Mechanism of Generation of Body Surface Electrocardiographic P-Waves in Normal, Middle, and Lower Sinus Rhythms

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SUMMARY We used comprehensive electrophysiological/anatomical digital computer models of atrial excitation and the human torso to study the mechanism of generation of body surface P-waves in normal sinus rhythm, and in middle and lower sinus rhythm. Simulated atrial surface isochrone maps for normal sinus rhythm support the validity of the atrial excitation model. The results suggest that the presence of specialized internodal tracts containing fast-conducting fibers is not essential to account for propagation of excitation in apparent preferential directions from the sinoatrial (SA) node to the interatrial septum. P-wave notches occur in the absence of specialized fast conducting atrial tracts and anisotropies due to fiber orientation. These notches are due to the atrial geometry and the separate contributions of the right atrium, left atrium, and interatrial septum to the P-waves, and become more pronounced as the pacemaker site shifts downward in the SA node. Thus, slight changes in the origin of excitation, which result in subtle changes in the atrial excitation isochrones, produce significant and complex changes in the simulated body surface P-waves.


THE site of origin of normal atrial pacemaker activity is not necessarily fixed. According to Merideth and Titus (Merideth and Titus, 1968) and James (James et al., 1966), it may vary as much as 15 mm. Spach (Spach et al., 1971) showed that in rabbits and dogs, the sinoatrial (SA) nodal impulse may vary within the crista terminalis from higher to lower locations down to the level of the limbus. (Durrer et al., 1970) indicated the difficulties in locating the origin of the SA node impulse in human atria. Major, if not insurmountable, difficulties have arisen in electrophysiological experiments to elucidate the mechanism of generation of body surface P-waves by an intact human heart.

Recent advances in developing realistic anatomical/electrophysiological digital computer models of human cardiac activation have demonstrated the usefulness of computer simulation as a basic investigative tool (Horacek and Ritsema van Eck, 1972; Horacek, 1973; Horacek et al., 1973; Horacek, 1974; Macchi, 1974; Ritsema van Eck, 1974). In the present investigation, a comprehensive electrophysiological/anatomical model of the human atria has been incorporated with a realistic replica of the inhomogeneous human torso and the numerical solution formulated by Horacek (1973) to generate body surface P-waves resulting from atrial activation originating at various sites within the SA node.

The primary purpose of this investigation was to examine the mechanism of generation of P-waves by studying the separate contributions by the right atrium, interatrial septum, and left atrium to the total composite P-waves as manifested in commonly used ECG leads. The second objective was to determine how SA nodal pacemaker shifts can best be identified from P-wave waveforms.

Methods

A digital model for simulating electrical activity in the human heart was used to simulate atrial activation and repolarization for upper, middle, and lower SA nodal rhythms. This model is described in detail in Appendix I. Each element of the model was assumed to be electrically homogeneous and isotropic. No specialized internodal atrial pathways were included in the model. Also, possible special electrical properties of gross structures such as the limbus of the fossa ovalis were not included. However, a region of slow conduction (1/5th normal conduction velocity) approximately 3 cm long and less than 1 cm wide was introduced along the crista terminalis from the superior vena cava to the interatrial septum. This slow conducting region represents the sole inhomogeneity in the atrial model. For upper, middle, and lower SA nodal rhythms, activation was assumed to start in an element in the center of the appropriate region of the SA node.

Using the procedure described in Appendix II, the resulting atrial activation sequences were used...
to calculate current dipoles at 41 locations in the atria, and these dipole vector functions were used in turn to calculate unipolar P-wave potentials at 128 sites on the surface of the inhomogeneous torso model. The unipolar potentials then were used to determine the standard 12 lead and Frank XYZ lead P-waves using standard lead equations. The separate right atrial (RA), interatrial septal (IAS), and left atrial (LA) contributions to the P-waves were determined from the appropriate subset of dipoles. Of the 41 atrial dipole source locations (DSLs), 18 were considered to be RA, 15 LA, and 8 IAS. There were 10,733 elements in the RA DSL fields, 8,003 in the LA DSL fields, and 5,677 in the IAS fields. Figure 1 shows the DSL fields on the superior and posterior-lateral atrial surfaces and on the right atrial surface of the interatrial septum, and indicates the relative position of the atria in the torso model. Note that the majority of the DSLs lie within the atrial walls and do not appear on the atrial surfaces. However, at least some portion of all DSL fields except that of DSL 33 does appear on the surface for one of the three views shown.

