A computer model of atrial fibrillation

*Gordon K. Moe, M.D.**
*Werner C. Rheinboldt, Ph.D.***
*J. A. Abildskov, M.D.****
Utica, N. Y.

Fibrillation can be initiated by premature excitation of some elements while others are still refractory. The induction of fibrillation should be facilitated by any agency which increases temporal dispersion of excitation and recovery.

It has been proposed that fibrillation can be initiated by unidirectional propagation of impulses about an obstacle. This mechanism can account for the rapid but still rhythmic activity of atrial flutter, but it is doubtful that a fixed circuit is compatible with the persistent chaotic activity characteristic of fibrillation.

A variant of the circus movement theory proposes that fibrillation is maintained by the irregular wandering of numerous wavelets generated by the fractionation of a wave front passing through tissue in a state of inhomogeneity with respect to excitability and conduction velocity.[1,2] The arrhythmia is assumed to sustain itself when the number of wavelets is so great that chance coalescence is improbable. The number of wavelets which can coexist in the tissue should be directly related to some function of the mass of the tissue, and inversely related to the duration of the refractory period and to the conduction velocity.

These three functions have been demonstrated to influence the probability of persistent fibrillation in the expected manner, but direct test of the hypothesis in vivo is difficult if not impossible. We do not know, for example, the critical number of wavelets below which spontaneous recovery is likely and above which persistence is possible, nor indeed whether multiple independent wavelets exist at all. It is known, however, that: (1) the atrium is not homogeneous with respect to the duration of refractory period in closely adjacent spots[3]; (2) the refractory period of the atrium is not uniformly abbreviated by vagal stimulation[3]; (3) the conduction velocity, approximately 80 cm./sec. in fully excitable atrial muscle, is depressed in the relatively refractory state; and (4) the duration of the functional refractory period is related to the preceding cycle duration.[4] Given reasonable approximations of these properties of atrial behavior, it was believed possible to construct a

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*Address: Masonic Medical Research Laboratory, Bleecker St., Utica 2, New York.
**Formerly, Director, Computing Center, Syracuse University. Now, Director, Computer Science Center, University of Maryland, College Park, Md.
***Associate Professor of Medicine, State University of New York, Upstate Medical Center, Syracuse, N. Y.

mathematical model in which the postulated mechanism of fibrillation could be tested on a digital computer.

Methods

A. The mathematical model. The model was designed on the basis of a number of simplifying assumptions: (1) The piece of atrial tissue under consideration consists of a finite number of discrete "units." No fine structure is considered within a unit. (2) The units are arranged in a regular hexagonal packing as a flat sheet one unit thick. Each unit, except those on the boundary, has six neighbors (see Fig. 2). (3) A unit, when fired, transmits excitation of a constant amplitude* to all its neighbors; after some delay these neighbors will fire or not, depending on their state of excitability.

To follow the propagation process in the computer, the time as well as the tissue was considered as discrete units. The fundamental time-step was chosen to give a conduction velocity of one unit per time-step in fully recovered tissue. If we assume the time-step to equal 5 msec., a conduction velocity of 80 cm. per second corresponds to a 4-mm. diameter of one tissue-unit.

Five states of excitability were assigned, as indicated in Fig. 1:

STATE 1, the absolutely refractory state, has a duration represented by the formula $R = K\sqrt{C}$, where C is the preceding cycle duration and K is a constant (K^2 has the dimension of time). The value of K is a property of the unit and is generally different from unit to unit. A unit in State 1 will be uninfluenced by discharge of a neighboring unit.

STATE 2, the first stage of excitability recovery, lasts two time-steps (10 msec.). During this period, discharge of a neighbor excites the unit, but only after the lapse of 4 time-steps, i.e., the conduction velocity has a lower limit equivalent to one fourth of the value obtaining in fully excitable tissue, or, transposed to real tissue, 20 cm. per second.

STATE 3, second stage of relative refractoriness, is assumed to last an additional two time-steps, and provides for discharge after the lapse of 3 time-steps.

STATE 4, persisting for two-time steps after State 3, permits firing two time-steps after a neighboring discharge.

STATE 5, which lasts until re-excitation, is the fully recovered state in which excitation requires only one time-step per unit.

The three stages of partial refractoriness correspond to a relatively refractory period

*The assumption of constant amplitude for the "action potential" is a convenient simplification of relative unimportance to the operation of the model. Conduction velocity, which is the important parameter to be considered, must in real tissue be a function of the "excitability" of a recipient unit, and of the amplitude and rate of rise of the action potential of the donor unit. It would be possible to incorporate these separate determinants of conduction velocity, and, in fact, this is planned for a later stage of the study. Spatial and temporal summation have also been disregarded in the preliminary model.

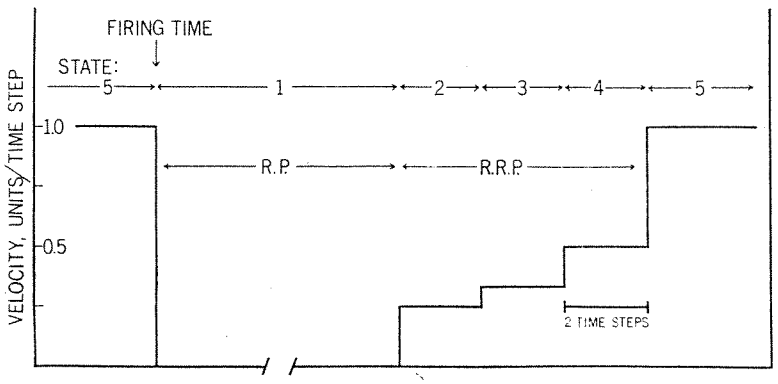

Fig. 1. Schematic representation of the five states of activity. Abscissae, "time"; ordinates, conduction velocity. *R.P.*: Duration of State 1 = absolutely refractory period. *R.R.P.*: Duration of States 2,3, and 4 = relatively refractory period.

of 30 msec., which is close to the observed values in the exposed atria of dogs under barbiturate anesthesia and is assumed to be independent of the cycle length.[5]

To start the propagation process certain units were externally stimulated. It was assumed that the external stimulus was delivered at a strength so much in excess of the normal "action potential" amplitude that the selected tissue-units, unless absolutely refractory, responded with a minimal delay of one time-step.

The only assigned variability from unit to unit was that of the parameter K. The size of the tissue-sheet, the distribution of the parameters K, and their range of variability were assumed to be primary factors in the initiation of turbulent propagation, i.e., atrial fibrillation.

B. The computer program. Two closely related programs were written for an I.B.M.-650 tape system with 4,000-word drum (three tape drives) and an on-line I.B.M.-407 printer. A more elaborate I.B.M.-7090 program is now in preparation. The details of these programs will be described separately[6]; we outline only some of the main points here.

To provide for hexagonal packing of the tissue-units a 60-degree coordinate system was used. In this coordinate system each unit is identified by two coordinates, n and m. The six neighbors of the unit (n,m) then are the units with the coordinates (n,m−1), (n,m+1), (n−1,m), (n−1,m+1), (n+1,m), (n+1,m−1). Each of the units of the sheet was represented in the main memory of the computer by two ten-decimal digit words. In order to find these words in memory a mapping function was needed correlating the coordinates n, m of the unit with the address in memory. To permit changes of geometry, a general mapping function was built into the programs. The words in memory describing one tissue-unit contained the coordinates of the unit, its state of excitability, its last time of firing, the time the unit was to remain in its present state of excitability, and, in case a neighbor fired, the time interval until the unit would fire next. Other information recorded in these words was of importance only for the actual details of programming.

At each time-step the program searched all units in memory. If a particular unit was to fire at that time-step, the refractory period was calculated, all excitable neighbors were stimulated, and appropriate information about the firing unit was printed out. Every unit not firing in that time-step was checked whether subject to a change in its state of excitability. As long as an external stimulus acted upon certain units of the tissue-sheet, these units were checked to find out whether they changed from total to partial refractoriness, in which case they were stimulated to fire in the next time-step. Once all units had been searched, the time was advanced and the process begun again.

The second program permitted replication of up to 9 copies of the same tissue-sheet. These copies were run in parallel; changes could be effected in the various copies, retaining the original sheet as a control. The different copies were kept on magnetic tape and were read-in and processed in succession at every time-step.

At a later stage a visual I.B.M.-407 printout of the tissue-sheet at a given time-step was incorporated (see Fig. 11). This was a slow process and was used only for a few selected time-steps.

The I.B.M.-650 programs were severely limited by the size of the 4,000-word main memory of the computer. By using a variety of special features, and in particular by applying certain overlay techniques, it was possible to permit flat tissue-sheets of up to 999 tissue-units. The first computer-runs performed with these programs used a diamond-shaped 31 × 32 matrix of 992 tissue-units.

Results

A. Behavior of 992-unit matrix (Program 1).

INITIATION OF SELF-SUSTAINED ACTIVITY. At the outset it was not known whether self-sustained activity could be accommodated within the framework of 992 units. The selection and distribution of the parameters K were obviously of crucial importance. For the original sheet a range of values was chosen which, assuming 1 time-step to be equal to 5 msec., would yield refractory periods in the approximate range observed in dog atria.[3] The 11 values $\sqrt{10}$, $\sqrt{11}$, ... , $\sqrt{20}$ were selected, and

were distributed at random among the tissue-units. The 11 classes of units comprised approximately equal proportions of the total population.

