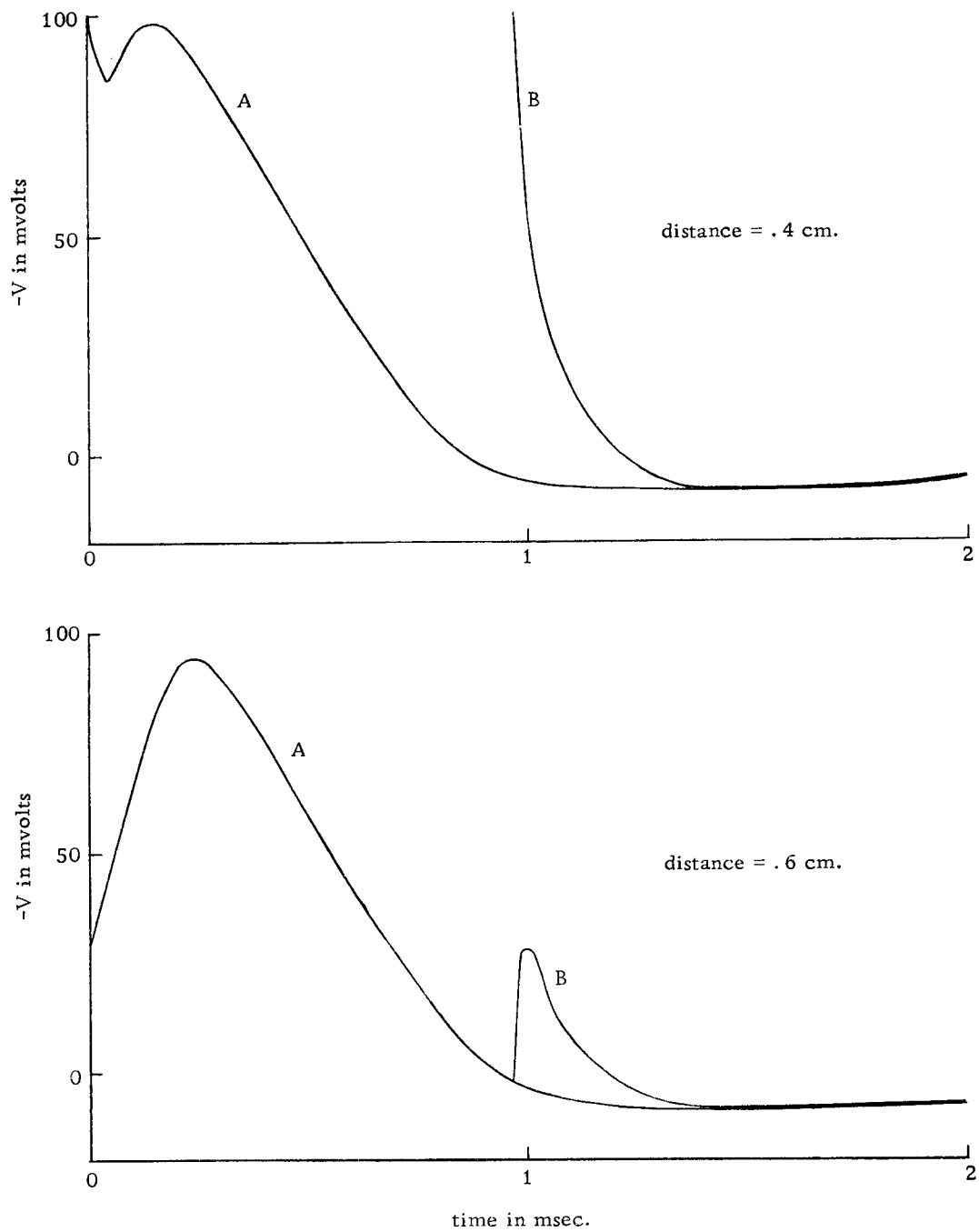


Figure 5. Numerical solution demonstrating absolute refractory period. In each frame curve A is the same solution that is illustrated in Figure 3 (page 32). Curves B show the result after applying the identical shock (that started the solution corresponding to curves A) at  $t = .97$  msec. Temperature  $18.5^{\circ}\text{C}$ . Graphs continued on next page.