Results

Atrial Activation Sequences for Upper, Middle, and Lower SA Nodal Rhythms

The atrial activation sequence for upper SA nodal rhythm is depicted in Figure 2 as isochronous maps of excitation arrival times on the superior and posterior-lateral atrial surfaces and the right side of the interatrial septum. Excitation spreads initially from the SA node in the right atrium anteriorly around the superior vena cava through the arch of the crista terminals and simultaneously inferiorly and to the right in the posterior RA free wall, along the sulcus terminals (Fig. 2B). The superior-anterior right atrial excitation wavefront proceeds anteriorly and to the left along the anatomical region of Bachmann's bundle where it reaches the border between the right and left atrium and the upper border of the interatrial septum after approximately 36 msec (Fig. 2, B and C). The tip of the right atrial appendage is excited after about 60 msec, and right atrial excitation is completed shortly after 84 msec from the initiation of excitation at the SA node.
After excitation of the thick musculature in the region of Bachmann’s bundle, the left atrium is excited in broad concentric semicircular rings which extend through the posterolateral free wall. The regularity of these excitation fronts is disturbed somewhat in the posterior left atrial wall by the right pulmonary veins. The tip of the left atrial appendage is excited at 120 msec, and at about the same time the left atrial excitation wavefronts extinguish below the left atrial appendage.

As the pacemaker site is shifted down the SA node, there is a progressive decrease in the time for completion of RA excitation, an increase in the times for initiation and completion of LA excitation, and a shift in the pattern of IAS excitation from the superior-inferior direction to a more posterior-anterior direction (Figs. 3 and 4). In addition, RA excitation assumes a posterior-anterior direction on the superior surface and a concentric pattern posteriorly.

P-Waves for Upper SA Nodal Rhythm

Figure 5A shows unipolar P-wave potentials at 128 sites on the surface of the inhomogeneous torso model for simulated upper SA nodal rhythm. The waves on the upper torso (rows 2–5) are predominantly negative, with late positivity in the left posterior region (columns L-P) in rows 4 and 5. On the lower torso (rows 8–10), the potentials are predominantly positive. In the midtorso region (rows 6 and 7, the 4th and 6th intercostal spaces), the waves are strongly biphasic on the mid-anterior surface (columns D-G) and predominantly positive in the left anterior and posterior regions (columns A-C, L-P).
The right-sided mid-torso potential waves (both anteriorly and posteriorly, columns H-K) show transitional forms between those characteristic of the upper and lower torso.

The simulated Frank XYZ lead P-waves for upper SA nodal rhythm are shown in Figure 5B (top), along with the RA, LA, and IAS components (R, L, and S, respectively) of these waves. From these tracings it is seen that the initial and secondary positive peaks in X and Y are caused mainly by RA activity. In Y, the tertiary positive peak is due primarily to LA activity. Septal activation gives very little contribution to X but adds to late RA and early LA activity to account for the large sharp tertiary peak in Y. The separate contributions of the right and left atria to the P-wave are seen most clearly in Z, with RA activity giving the initial negative wave, and LA activity the succeeding positive wave. Septal activity reduces the magnitude of the negative peak in Z and adds to the early portion of the positive wave. The small notch early in the positive wave in the Z lead is due to late RA and mid IAS activity subtracting from early LA activation.

The right-sided mid-torso potential waves (both anteriorly and posteriorly, columns H-K) show transitional forms between those characteristic of the upper and lower torso.

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The corresponding P-III and P-aVL are shown in Figure 5C. Note that P-III is a relatively large positive wave for upper SA nodal rhythm, whereas P-aVL is a negative wave of smaller magnitude.

Although all 15 standard leads are not shown in Figure 5, the simulated P-waves for upper SA nodal rhythm show the basic features of normal ECG's, being positive in leads I, II, III, (and tallest in II), aVF, X, and Y, and negative in aVR (and aVL). The Z lead is biphasic and the chest leads (as may be deduced from Figure 5A) show a gradual transition, being biphasic in V1, but positive in V4, V5 and V6. P-amplitude in the chest leads is greatest in V2 and least in V6. The waveforms in I and V6 are quite similar to X, and II and aVF are similar to Y. As in the Z-lead, the separate contributions of RA and LA activity to the P-waves are also clearly seen in V1, where RA excitation causes an early positive deflection and LA excitation a succeeding negative deflection.

P-Waves for Middle SA Nodal Rhythm

Figure 6 shows the 128 body surface unipolar P-wave potentials (A), the Frank XYZ lead P-waves along with the separate RA, LA, and IAS contributions to these waves (B), and P-III and P-aVL
(C) for simulated middle SA nodal rhythm. For middle SA nodal rhythm, the potentials on the upper and lower torso generally are diminished in magnitude and there is now late positivity in the upper right posterior waveforms and late negativity in the lower right anterior waves (Figure 6A). The potentials in the midtorso are now all negative in the right mid-axillary region (columns G-J), positive in the left anterior and left to mid-posterior regions (columns A-C, K-P), and biphasic in the mid-sternal region (columns D-F), including rows 5 and 8.

From Figure 6B it is seen that RA activity again gives rise to the initial positive wave in X and Y and the initial negative wave in Z. LA activity accounts for the secondary positive wave in all three leads. Because of the difference in sign, the separate contributions from RA and LA activity are seen most clearly in Z. IAS activity is masked in X, and adds to late RA and early LA activity to give the secondary peak on the initial positive wave in Y. In the Z lead, IAS activity reduces the negative deflection and contributes to the initial peak on the positive wave.

