

TABLE I

HF-ECG	BCG
(1,5)*	(1,5)*
(2,3)	(2,6)
(3,8)	(3,17)
(4,5)	(4,17)
(5,1)*	(5,1)*
(6,11)	(6,2)
(7,10)*	(7,10)*
(8,3)	(8,17)
(9,18)	(9,14)
(10,7)	(10,5)
(11,6)	(11,10)
(12,10)	(12,8)
(13,2)	(13,17)
(14,15)	(14,19)
(15,14)	(15,5)
(16,11)*	(16,11)*
(17,12)	(17,8)
(18,19)	(18,3)
(19,12)	(19,1)
(20,11)*	(20,11)*

Pattern classification table for twenty HF-ECG and twenty BCG complexes. Asterisks indicate the cross matches.

TABLE II

Subject	No. of cross matches
1	6
2	14
3	14
4	5
5	7
6	13
7	3

The number of cross matches between HF-ECG and BCG in 7 subjects for 60 consecutive beats/subject.

TABLE III

Subject	Number of Matches	Subject	Number of Matches
1	1	10	1
2	3	11	2
3	2	12	1
4	1	13	1
5	0	14	2
6	1	15	0
7	3	16	1
8	2	17	0
9	1	18	0
		19	0

Matches for 19 normal subjects using data from 20 beats.

this would indicate a correlation between the two signals for those two beats.

## RESULTS AND DISCUSSION

Table I shows the computer matching of both HF-ECG and BCG for the first twenty beats for one subject. The asterisk indicates a cross match. Note that the match (1, 5) does not necessarily imply the match of (5, 1) (since the first number in the bracket, the vector  $\vec{X}$ , has been removed from the pattern space). The cross matches for all seven subjects are given in Table II. Table III shows the results of cross matches found for the group of 19 normals. The oc-

currence of cross matches for the abnormal group were found significant at a level of  $\alpha = .05$  when compared to the normal group using the Welch's  $t$ -test (8). This indicates that the presence of aberrant electrical pathways represented as the notching and slurring of the QRS complex corresponds to a change in the muscular activity of the heart reflected by the BCG. Further studies on the irregularity problem of BCG's are desirable, since it is a major obstacle to a more refined classification of ballistocardiograms and has impeded a more widespread acceptance of ballistocardiography as a non-invasive diagnostic tool for detection of abnormal myocardial contraction.

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## A Practical Algorithm for Solving Dynamic Membrane Equations

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**Abstract**—Many investigators work with the Hodgkin-Huxley model of membrane behavior or extensions thereof. In these models action potentials are found as solutions of simultaneous non-linear differential equations which must be solved using numerical techniques on a digital computer. Recent membrane models showing pacemaker activity, such as that of McAllister, Noble, and Tsien, involve solutions covering long periods of time, up to five seconds, and many ionic currents. Those added requirements make it desirable to have an efficient algorithm to minimize computer costs, and a systematic and simple solution method to keep the program writing and debugging to manageable levels.

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This paper shows that an iterative procedure using only one differential equation is possible and desirable and that the simplest numerical integration method is adequate. Graphical solutions for the action potentials and all nine components of the membrane ionic current over four action potential cycles are provided for the McAllister, Noble, and Tsien model; these are of intrinsic interest and helpful as a program debugging aid. A specific procedure for adjusting step-size during the iterative solution is given and it is shown that 4.5 minutes of repetitive membrane activity requires only 4 minutes of computer time. The procedure and model is shown to be intrinsically stable over this time duration with respect to computer and numerical integration errors.

Studies of cell membrane behavior are often based on the classic research of Hodgkin and Huxley (H-H) [1]; an example is the work of McAllister, Noble, and Tsien (M-N-T) [2] whose model for the dynamics of myocardial Purkinje fibers includes pacemaker characteristics. Some aspects of the digital computer programming required have been described by McAllister [3], without, however, giving a clear picture of the practical considerations that lead to efficient algorithms, an essential goal for the M-N-T formulation which can consume exorbitant amounts of computer and debugging time. This communication describes an alternative formulation of the solution which should make it convenient for investigators having limited knowledge of programming and numerical analysis to write their own programs. The description will specifically relate to the (H-H) and (M-N-T) models for giant squid axon and Purkinje fiber, respectively. To assist in debugging and interpretations, plots of all nine components of the M-N-T membrane current over four cycles of the action potential are provided.