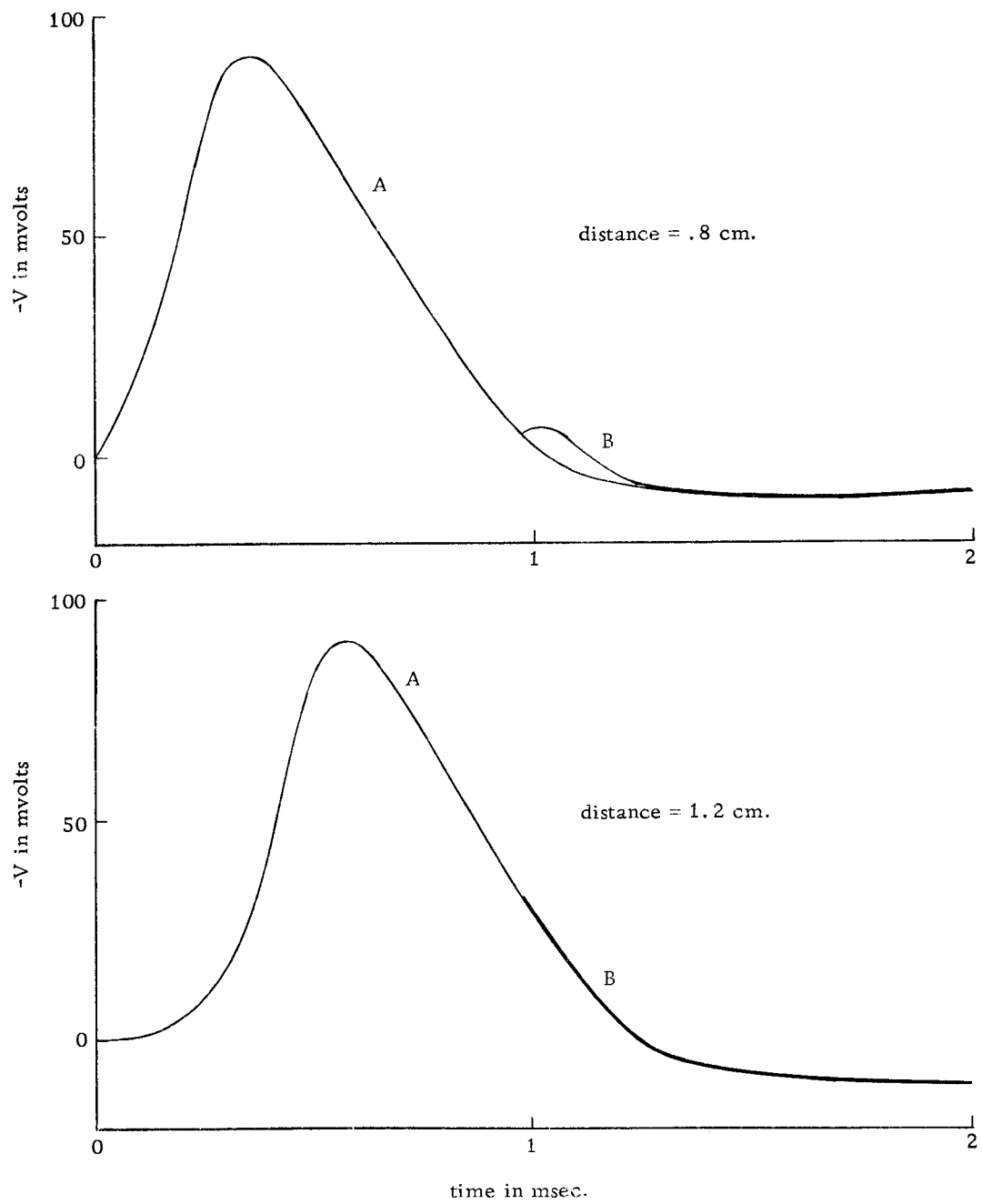


Figure 5. (Continued)

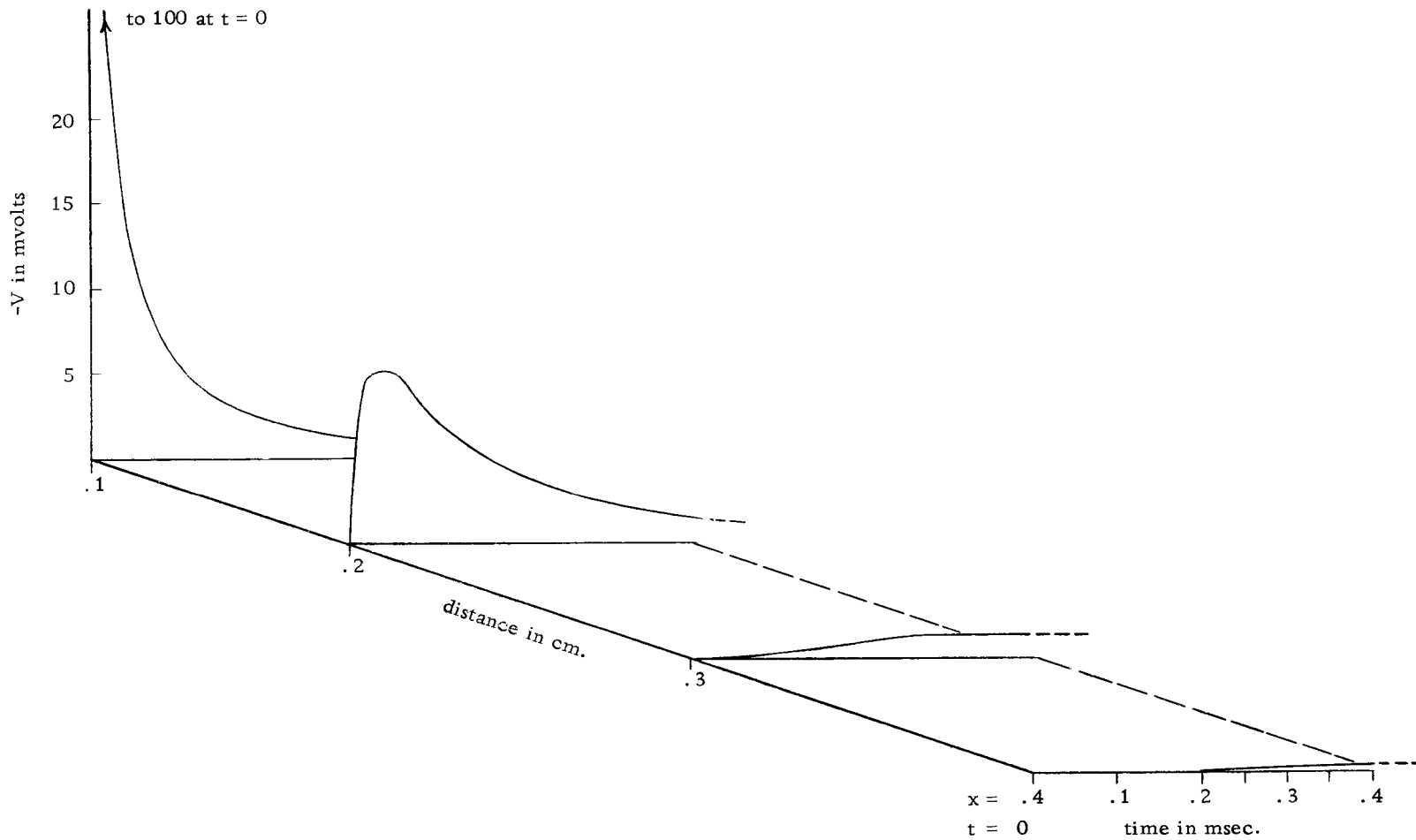


Figure 6. Numerical solution (of Hodgkin-Huxley's partial differential system) which was started with a shock of -100 mvolts at  $x = .1$  cm. and the resting values of the dependent variables at other points along starting time row. Temperature  $18.5^{\circ}\text{C}$ .

to Hodgkin and Huxley's partial differential system was impractical, results reasonably in agreement with experimental data have been obtained. The solution obtained for the propagated action potential is essentially the same result as Hodgkin and Huxley (53) and others (27, 34) have obtained using an assumption which simplified the system from a partial differential system to an ordinary differential system. Since this analysis originated as an investigation of this assumption, it is concluded that the assumption is valid. In addition a three dimensional demonstration of the absolute refractory period has been presented. Lastly and perhaps most significant, computational evidence supporting Rushton's hypothesis has been presented.