The general features of the simulated P-waves in the 15 standard leads for middle SA nodal rhythm are similar to those resulting from upper SA nodal rhythm. The major differences are that the magnitude of P-III is decreased and polarity of P-aVL is reversed, becoming predominantly a positive wave, as shown in Figure 6C. In addition, the peaks in leads I (similar to X), V1-V6 (as may be deduced from Fig. 6A), X and Z (Fig. 6B) are sharper.

P-Waves for Lower SA Nodal Rhythm

For lower SA nodal rhythm, the potentials on the upper and lower torso are further diminished in magnitude and become positive on the upper torso with the exception of the right mid-axillary region, and negative in the lower torso in the right mid-axillary region (Fig. 7A). In the midtorso region, the waveforms are negative on the right and positive on the left, both anteriorly and posteriorly. Notches are apparent near the peak of the early positive wave in the right mid-torso region. In the mid-sternal region, biphasic waveforms are apparent in rows 4 through 9.

As in the two previous cases, the separate contributions of RA and LA activity are seen most readily in the Z lead, but are now also apparent in Y (Fig. 7B). The notch near the peak of the early dominant wave in lead X arises from RA activity. There is a discernable IAS contribution to lead X giving rise to a positive peak near the tail of the P-wave.
P-WAVES AND SA NODAL SHIFTS/Eifler et al.

**Figure 5** Simulated P-waves on the surface of the inhomogeneous torso model for upper SA nodal rhythm. A: Body grid P-waves. RMAL and LMAL = right and left mid-axillary lines. MSL = mid-sternal line. VC = vertebral column. Rows 6 and 7 represent the levels of the 4th and 6th intercostal spaces. Note that the RMAL potentials (column 1) are repeated at the extreme left and right. B: Frank XYZ lead P-waves (top) and the separate RA, LA, and IAS contributions to these P-waves (R, L, and S, respectively). C: P-III and P-aVL. Horizontal bar represents 50 msec and vertical bar 50 V.

The general form of the simulated P-waves for lower SA nodal rhythm is again similar to that for upper SA nodal rhythm but here, in addition to a positive aVL as in middle SA nodal rhythm, lead III becomes predominantly negative (Fig. 7C). Also, II and aVF (both similar to Y) show early negativity and there is a distinct notch near the positive peak in leads I (similar to X), II, aVR, aVF, and V1-V6 (as may be deduced from Fig. 7A) arising from RA activity.

**Discussion**

The existence of notches (local maxima or minima) in the P-wave has been known for some time (Takayasu, 1937a, 1937b, 1937c; Langner, 1952; DeCommence et al., 1955; Abildskov et al., 1955; Irisawa and Seyama, 1966; Brody et al., 1967a, 1967b; Woolsey et al., 1967; Brody et al., 1969; Selvester and Pearson, 1971; Duchosal et al., 1971), and the relationship between this notching and shifts in the site of origin of pacemaker activity within the SA node has been the subject of often contradictory speculation (Sano and Yamagishi, 1965; James et al., 1966; Merideth and Titus, 1968; Durrer et al., 1970; Goodman et al., 1971; Spach et al., 1971; Spach et al., 1972). No single explanation has emerged. Brody et al. (1967b) proposed three possible mechanisms for P-wave notching: (1) small shifts in pacemaker location within the SA node, (2) variable exit from the SA node, and (3) changes in dominance of preferential conduction pathways in the atria, the very existence of which has been
the subject of much controversy (Janse and Anderson, 1974). Boineau et al. (1978) have proposed mechanisms similar to (1) and (2) to explain varying dominance of trifocal origin of atrial excitation observed in the dog heart. To elucidate the problem, a comprehensive anatomical/electrophysiological model of the human atria has been used in conjunction with a realistic model of the inhomogeneous human torso (Horacek, 1973) to investigate the effects of SA nodal shifts on standard lead P-waves as well as the separate contributions of RA, IAS, and LA activity to these P-waves.

The simulated atrial excitation patterns generated by our atrial model agree with a number of reports on experimental observations. The 1916 report by Bachmann (1916) states that, in the dog, "the most important path of conduction between the two auricles appears to be the interauricular band." This observation has been confirmed by a number of other investigators (Puech et al., 1954; Matsuoka, 1957; Oishi, 1967; Spach et al., 1969). Matsuoka (1957) also noted that the activation wave propagates from the posterior inferior region of the right atrium to a small region of the lower left atrium. Oishi (1967) also produced evidence that, in addition to Bachmann's bundle, the left atrium is excited through a pathway between the inferior vena cava and the right lower pulmonary vein. The changes in atrial excitation patterns associated with shifts in the site of initiation within the SA node are consistent with those recently observed in the dog atria (Boineau et al., 1978).

Of particular importance regarding the validity of our atrial model are experimental observations on the pattern of activation of the interatrial septum and the intercaval region. A region with very slow conduction between the crista terminalis and septum has been identified in the rabbit atria (Sano...
and Yamagishi, 1965). It also has been reported
that serial sections of the intercaval region showed
fiber-to-fiber connection only along three anatomical
"internodal" routes, these tracts being surrounded by extensive connective tissue (Meridith
and Titus, 1968). Earlier (Yamada et al., 1965), it
was demonstrated that in dog and rabbit the sep-
tum receives excitation through the arch of the
crista from above downward.