In both formulations involving space clamp conditions, the membrane is treated as a circuit node at which Kirchhoff's current law is applied; the stimulus current entering the node is equal to the sum of all currents leaving, (1).

$$I_s = I_c + \sum_{k=1}^N I_k = C \frac{dV}{dt} + \sum_{k=1}^N g_k (V - V_k). \quad (1)$$

$I_s$ ,  $I_c$  and  $I_k$  are the stimulus, capacitive and  $k$ th ionic currents, respectively. The terms on the right are then expressed in terms of the membrane voltage,  $V$ .  $I_c = C dV/dt$  and  $I_k = g_k (V - V_k)$ , in which  $C$  is the capacitance per unit area;  $g_k$  is a conductance for the  $k$ th channel which may be voltage and time dependent; and  $V_k$  is the equilibrium voltage of the  $k$ th channel (physically related to the Nernst potential). In general, the conductances are expressed as functions of gating variables,  $y$ , in the form

$$g_k = \bar{g}_k f_k(y_1, y_2, \dots) \quad (2)$$

in which  $\bar{g}_k$ 's are experimentally determined constants and the  $f_k$ 's are experimentally determined functions. The gating variables satisfy first order ordinary differential equations

$$\frac{dy_i}{dt} = \alpha_{y_i}(1 - y_i) - \beta_{y_i}y_i \quad (3)$$

The rate constants  $\alpha$ ,  $\beta$  are specifically voltage dependent, through empirically derived equations containing voltage terms, so that  $\alpha_{y_i} = \alpha_{y_i}(V)$  and  $\beta_{y_i} = \beta_{y_i}(V)$ .

The solution of the H-H equations thus requires the simultaneous solution of four differential equations, namely the three expressed by (2) and the fourth by (1). Six additional equations are required to update the  $\alpha_{y_i}(V)$ ,  $\beta_{y_i}(V)$  [1] for each new value of  $V$ . The M-N-T program has nine ionic currents and a corresponding larger number of gating variables to be solved by (3).

The differential equations have typically been integrated numerically, a Runge-Kutta procedure [4] is common. An alternate algorithm, however, recognizes that the solution to

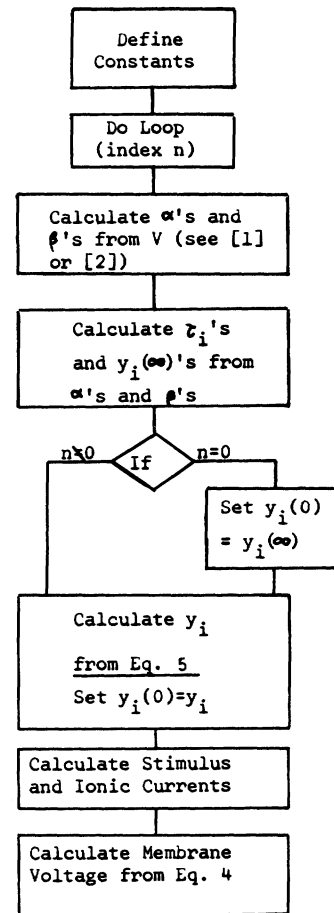


Fig. 1. Flow diagram for major segments of H-H and M-N-T programs described in text.

(3) would be a simple exponential if the  $\alpha$ 's and  $\beta$ 's were constant. Rewriting (3) as

$$\frac{dy_i}{dt} = y_i(\alpha_{y_i} - \beta_{y_i}) = \alpha_{y_i} \quad (4)$$

it is clear that the steady state solution is a constant, at which time  $dy_i/dt = 0$ ,  $y_i(\infty) = \alpha_{y_i}/(\alpha_{y_i} + \beta_{y_i})$ . The solution to the homogeneous portion is  $y_i = K e^{-t(\alpha_{y_i} + \beta_{y_i})}$  in which the constant  $K$  is determined to satisfy the initial condition  $y_i = y_i(t=0)$ . Thus, with the  $\alpha$ 's and  $\beta$ 's assumed constant over a time increment of  $\Delta t$  the complete solution to (4) becomes, with time constant  $\tau_i = 1/(\alpha_{y_i} + \beta_{y_i})$

$$y_i = y_i(\infty) - [y_i(\infty) - y_i(0)] e^{-\Delta t/\tau_i} \quad (5)$$

Eq. 5 appears in the literature [1], [6] and is mentioned as a solution method [6] but apparently has not been used in model studies. The main purpose of this paper is that of providing a straightforward and practical algorithm based on the use of (5), for solving the membrane potential as follows.

