Variations in the Functional Electrical Coupling between the Subendocardial Purkinje and Ventricular Layers of the Canine Left Ventricle

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SUMMARY. Action potential propagation from the subendocardial Purkinje network into the ventricular muscle is an essential link in cardiac activation. Studies of papillary muscles have indicated that ventricular muscle activation by the Purkinje network occurs only at discrete, localized regions near the papillary muscle base. Over the rest of the endocardial surface, however, the spatial distribution of these subendocardial Purkinje to ventricular muscle connections has been less well defined. We therefore studied in vitro 12 canine left ventricular preparations (eight from the septum, four from the lateral wall), using a high-density (1-mm spacings), high-resolution extracellular mapping technique to determine the subendocardial Purkinje and ventricular muscle activation sequences. These studies show that the distribution of subendocardial Purkinje to ventricular muscle electrical coupling is spatially inhomogeneous, and that the junctional regions themselves have variable degrees of electrical coupling. We also attempted to determine whether ventricular muscle coupling to the Purkinje network might influence Purkinje network conduction velocity. We found that on the papillary muscle apex, a region without direct Purkinje to ventricular muscle propagation, Purkinje network conduction velocity was slowed, suggesting that the Purkinje network might be electrically loaded by the underlying ventricular muscle. Finally, we performed numerical simulations using a model consisting of two layers of excitable cells to evaluate the effects that different electrical coupling patterns and/or different coupling resistivities between the two layers might have on activation of each layer. These simulation studies suggest that a coupling pattern having discrete junctional sites between the two layers (similar to our findings for subendocardial Purkinje to ventricular muscle coupling) is beneficial, as this arrangement allows more rapid activation of both layers by minimizing electrical loading of the thin Purkinje layer by the thicker ventricular muscle layer. (Circ Res 57: 252-261, 1985)

PROPAGATION of action potentials through the rapidly conducting Purkinje (P) network and into the subendocardial ventricular muscle (VM) cells forms an essential part of the normal cardiac activation sequence. The importance of this arrangement was first appreciated by Lewis and Rothschild in 1915. From activation time recordings made in vivo from the epicardial and endocardial surfaces of dog hearts, they concluded that the P network serves to distribute rapidly the excitation wave to the VM, with the excitation wave penetrating the VM at "innumerable points."

Subsequent detailed studies of VM activation using epicardial and endocardial surface, as well as transmural, recording electrodes have confirmed the importance of the P network in coordinating ventricular activation (Scher et al., 1953; Durrer et al., 1955; Sodi-Pallares et al., 1961; Scher and Spach, 1979). A problem with these studies, however, is that, with the techniques used, action potential propagation at the sites of P-to-VM conduction (termed Purkinje-ventricular junctions) could not be examined directly.

Other groups have focused on conduction at the Purkinje-ventricular muscle junction (PVJ). Using microelectrodes, they studied preparations consisting of canine papillary muscles and attached P fibers (Alanis et al., 1961; Alanis and Benitez, 1967; Matsuda et al., 1967; Benitez and Alanis, 1970; Mendez et al., 1970; Evans et al., 1984). Early studies (1970 and before) found: (1) significant, and often quite variable, conduction delays during P-to-VM action potential propagation across the PVJ; (2) marked differences in conduction delays during orthodromic (P-to-VM) vs. antidromic (VM-to-P) propagation; (3) an increased safety margin for antidromic vs. orthodromic conduction. One problem with these early studies, however, is that the investigators assumed that the area where a P fiber merged with the papillary muscle surface was the location of a PVJ.

In an attempt to resolve some of the above differences, Myerburg et al. (1972, 1975, 1978) determined the P and VM activation sequences on the
endocardial surfaces of dog hearts using microelectrode and extracellular bipolar recordings. Their two major findings were: (1) there are limited sites of orthodromic conduction, and these same sites are the only sites of antidromic conduction, and (2) there are marked regional differences in the degree of P-to-VM electrical coupling. For example, on the upper halves of the papillary muscles, the basal regions of both ventricles, and the upper two-thirds of the right ventricular (RV) septum, they found no functional coupling between the P network and the underlying VM. Conversely, on the papillary muscle bases, the RV free wall, and the apical third of the LV cavity they found VM activation to closely follow overlying P activation; this they interpreted as indicating dense P-to-VM interconnections.