As in real tissue, the refractory periods (i.e., K values) assigned to the model determined the maximum frequency at which a unit could fire. For the lowest value of K the minimum cycle duration was 17 time-steps (State 1 = 13 plus 4 for excitation); for the highest value the minimum cycle duration was 28 time-steps. Since the maximum frequency which the whole tissue could follow uniformly was determined by those units which had the longest refractory period, the maximum regular frequency would be 1 response per 28 time-steps, or the equivalent of 7.15 impulses per second. This is roughly comparable to what has been observed in the exposed dog atrium.[1]

At the start of the first run, it was assumed that the duration of the preceding cycle for all units was 40 time-steps, corresponding in "real" time to a frequency of 5 per second, a frequency which the atria may be expected to follow with regularity and at uniform conduction velocity. Stimulation was applied to a cluster of 4 units at a frequency of 1 stimulus per time step. By convention, a stimulated unit having a refractory period of 20 time-steps ($R = 3.16\sqrt{40}$) would be excited at time-step 1, recover at time-step 21, and would respond again at time-step 22. The units chosen for stimulation were selected to permit the escape of an early premature beat. Selection was necessary, for if stimulation were applied only to units with maximal K values, or those surrounded by neighbors with high K values, then re-excitation could not lead to self-sustained activity; the tissue would merely be driven at the highest rate permitted by those units with the longest refractory periods. The site of stimulation was selected as a cluster containing low K values, and with a pathway of neighbors of suitably low values.

Propagation of the first beat progressed uniformly at the maximum velocity of 1 unit per time-step; the excitation wave reached the most remote extremity of the matrix at time-step 32. The duration of State 1 ranged from 20 to 28 time-steps. At the earliest possible moment, an additional response was induced in one of the stimulated units. At this moment regular and concentric propagation of the impulse was impossible because of nonuniform excitability among neighboring units. The orderly progress of the first impulse, and the necessarily irregular escape of the second, are illustrated in Fig. 2, which indicates those units which fired in time-steps 20 to 34. The four units enclosed by the heavy beaded line were subjected to the external stimulus. Escape of the premature response occurred as individual small wave

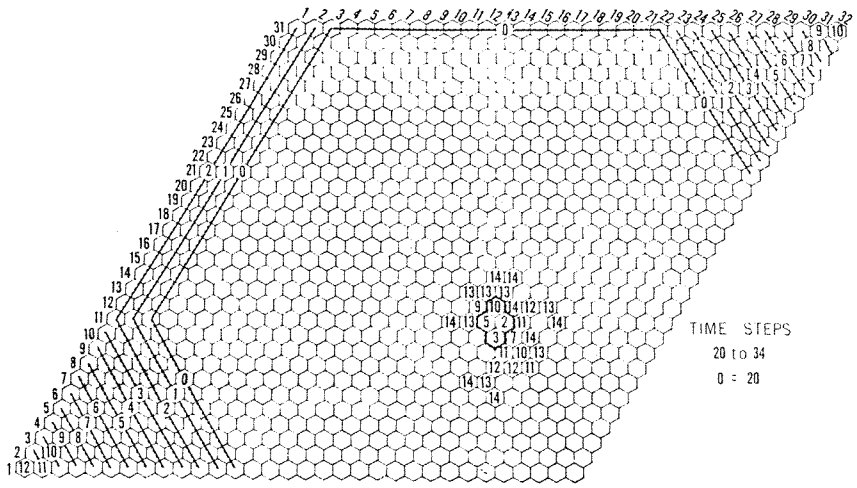

Fig. 2. Pattern of activity during time 20 to 34, Program 1. Regular patterns labeled 0-12 represent position of excitation wave of first response. Irregular patterns around stimulated units indicate escape of first "premature" beat.

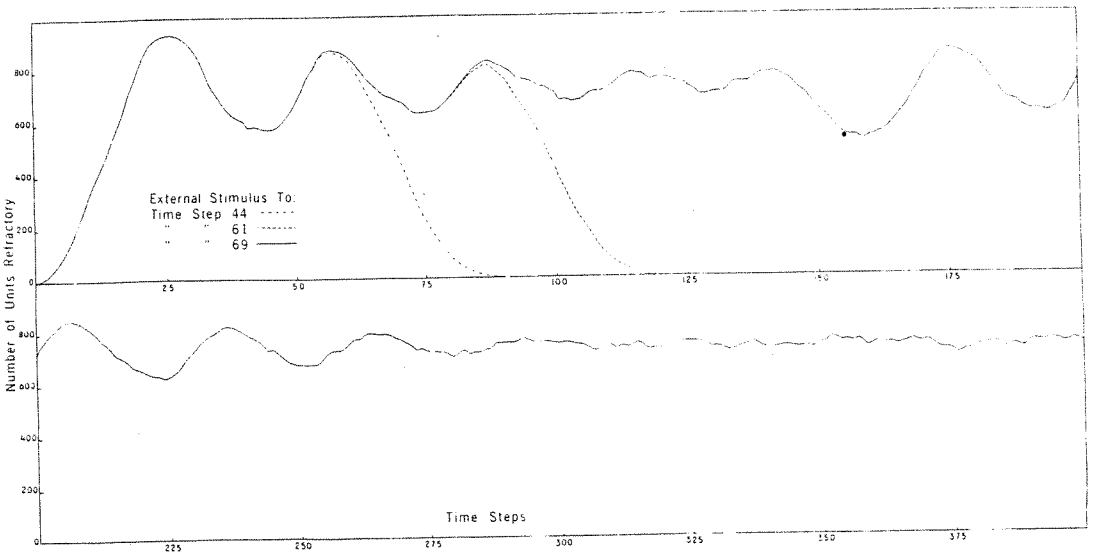

Fig. 3. "Electrogram" of activity in 992-unit matrix from time 0 to 400. Abortive responses are indicated by broken line.

fronts arising from the units which were fired at t=23 (3→7→11, etc.), at t=25 (5→9→13), and at t=30 (10→13 and 14). Because of slow conduction in the relatively refractory units near the site of stimulation, additional time was available for the recovery of more remote units; accordingly, acceleration of the premature wave fronts occurred, with fusion into a single wave similar in contour to the initial one.

In preliminary trial runs, the external stimulus was turned off at each successive time when any one of the four stimulated units was re-excited. Stimulation through time-step 44 resulted in a single premature beat which involved the whole matrix, followed by an abortive re-entry which invaded only a few central units. Stimulation through time 61 caused two successive premature responses, but again permitted re-entry of only a few units before the process expired. Stimulation through time 69 caused a self-sustained arrhythmia which persisted with no apparent tendency for spontaneous arrest for some 1,500 time-steps, at which time the run was terminated.

Fig. 3 represents an "electrogram" of the activity through the first 400 time-steps. The ordinates represent the total number of units in State 1 (i.e., "depolarized"), plotted against time. A flutter-like oscillation persisted until about time-step 300, after which the number of active units fluctuated irregularly within a narrow range, much like the over-all electrical record of activity in fibrillating atria. The abortive responses to stimulation through times 44 and 61 are shown for comparison.

DEVELOPMENT OF ASYNCHRONY. To illustrate the influence of inhomogeneity on impulse transmission, the times of excitation and recovery were tabulated for two different groups of units for four successive discharges, including the three initial responses induced by external stimulation. A near group of 15 units fired for the first time at t=5. For comparison, a more remote group firing at t=19 was selected. The behavior of these two groups is illustrated in Fig. 4.

The proximal group is displayed in the lower half of Fig. 4, and the distal group in the upper half. In the near group the time of successive discharges was greatly influenced by the time of recovery from preceding activations, i.e., the advancing wave front was molded by the "retreating" edge of a prior response, so that neighboring units were forced out of phase with each other. More distant units preserved their temporal "unity" for a longer period, having been protected by the transmission delay near the site of initial re-excitation. The average "excitable gap" (i.e., the

interval between the end of State 1 and re-excitation) was considerably briefer for the proximal gang of units than for the distal elements. In other words, many of the distal elements were allowed time for full recovery (to State 5) before discharge of neighboring elements caused re-excitation.

Spreading of the turbulence and progressive conduction delay due to repeated premature activations is apparent in Fig. 5, which illustrates the first 5 activations of a unit on the periphery of the matrix, 21 units away from the stimulated site. The first impulse (*A*) traversed the 21 units in 21 time-steps. Impulse *B* was delayed near its origin, then accelerated to full speed. To reach the same goal, *B* traversed 24 units in 31 time-steps. Further delay and increasing tortuosity of the path occurred, until response *E* required 75 time-steps and traversed 40 units in passage.