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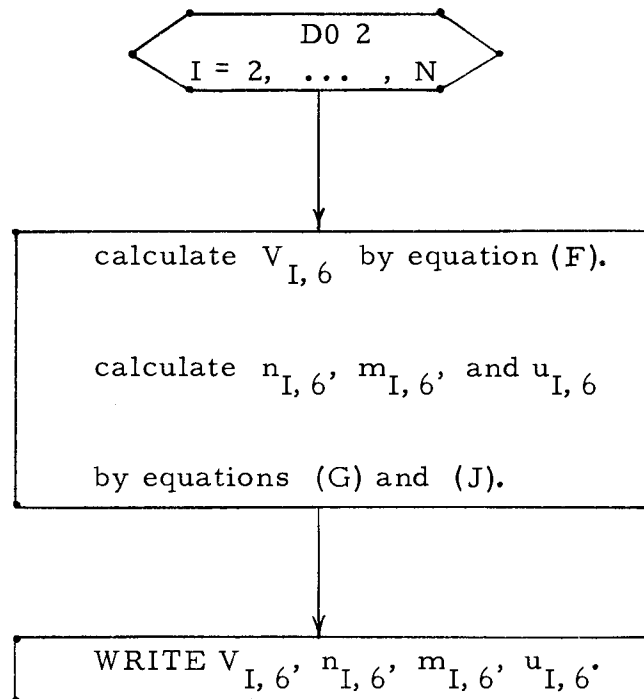
## APPENDICES