In 1981, Nagao et al. also used extracellular and microelectrode recording techniques to study RV, P, and VM activation sequences. Like Myerburg et al. (1972, 1978), they found VM activation to be independent of P activation on the basal portions of the RV septum and free wall. Over the remainder of the RV, they found VM activation to almost always follow P activation by 2–6 msec; they felt this suggested electrical continuity between the P and VM layers in these regions.

We have recently examined papillary muscle P and VM activation using high-density, high-resolution extracellular mapping (Overholt et al., 1984; Veenstra et al., 1984). Our results during P stimulation are similar to those of Myerburg et al. (1972, 1975), but clearly demonstrate that on the papillary muscle base, P-to-VM action potential conduction occurs at discretely located sites. Also [in contrast to the results of Myerburg et al. (1972, 1975)], when we directly stimulated the VM on the papillary muscle apex, we found that antidromic propagation could occur at other locations apical to the basal PVJ sites (the latter determined from orthodromic propagation).

In this paper we have used the extracellular mapping technique to study the extent of subendocardial P-to-VM electrical coupling by recording from the endocardial surfaces of canine left ventricular (LV) septum and lateral free wall. The purpose was to test the hypothesis that subendocardial P-to-VM electrical coupling in these areas is spatially discrete, and not "continuous," as suggested by Nagao et al. (1981).

We also examined whether the presence of subendocardial P-to-VM electrical coupling might influence the subendocardial P layer action potential conduction velocity. We predicted that if electrical loading of the P layer by the VM could take place: (1) the action potential conduction velocity in a free-running P strand should be greater than in a P layer in contact with VM, and (2) action potential conduction velocity in this same P layer should be much greater than in its underlying VM.

Finally, we performed numerical simulations using our model of two interconnected layers of excit-
amplifiers was connected to a second variable gain amplification stage to obtain a signal amplitude of up to ±5 V for digital sampling. With an interactive data acquisition system operating on a VAX 11/780 computer (Digital Equipment Corp.), 100 nsec of data (sampled with 12-bit precision at 10,000 samples/sec) were stored on magnetic disk for each monopolar electrode recording.

Microelectrode Recording Techniques

Intracellular recordings were obtained using conventional glass microelectrodes filled with 2.5 M KCl, with tip resistances of 15–25 MΩ. The microelectrodes were connected to the probe input of a WPI M707 DC preamplifier (WPI Inc.), with capacity neutralization, adjusted to give a 10-fold gain. Intracellular signals were recorded simultaneously with those from an extracellular electrode placed on the muscle surface within a few hundred microns of the microelectrode.

Analysis of the Extracellular Recordings

Our method of analysis has been previously published in detail (Veenstra et al. 1984). Briefly, the digitally recorded waveforms were redisplayed on a Tektronix 4014 graphics terminal (Tektronix, Inc.), where an interactive computer program calculated the local P and VM activation times relative to the stimulus artifact. For these calculations, the peak negative P and VM deflections were used to mark local activation of the respective waveforms. The peak negative deflection was used, as it has previously been shown to correlate with the time of occurrence of the peak local membrane current density (Spach et al., 1972; Joyner, 1982). If more than one P or VM signal was noted at a particular point, the activation time of the duplicated signal with the largest negative deflection was taken as the respective activation time at that point. These activation times were then used to construct activation time maps. In occasional records, the P and/or VM deflections were difficult to interpret due to signal fractionation and/or small signal amplitude; these records were not included in the analysis. Activation maps were sketched onto a scale drawing of the tissue piece on which each recording site was marked.

Our criteria for identifying a Purkinje-ventricular muscle junction (PVJ) have been modified slightly from those described by Veenstra et al. (1984). For this paper they are (1) during P stimulation, a PVJ site is one in which there is earlier VM activation relative to VM activation in the surrounding area; (2) the delay between P and VM activation at the proposed site is less than in the surrounding area; (3) the extracellular VM signal at the site must be uniphasic and negative.