If (5) is assumed sufficiently accurate over one time increment, it can be utilized in an iterative scheme. In any iteration the term  $y_i(0)$  is the value of  $y$  at the start,  $y_i(\infty)$  is the asymptotic value of  $y_i = \alpha_{y_i}/(\alpha_{y_i} + \beta_{y_i})$  which depends on the current value of  $V$ . The computed value,  $y_i$ , on the left becomes  $y_i(0)$  for the next iteration. Otherwise the program is similar to the conventional one and contains the following principal components, Fig. 1. Constants such as capacitance, time step, resting potential, conductance constants and Nernst potentials to be used in subsequent equations are assigned numerical values. A "Do Loop," with index ( $n$ ) used

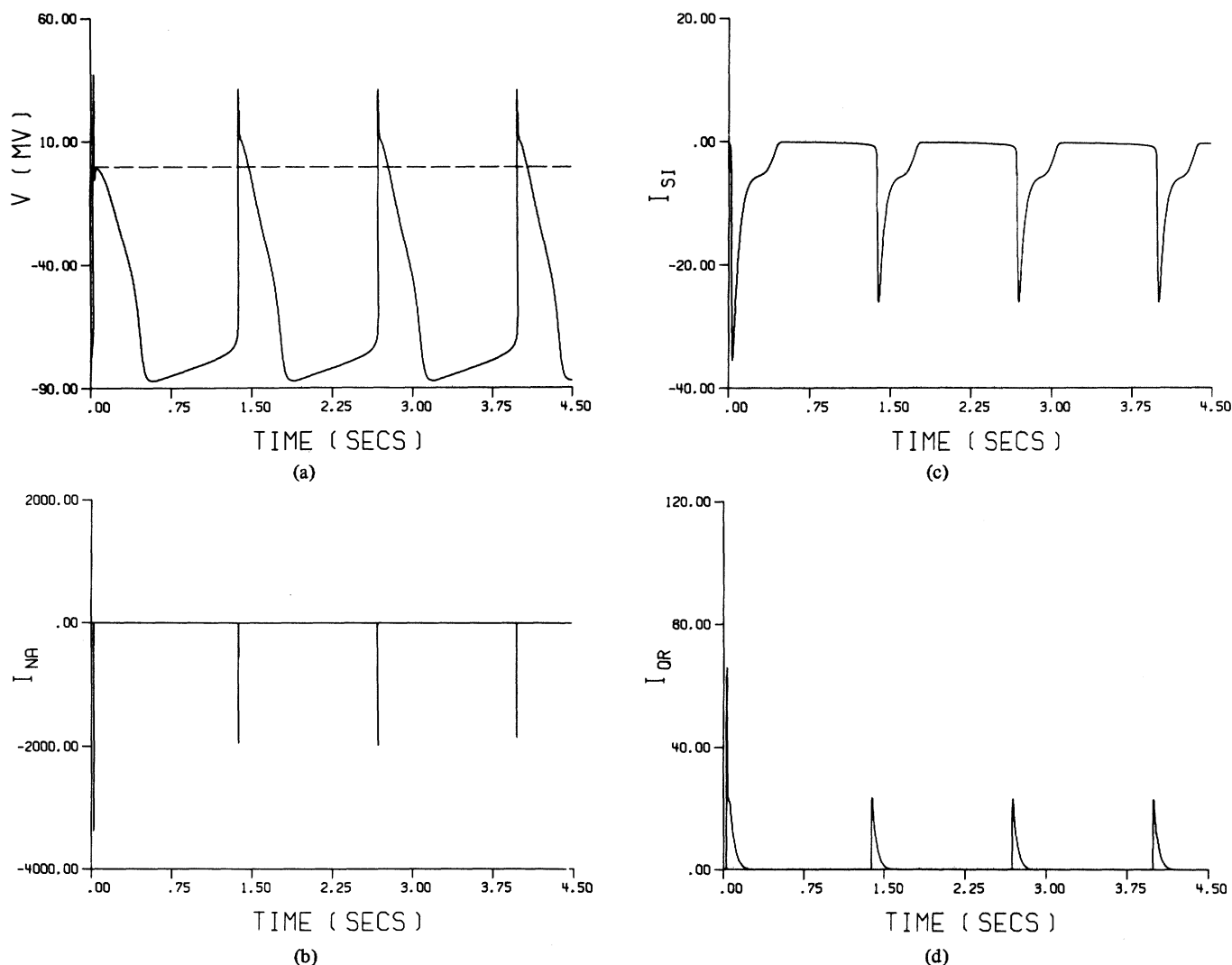


Fig. 2. Action potential ( $V$ ) and seven components of membrane current ( $\mu\text{Amp}/\text{cm}^2$ ) found from the McAllister-Noble-Tsien model. The two missing components,  $I_{Na,b}$  and  $I_{Cl,b}$  are linearly related to the action potential and thus differ from it only in scale. The stimulus is a 2 ms decaying exponential current started with  $V = -80\text{ mV}$ .

as a time-increment multiplier begins the iteration. The  $\alpha$ 's and  $\beta$ 's are found using the most recently calculated membrane voltage. From these the time constants and  $y_i(\infty)$ 's are computed. An "If" statement permits  $y_i(0)$  to be set equal to  $y_i(\infty)$  when  $n=0$ , otherwise  $y_i(0)$  equals the  $y_i$  of the previous step. The stimulus strength is calculated, equations for  $y_i$  of the form (5) are evaluated, and the  $y_i(0)$ 's for the following iterations are set equal to these. The ionic currents are then calculated and used in an equation of the form (5) to find  $V$  at the end of  $\Delta t$  in terms of  $V$  at the beginning. After this step the latter is reset to the former