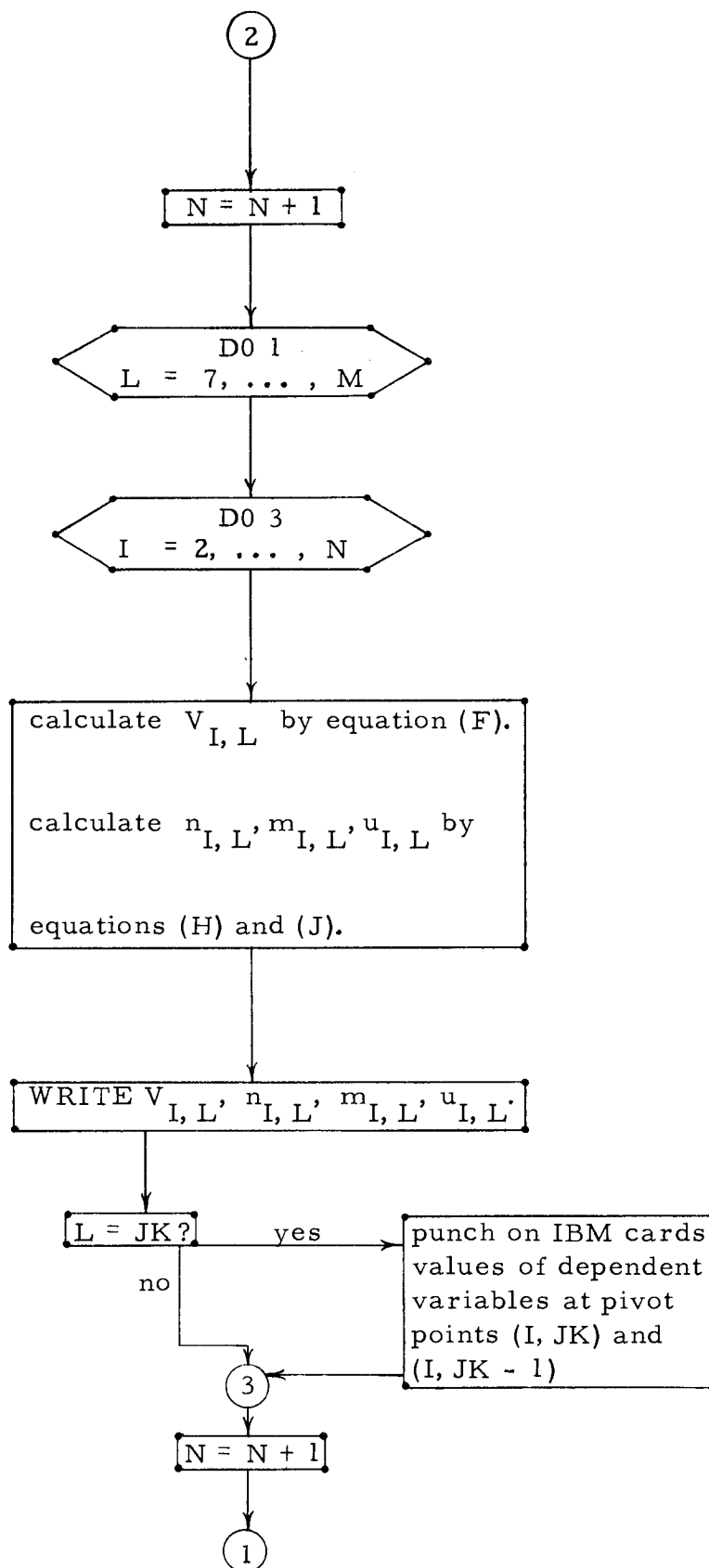
## APPENDIX 1

## EXPLICIT METHOD FOR STARTING SOLUTION

Summary Flow Diagram for Program PDIFF

- I = index with respect to distance ( $x = 0$  corresponds to  $I = 1$ ).
- JK and JK - 1 = the fixed time indices of the time rows whose dependent variables are punched out on IBM cards for future use.
- L = time row index ( $t = 0$  corresponds to  $L = 5$ ).
- M = index of last time row.
- N = last pivot point in L th time row





```

C CONTROL CARDS GO HERE.  SEE REFERENCE MANUAL.
  PROGRAM PDIFF
C WARNING. ALL CONTINUED STATEMENTS SHOULD BE CARRIED TO
C COLUMN 72.
  DIMENSION V(600,3),XN(600,3),XM(600,3),XH(600,3)
101 FORMAT(1H ,3HI= ,I3,2X,3HJ= ,I3,2X,3HV= ,E16.8,/1H ,
  19HXN,XNT,DN,2X,3(E16.8,2X),/1H ,9HXM,XMT,DM,2X,3(E16
  2.8,2X),/1H ,9HXH,XHT,DH,2X,3(E16.8,2X),/)
106 FORMAT(4E16.8,8X,I3,1X,I3,/4E16.8,8X,I3,1X,I3)
  EX=EXP(1.)
  XNO=XN(2,1)=XN(3,1)=XN(4,1)=XN(5,1)=XN(6,1)=XN(7,1)=
  14./(5.*EX-1.)
  XMO=XM(2,1)=XM(3,1)=XM(4,1)=XM(5,1)=XM(6,1)=XM(7,1)=
  15./(8.*EX**2.5-3.)
  XHO=XH(2,1)=XH(3,1)=XH(4,1)=XH(5,1)=XH(6,1)=XH(7,1)=
  1(7.*(EX**3+1.))/(7.*EX**3+107.)
C V(2,1) = THIS WILL BE THE SHOCK
  V(2,1)=V(3,1)=V(4,1)=V(5,1)=V(6,1)=-100.
C XK = TIME INCREMENT
  XK=.005
C H = SPACE INCREMENT
  H=.1
  C=(23.8*XK)/(2.*35.4*H**2)
  GK=XK*36.
  GN=XK*120.
  GL=XK*.3
  GLC=GL*10.5989
C SECOND TIME ROW
C N = LAST PIVOT POINT IN I TH TIME ROW
  N=7
  L=6
  J=1
  V(1,1)=V(N,1)=V(N+1,1)=0.
  DO 2 I=2,N
  V(I,2)=V(I,1)+C*(V(I+1,1)-2.*V(I,1)+V(I-1,1))-(GK*XN
  1(I,1)**4*(V(I,1)-12.))-(GN*XM(I,1)**3*XH(I,1)*(V(I,1
  2)+115.))-(GL*V(I,1))-GLC
  ZN=XNP(XN(I,J),V(I,J))
  ZM=XMP(XM(I,J),V(I,J))
  ZH=XHP(XH(I,J),V(I,J))
  XNT=XN(I,J)+XK*ZN
  XMT=XM(I,J)+XK*ZM
  XHT=XH(I,J)+XK*ZH
  XN(I,J+1)=XN(I,J)+.5*XK*(ZN+XNP(XNT,V(I,J+1)))
  XM(I,J+1)=XM(I,J)+.5*XK*(ZM+XMP(XMT,V(I,J+1)))
  XH(I,J+1)=XH(I,J)+.5*XK*(ZH+XHP(XHT,V(I,J+1)))
  DN=XN(I,J+1)-XNT
  DM=XM(I,J+1)-XMT
  DH=XH(I,J+1)-XHT
  WRITE(61,101)I,L,V(I,J+1),XN(I,J+1),XNT,DM,XM(I,J+1)

```

```

1,XMT,DM,XH(I,J+1),XHT,DH
2 CONTINUE
  N=N+1
  V(1,2)=V(N,2)=V(N+1,2)=0.
  XN(N,2)=XN(N,1)=XNO
  XM(N,2)=XM(N,1)=XMO
  XH(N,2)=XH(N,1)=XHO
C THIRD, FOURTH, ... TIME ROWS
C M= NUMBER OF TIME STEPS
  M=10
C JK AND JK-1 ARE THE PUNCHED OUT TIME ROLLS
  JK=21
  J=2
  JJ=J+1
  NN=N-1
  DO 1 L=NN,M
  DO 3 I=2,N
    V(I,3)=V(I,2)+C*(V(I+1,2)-2.*V(I,2)+V(I-1,2))-(GK*XN
1(I,2)**4*(V(I,2)-12.))-(GN*XM(I,2)**3*XH(I,2)*(V(I,2
2)+115.))-(GL*V(I,2))-GLC
    ZN=XNP(XN(I,2),V(I,2))
    ZM=XMP(XM(I,2),V(I,2))
    ZH=XHP(XH(I,2),V(I,2))
    XNT=XN(I,1)+2.*XK*ZN
    XMT=XM(I,1)+2.*XK*ZM
    XHT=XH(I,1)+2.*XK*ZH
    XN(I,3)=XN(I,2)+.5*XK*(ZN+XNP(XNT,V(I,3)))
    XM(I,3)=XM(I,2)+.5*XK*(ZM+XMP(XMT,V(I,3)))
    XH(I,3)=XH(I,2)+.5*XK*(ZH+XHP(XHT,V(I,3)))
    DN=XN(I,3)-XNT
    DM=XM(I,3)-XMT
    DH=XH(I,3)-XHT
C J IN FORMAT STATEMENT IS A DIFFERENT J
  WRITE(61,101)I,L,V(I,J+1),XN(I,J+1),XNT,DM,XM(I,J+1)
  1,XMT,DM,XH(I,J+1),XHT,DH
  IF(L.EQ.JK) 5,3
5 PUNCH 106, V(I,2),XN(I,2),XM(I,2),XH(I,2),I,J,V(I,3)
  1,XN(I,3),XM(I,3),XH(I,3),I,JJ
3 CONTINUE
  DO 4 K=2,N
    V(K,1)=V(K,2)
    V(K,2)=V(K,3)
    XN(K,1)=XN(K,2)
    XN(K,2)=XN(K,3)
    XM(K,1)=XM(K,2)
    XM(K,2)=XM(K,3)
    XH(K,1)=XH(K,2)
    XH(K,2)=XH(K,3)
4 CONTINUE
  N=N+1