P and VM activation maps were derived from extracellular recordings made sequentially from multiple points on a section's endocardial surface. These points were taken at 1-mm horizontal and vertical spacings; distances were measured with a calibrated grid micrometer eyepiece. During the period (1–2 hours) of data acquisition, an additional extracellular electrode was placed in a fixed position at each end of the mapped area, and these were continuously recorded to ensure stability of the preparation during the study period. This was done even though such tissue pieces survive for several hours before any deterioration occurs (Veenstra et al., 1984). After data acquisition was complete, the signals from these two sites were reviewed and the study was discarded if either the P or VM activation times at either point had changed by more than 10%, or if there was a significant change in any waveform morphology.

On the papillary muscle surface, P and VM isochronal maps were constructed from extracellular recordings made at 2-mm spacings. P and VM layer action potential conduction velocities were then calculated from regions of parallel isochrones. P strand action potential conduction velocity was measured between two extracellular recording sites separated by 2 mm along the P strand. Also, in addition to apical P strand stimulation, a second stimulating electrode was placed on the basal surface of the papillary muscle, and data with basal P layer stimulation were alternately recorded with those with apical stimulation. For these experiments, conduction velocity measurements were accepted for analysis if the directional differences in conduction velocity (with apical vs. basal stimulation) for all three regions (P strand, P layer, VM layer) were less than 10%.

### Theoretical Simulations

Numerical simulations of a two-layer model of coupled excitable cells were performed using a method described in detail by Joyner et al. (1984). Specific model assumptions are discussed in the results.

### Statistical Methods

In Table 1, group conduction velocities were compared using standard analysis of variance. Conduction velocity differences were compared using Student’s t-test for paired samples (Snedecor and Cochran, 1967). Least-squares curve fitting was done using standard algorithms.

### Results

#### Purkinje and Ventricular Muscle Activation Patterns

In these experiments we studied a total of 12 LV preparations, eight from the septum and four from the lateral wall. Figure 1 shows a set of P and VM activation maps derived from recordings made on the endocardial surface of one septal preparation; similar results were seen on two other septal preparations. Part A shows the P layer activation isochrones, in msec, measured from the onset of the stimulus artifact. Part B is a similar plot for the VM layer. (Each dot in this and subsequent figures represents a point where an extracellular recording was...
Rowling et al. / LV Purkinje Ventricular Muscle Coupling

PURKINJE ACTIVATION TIME (ms)

VENTRICULAR ACTIVATION TIME (ms)

FIGURE 1. P and VM activation time maps for an LV septal preparation. Each dot represents an extracellular recording point; these are spaced 1 mm apart on the endocardial surface. The preparation was stimulated at 1 Hz on a free-running P strand. In part A, the dashed lines show selected isochrones for P layer activation. The isochrones represent the delay, in msec, from onset of the pacing stimulus to time of local P cell activation. Part B is a similar plot for VM layer activation. See text for discussion.

Eight of the LV preparations we studied had more complex VM activation sequences than those shown in Figure 1. On these preparations, four from the septum and four from the lateral wall, clearly discrete PVJ regions were found. An example of this pattern of VM activation is shown in Figure 3; this preparation was taken from the lateral LV wall. As before, the P activation front propagated quite uniformly across the mapped region. Initially, the VM activation front also propagated quite uniformly, although at a much slower velocity. Because of this
velocity difference, the P activation front reached a second PVJ site (marked by the star within the top 17-msec isochrone) before the arrival of the initial VM activation front, and therefore started up a second VM activation front at this second PVJ site. As this second VM activation front spread to the left, it collided with the initial VM activation front and they extinguished each other; this was confirmed by finding the extracellular waveform morphology to be uniphasic and positive at collision points (Spach et al., 1971). In other areas, the two activation fronts merged, finally forming a continuous activation front (21-msec isochrone), which then slowly continued on.

Figure 4B shows averaged P and VM activation times for this preparation. Only the top three data rows (shown in Fig. 4A) from the activation maps were used for this figure in order to emphasize the presence of the second PVJ site (again marked by a star). As before, P and VM activation times, averaged by column, are plotted against distance along the mapped region. P layer activation was quite uniform. For the first 7 mm, VM layer activation (dashed line) was also quite uniform, but much slower than that of the P layer. VM layer activation time then shortened due to the initiation of the second VM activation front at the second PVJ (at 11-mm distance). Then VM layer activation continued at the low conduction velocity intrinsic to VM.