for the next iteration and  $V$  is stored, printed or plotted prior to the next iteration. With this very elementary scheme, it is possible with a time increment as large as .02 ms, to duplicate the performance of the considerably more sophisticated and complex Hodgkin-Huxley algorithm. With the H-H model action potential having a time duration of only 5 ms the principal advantage of the method proposed here is that of simplicity; only elementary programming and the most rudimentary differential approximations, Eq. (6), to (1) is needed.

$$V[(n+1)\Delta t] = V(n\Delta t) + \frac{\Delta t}{C} \{I_s(n\Delta t) - \sum I_k(n\Delta t)\}. \quad (6)$$

Further, increases in efficiency, as required for M-N-T model studies of arrhythmias, for example, can be obtained by lengthening the step size when the variables are not changing rapidly. The control for the step size changes must be generated internally since one cannot predict in advance when the next upstroke, for example, will occur. The technique we have employed monitors  $dV/dt$ , the rate of change of the membrane potential, and adjusts the step size over a range from .01 to 1 ms. Specifically, the program calls for the step size  $\Delta t$ 's to equal .01 during the stimulus or if  $dV/dt$  exceeds 5 mV/ms. Otherwise  $\Delta t$  is calculated according to  $\Delta t = (.01) (5/dV/dt)$ . If the calculated  $\Delta t$  exceeds 1 ms, it is reset to 1 ms as an upper bound. The time variable is the accumulated sum of the  $\Delta t$ 's.

## RESULTS

The M-N-T program, with line printer output commands, requires about 150 Fortran statements. A first order Euler method (6) proved to be entirely satisfactory from tests run so far; more sophisticated integration methods are readily available if necessary. With the program described above, the four action potentials shown in Fig. 2 extended over 4.5 s