Inhomogeneity, built into the program as a range of K values, was increased by re-excitation. "Premature" excitation resulted in a molding of subsequent responses by the recovery pattern of the preceding event (Fig. 4). As a result, dispersion of refractory periods due to variation in preceding cycle length was added to the initial inhomogeneity. After the lapse of 100 time-steps, the average refractory period dropped to 20.4, with a range of 14-24, and the average cycle length to 27.9, with a range of 20-29. The range of variation of cycle lengths and refractory periods then increased progressively with time, although the mean values did not change appreciably. By time 900, some units were responding 5 times per 100 time-steps, whereas others responded less than twice during the same interval. This result is in conformity with experimental observations of different frequencies recorded simultaneously from two microelectrodes inserted into fibrillating tissue.[7]

DEVELOPMENT OF CIRCUITS. It will be noted in Fig. 5 that the responses *D* and *E* were traced back to the same time of origin, at t=69. It is obvious that a circuit occurred in the pathway, and this can indeed be traced out. The impulse *D*, which reached the "goal" over an irregular path,

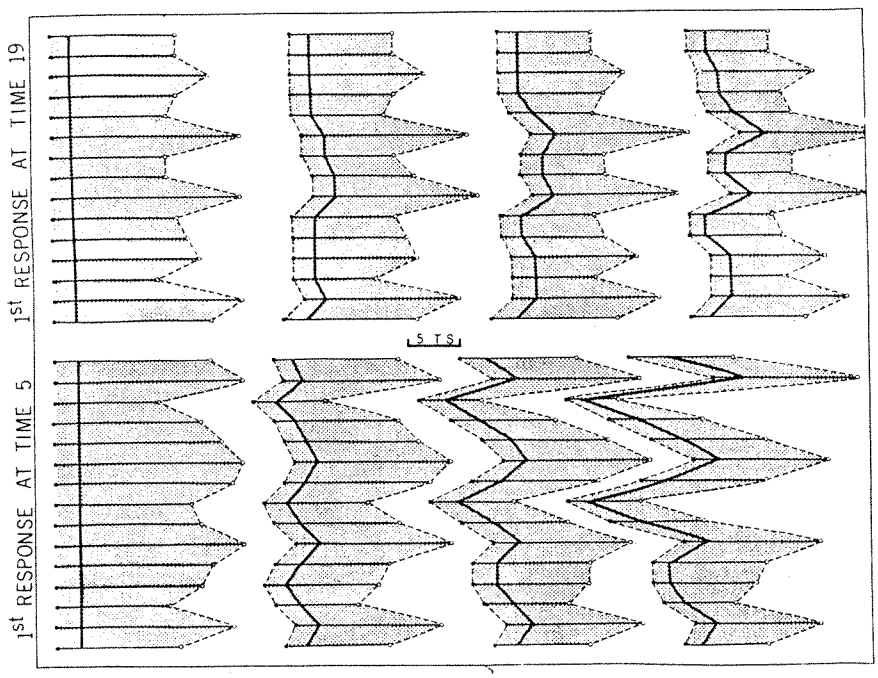

Fig. 4. First 4 responses of 15 units near stimulated site (*1st response at time 5*) and of 15 remote units (*1st response at time 19*). Shaded area represents duration of State 1; heavy black line represents deletion of 10 time-steps. First three responses resulted from stimulation; fourth response, first spontaneous re-entry.

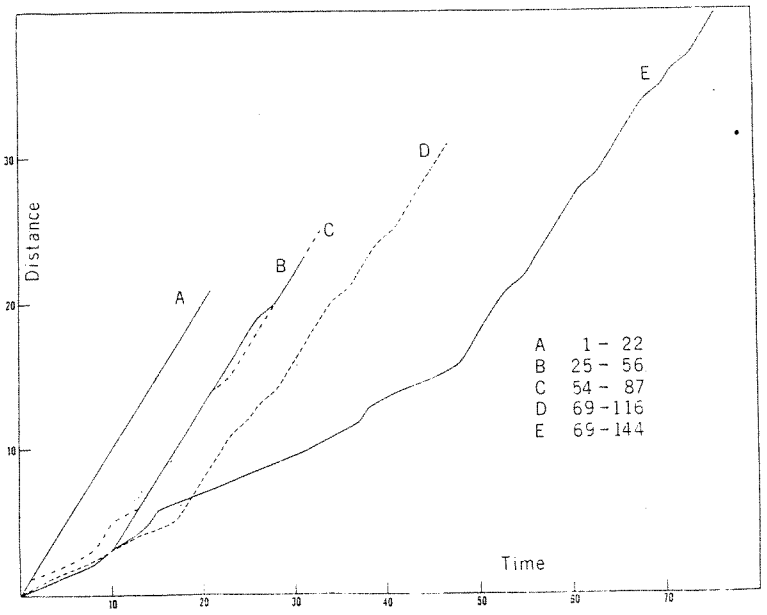

Fig. 5. First 5 responses traced to a unit on the periphery of the matrix, 21 units distant from site of stimulation. Time 0 in each case represents parent response at stimulated site. Upper end of each line represents arrival at goal. Distance in units; time in steps.

generated a vortex which again resulted in excitation of the peripheral unit. The existence of such circuits is illustrated in Fig. 6, in which the source of activity of three corner elements firing at t=857, 864, and 875 was traced through nearly 200 time-steps. The routes indicated by arrows were traced backward in time, for it can be established from whence a given unit was excited, but it cannot readily be determined that a given wave front will reach a unit at some later time, or indeed that the wave front will survive at all. Circuits occurred in all three pathways, and all can be traced to a common origin at time 686. Each of the "goal" units fired several times during the period covered by the wandering of these impulses.

The fact that the excitation pathways for three widely separated units were traced back to a common trunk might suggest that a basic circuit existed which repeatedly discharged the rest of the matrix. When the self-sustained arrhythmia was initiated, and for about 300 subsequent time-steps, re-excitation occurred repeatedly, although irregularly, near the stimulated site where turbulence was most pronounced. Progressive disorganization occurred, however, and spread to all areas of the matrix, with many scattered and varying sites of "re-entry." Plots of the sequence of discharge of all units firing over a period of several hundred time-steps failed to reveal any fixed re-entrant pathway. Many circuits developed in widely scattered areas, circuits which shifted position, frequency, and direction with time, and which died and were replaced by others.

WAVE FRONTS. The nature of the simulated arrhythmia can be illustrated by plotting the wave fronts coexisting at a given instant. The term "wave front" is used to indicate those contiguous units which, at a given instant, are being excited by neighboring elements. Since we have decided that an element in State 2 cannot fire until 4 time-steps after the discharge of a neighbor, we must include events both before and after the selected moment. Consider the wave fronts existing at the imaginary instant between time-steps t and $t+1$. Any unit which fires in time-step $t+1$ will be included, since it must have received the impulse from a neighbor firing at t or earlier. Not all units firing in time-step $t+2$ can be included, for some of these

will have received activity from neighbors firing at $t+1$, i.e., after the selected instant. Similarly, some units firing at $t+3$ and $t+4$ will be included in the wave front, for they will have fired in response to events at $t-1$ or t, but others will be excluded because they responded to events at $t+1$ or later.

Fig. 7 depicts the wave fronts existing between time-steps 527 and 528. All units firing at 528 (labeled *8* in the diagram) are included, and those units which fired at 529, 530, and 531 in response to events prior to t 528 are also included. Contiguous units constituting an entity are enclosed by heavy beaded lines; a total of 30 wave fronts coexisted at that instant.

The further progress, if any, of these wavelets is indicated by small arrows. If activity passed to additional units after the moment under consideration, an arrow indicates the recipients. These waves are considered to be "active." Some wave fronts were enclosed by refractory tissue or had encountered a boundary and would, therefore, be snuffed out. These are considered "dead." It is apparent that fusion of some wavelets, particularly those to the

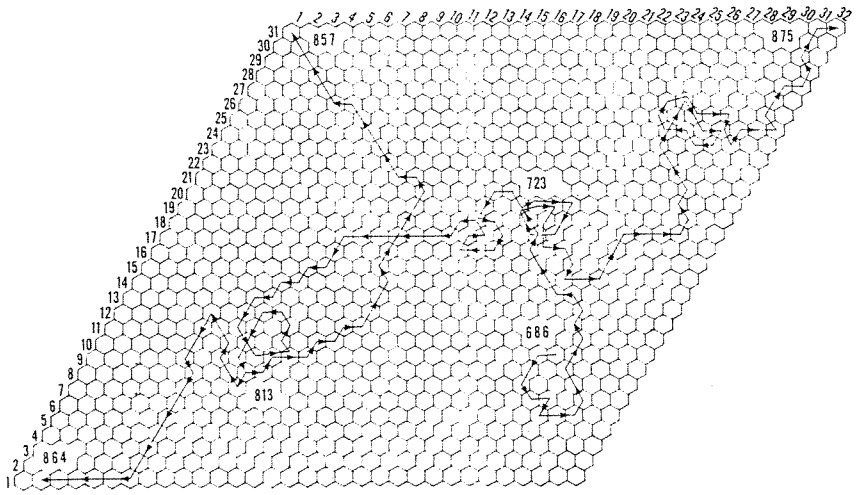

Fig. 6. Impulse pathways traced to three peripheral units firing at time 857, 864, and 875.

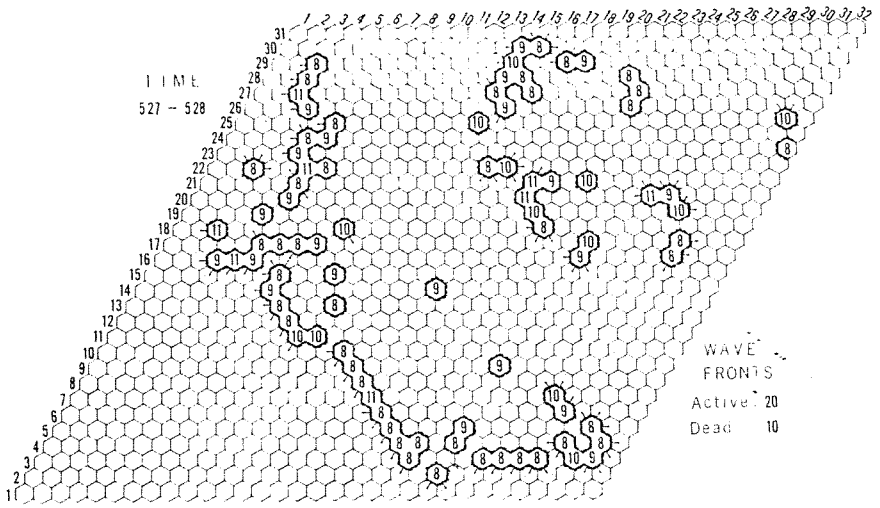

Fig. 7. Wave fronts mapped at time 528 in Program 1. Arrows indicate direction of progress of wave fronts; numbers indicate firing time (528 = 8, etc.).

left, would occur within the subsequent time-step, but others would become discontinuous at the same time. Similar diagrams were plotted at many times during the program. During the initial phases of the "arrhythmia" most of the turbulence and re-entry were confined to the region immediately surrounding the stimulated site. During this period (i.e., up to about t=300) the number of wave fronts was relatively small, ranging from 4 to 11 active, 0 to 6 "dead," and 5 to 14 total. At time-step 103, for example, two large wave fronts were progressing toward the periphery in a nearly regular sweep, whereas re-entry spawned two single-unit wavelets near the site of original stimulation. A fifth wave was about to be extinguished at a boundary of the matrix.