The solid lines in Figure 4B were least-squares fit to the averaged P and VM activation time data. Note that despite areas of slow VM action potential propagation, the presence of the second PVJ serves to enhance the overall rate of VM activation such that the average VM conduction velocity of 2.01 m/sec, calculated over the length of the mapped region (18 mm), is the same as that of the uniformly activated P layer (conduction velocity = 2.04 m/sec).

**Microelectrode Recordings**

If the PVJ represents a region of better P-VM electrical coupling, compared to nonjunctural areas, then microelectrode recordings from VM cells at a PVJ, during P stimulation, should show current spread during propagation from PVJ P cells into the underlying VM cells. In nonjunctural areas, P cell-to-VM cell current spread would not be expected.

Figure 5 shows microelectrode recordings made from a PVJ site and a nonjunctural site on one LV lateral wall preparation. Parts A and B show, respectively, the P and VM activation maps; the circled sites were the locations of the microelectrode recordings. In parts C and D, the top trace is the extracellular signal recorded from the site of, and during the time of, the microelectrode recordings. The bottom traces show the initial portions of P and VM action potentials recorded by serially penetrating P and VM cells at the indicated sites.

Part C shows the action potentials recorded from site A. This site was located within a PVJ, as shown by the activation maps and confirmed by the morphology of the extracellular VM waveform (Veenstra et al., 1984). Note that shortly after the overshoots of the P cells' action potentials, a smooth pre-potential began in the VM cell and culminated in its action potential. Part D shows a P cell and two VM cell action potentials recorded from site B, located in a nonjunctural area. No pre-potential is seen in these VM cells, nor was any seen in other VM cells recorded at several nonjunctural sites on this section. Similar results were found on two other preparations.
Purkinje Strand and Purkinje Layer Action Potential Conduction Velocities

To compare action potential conduction velocities in free-running P strands with those in P layers overlying VM and the VM itself, we studied nine LV papillary muscle preparations, of which six fulfilled our acceptance criteria. Table 1 shows the results of these six experiments.

Mean conduction velocity values were significantly different ($P < 0.005$) for the three regions, with P strand $>$ P layer $>$ VM layer. In addition, the difference between the P action potential conduction velocities ($P_{\text{strand}} - P_{\text{layer}}$) was significantly less ($P < 0.001$) than that between the $P_{\text{layer}}$ and VM layers ($P_{\text{layer}}$ conduction velocity $-$ VM layer conduction velocity).

Theoretical Results

We have extended our previous methods of numerical simulation of action potential propagation in one-dimensional strands to model the propagation of action potentials in two layers of excitable tissue, as diagrammed in Figure 6 (see Joyner et al., 1984 for a complete description and methodology). Note that in the present model, however, each element of each layer is assumed to be isopotential along the $Z$ axis, thus producing a one-dimensional approximation to each layer. Although real LV tissue is certainly three-dimensional, the limited depth of surviving tissue under in vitro conditions (see Spach et al., 1979) supports our approximation of the surviving subendocardium as a thin P layer (50 $\mu$m in the model) and a thicker VM layer (250 $\mu$m in the model) with all corresponding elements of the two layers connected by some resistance. Assuming that electrical coupling between these two layers is produced by gap junctions between P and VM cells, we define a resistivity $R_c$ (ohm-cm) for this P-VM interface region and calculate the resistance (ohms) between two corresponding elements by assuming that the resistivity $R_c$ represents the combined cytoplasmic and junctional resistivity for a specific interface region composed of the lower 25 $\mu$m of the
Figure 7. Numerical simulation of propagating action potentials in two layers of excitable cells (as diagrammed in Fig. 6). Parts A and B illustrate action potential propagation in response to stimulation of the left end of layer one (P layer). Plotted in each part are membrane potentials at selected distances (labeled in millimeters) as functions of time, with vertical separation for clarity. The two spatial patterns of coupling resistivity between the two layers are:

- Part A—a value of 4000 ohm-cm everywhere; part C—4000 ohm-cm for distances 4.5-5.5 and 14.5-15.5 mm only; elsewhere, infinite coupling resistance. Parts B and D are plots of activation time vs. distance for the simulations of parts A and C, respectively, with open symbols for the P layer and filled symbols for the VM layer. See text for discussion.