Clear evidence of the excitation traveling to the
left atrium superiorly across the region of Bach-
mann's bundle and inferiorly in a leftward direction
across the area adjacent to the coronary sinus is
displayed by the potential maps on the dog's atrial
surface (Spach et al., 1969). A precise analysis of
the septal excitation sequence (Spach et al., 1971)
indicates no conduction between the crista termi-
nalis and the adjacent intercaval area of the upper
septum of the adult dog. In the rabbit, the septum
was excited only from the arch of the crista and
from above downward. These observations agree
with the septal excitation maps in rabbit atria
(Janse and Andersen, 1974) supporting the validity
of our model.

The above observations substantiate the pres-
ence of a slower conducting region parallel to the
crista terminalis toward the interatrial septum. The
addition of this slow conducting region was neces-
sary to achieve the correct sequence of septal acti-
vation.

It should be recognized that excitation waves in
the atria—by necessity—take the route between
natural anatomical obstacles. This fact, in itself,
may adequately account for the observations of
Matsuoka (1957) and Oishi (1967) regarding the
preferential pathways in the atria. It is important
to recognize the meaning of so-called preferential
pathways in a model or real structure if it is as-

**FIGURE 7** Simulated P-waves on the surface of the inhomogeneous torso model for lower SA nodal rhythm. A, B, C,
symbols and scaling as in Figure 5.
sumed that there are no fast conducting fibers. Preferential propagation will appear to take place in a given direction where there are no anatomical obstacles. Such obstacles occur (1) where vessels penetrate into the atria and (2) where muscle fibers are sparse or absent. In addition, (3) surface irregularities can produce the appearance of faster conduction across less undulated regions. For example, wavefront propagation appears slower along the line from the SA node to the RAA in Figure 2A than in adjacent tissue. This is due to the existence of an elevated region along this line that does not appear in the planar projection. Any appearance of preferential propagation in Figures 2, 3, or 4 can be accounted for by the three factors mentioned above.

Using the 15 common ECG leads (standard 12-leads plus XYZ) resulting from simulated atrial excitation, shifts in the site of origin within the SA node are most clearly evident from examination of leads aVL and III. As seen from a comparison of Figures 5C and 6C, a shift in the origin of excitation from the upper to the middle SA node is discernable by a change in polarity in the P-wave in lead aVL from negative to positive. At the same time, P-III decreases in magnitude. The positivity of aVL increases when the site of excitation shifts to the lower SA node (Figure 7C), and the lead III P-wave changes sign (from positive to negative); this is in agreement with the findings of Brody et al. (1967a). In addition, a prominent notch appears near the peak of the positive wave in the precordial leads, as may be deduced from Figure 7A.

The effects of SA nodal shifts on P-aVL and P-III can be explained by examining the atrial excitation sequences (Figs. 2-4) and the appropriate unipolar P-waves (Figs. 5A, 6A, and 7A). As the origin of excitation shifts down the SA node, the shift in RA and IAS excitation patterns causes the potentials in the region of the right arm (ra) to become less negative, those in the region of the left arm (la) to reverse polarity, and the left leg (ll) potentials to become less positive. Therefore, P-III (= II-la), which is positive for upper SA nodal rhythm, decreases in magnitude as pacing shifts to the middle SA node, and becomes negative for lower SA nodal rhythm. P-aVL (= la − ½ ra − ½ ll), which is initially negative, reverses polarity, then increases in magnitude.

For all three SA nodal rhythms, RA activity contributes to the early portion of the P-wave and LA activity to the later portion in all leads. Although the separate RA and LA contributions cause separate peaks in the P-waves in all 15 leads, the effects are most readily discernable in lead Z (Figs. 5B, 6B, and 7B) because the RA and LA activity here give rise to waves of opposite polarity. As the stimulus site moves from the upper, to the middle, to the lower SA node, there is a progressively greater delay between RA and LA activation (Figs. 2-4); RA excitation becomes closer to completion prior to the onset of LA excitation, and the separation between the RA and LA contributions to the P-waves becomes more pronounced in all 15 leads. This is particularly evident in the V lead in Figures 5-7 and is consistent with recent observations in the dog (Boineau et al., 1978), where shifts in early atrial epicardial activation to lower centers in the region of the superior vena cava resulted in increased P-wave notching. The impact of IAS activity on the body surface P-waves comes during the end of the RA contribution and the beginning of the LA contribution, giving rise to small, though generally not easily discernable notches. The contribution of the IAS is most clearly discernable in lower SA nodal rhythm (Fig. 7), giving rise to a positive peak near the tail end of the P wave in X (as well as I, V5, and V6).