After the development of widespread turbulence, the number of wave fronts increased, whereas the average number of units in each wavelet diminished, i.e., further fractionation occurred. Between t=300 and t=816 the number of active wavelets varied between 15 and 33 (average of 17 samples = 20.6), the number of "dead" wavelets varied between 4 and 16, with an average of 10.8, and the total number fluctuated between 23 and 40.

No sign of repetition of patterns was discovered, although it is certain that periodicity would eventually have to appear, since behavior of the matrix was not truly up to chance but was predestined. However, the number of permutations is so large as to preclude any obvious tendency toward periodicity.

EFFECT OF REDUCTION IN SIZE AND PROLONGATION OF REFRACTORY PERIOD. The program as developed to this point demonstrates that self-sustained activity can be induced in the matrix as designed, and that in some respects the activity resembles fibrillation. The next step was to test some of the variables known from animal experimentation to influence fibrillation, namely, tissue mass, geometry, and refractory period.

A preliminary test of reduction in size and of prolongation of the refractory period was made in the first run. At t=810, the matrix was nearly bisected by removal of elements along a straight line, leaving an isthmus of 4 units in the center. The arrhythmia continued on either side of the scission. In effect, the area had been bisected, for wave fronts from each side repeatedly collided, with mutual extinction, at the isthmus. After an additional 400 time-steps, the refractory periods (i.e., the K values) of all units on one side of the isthmus were increased by 50 per cent. As soon as this change in behavior became effective, that half of the matrix ceased to exhibit spontaneous activity, but it continued to be excited by impulses transmitted through the isthmus from the fibrillating portion. At t=1350, the isthmus was severed; fibrillation continued in the "control" half, but activity ceased in the altered portion, even though the latter contained the initially stimulated units and the area of earliest turbulence and re-entry.

B. Comparative behavior of smaller matrices (Program 2).

Although the preliminary results suggested that the initial matrix was larger than need be for self-sustained activity, and that prolongation of the refractory period might terminate the arrhythmia, they also indicated the necessity of maintaining a control matrix for comparison with experimental patterns.

Program 2 was designed to permit a simultaneous comparative study of several matrices of originally identical geometry and parameters. One group was maintained as a control, whereas changes which might be expected to alter the arrhythmia were imposed on parallel groups. To save computer time, and also to make the model more critically balanced with respect to continued activity, the matrix was reduced in "mass" to a regular hexagon composed of 547 units. The hexagon, cut out of the original parallelogram, included the area initially subjected to stimulation. The distribution of K values was the same as in the comparable area of the original program.

ALTERATION OF REFRACTORY PERIODS (PROGRAM 2-A.)* As before, stimulation was continued through t=69, and a self-sustained arrhythmia resulted. By t=300, as

*Only two programs were written for these studies. In the text of the paper and in the tables and illustrations the several runs of Program 2 are identified as Program 2-A, 2-B, and 2-C.

Table I. *Effects of alteration of refractory periods (Program 2-A)*

Group	*K (avg.)*	*K (range)*	*R*	*C*	n_1	n_f	*S*	*T*	λ
2	3.46	2.84–4.02	16.8	23.6	363	23.2	54	2.34	10.1
1	3.85	3.16–4.47	19.8	26.4	384	20.7	48	2.32	11.4
3	4.23	3.48–4.92	23.6	31.2	394	17.5	40	2.28	13.7
4(A)	4.62	3.79–5.36	27.9	36.3	404	15.1	33	2.19	16.6
4(B)	4.62	3.79–5.36	28.1	36.9	365	14.8	23	1.55	23.8

K: Constant in relation $R = K\sqrt{C}$. R: Average refractory period (duration of State 1). C: Average cycle duration $= \frac{N}{n_f}$, where N = total number of units in matrix. n_1: Average number of units in State 1. n_f: Average number of units firing per time-step. S: Average number of units in excited state but not yet fired. T: Average excitation time $= \frac{S}{n_f}$. λ: Average "wave length" $= \frac{N}{S} = \frac{C}{T}$

In groups 2,3, and 4 the values of K were changed from those of Group 1 after self-sustained activity had progressed for 300 time-steps. The other values listed in the table represent the average behavior between t = 400 and t = 500, for Groups 2,1,3 and 4(A) and between t = 684 and 719 for Group 4(B). At the latter time, Groups 1,2, and 3 had not changed significantly from the listed values.

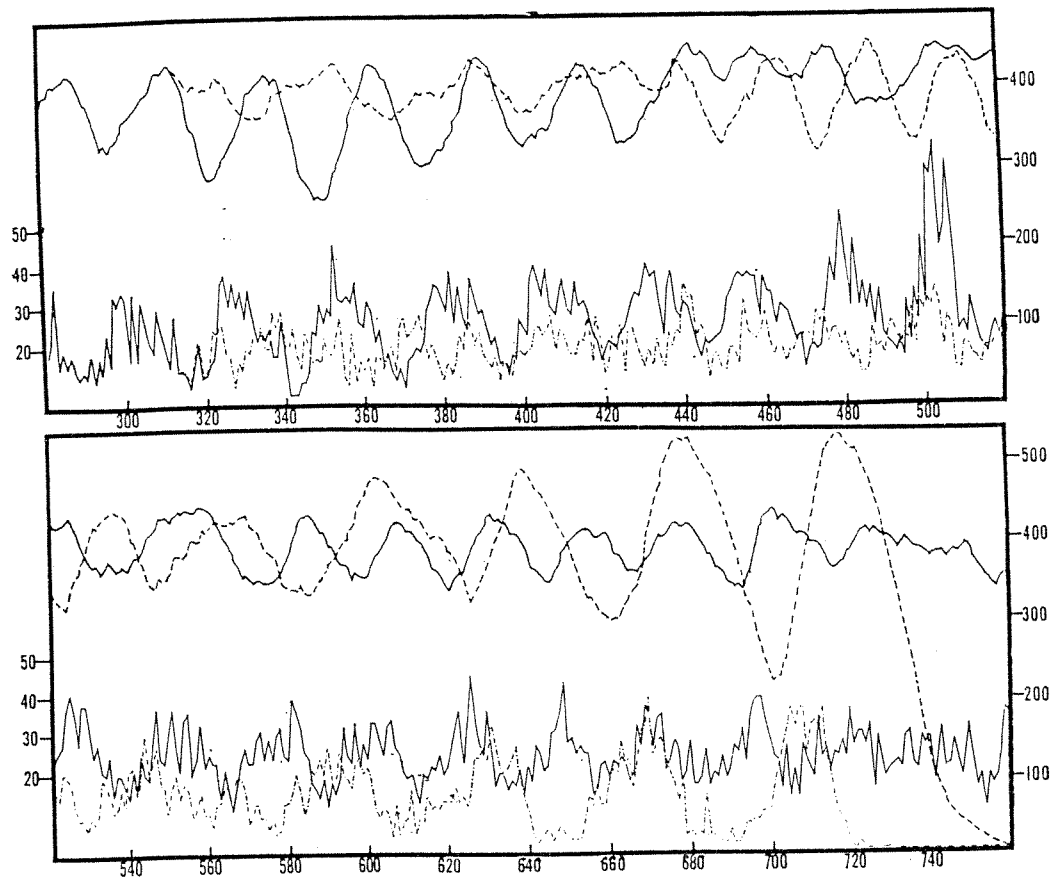

Fig. 8. "Electrogram" of Groups 2 and 4 of Program 2-A in which K values were reduced from initial values by 10 per cent (Group 2, *solid lines*) and increased by 20 per cent (Group 4, *broken lines*). Change in K values instituted at time 300. Upper curves, number of units in State 1 (scale at right); lower curves, number of units firing in each time-step (scale at left).

in the first program, turbulence was widespread and a diagnosis of fibrillation was made. At that time the program was replicated to create 4 groups, all of which started in the same condition. Group 1 was continued with the original K values; in Group 2, all K values were reduced by 10 per cent; in Groups 3 and 4, the K values were increased by 10 and 20 per cent, respectively. At t=730, Group 4 ceased firing.

It should be pointed out that inhomogeneity, the *sine qua non* of *inducing* sustained activity in the model, was retained in all groups; the refractory periods of all units were altered in proportion. It follows that, for a given area and configuration of the model, the likelihood of continued self-sustained activity was reduced by prolongation of the absolutely refractory period.

Fig. 8 illustrates the behavior of Groups 2 and 4 (the extremes of the K values) after the parameters were changed. Oscillation of the number of units active in Group 4 became accentuated beginning at about t=580 as the active wave fronts began to coalesce.

A statistical comparison of the effects of alteration of the refractory periods is presented in Table I. The average and range of K values for the various groups are the independent parameters introduced at time 300. The computed parameters R, C, n_1, n_f, S, T, and λ are listed for Groups 2, 1, 3 and 4(A) as average values derived from 5 samples of 16 consecutive time-steps each, taken between t=400 and 500. The values tabulated for Group 4(B) are the average for these same parameters over 36 consecutive time-steps (684 to 719) shortly before spontaneous arrest. Between t 400 and 500 the four groups had become differentiated with respect to the computed parameters, but Group 4 had not yet clearly exhibited the signs of progressive organization which preceded its arrest.