```

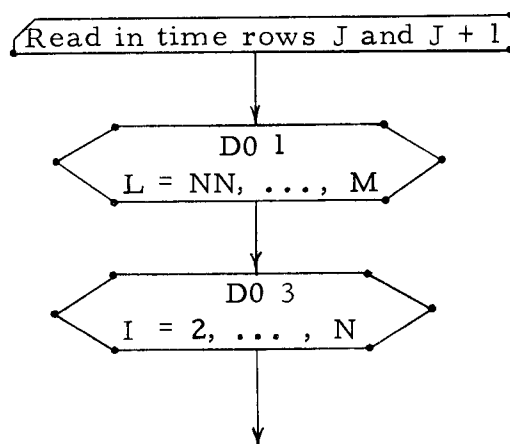


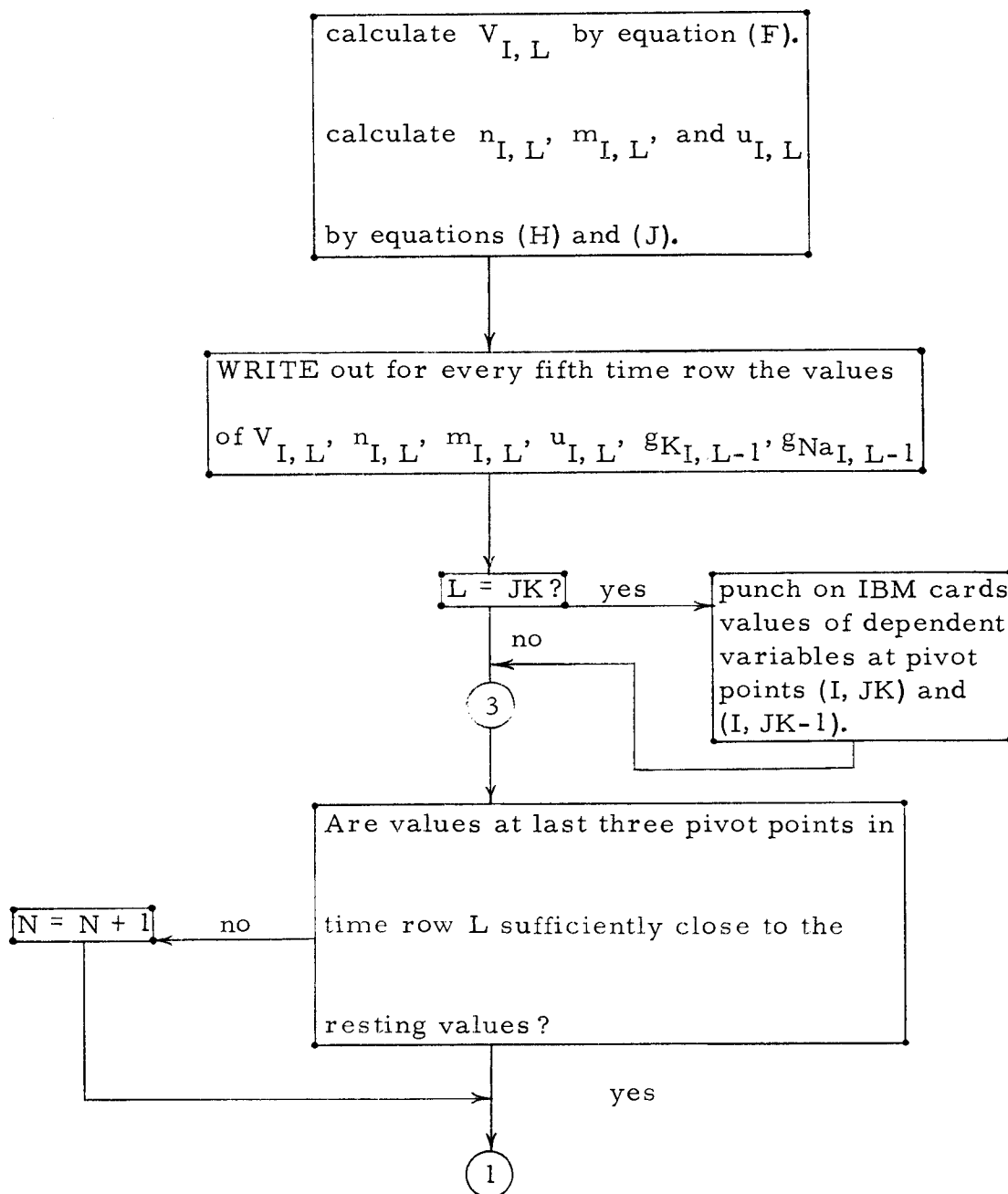
```
V(N,2)=V(N+1,2)=0.  
XN(N,2)=XN(N,1)=XNO  
XM(N,2)=XM(N,1)=XMO  
XH(N,2)=XH(N,1)=XHO  
1 CONTINUE  
END  
C FUNCTION SUBPROGRAMS, DATA, AND CONTROL CARDS GO HERE.  
C SEE REFERENCE MANUAL.
```

## APPENDIX 2

EXPLICIT METHOD FOR USE AFTER SOLUTION  
HAS BEEN STARTEDSummary Flow Diagram for Program PDIF2

- I = index with respect to distance ( $x = 0$  corresponds to  $I = 1$ ).
- J = index of starting time row.
- J + 1 = index of other starting time row.
- JK and JK - 1 = the fixed time indices of the time rows whose dependent variables are punched out on IBM cards for future use.
- L = time row index ( $t = 0$  corresponds to  $L = 5$ ).
- M = index of last time row.
- N = distance index of last pivot point in L th time row.
- NN = J + 2 = time index of first calculated time row.





```

C CONTROL CARDS GO HERE.  SEE REFERENCE MANUAL.
  PROGRAM PDIF2
C WARNING. ALL CONTINUED STATEMENTS SHOULD BE CARRIED TO
C COLUMN 72.
  DIMENSION V(600,3),XN(600,3),XM(600,3),XH(600,3),CK
  1(600),CN(600)
101 FORMAT(1H ,3HI= ,I3,2X,3HJ= ,I3,2X,3HV= ,E16.8,2X,4H
  1GK= ,E16.8,2X,4HGN= ,E16.8,/1H ,3(E16.8,2X),/)
105 FORMAT(1H ,3HN= ,I3,/)
106 FORMAT(4E16.8,8X,I3,1X,I3,/4E16.8,8X,I3,1X,I3)
120 FORMAT(1H ,3HN= ,I3,2X,25HV(N-2,3),V(N-1,3),V(N,3) ,
  13(E16.8,2X),/)
500 FORMAT(4E16.8,/4E16.8)
  EX=EXP(1.)
  XNO=4./(5.*EX-1.)
  XMO=5./(8.*EX**2.5-3.)
  XHO=(7.*(EX**3+1.))/(7.*EX**3+107.)
C XK = TIME INCREMENT
  XK=.005
C H = SPACE INCREMENT
  H=.1
  C=(23.8*XK)/(2.*35.4*H**2)
  GL=XK*.3
  GLC=GL*10.598921
C N= LAST PIVOT POINT IN L TH TIME ROW
C J= STARTING TIME ROW AND J+1= STARTING TIME ROW + 1
  J=198
  JJ=J+1
C JK AND JK-1 ARE THE PUNCHED OUT TIME ROWS
  JK=304
C N MUST CORRESPOND TO STARTING TIME ROW +1
  N=45
  DO 400 I=2,N
  READ(60,500) V(I,1),XN(I,1),XM(I,1),XH(I,1),V(I,2),X
  1N(I,2),XM(I,2),XH(I,2)
400 CONTINUE
  N=N+1
  V(N,2)=V(N+1,2)=V(1,2)=0.
  XN(N,2)=XN(N,1)=XNO
  XM(N,2)=XM(N,1)=XMO
  XH(N,2)=XH(N,1)=XHO
C M= TOTAL NUMBER OF TIME STEPS
  J=2
  JJ=J+1
  M=306
  NN=200
C L= TIME ROW
  DO 1 L=NN,M
  XL=L
  DO 3 I=2,N
C CONDUCTANCES IN WRITE OUT ARE FOR PREVIOUS TIME ROW