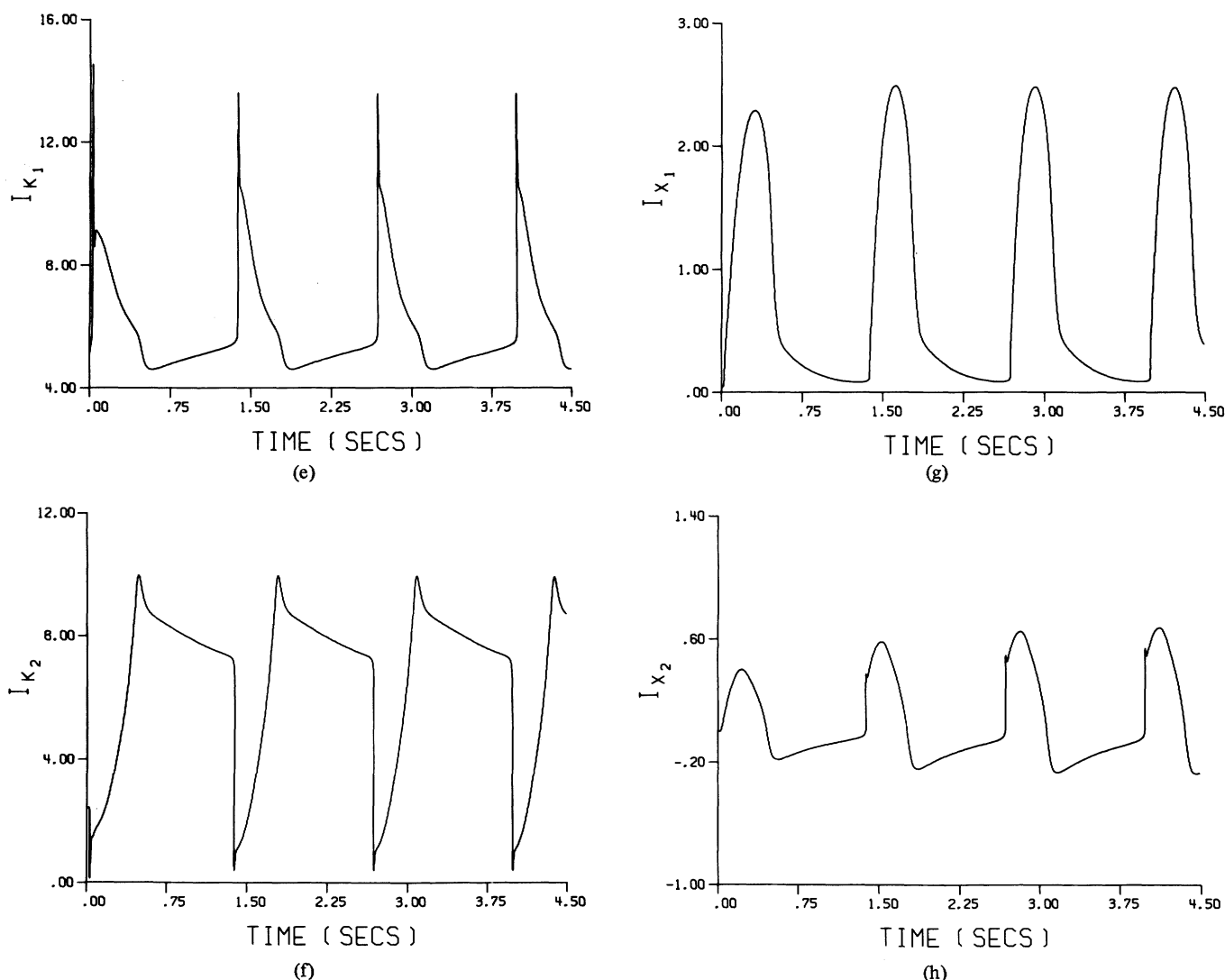


Fig. 2. (Continued).

and 15,000 iterations and were calculated in four minutes; fixed step sizes were used during the stimulus interval to minimize problems due to variable step sizes [6].

Fig. 2 shows a typical graphical output of all the ionic current components as well as the membrane potential. There are slight changes from cycle to cycle visible but, as is apparent from  $I_{X_2}$ , these are part of a transient which appears to be decaying exponentially to a steady state condition. Thus, after four cycles of the action potential, the algorithm gives no sign of a worsening solution due to numerical errors or other causes.

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#### A 60-Hz Harmonic Eliminator

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**Abstract**—A 60-Hz harmonic eliminator has been designed to remove dc and 60-Hz line frequency and its harmonics. By triggering a 1024-point sliding average on each cycle of the line voltage, the harmonics of 60 Hz and dc are averaged from the input. This average is then subtracted from the input to eliminate these components, leaving the rest of the signal unaffected. The circuit is equivalent to 500 notch filters at every harmonic of 60 Hz with each notch about 48 dB deep and less than 2 Hz wide.

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