It is predictable that increasing the value of K must increase the average refractory period (R) and cycle duration (C). The average frequency of excitation, in other words, must diminish. Accordingly, given a fixed number of units, the increased refractory periods must be accompanied by a reduction in the average number of units firing per time-step (n_f). The value of n_f was roughly inversely proportional to the average K value in the four groups. One might also expect the average number of units in State 1 (n_1) to be increased by prolongation of the refractory period, but since fewer units entered State 1 during each time-step as the average value of K was increased, the difference between the several groups was not great, ranging from 363 in Group 2 to 404 in Group 4.

It was expected that the progressive organization of activity preceding arrest in Group 4 (highest K value) would be accompanied by a progressive increase in the conduction velocity, i.e., by a decrease in excitation time. At time 400 to 500, however, this trend was not yet apparent. The average excitation time, T, is represented by

$$\frac{(4n_2 + 3n_3 + 2n_4 + n_5)}{n_f}$$

where n_2, n_3, n_4, and n_5 represent the number of units firing per time-step from States 2, 3, 4, and 5, respectively, and n_f represents the total number of units firing per time-step. The sum $(4n_2 + 3n_3 + 2n_4 + n_5)$ is represented in the table as S. There is no significant systematic relationship between the average K and the average excitation time in the several groups. Shortly before arrest of Group 4, however, mean conduction velocity did indeed increase (Group 4(B), t=684 to 719).

The values for wave length (λ) in the table are average values computed from the ratio of N (the total number of units in the matrix) to S (the number of units in the excited state, i.e., the number of units comprising wave fronts).* The average value of λ increased in proportion to the value of K.

Details of the events prior to arrest of Group 4 are displayed in Fig. 9, which

*Since it may not be immediately apparent that the ratio N/S yields λ, the following derivation is appended: Let S = the average number of stimulated units, T = the average excitation time, and n_f = the average number of units firing per time-step. Then, $S = n_f T$. The average cycle duration, C, can be defined as $\frac{N}{n_f}$, where N represents the total area of the matrix. The wave length, which is equal to velocity divided by frequency, must also be equal to cycle duration (inverse of frequency) divided by excitation time (inverse of velocity). Accordingly, $\lambda = \frac{C}{T} = \frac{N}{n_f T} = \frac{N}{S}$.

encompasses the last major excitation process in that group. At the start of the figure, the number of units firing was at a low ebb, falling to one or two units per time-step. This was at a time when a single re-entrant circuit was progressing not far from one corner of the matrix. During the time that this excitation process was slowly escaping through a barrier of relatively refractory units (excitation time averaging more than 2.5 time-steps per unit), more peripheral units were emerging from the refractory state. The fractionated wave fronts progressed more and more rapidly, merged, and eventually swept out the whole matrix at full speed. The number of units firing increased to more than 30 per time-step, average excitation time decreased to 1.3 time-steps per unit, and the number of units in State 1 increased rapidly. As the united wave front encountered the boundary of the matrix, the number of firing units rapidly declined, until the excitation process died out.

Over the span of 36 time-steps represented in Fig. 9, the average number of units in State 1 was 365, significantly less than at the time of the sample 4(A) in Table I. The average figure is relatively less significant than the fluctuation of that number, but even the apparently periodic behavior in Fig. 8 is not necessarily indicative of periodically repetitive activity. Periodic behavior in the model could be accompanied by little or no fluctuation of the "electrical" correlates of activity, whereas aperiodic behavior could result in wide oscillations. For example, it is true that a stable circus movement flutter about an obstacle eccentrically located in a relatively small matrix would yield waves of regular amplitude, contour, and period, but it is also true that the swings would be damped out if the obstacle were centrally located or if the matrix were great in area. It could be shown that the increasing amplitude of oscillations of Group 4 was associated with a progressive decrease in the number of vortices until, at the time represented in Fig. 9, a single re-entrant circuit accounted for the last major activation of the model. It is apparent, then, that the shrinkage of turbulence imposed by the increased K value left a large area of the matrix free to recover to State 5, and to respond at full velocity. Re-entrant activity was wiped out as inhomogeneity of excitability was erased.

The very slight effect of K on conduction velocity while turbulence was still manifest in all groups merits some detailed analysis. Short of arrest of turbulent activity it can be shown, in a reduced model, that alteration of the refractory period should not

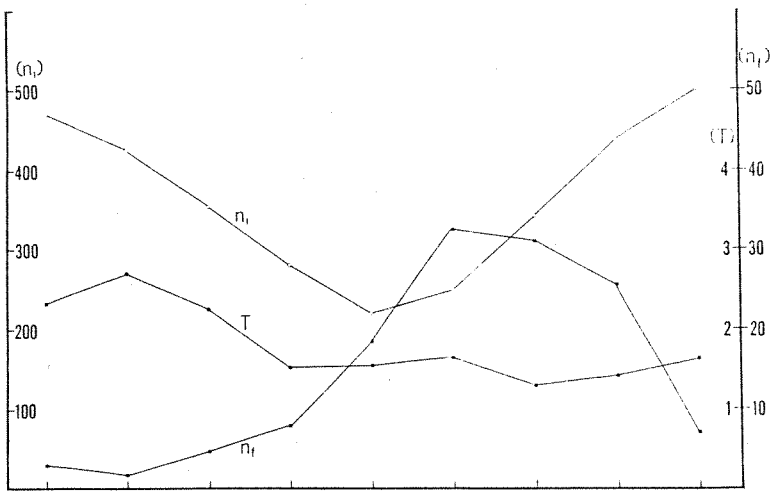

Fig. 9. Group 4, Program 2-A; events from t = 684 to 719, just prior to spontaneous arrest. Abscissae, time; intervals of 4 time-steps. Ordinates, number of units in State 1 (n_1); number of units firing per time-step (n_f); average excitation time (T). Each plotted value represents the average of 4 successive time-steps.

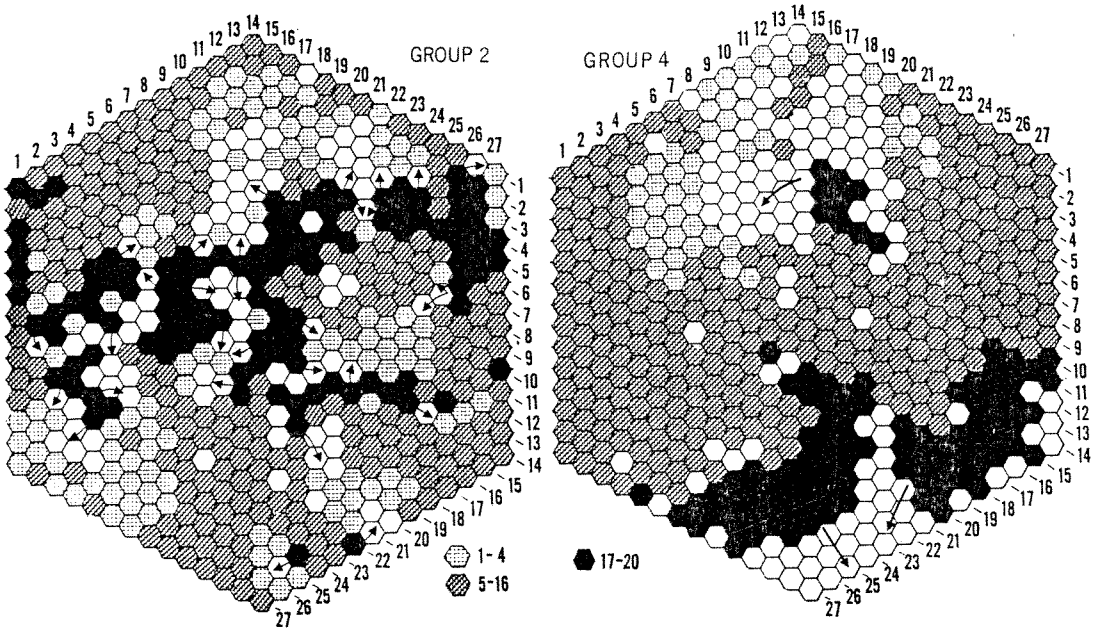

Fig. *10*. Comparison of Groups 2 and 4 of Program 2-A shortly before arrest of activity in Group 4. Group 2 on left, time 578-597, inclusive (578 = 1); Group 4 on right, time 656-675 (656 = 1). Arrows indicate direction of further activity.

significantly alter the average excitation time. In a cluster of units having the same refractory period, determined by K=5, consider 12 arranged in two contiguous columns of 6 units each, such that unit 1 is a neighbor of units 2, 3, and 4. Assume that one-way transit has been established, up one column and down the other, with a conduction time of 3 time-steps per unit. Total circuit time will be 36 time-steps, and the refractory period will be $5\sqrt{36}$ or 30 time-steps. If, now, the value of K were reduced by 10 per cent, to 4.5 a "short circuit" would occur, resulting in a 10-unit path. Total circuit time would drop to 31 time-steps, and the refractory period to 25 time-steps, but the average conduction time would increase to only 3.1 time-steps per unit. Conversely, an increase of K by 10 per cent would result in an addition of one unit to the path length. Total circuit time would increase to 41 time-steps, refractory period to 35 time-steps, and the average conduction time would become 3.15 time-steps per unit. If the system were more finely resolved, it is apparent that the net effect of a change in K would be a corresponding change in refractory period, transit time, and path length, *without any change in excitation time*. The data of Table I show that the average behavior of the four groups of Program 2 at t 400 to 500 fits this reduced conjectural model. The average wave length increased with the value K, and a further increase occurred in Group 4 as turbulence diminished, conduction velocity increased, and wave fronts coalesced.