```

```

      CK(I)=36.*XN(I,2)**4
      CN(I)=120.*XM(I,2)**3*XH(I,2)
      V(I,3)=V(I,2)+C*(V(I+1,2)-2.*V(I,2)+V(I-1,2))-(XK*CK
1(I)*(V(I,2)-12.))- (XK*CN(I)*(V(I,2)+115.))- (GL*V(I,2
2))-GLC
      ZN=XNP(XN(I,2),V(I,2))
      ZM=XMP(XM(I,2),V(I,2))
      ZH=XHP(XH(I,2),V(I,2))
      XNT=XN(I,1)+2.*XK*ZN
      XMT=XM(I,1)+2.*XK*ZM
      XHT=XH(I,1)+2.*XK*ZH
      XN(I,3)=XN(I,2)+.5*XK*(ZN+XNP(XNT,V(I,3)))
      XM(I,3)=XM(I,2)+.5*XK*(ZM+XMP(XMT,V(I,3)))
      XH(I,3)=XH(I,2)+.5*XK*(ZH+XHP(XHT,V(I,3)))
      IF(FLOAT((L-1)/5).EQ.(XL-1.)/5.) 32,33
32  DN=XN(I,3)-XNT
      DM=XM(I,3)-XMT
      DH=XH(I,3)-XHT
C J IN FORMAT STATEMENT IS A DIFFERENT J
      WRITE(61,101) I,L,V(I,J+1),CK(I),GN(I),DN,DM,DH
33  IF(L.EQ.JK) 5,3
      5 IF(I.EQ.N)6,7
      6 WRITE(61,105) N
      7 PUNCH 106, V(I,2),XN(I,2),XM(I,2),XH(I,2),I,J,V(I,3)
      1,XN(I,3),XM(I,3),XH(I,3),I,JJ
      3 CONTINUE
      DO 4 K=2,N
      V(K,1)=V(K,2)
      V(K,2)=V(K,3)
      XN(K,1)=XN(K,2)
      XN(K,2)=XN(K,3)
      XM(K,1)=XM(K,2)
      XM(K,2)=XM(K,3)
      XH(K,1)=XH(K,2)
      XH(K,2)=XH(K,3)
      4 CONTINUE
      IF(V(N,3).LE..0005.AND.V(N,3).GE.-.0005.AND.V(N-1,3)
1.LE..0005.AND.V(N-1,3).GE.-.0005.AND.V(N-2,3).LE.
2.0005.AND.V(N-2,3).GE.-.0005) 30,31
31  N=N+1
      V(N,2)=V(N+1,2)=0.
      XN(N,2)=XN(N,1)=XNO
      XM(N,2)=XM(N,1)=XMO
      XH(N,2)=XH(N,1)=XHO
      GO TO 1
30  WRITE(61,120) N,V(N-2,3),V(N-1,3),V(N,3)
      1 CONTINUE
      END
C FUNCTION SUBPROGRAMS, DATA, AND CONTROL CARDS GO HERE.
C SEE REFERENCE MANUAL.

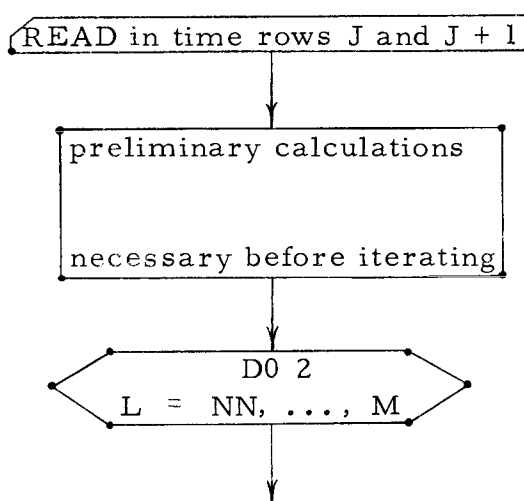
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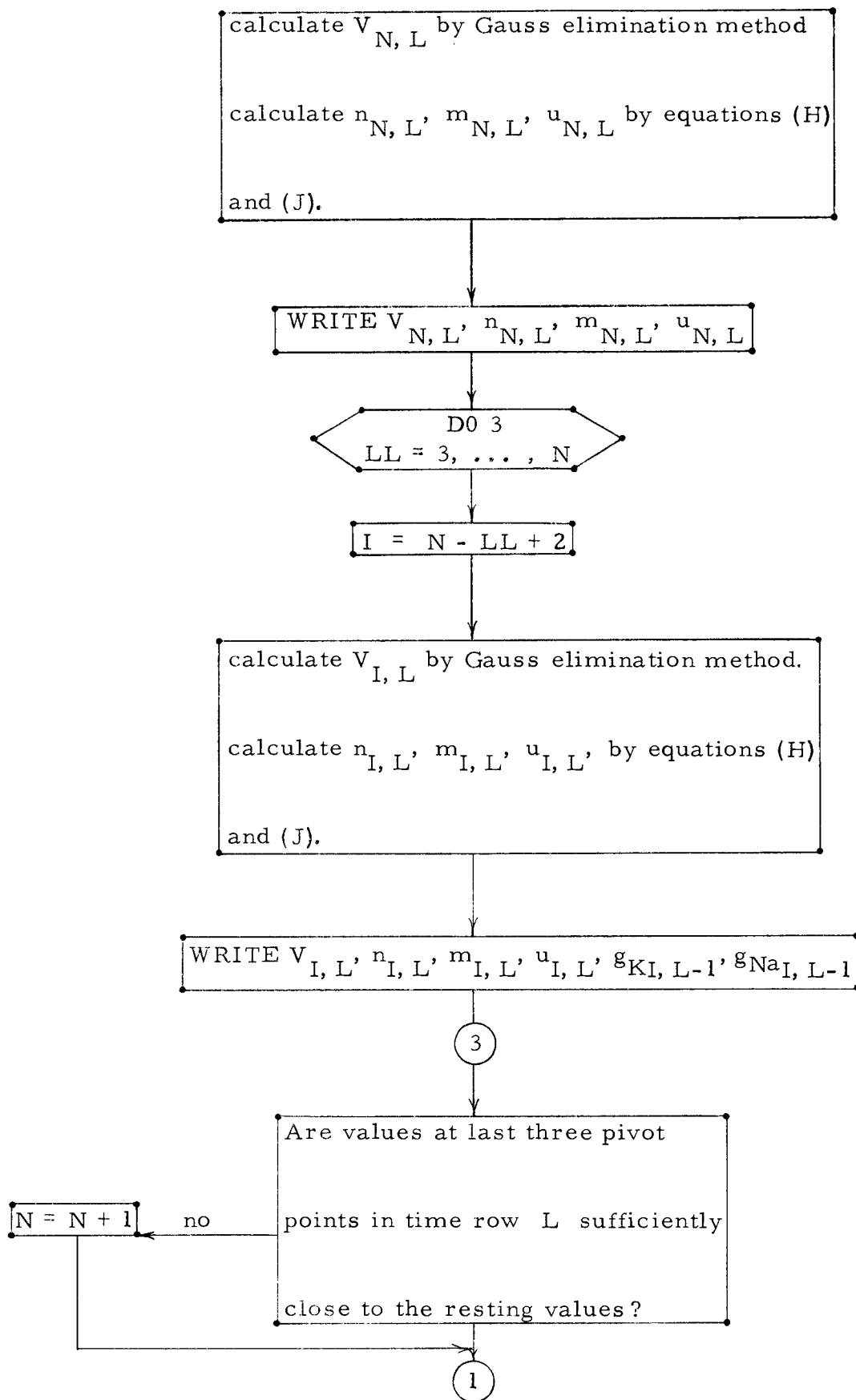
## APPENDIX 3

## CRANK-NICOLSON IMPLICIT METHOD

Summary Flow Diagram for Program CRNC

- I = index with respect to distance ( $x = 0$  corresponds to  $I = 1$ ).
- JK and JK-1 = the fixed time indices of the time rows whose dependent variables are punched out on IBM cards for future use.
- L = time row index ( $t = 0$  corresponds to  $L = 5$ ).
- M = index of last time row.
- N = distance index of last pivot point in L th time row.
- NN = time index of first calculated time row.





C CONTROL CARDS GO HERE. SEE REFERENCE MANUAL.

PROGRAM CRNC

C WARNING. ALL CONTINUED STATEMENTS SHOULD BE CARRIED TO  
C COLUMN 72.