In interpreting the results of the model simulation of body surface P-waves, the limitations of the model (and modeling) must be kept in mind. Of particular importance to this study are the following: (1) Atrial tissue has been assumed to be isotropic, with radial spread of activation from a given element to each of its 12 neighbors at the same velocity. That is, there are no directional differences in propagation velocity despite the probability of higher velocity of propagation of the activation wavefronts in the fiber direction (Eiffer and Plonsey, 1975), particularly along the axis of the atrial trabecula. (2) No special internodal conduction pathways have been included in the atrial model. The possible existence of such pathways remains controversial (Janse and Andersen, 1974). (3) A region of slow conducting fibers has been introduced along the crista terminalis. Evidence for its existence, though inconclusive, is based on histological and electrophysiological observations (Meredith and Titus, 1968; Spach et al., 1971; Sano and Yamagishi, 1965). (4) The potential of each individual cardiac element has been assumed to be uniform at each instant of time. The current dipoles existing at the interfaces between neighboring elements by virtue of the potential difference across the interface have been referred to the appropriate DSL via vector addition with all such dipoles in the DSL field. Higher moments have been ignored. (5) The potential of the boundary shell elements in the region of an interface with an atrial element has been assumed to be equal to that of the atrial element. Since a typical shell element borders several different atrial elements, each at a different potential at a given instant of time, a potential gradient must exist within the shell element. Dipoles arising as a consequence of this potential gradient have been ignored.

Some of these assumptions are rather crude. However, despite the first two, the resulting activation sequences are quite similar to those observed in the normal atria, in part because of the third assumption. Further, as seen from the isochronous activation maps of Figures 2-4, the overall spread of excitation does not appear uniform in planar.
projections of the atrial surfaces, giving an impression of increased conduction velocity along preferential pathways. This is a result of natural anatomic obstacles, not the presence of fast conducting pathways, and occurs despite the assumption of uniform radial spread of activation from element to element. Despite the last two assumptions, the simulated P-waves have both the same form and order of magnitude as those obtained from the normal human subject. Perhaps the major advantage of the atrial-torso models is that they allow rigid control of the experimental situation and separation of the effects of RA, LA, and IAS activity on the resulting waveforms.

Bearing in mind the limitations of the models, one can make several conclusions from the simulation studies: (1) Special conducting atrial pathways are not a prerequisite for normal P-wave morphology. The model simulations give rise to normal atrial activation sequences and normal P-waves on the surface of the inhomogeneous torso model via the inclusion of a slow conducting region along the crista terminalis, without the inclusion of specialized fast conducting bundles in the atria. This observation supports arguments in favor of the existence of such a slow conducting region as well as those against the existence of fast conducting atrial pathways. (2) P-wave notching under normal conditions results from separate RA, IAS, and LA contributions to the body surface potentials, and need not be explained as resulting from separate waves propagating along preferential conduction routes, or simply the delay between depolarization of the left and right atrial appendices. The separate peaks resulting from RA, IAS, and LA activity, and hence the P-wave notches, become more apparent as the pacemaker site shifts from the upper to the lower SA node. In addition, notching appears near the peak of the early (RA) wave, particularly in X and the precordial leads, in lower SA nodal rhythm due to separate excitation fronts propagating simultaneously inferiorly and superiorly along the RA free wall. The presence of these separate fronts is due to the downward shift in the site of initiation of excitation within the SA node. Hence, such variations in P-wave morphology can be explained on the basis of SA nodal shifts without the need to postulate conduction blocks in preferential inter nodal pathways or variable sites of exit from the SA node. (3) Small shifts in pacemaker site within the SA node can be detected from standard body surface P-waves. A shift in pacemaker site from the upper to the middle SA node (representing a distance of less than 0.5 cm) results in a change in polarity in P-III and P-aVL, and increased prominence of P-wave notches may be indicative of shifts in the SA nodal pacing site.

Thus, comparison with experimental results indicate that, for normal SA nodal rhythm, the atrial model is quite good for generating overall activation sequences for the calculation of body surface electrocardiographic potentials. The simulation studies indicate that, even in the absence of anisotropies or specialized fast conducting pathways, slight changes in the location of the SA nodal pacing site produce subtle changes in the atrial excitation pattern that result in significant and complex changes in the body surface P-waves. This indicates the difficulty in predicting local events in the atrial myocardium from potentials measured on the body surface.

Appendix I

A Digital Computer Model for the Simulation of Activation and Repolarization in the Human Heart

This appendix describes the comprehensive anatomical/electrophysiological digital computer models of the human atria and ventricles developed in our laboratory and is based on the work of Ritsema van Eck (1972) and Macchi (1973). Emphasis is placed on the atrial model. The general principles apply to the ventricular model as well, only the details (conduction velocity and representative majority-type action potential waveforms) differ.