Coalescence of wave fronts is illustrated by Fig. 10, which compares Groups 2 and 4 at a time shortly before the spontaneous arrest of the arrhythmia in Group 4. The times were not identical, for Group 4, with higher K values, was forced to operate at a slower average frequency than Group 2. Accordingly, a time was chosen when a particular "indicator" unit had fired, in both groups, for the twenty-second time. In each matrix, the units which fired during a span of 20 time-steps are represented as crosshatched areas (time t+1 to 4), diagonally striped areas (time t+5 to 16), and black areas (t+17 to 20). Where the black areas, which include the advancing wave fronts, are separated from the Class 1-4 by white areas, potential sites of re-entry exist. In Group 2, in which the average refractory period was less than 17 time-

steps, re-entry was possible without an intervening white area; in Group 4, with an average refractory period of 28 time-steps, re-entry could not occur without at least one intervening white unit. In Group 4, waves of activity swept downward on both sides, converged in the center, and emerged at the top of the diagram as a single wave front which accomplished one more activation of the matrix before expiring.

EFFECT OF UNIFORM K VALUES (PROGRAM 2-B). An additional series, also starting with 4 groups under initially identical conditions, was set up to test whether abolition of the inhomogeneity of K values would alter the behavior of the tissue. Group 1 was maintained as a control. At t=300, all K values in Group 2 were changed to the average of K values in the control group, namely, 3.85. In Groups 3 and 4 they were reduced to 3.5 and 3.16.

At the outset, all groups were inhomogeneous because of a range of K values to which was added the dephasing due to variation in the preceding cycle lengths for individual units. It was expected that the assignment of constant K values would reduce the inhomogeneity, that is, the cycle lengths would become equal. After the lapse of about 300 additional time-steps, the variation in cycle lengths disappeared in Groups 2, 3, and 4. Periodicity, however, also became apparent. Exact repetition of behavior was not apparent during the time the program was allowed to run, but in Group 3, an approximate period of 84 time-steps (involving, on the average, 4 successive excitations) was discerned. Repetitive circuits occurred at several sites in the matrix. Because the parameters of all units were equal, exact periodicity at some multiple of 21 time-steps should be expected. The run was terminated when it was decided that spontaneous arrest was unlikely.

In Fig. 11, the behavior of the control group, in which the average value of K was 3.85, is compared with Group 2, in which all units were assigned the value K = 3.85. The two patterns are reproductions of the I.B.M.-407 printout sheets taken at time-step 1505. Units labeled *S* represent those units which have been stimulated but have not yet fired. Contiguous *S* units are outlined to indicate the number of wave fronts coexisting at the selected moment.

In this program a given unit would be expected to fire repeatedly with the same cycle length; many "electrodes" spotted at various points on the surface would yield the same frequency. In other words, the deliberate introduction of homogeneity resulted in periodicity more characteristic of flutter than fibrillation.

EFFECT OF CHANGES IN GEOMETRY (PROGRAM 2-C). In the final run of this series, an attempt was made to study the influence of the size of the matrix. Group 1 of the

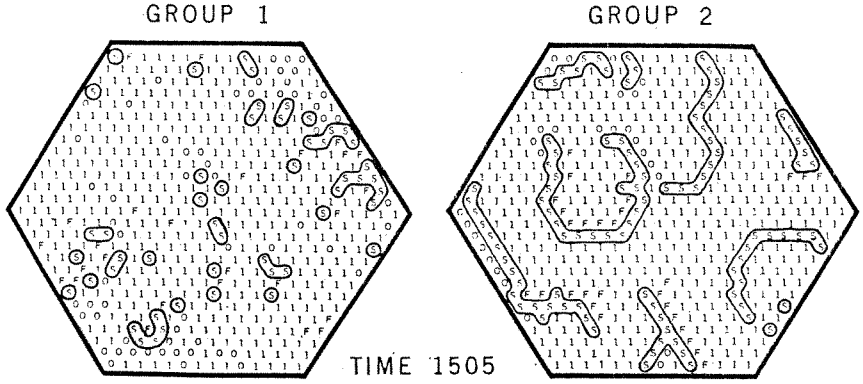

Fig. 11. Sample of hexagonal printout for Groups 1 and 2 of Program 2-B. Group 1, control with unchanged parameters. Group 2, all K values changed to 3.85 (mean of values in Group 1). Printed characters indicate state of activity: *0* = excitable (i.e., units in States 2,3,4, or 5); *1* = refractory (State 1); *S* = units excited but not yet fired. *F* = units firing in that time-step (time 1505). *S* units are outlined to define coexisting wave fronts.

prior series continued as a control. Group 2 differed by the removal of the 78 units of the outer shell; in Group 3 the two marginal layers (150 units) were removed; Group 4 was subjected to removal of 79 units by the creation of a central hole, and Group 5 was slit internally by the excision of 4 noncontiguous columns of cells. The values of K were not altered.

The number of wavelets, by comparison with Group 1, was reduced in all the experimental groups, but turbulent activity continued in all except Group 5. In this group, as illustrated in Fig. 12, activity was converted to a circus movement flutter about one of the internal obstacles. The obstacle was sufficiently large to sustain periodic behavior in perpetuity (average cycle length, 32 time-steps), and the run was therefore terminated. At the time that such periodic behavior was evident, turbulence still existed in Groups 2 and 3, but had become restricted in Group 4 to one corner of the matrix, from which nearly regular wave fronts spread in both directions about the obstacle, colliding at the opposite side. Truly periodic activity, however, had not yet developed even in this group.

Table II lists a statistical comparison of the five groups. The average refractory periods and cycle lengths of Groups 2 and 3 remained approximately equal to the control values. The average number of units firing in each time-step was reduced in the smaller matrices, and the number of stimulated units (S) was reduced out of proportion to the reduction in size. The excitation time (T) was reduced and the wave length (λ) increased in the smaller groups. The changes in the derived parameters are consistent with a reduction in turbulence, and they indicate that the chance of persistent, self-sustained, aperiodic activity was correspondingly reduced.

That size alone is not a simple determinant of the possible persistence of turbulence is apparent from the comparative behavior of Groups 4 and 5. A more appropriate factor, N/P, incorporates both size and shape. This factor, the ratio of the total number of units to the number of boundary units, provides an index of the latitude available for turbulent activity. It is approximately equal to one half the radius in the solid sheets (Groups 1, 2, and 3), or to one half the average diameter of cell columns in the groups with internal obstacles (Groups 4 and 5). It is roughly proportional to excitation time, or inversely proportional to λ, in all of the groups of Table II.

Discussion

The self-sustained activity exhibited by the model resembles experimental atrial fibrillation in several respects. The activity can be initiated by repetitive "premature" excitation, and it maintains itself after the external stimulus is withdrawn. The activity is turbulent rather than rhythmic and regular; the simulated electrical activity begins with periodic flutter-like waves which disintegrate as turbulence spreads. Like true fibrillation, the process can be arrested by sufficient prolongation of the refractory period, and, as in true fibrillation, the activity appears to become "organized" and periodic before arrest occurs. In other words, the model demon-

Table II. Effects of alteration of geometry (Program 2-C)

Group	*N*	*R*	*C*	n_t	*S*	*T*	λ	*P*	*N/P*
1	547	19.6	25.9	21.0	50.5	2.40	10.8	78	7.0
2	469	19.2	24.9	18.8	38.1	2.02	12.3	72	6.5
3	397	19.2	24.8	16.0	30.2	1.95	13.1	66	6.0
4	468	24.2	39.3	11.9	22.5	1.89	20.8	112	4.2
5	500	21.8	32.0	15.6	16.9	1.08	29.5	188	2.7

Average values based on 3 samples of 16 time-steps each, taken from 1485-1500, 1545-1560, and 1565-1580 for Groups 1,2,3, and 4. Thirty-two consecutive time-steps, 1547-1576 for Group 5. *Group 1:* Control (same independent parameters as Group 1 in Table I). *Group 2:* Outer shell removed. *Group 3:* Two outer shells removed. *Group 4:* Central hexagonal core removed. *Group 5:* Four internal columns removed. P = number of units on perimeter; other symbols as in Table I.