```

      DIMENSION V(100,3),XN(100,3),XM(100,3),XH(100,3),ALP
      1(300),D(300),S(600),AOA(600),CK(600),CN(600)
101 FORMAT(1H ,3HI= ,I3,2X,3HJ= ,I3,2X,3HV= ,E16.8,/1H ,
      19HXN,XNT,DN,2X,3(E16.8,2X),/1H ,9HXM,XMT,DM,2X,3(E16
      2.8,2X),/1H ,9HXH,XHT,DH,2X,3(E16.8,2X),/1H ,15HCK(J-
      31),CN(J-1),2(E16.8,2X),//)
107 FORMAT(4E16.8,/4E16.8)
108 FORMAT(1H ,3HK= ,I3,2X,21H AOA(K),ALP(K),D(K),SK,2X,4
      1(E16.8,2X),//)
109 FORMAT(1H ,6HD(2)= ,E16.8,//)
110 FORMAT(1H ,3HK= ,I3,2X,6HD(K)= ,E16.8,//)
111 FORMAT(1H ,3HI= ,I3,2X,3HJ= ,I3,2X,30HV(I,J),XN(I,J)
      1,XM(I,J),XH(I,J),2X,4(E16.8,2X)/1H ,3HI= ,I3,2X,3HJ=
      2 ,I3,34X,4(E16.8,2X)//)
120 FORMAT(1H ,3HN= ,I3,2X,25HV(N-2,3),V(N-1,3),V(N,3) ,
      13(E16.8,2X),//)

```

C MAY NEED NEW N TO CORRESPOND TO N IN PDIF2

N=12

EX=EXP(1.)

XNO=XN(N,1)=XN(N+1,1)=XN(N+1,2)=4./(5.\*EX-1.)

XMO=XM(N,1)=XM(N+1,1)=XM(N+1,2)=5./(8.\*EX\*\*2.5-3.)

XHO=XH(N,1)=XH(N+1,1)=XH(N+1,2)=(7.\*(EX\*\*3+1.))/(7.\*  
1EX\*\*3+107.)

C XK = TIME INCREMENT

XK=.01

C H = SPACE INCREMENT

H=.1

C C DIFFERENT C THAN IN PDIFF

A=C=(23.8\*XK)/(4.\*35.4\*H\*\*2)

ALP(2)=B=2.\*A+1.

GL=XK\*.3

GLC=GL\*10.598921

V(1,2)=V(1,3)=0.

V(N+1,2)=V(N+2,2)=V(N+2,3)=0.

J=10

JJ=J+1

DO 1 I=2,N

READ(60,107) V(I,1),XN(I,1),XM(I,1),XH(I,1),V(I,2),X  
1N(I,2),XM(I,2),XH(I,2)

WRITE(61,111) I,J,V(I,1),XN(I,1),XM(I,1),XH(I,1),I,J  
1J,V(I,2),XN(I,2),XM(I,2),XH(I,2)

1 CONTINUE

K=2

CK(K)=36.\*XN(K,2)\*\*4

CN(K)=120.\*XH(K,2)\*XM(K,2)\*\*3

D(K)=V(K,2)+A\*(V(K-1,2)-2.\*V(K,2)+V(K+1,2))-(XK\*CK(K  
1)\*(V(K,2)-12.))-(XK\*CN(K)\*(V(K,2)+115.))-GL\*V(K,2)-