Preparation of the Heart Specimen

The heart of a 25-year-old male was obtained at necropsy along with the appropriate consent forms; he had died approximately 10 hours earlier from head injuries. Thoracotomy was performed and two orientation needles were inserted into the heart. The organ was removed from the thorax, washed with fresh water, submerged in a solution of 20% gelatine with 5 ml carbolic acid per liter, and incubated for 4 days at 37°C. On day 5, the openings of the large vessels were ligated around cork stoppers and heated gelatine (40°C) was injected via a needle through the corks into the right and left sides of the heart. Two syringe needles (Luer-Lock) with 3-way valves attached were inserted through the ventricular walls into the ventricular cavities. Gelatine was injected until pressures of 20 and 80 mm Hg were reached in the right and left ventricular cavities, respectively. The whole preparation was cooled gradually to 4°C and kept at this temperature for 48 hours. With the orientation needles as guides to the body axes, the heart was positioned in a wooden box as in the body; the box was filled with fresh warm gelatine and was frozen (~20°C). Forty-eight hours later, the frozen block was removed, positioned on the object plate of a large microtome (Tetramder 1, R. Jung AG), and cut in the transverse.
plane in 1-mm slices to produce 84 sections containing the entire heart. Each section was photographed on a paper sheet with reference scale; on enlarged prints, the boundary lines of cardiac muscle were identified, converted into a series of coordinate-pairs (using a D-Mac pencil follower digitizer; Computer Equipment Corp., Peripheral Systems Division) and stored on magnetic tape.

The data were processed by a digital computer (XDS Sigma 5). Second-order interpolation was used to convert coordinate series of unequally spaced sample points into equidistant (0.5-mm) points, and the series were smoothed (nine-point weighted moving average).

The X-Y coordinates of all points were transformed into an oblique reference system of 60° axes. In this reference system, each point is defined by three integer coordinates which locate the center of a cardiac element. The distance between the centers of adjacent elements is 1.225 mm and each element has 12 neighbors at an equal spatial distance. Thus, the cardiac structure is filled by a honeycomb of rhombododecahedra, as illustrated in Figure 8 for the atria. The basic volume element of the heart model represents a muscle mass of approximately 1.3 mm$^3$, thus comprising several thousand actual muscle fibers. There are a total of 24,413 excitable elements in the atrial structure spanning through 67 sections of the heart. The ventricular structure is composed of 156,349 elements in 84 sections. The excitable muscle tissue is separated from the intercavitary blood masses and the surrounding body tissues by a nonexcitable layer of “shell” elements representing the boundary between excitable cardiac muscle and the surrounding inexcitable conducting medium.

**Functional Properties of the Heart Model’s Elements**

Three parameters, TYPE, STATE, and TIMER, define each element’s behavior; STATE and TIMER are updated during simulation. Elements with identical TYPE share the same functional properties given as functions for duration of states and a concomitant action potential function. STATE signifies an element’s ability to interact with its neighbors. Four distinct states—resting, depolarizing, absolutely refractory and relatively refractory—are recognized and normally follow the sequence presented. TIMER indicates duration of states: in the resting state it indicates the previous time of recovery.

**Figure 8** Horizontal section, 33 mm from the base of a normal human heart. A: Gelatine fixed slice. RA = right atrium, LA = left atrium, PV = pulmonary vein, S = septum, CT = crista terminalis. B: The atrial myocardium represented as a honeycomb of equal rhombododecahedral elements which appear as hexagons in this cross-sectional plan. Black elements are located in the slow-conducting intercaval region.
The spread of activation is governed by a set of rules for transitions between states that concur with the assumption that each element is electrically homogeneous and isotropic so that activation spreads with equal velocity from an element to all its neighbors, when their state allows. An activated element's behavior is autonomic, predetermined only by its history and the properties corresponding to its TYPE.

An element's resting state can be transformed into the depolarizing state by an external stimulus or by a neighboring element whose depolarizing state has just elapsed. Hence, the duration of the depolarizing state determines the lag time for the spread of excitation from element to element and is thus assumed to be inversely proportional to the element's conduction velocity. That is, the duration of the depolarizing state is assumed to correspond to the element-to-element conduction time. Activation thus spreads from element to element with a delay corresponding to the duration of the depolarizing state of the donor element—i.e., to the donor's conduction delay. Following the depolarizing state, an element automatically enters the absolutely refractory state during which it does not respond to further stimuli, then reaches the relatively refractory state, and finally reverts to the resting state. The duration of the relatively refractory state is considered constant, and the duration of the absolutely refractory state is dependent upon the duration of the previous recovery (resting) state. Any element in the relatively refractory state may surpass the resting state when reactivated by a neighbor or an external stimulus and, with imposed delay, enter the depolarizing state of a new cycle.

**Action Potential Waveforms**

The intricacies of simulation experiments can be appreciated by considering the variations in intracellular action potential waveforms in different cardiac tissues as demonstrated in the classic work by Hoffman and Cranefield (1960). The details of these waveforms are significant when determining the cardiac generators (see Appendix II), but for activation sequence simulation, representative majority type action potentials were used to determine state durations.

**Conduction Velocity and Initiation and Spread of Excitation in the Atrial Model**

The atrial structure was assumed to be homogeneous and conduction uniform in all directions with a velocity of 0.8 m/sec. The SA node is represented in the model by a group of 16 elements in a tract approximately 2 mm wide and 2 cm long, extending from the right superior aspect of the junction of the superior vena cava with the right atrium downward along the crista terminalis through 14 sections of the atrial structure. This tract is subdivided into three approximately equal groups of elements which represent the upper, middle, and lower SA nodal regions. For normal sinus rhythm, atrial activation was assumed to start in an element located in the center of the upper part of the SA node. The computer program propagated the activation throughout the atrial structure, updating in 1.5-msec time-steps each element's STATE and TIMER when required by the rules.