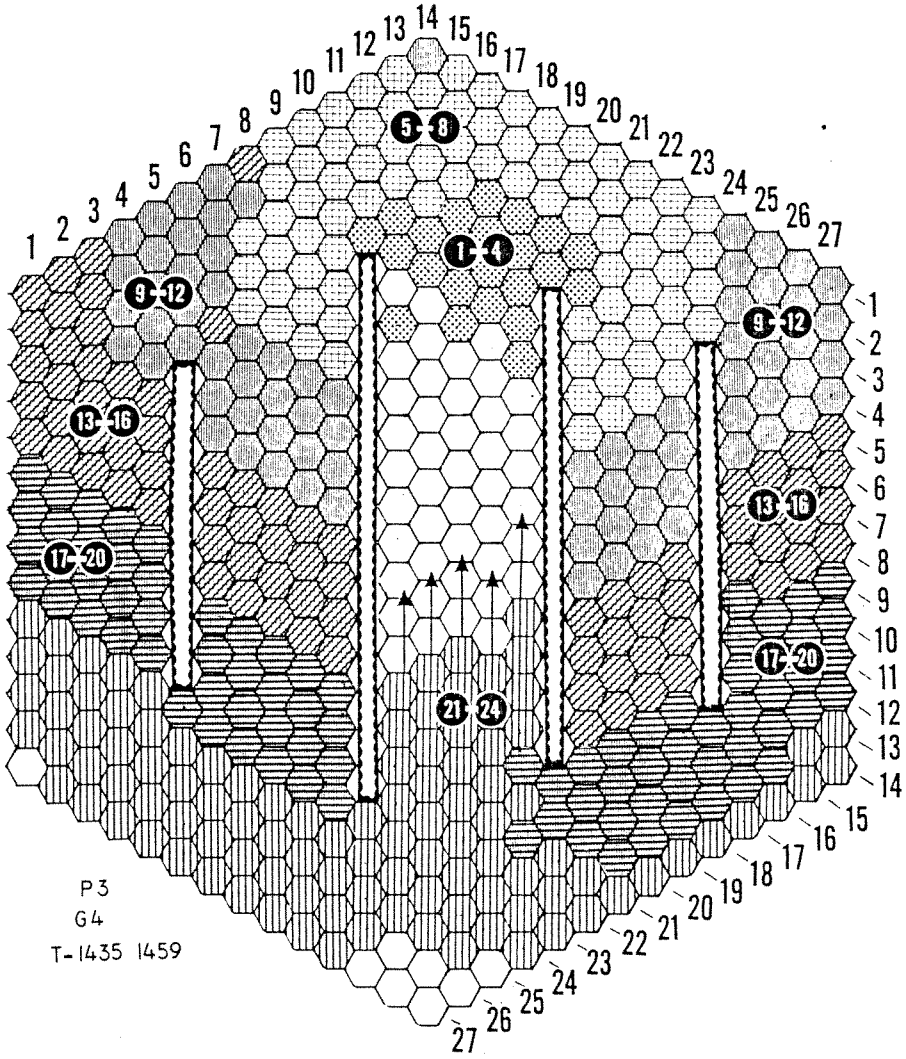

Fig. 12. Circus movement flutter in Group 5 of Program 2-C. Arrows indicate direction of advancing wave fronts.

strates that something akin to fibrillation can sustain itself in a limited system in which inhomogeneity, comparable to that observed in exposed dog atria, is built in.

Differences between the model and real tissue. In many respects the model departs from the structural and functional characteristics of living tissue. One of these, although perhaps not of cardinal importance in an assessment of the validity of the hypothesis, is the geometry. The model is a flat sheet. Topologically it could be assumed to be a sphere with a large obstacle; but the perimeter of the obstacle, unlike the boundaries of the several orifices in real atria, is large with respect to the total "mass" of the sheet. Closer simulation could be incorporated in a more complete program; for example, all units on one margin of the original sheet could be made neighbors of the units of the opposite edge; all margins could be fused to create a sphere, with or without orifices; the sheet could be folded to simulate a three-dimensional system two or more units thick. Until these extensions of the program have been studied, it is difficult to predict their influence on the activity of the network. For example, in the present simple sheet it has been obvious that many marginal

units did not participate fully in the turbulent activity characteristic of the interior of the model. Presumably this is because, having fewer neighbors, they were exposed to fewer possible routes for re-entry.

The packing of units in the model was arbitrarily chosen to provide six neighbors for each internal unit. We do not know how far this may depart from the functional anatomy of atrial tissue, but systems with smaller or greater numbers of potential contacts can be readily devised.

The model differs from living tissue in physiologic as well as anatomic features. Inhomogeneity was introduced as a random distribution of K values. Once assigned, these values remained attached to the individual units, except for major changes introduced for specific study. It is certain, however, that the "K values" in real tissue cannot be invariant. Irregular fluctuations of local refractory periods might be expected to favor persistence of truly turbulent activity.

No preferential conduction pathways were incorporated into the model, although evidence indicates that the propagation of impulses in living atria is not uniform in all directions from a stimulated site. Conduction velocity is faster in the direction of the longitudinal axes of the trabeculae than transversely.[8] This feature would probably be of little significance in the model; if we assume, for example, that the tissue units are "longer" in the *n*-axis than in the *m*-axis of the matrix, then the "velocity" of propagation is faster in that direction.

The model was constructed with fixed definition of neighbors, and with no provision for temporal or spatial summation. Models of nerve-nets incorporating summation, together with axonal transmission from remote units, have been constructed, and have been shown to exhibit more or less rhythmic self-sustained activity.[9] It is perhaps significant that the atrial model is capable of "fibrillation" without the incorporation of these additional complexities.

Analysis of turbulent impulse propagation. Admittedly, the model bears only a superficial resemblance to real atrial tissue. Nevertheless, it provides a means of examining some features of propagation in a nonuniform two-dimensional excitable medium in a manner which cannot be approached in living tissue.

The model illustrates that re-entrant circuits can be generated without an anatomic obstacle. Islands of refractory tissue have long been assumed to provide opportunities for circuit formation, although it is commonly supposed that such islands result from pathologic alteration of the properties of the tissue, and that the resultant circuits continue as fixed sources of repeated excitation of the atria or, in effect, pacemakers. In the model, numerous vortices, shifting in position and direction like eddies in a turbulent pool, accounted for the sustained activity in all programs except those in which the parameters were changed to permit fixed circuits.

Inhomogeneity was clearly necessary for the induction of self-sustained activity in the model and must be responsible for continued turbulence, but inhomogeneity was not necessary for perpetuation of a periodic flutter-like process. In the groups in which all K values were made identical, two or three residual circuits continued to operate through fixed pathways of 5 or 6 units. These conditions were grossly artificial, for exact uniformity could hardly be expected in a biologic system. If the values of K, instead of being made identical, were limited to a narrower range about the same mean value (3.85) as the control group, it is possible that the model would show an increase in apparent periodicity and a decline in turbulence. In other words, there might be no sharply defined boundary between what we may call "true" fibrillation and "true" flutter. At least in this respect the model appears to resemble certain cases of atrial dysrhythmia as observed in the clinic.

The statistical comparison in Tables I and II permit conjecture of the nature of turbulent activity in the model and of the influence of the induced alterations in K values and size upon it. It is clear that, if turbulence is characterized by drifting eddies or wave fronts, then some spatial latitude is necessary for persistent activity. To cite the extreme case, turbulence cannot be maintained in a single column of cells; even if the ends of the column were joined to form a ring, only periodic activity

would be possible. In other words, not only the total area (N) but the *shape* of the matrix is important. In the regular hexagon of unit thickness used in the present studies the "latitude" or space available for turbulent activity must be some function of the radius or total area, but it is apparent that the "space" factor would be a different function of area in matrices of different shapes. Two hexagons of equal area connected by a narrow isthmus would not be expected to sustain turbulent activity any more readily than either member alone. The probability of self-sustained aperiodic activity should be related, therefore, to the area or mass of the matrix multiplied by a constant which would be characteristic for a given shape. The preliminary correction for shape (N/P) as listed in Table II cannot be universally applicable, for such a ratio would be infinity in a closed spherical surface, yet a small sphere would be unlikely to support self-sustained turbulence.

Persistence of arrhythmia was clearly related to the mean value and the range of the assigned K values, i.e., upon the duration of the refractory periods. Fibrillation could not have been induced without the initially programmed inhomogeneity, and the self-sustained activity quickly became organized and periodic when the K values were equalized. It is safe to conclude that persistence is directly related to some function of the range of K and inversely related to some function of the mean value. The precise definition of the appropriate functions, however, is not yet apparent. For example, persistence is not simply related to the ratio of the range of K to the mean of K, for this ratio was constant in the four groups of Program 2-A (Table I). Nor does the range of K describe the full influence of the frequency distribution and the random geometric distribution of the 11 families of K. If, for example, only the classes $K = \sqrt{10}$ and $K = \sqrt{20}$ were included, and if all the values $\sqrt{10}$ were placed on one side and all the values $\sqrt{20}$ on the other side of a dividing line, then turbulent activity would surely be impossible, yet the range and the mean of K would be the same as in Program 1. "Some function of the range" would, therefore, have to take into account the range, frequency distribution, and random disposition of K values.

It is probable that the influence of the range of K becomes incorporated into the dependent variable, T. It was shown in Table I that the average value of T did not change very much as the value of K increased, and an argument was presented to explain the apparent insensitivity of that parameter. It should be obvious that during self-sustained activity a wave front will move at the maximum velocity permitted by the state of recovery of the surrounding units, and that re-entry of any given unit in a circuit will, correspondingly, occur over the briefest (not necessarily the *shortest*) possible pathway. If such a pathway includes units with different values of K, as it must do in the several groups of Program 2-A, then the conduction velocity cannot be constant. The impulse will be maximally delayed by units which are in State 2, and will accelerate when traversing units in a more advanced stage of recovery. The mean excitation time will accordingly have to be less than 4 and more than 1, but the range of T will be wide. If all the values of K are made equal, as in Program 2-B, the briefest path will also be the shortest in distance, but the excitation time at each unit in the circuit will be maximal. On the other hand, in the group in which a stable circus movement resulted, the excitation time was reduced to the minimal value of 1 in all but a few units. In the latter case, the programmed inhomogeneity, although still present, was no longer operative; nearly all units were in State 5 when the excitatory process reached them. In both cases, self-sustained activity continued, but in a completely periodic manner. Turbulence, in other words, was eliminated when inhomogeneity with respect to conduction velocity was abolished, whether by eliminating the initial variation of K values or by introducing anatomic barriers.