```

2GLC
  S(K)=D(K)
  WRITE(61,109) D(K)
  N=N+1
  DO 6 K=3,N
    AOA(K)=A/ALP(K-1)
    ALP(K)=B-AOA(K)*C
11  CK(K)=36.*XN(K,2)**4
    CN(K)=120.*XH(K,2)*XM(K,2)**3
    D(K)=V(K,2)+A*(V(K-1,2)-2.*V(K,2)+V(K+1,2))-(XK*CK(K
1) *(V(K,2)-12.))- (XK*CN(K)*(V(K,2)+115.))-GL*V(K,2)-
2GLC
12  S(K)=D(K)+AOA(K)*S(K-1)
    WRITE(61,108) K, AOA(K), ALP(K), D(K), S(K)
6  CONTINUE
  J=2
  JJ=3
  M=14
  NN=N-1
  DO 2 L=NN,M
    XL=L
    V(N,3)=S(N)/ALP(N)
    ZN=XNP(XN(N,2),V(N,2))
    ZM=XMP(XM(N,2),V(N,2))
    ZH=XHP(XH(N,2),V(N,2))
    XNT=XN(N,1)+2.*XK*ZN
    XMT=XM(N,1)+2.*XK*ZM
    XHT=XH(N,1)+2.*XK*ZH
    XN(N,3)=XN(N,2)+.5*XK*(ZN+XNP(XNT,V(N,3)))
    XM(N,3)=XM(N,2)+.5*XK*(ZM+XMP(XMT,V(N,3)))
    XH(N,3)=XH(N,2)+.5*XK*(ZH+XHP(XHT,V(N,3)))
    DN=XN(N,3)-XNT
    DM=XM(N,3)-XMT
    DH=XH(N,3)-XHT
    I=N
    WRITE(61,101) I,L,V(I,J+1),XN(I,J+1),XNT,DM,XM(I,J+1)
1  ,XMT,DM,XH(I,J+1),XHT,DH,CK(I),CN(I)
    DO 3 LL=3,N
      I=N-LL+2
      V(I,3)=(1./ALP(I))*(S(I)+C*V(I+1,3))
      ZN=XNP(XN(I,2),V(I,2))
      ZM=XMP(XM(I,2),V(I,2))
      ZH=XHP(XH(I,2),V(I,2))
      XNT=XN(I,1)+2.*XK*ZN
      XMT=XM(I,1)+2.*XK*ZM
      XHT=XH(I,1)+2.*XK*ZH
      XN(I,3)=XN(I,2)+.5*XK*(ZN+XNP(XNT,V(I,3)))
      XM(I,3)=XM(I,2)+.5*XK*(ZM+XMP(XMT,V(I,3)))
      XH(I,3)=XH(I,2)+.5*XK*(ZH+XHP(XHT,V(I,3)))
32  DN=XN(I,3)-XNT
      DM=XM(I,3)-XMT

```

```

      DH=XH(I,3)-XHT
C J IN FORMAT STATEMENT IS A DIFFERENT J
C J IS TIME ROW IN PRINT OUT
      WRITE(61,101)I,L,V(I,J+1),XN(I,J+1),XNT,DN,XM(I,J+1)
      1,XMT,DM,XH(I,J+1),XHT,DH,CK(I),CN(I)
33 CONTINUE
3 CONTINUE
      DO 4 K=2,N
      V(K,1)=V(K,2)
      V(K,2)=V(K,3)
      XN(K,1)=XN(K,2)
      XN(K,2)=XN(K,3)
      XM(K,1)=XM(K,2)
      XM(K,2)=XM(K,3)
      XH(K,1)=XH(K,2)
      XH(K,2)=XH(K,3)
4 CONTINUE
      IF(L.EQ.M)2,13
13 IF(V(N,3).LE..0005.AND.V(N,3).GE.-.0005.AND.V(N-1,3)
      1.LE..0005.AND.V(N-1,3).GE.-.0005.AND.V(N-2,3).LE.
      2.0005.AND.V(N-2,3).GE.-.0005) 30,31
31 N=N+1
      V(N,2)=V(N+1,2)=V(N+1,3)=0.
      XN(N,2)=XN(N,1)=XNO
      XM(N,2)=XM(N,1)=XMO
      XH(N,2)=XH(N,1)=XHO
      AOA(N)=A/ALP(N-1)
      ALP(N)=B-AOA(N)*C
      GO TO 34
30 WRITE(61,120) N,V(N-2,3),V(N-1,3),V(N,3)
34 K=2
      CK(K)=36.*XN(K,2)**4
      CN(K)=120.*XH(K,2)*XM(K,2)**3
      D(K)=V(K,2)+A*(V(K-1,2)-2.*V(K,2)+V(K+1,2))-(XK*CK(K
      1)*(V(K,2)-12.))-(XK*CN(K)*(V(K,2)+115.))-GL*V(K,2)-
      2GLC
      S(2)=D(2)
      WRITE(61,109) D(K)
      DO 5 K=3,N
21 CK(K)=36.*XN(K,2)**4
      CN(K)=120.*XH(K,2)*XM(K,2)**3
      D(K)=V(K,2)+A*(V(K-1,2)-2.*V(K,2)+V(K+1,2))-(XK*CK(K
      1)*(V(K,2)-12.))-(XK*CN(K)*(V(K,2)+115.))-GL*V(K,2)-
      2GLC
22 S(K)=D(K)+AOA(K)*S(K-1)
      WRITE(61,110) K,D(K)
      5 CONTINUE
      2 CONTINUE
      END
C FUNCTION SUBPROGRAMS, DATA, AND CONTROL CARDS GO HERE.
C SEE REFERENCE MANUAL.

```

## APPENDIX 4

## FUNCTION SUBPROGRAMS

C WARNING. ALL CONTINUED STATEMENTS SHOULD BE CARRIED TO  
C COLUMN 72.

```

      FUNCTION XNP(PN,PV)
      IF(PV.GE.-10.00001.AND.PV.LE.-9.99999)201,202
201 AN=.1
      GO TO 203
202 AN=(.01*(PV+10.))/(EXP((PV+10.)/10.)-1.)
203 XNP=3.8202161*((1.-PN)*AN-PN*.125*EXP(PV/80.))
      END

```

```

      FUNCTION XMP(PM,PVA)
      IF(PVA.GE.-25.00001.AND.PVA.LE.-24.99999)301,302
301 AM=1.
      GO TO 303
302 AM=(.1*(PVA+25.))/(EXP((PVA+25.)/10.)-1.)
303 XMP=3.8202161*((1.-PM)*AM-PM*4.*EXP(PVA/18.))
      END

```

```

      FUNCTION XHP(PH,PVB)
      XHP=3.8202161*((1.-PH)*.07*EXP(PVB/20.)-(PH/(EXP((PV
1B+30.)/10.)+1.)))
      END

```