After initial simulation experiments, it was decided to make one modification to the assumption of homogeneity in the atria. Histological and electrophysiological observations (Spach et al., 1971; Meredith and Titus, 1968; Sano and Yamagishi, 1965), although not fully conclusive, suggest a paucity of excitable tissue in the structure of the intercaval region. These observations were supported by inspection of the histological sections from our own heart preparation. For this reason, a small, slowly conducting segment extending 3 cm down to the limbus with a width less than 1 cm was incorporated in the superior-posterior intercaval region of the atrial model between the crista terminalis and the posterior aspect of the interatrial septum. A total of 507 elements described this slow conducting region. Conduction velocity was sequentially reduced to 1/2, 1/3, etc., of its normal value, and the resulting simulated isochronal excitation maps were examined to determine the appropriate value.

When the conduction velocity in the slow conducting segment in the intercaval region of the atrial model was reduced to 1/5 of its normal value, the pattern of excitation in the interatrial septum closely resembled the reported course for upper SA nodal rhythm, i.e., the wavefront reaches the AV node via the septum from top to bottom (Yamada et al., 1965; Spach et al., 1971; Janse and Anderson, 1974). Without this slow conducting region, septal activation proceeded obliquely from the superior posterior aspect down toward the AV node. The conduction velocity in the slow conducting region was therefore chosen to be 0.16 m/sec—one fifth that in the rest of the atria.

**Appendix II**

**Calculation of Cardiac Generators and Body Surface Potentials for the Heart-Torso Model**

This appendix describes the selection of the dipole source locations and the calculation of the dipole current sources and body surface electrocardiographic potentials for the atrial and inhomogeneous torso models. The method described applies to the ventricular model as well; only the number and location of the sources and the waveform selected for calculation of the dipole vector functions differ.

**Selection of Atrial Dipole Source Locations**

The atrial generators are assumed to be represented adequately by 41 dipole current sources whose magnitude and direction are determined at each instant of time by the atrial excitation se-
The field of each DSL is defined as consisting of all atrial structure within each of these layers with a separation of 12 elements in the right-left (Frank X-) and anterior-posterior (Frank Z-) directions. The dipole source locations (DSLs) are selected to simultaneously stimulating the elements at the 41 DSLs and allowing activation to spread (with the assumption that conduction velocity is the same for all elements in the atria) until the fronts collide and activation ceases. The result is a group of 41 closed surfaces defined by the collision of the activation wavefronts from each DSL with those from nearby DSLs or with the atrial boundaries. Each such surface encloses 1 DSL, and all elements enclosed within each surface are defined to be in the field of the enclosed DSL. A DSL is considered to be left atrial (LA), right atrial (RA), or interatrial septal (IAS), depending on the location of the major portion of its DSL field, which may differ from the DSL because of the irregular geometry of the atrial structure.

Calculation of Cardiac Generators

The resultant current dipole (D) at each DSL is calculated as the vector sum of the dipoles existing at each interface between elements in the DSL field and adjacent elements (either in the same or an adjacent DSL field, or a boundary “shell” element) by virtue of a potential difference across the interface (Plonsey, 1969), times a coefficient (ξ) equal to the ratio of cardiac tissue to tissue plus interstitial space. The current dipole at the interface between the i-th and j-th elements (di,j) is equal to the product of the conductivity of the conducting medium (α), the surface area (Aij), and is oriented along the unit surface normal (aij) in the direction of the potential gradient. Thus

\[ \vec{d}_{ij} = \alpha A_{ij} \left( V_i - V_j \right) \vec{a}_{ij} \]  

(1)

In general, there are three types of interfaces in a given DSL field at which current dipoles of the form given in Equation 1 exist; interfaces between two elements in the DSL field (I, or internal interfaces), interfaces between an element in the DSL field and an atrial boundary shell element (S, or shell interfaces), and interfaces between an element in the DSL field and an element in a neighboring DSL field (N, or neighboring interfaces). Since the third type of interface is shared by two adjacent DSL fields, ½ the current dipole at each such interface is referred to each of the two DSLs. Thus, for the k-th DSL,

\[ D_k = \xi \left( \sum_i d_i + \sum_s d_s + \frac{1}{2} \sum_N d_N \right) \]  

(2)

where \( d_i \), \( d_s \), and \( d_N \) are given by Equation 1. Assuming \( \alpha \) and \( A_{ij} \) to be the same for all elements of the atrial structure, it is easily seen that the sum of all dipoles at the internal (I) interfaces is equal to the negative of the sum of the dipoles which would exist at the interface at the boundary of the DSL field (S plus N interfaces) if the region external to the DSL field were at zero potential. For example, consider a three-element DSL field bounded on the left by an element in a neighboring DSL field and on the right by a boundary shell element as illustrated in Figure 9. Considering the x-direction only, there are two internal (I) interfaces and two external (E) interfaces, N and S. The sum of the x-components of the current dipoles at the internal interfaces is given by

\[ \sum_i d_{ix} = \xi \alpha A_{ij} (V_i - V_j) \vec{a}_{ij} \]  