The inhomogeneity with respect to conduction time can be expressed as the standard deviation of T. The deviation is the result of the programmed spread of K values, but it is also influenced by the geometric configuration. A wide range of K has no significance if the system is driven at slow frequency, for all units will re-

spond at full speed; the group in which circus movement flutter became established (Table II) is a case in point. These considerations lead to the conclusion that turbulent activity was characterized by a wide range of variation of conduction velocity, whereas periodic activity was associated with more nearly constant velocity at either minimal or maximal values.*

The parameters of size, shape, and range and mean value of K, do not provide a direct index of the likelihood of persistence of turbulence. The comparison of Group 4 of Program 2-A at the times represented in Table I indicates that the parameters directly derived from K (i.e., R and C) did not change appreciably as turbulence abated, whereas the parameters T and λ clearly indicated the approaching arrest. Similar conclusions can be drawn from Table II. In Groups 1,2,3, all of similar shape but differing in size, neither R nor C provides a measure of the stability of the arrhythmia, whereas T and λ differentiate the groups.

It is clear enough that the wave length must increase as R and C are increased. It is perhaps less obvious that λ must also increase when the "spatial freedom" available for turbulent activity is constricted. A re-entrant circuit may be responsible for the excitation of its surrounding domain for one or more successive passages. In a matrix of sufficient size, this domain may be invaded and the re-entrant circuit wiped out by newly generated circuits in closely adjacent areas, with the result that most of the units within that domain are again excited while they are still relatively refractory. If, however, a circuit becomes extinguished and is not replaced at once, as is likely when the distance to boundaries is diminished, the units in its field will be permitted to advance to a more complete stage of recovery, with the result that wave fronts entering from more remote sites of impulse generation will accelerate and coalesce. Adjacent units will, in other words, become "re-phased," and the possibility of renewed turbulence will be reduced. This will deprive still existing re-entrant circuits of possible substitute excitation sources when they, in turn, fall victim to chance extinction. The result will be an acceleration of conduction (reduction of T) and an increase of λ, together with a further regression of turbulence.

The changes in λ and T can occur without comparably striking changes in R and C (Table I, Groups 4(A) and 4(B); Table II, Groups 1,2, and 3). This is not surprising, for a shift from an average excitation time of 2 time-steps to 1 time-step could be accomplished by allowing a single additional time-step for recovery. For example, a unit with cycle duration of 25 time-steps and a refractory period of 18, determined by K = 3.6, would have an excitation time of 2 time-steps if a neighbor fired during the twenty-fourth time-step of the cycle; but if the neighbor fired at the twenty-fifth time-step, excitation time would be reduced to 1 time-step, while C and R remained unchanged.

A "fibrillation number." The considerations outlined above suggest that the conditions which permit turbulence may be expressed in a form resembling the definition of the Reynolds number in fluid dynamics. Let us assume that the atrial model, instead of being "discretized" in time and space, is a continuous model. Then, as applied to geometrically similar atrial models, equality of a suitable "fibrillation" number at all corresponding points and times would be a condition for dynamic similarity of the propagation pattern in the models. If the propagation pattern is defined by the conduction time T (the inverse of conduction velocity) as the dependent variable, and by the parameters K as "materials" constants, then it can be shown by dimensional-analytic arguments that the fibrillation number has to have the form

$$\frac{LT}{K^2},$$

in which L is a characteristic length that identifies the size of the particular model within the set of geometrically similar models. The fibrillation number will depend

*Clearly this does not imply that periodic activity is possible only at the limiting values of T. Intermediate values would be obtained if appropriate *constant* values of K were assigned in association with an obstacle of smaller size. If, however, nonuniform distribution of K values were retained, a sufficient reduction in obstacle perimeter would again yield turbulence, and would be incompatible with a stable circus movement flutter.

on the particular point and on the time. Two geometrically similar continuous models will exhibit a dynamically similar propagation pattern if at all corresponding points the above dimensionless numbers are identical for all corresponding times.

For the discrete model this does not immediately apply, since point-by-point dynamic similarity cannot exist unless the models are geometrically equal (not just similar). However, in similarity with the properties of the Reynolds number, one may conjecture that the number indicates whether the propagation pattern in a continuous model is laminar or turbulent. For the discrete model we may ask whether, instead of a "local" fibrillation number changing from point to point, a suitable "global" index exists which indicates whether propagation is laminar or turbulent. As such a global index, one might use the average of the individual local fibrillation numbers. However, the discussions presented earlier suggest that an empirical relationship which permits comparison of some of the groups of Program 2 may be expressed in the form:

$$F' = \frac{L\sigma_T}{\bar{K}^2},$$

where σ_T represents the standard deviation of T, and $\bar{K}$ represents the average value of K. This dimensionless index is obviously related to the local fibrillation number, LT/K^2, but further study of the model and its mathematical properties will be necessary to arrive at a clearer understanding of these numbers and their properties as indicators of laminar or turbulent propagation patterns.

Application of this formula to the results obtained in the groups studied so far is illustrated in Table III. The expression N/P (i.e., the ratio of area to perimeter) is substituted as a convenient approximation of L, recognizing that it cannot be strictly appropriate for comparison of dissimilar groups. The data suggest that the critical value of F′ is close to 0.5 within the four groups of Program 2-A, in which only the assigned values of K were changed; and in Groups 1,2, and 3 of Program 2-C, which differed in size but not in shape. Groups 4 and 5 of Program 2-C, in which internal obstacles were created, cannot be directly compared with each other or with the other groups; but in Group 4, arrest or periodicity was approaching, and in Group 5 a circus movement flutter had established itself at the time of the samples from which the tabulated values were calculated. Group 2 of Program 2-B had also become periodic.

The wavelet hypothesis. Beyond providing an opportunity to relate the number of individual wave fronts to various induced alterations in the parameters of the matrices, the model adds little to the wavelet

Table III. *Average values used in calculation of F′**

Group	*N/P*	*T*	σ_T	K^2	*F′*	*Remarks*
2A-2	7.0	2.34	1.20	12.0	.70	
2A-1	7.0	2.32	1.23	14.8	.58	
2A-3	7.0	2.28	1.25	17.9	.49	
2A-4(A)	7.0	2.19	1.23	21.3	.40	
2A-4(B)	7.0	1.55	1.04	21.3	.34	Arrested
2C 1	7.0	2.32	1.23	14.8	.58	
2C 2	6.5	2.02	1.18	14.8	.52	
2C 3	6.0	1.95	1.13	14.8	.46	
2C 4	4.2	1.89	1.13	14.8	.32	
2C 5	2.7	1.08	.28	14.8	.05	Periodic
2B 2	7.0	3.96	.21	14.8	.10	Periodic

*In relation: $F' = \frac{L\sigma_T}{\bar{K}^2}$. Samples cover same time span as corresponding groups in Tables I and II. N/P has been used as an approximation of L.

hypothesis as originally proposed. Alterations expected to reduce the likelihood of persistence (increased refractory period, decreased size) do indeed reduce the number of wavelets, but it is apparent that a mere numerical tally provides neither an adequate description of mechanism nor a basis for predicting future status. Numerous wavelets, fractionated in the sense of noncontiguity, may represent fragments of a relatively uniform process, sweeping across relatively large areas without providing opportunity for re-entry. In other words, a single impulse generator beating at a sufficiently high frequency could yield as many individual wavelets as the more complex self-sustained activity described above. Previously published studies have indicated the superficial similarity but difference in mechanisms between these two forms of dysrhythmia.[1] To assess the functional significance of the number of wavelets in existence at a given moment it would be necessary to know their past history and future course, attributes difficult to describe quantitatively. In short, the model supplies insight into possible mechanisms of sustained turbulent impulse propagation, but has not yet provided a stringent and exclusive definition of fibrillation.

Summary

A mathematical model of impulse propagation in a nonuniform two-dimensional system was prepared as a program for a digital computer. The model exhibited self-sustained turbulent activity having many similarities to atrial fibrillation. The activity was not the result of fixed impulse generators or circuits, but was sustained by irregular drifting eddies which varied in position, number, and size. Increasing the refractory periods while retaining nonuniformity resulted in arrest of activity. Restoration of absolute uniformity resulted in periodic activity characterized by fixed re-entrant circuits without obstacles. Reduction of the area of the model altered the self-sustained activity in the direction of arrest, and the creation of internal obstacles resulted in a periodic circus movement flutter. The behavior of the model suggests the formulation of a "fibrillation" number, similar in concept to the Reynolds number related to turbulence in fluid flow.

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REFERENCES

1. Moe, G. K., and Abildskov, J. A.: Atrial fibrillation as a self-sustaining arrhythmia independent of focal discharge, Am. Heart J. **58**:59, 1959.
2. Moe, G. K.: On the multiple wavelet hypothesis of atrial fibrillation, Arch. int. pharmacodyn. **140**:183, 1962.
3. Alessi, R., Nusynowitz, M., Abildskov, J. A., and Moe, G. K.: Nonuniform distribution of vagal effects on the atrial refractory period, Am. J. Physiol. **194**:406, 1958.
4. Mendez, C., Gruhzit, C., and Moe, G. K.: Influence of cycle length upon refractory period of auricles, ventricles, and A-V node in the dog, Am. J. Physiol. **184**:287, 1956.
5. Siebens, A. A., Hoffman, B. F., Gilbert, J. L., and Suckling, E. E.: Effect of rate on excitability of dog's ventricle, Am. J. Physiol. **166**:610, 1951.
6. Rheinboldt, W. C., and Mesztenyi, C. K.: Computer simulation of propagation phenomena in atrial tissue. (To be published.)
7. Sano, T., Tsuchihashi, H., and Shimamoto, T.: Ventricular fibrillation studied by the microelectrode method, Circulation Res. **6**:41, 1958.
8. Woodbury, J. W., and Crill, W. E.: On the problem of impulse conduction in the atrium, *In* International Symposium on Nervous Inhibition, 1960, New York, 1961, Pergamon Press, pp. 124-135.
9. Farley, B. G.: Some results of computer simulation of neuron-like nets, Fed. Proc. **21**:92, 1962.