(3)

The sum of the x-components of the current dipoles at the external interfaces, assuming the region external to the DSL field to be at zero potential (\( V_N = V_S = 0 \)), is given by

\[ \sum_N d_{nx} = \sum_N d_{n=N,NO} = \xi \alpha A_{nj} (V_i - V_j) \vec{a}_{nj} \]  

(4)

This argument is easily extended to three dimensions. Thus

\[ \sum_I d_i = -\sum_N d_{NO} - \sum_S d_{SO} \]  

(5)

where \( d_{SO} \) and \( d_{NO} \) indicate the current dipoles that would exist at the external (S and N) interfaces if the media external to the DSL field were at zero potential (\( V_i = 0 \)). Thus, Equation 2 becomes

\[ D_k = \xi \left( \sum_S (d_{N} - d_{SO}) + \sum_N (\frac{1}{2} d_{N} - d_{NO}) \right) \]  

(6)

and to evaluate the resultant current dipoles at each DSL, we need only look at the interfaces at the boundary of the DSL field. Substituting from Equation 1 into 4 and assuming that there is no potential gradient (\( V_i = V_j \)) across S interfaces (i.e., \( d_S = 0 \)) gives

\[ D_k = \xi \alpha A \left( \sum_S V_i \vec{a}_{ik} + \frac{1}{2} \sum (V_i + V_n) \vec{a}_{ik} \right) \]  

(7)

where \( V_i \) is the potential of the i-th boundary element of the k-th DSL field, \( V_n \) is the potential of the n-th neighbor of i lying in a neighboring DSL field, \( \vec{a}_{ik} \) is the unit surface normal from the i-th element in the k-th DSL field to the s-th shell element neighboring i, \( \vec{a}_{ik} \) is the unit surface normal from the i-th element in the k-th DSL field to the n-th neighbor of i in a different DSL field, \( \sum_S \) indicates the sum on all interfaces between an element in the k-th DSL field and a boundary shell element, and \( \sum_N \) indicates the sum on all interfaces between an element in the k-th DSL field and an element in a neighboring DSL field.
The potentials \( V_i \) and \( V_a \) are determined at each instant of time from a realistic majority-type transmembrane action potential modeled on the experimental results of Gelband et al. (1972). This waveform is assumed to characterize each element of the model with the upstroke beginning at the time of activation of each element as determined by the model simulation. Thus, \( V_i \) and \( V_a \) are given by

\[
V(t) = \begin{cases} 
-0.083 \text{ for } t < t_0 \\
0.097e^{-\frac{(t-t_0)^2}{2}} - 0.083 \text{ for } t \geq t_0
\end{cases}
\]

where \( t_0 \) is the activation time of the given element and \( \alpha \) and \( \tau \) are constants determined by fitting Equation 6 to the experimental data (Gelband et al., 1972; Fig. 1B). Assuming the zero crossing to be at 21 msec and the membrane to be 70% repolarized at 115 msec, \( \alpha \) and \( \tau \) are found to be 137.5 and 10.3, respectively.

Since 15-20% of the total volume of cardiac tissue is interstitial space (Vick et al., 1970), the coefficient \( \xi \) is assumed to be 0.85. The interface area between adjacent elements of the model is 0.53 \( \times 10^{-3} \) m\(^2\) and \( \sigma \) is assumed to be 0.2 mho/m. With \( V_i \) and \( V_a \) determined from Equation 6 in volts, \( D_k \) is given in amp-meters.

**Calculation of Body Surface Potentials**

Having determined the resultant dipole vector potentials at the 41 DSLs, the body surface potentials are calculated using the concept of lead vectors (Burger and van Milaan, 1946, 1947, 1948), using a torso model which includes inhomogeneities due to the lungs, blood, and skeletal muscle (Horacek, 1973). In this torso model, the conductivity of the lungs is assumed to be one-fourth that of skeletal muscle and blood conductivity is assumed to be three times the conductivity of skeletal muscle; only the ratios of these conductivities are important in the calculation of the lead vectors. The lead vector from the \( k^{th} \) DSL to the \( j^{th} \) body surface point (\( L_{kj} \), in ohm/m) is calculated for 128 body surface points. The potential (in volts) at each electrode location is calculated from

\[
\phi_j(t) = \sum_{k=1}^{128} \frac{D_k(t) - L_{kj}}{r_{kj}}
\]

The standard 12-lead and Frank XYZ lead voltages are then calculated from the appropriate body surface potentials using the standard equations. To separate the effects of RA, LA, and IAS activity from that of the atria as a whole, the appropriate subsets of \( D_k \) and \( L_{kj} \) are used to calculate the \( \phi_j \).

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Mechanism of generation of body surface electrocardiographic P-waves in normal, middle, and lower sinus rhythms.

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