The spatial increment for each layer was 100 μm, and each layer had 200 elements, giving a total length of 20 mm. The stimulus was applied to element 1 of the P layer (left end). For parts A and C, we used a constant value of 4000 ohm-cm for \( R_c \) between the corresponding elements of the two layers. Part A shows \( V_m \) as functions of time for elements of the P layer (upper traces) and the VM layer (lower traces), with vertical separation of the \( V_m \) solutions at increasing distances (labeled in millimeters on the traces) for clarity. The action potential initiated by the stimulus in the P layer activates the VM layer with a short delay and then the two action potentials travel at the same velocity in a "continuous" manner, as shown by part C, in which we plot the activation time (time of peak inward current) for the P elements (open symbols) and VM elements (filled symbols) as functions of distance. Their common conduction velocity (69 cm/sec) is greater than the intrinsic VM conduction velocity (47 cm/sec in the model) and less than the intrinsic P conduction velocity (87 cm/sec in the model). For parts B and D, we modified the spatial distribution of \( R_c \) such that \( R_c \) was infinitely large (complete uncoupling) except for distances from 4.5-5.5 mm and from 14.5-15.5 mm, thus producing two discrete junctional sites, each 1 mm long, with the resistivity at the junctional sites being 4000 ohm-cm. Part B shows that the P action potential (upper traces) propagates from left to right, with alterations in the upstroke at the junctional sites. The VM action potential (lower traces) originates at distance 5 mm, which is the first junctional site encountered by the P action potential. Note the presence of a prepotential on the VM action potential at this junctional site. Propagation within the VM layer occurs from both left to right and right to left from this junctional site, as shown by the activation time plot of part D. When the P action potential encounters the second junctional site (at distance 15 mm) a second VM action potential, also having a prepotential, is initiated. This action potential also propagates in both directions.

In contrast to part B, in part D VM action potential conduction velocity (the inverse of the slope of the activation time plot) varies with distance. In the regions between the junctional sites, VM conduction velocity is slow, reflecting the lower intrinsic VM excitability. However, the periodic initiation of VM action potentials at each junctional site makes the
overall conduction velocity in the VM layer the same as that of the P layer. Further, P layer action potential conduction velocity is now essentially the same as the intrinsic P action potential conduction velocity because most of the P layer is now unaffected by the electrical load of the VM layer.

In Figure 8 we demonstrate further how variations in junctional resistivity can effect VM activation time. As diagrammed at the top of the figure, for these simulations we established three junctional regions between our simulated P and VM layers. The results of the simulations are shown as activation times vs. distance, with the open symbols representing the P layer and the filled symbols representing the VM layer.

For all three simulations, site 1 had a junctional resistivity of 4000 ohm-cm over 1 mm. As expected from Figure 7B (where both junctions had resistivities of 4000 ohm-cm), this resistivity allowed the action potential originating in the P layer to propagate into the VM layer. For the results labeled “A” in Figure 7, sites 2 and 3 were given infinite resistivities. In this case, following VM layer activation at site 1, the VM action potential propagated on at its slow intrinsic conduction velocity. For the results labeled “C,” sites 2 and 3 were given junctional resistivities of 4000 ohm-cm (the same as site 1), and the activation time plot for the VM layer shows its periodic coupling to the P layer, as expected from the results of Figure 7C. For the results labeled “B,” sites 2 and 3 were given junctional resistivities of 7500 ohm-cm, too high for direct P to VM propagation. (From other simulations, for the particular model parameters used, we had found that a junctional resistivity greater than 7000 ohm-cm over a 1-mm length would not allow propagation from the P layer to the VM layer to occur.) Despite these high resistivities at sites 2 and 3, activation times for the segments from site 2 on are all decreased with respect to curve “A” (infinite junctional resistivity) showing that current flow through these two junctions increased conduction velocity in the VM layer even when direct activation of the VM layer by the P layer at sites 2 and 3 could not occur.

Discussion

Observations on Purkinje to Ventricular Muscle Conduction

We propose that there are two forms of conductional discontinuity between the subendocardial P and VM layers: spatial and temporal. By spatial discontinuity we mean that the distribution of subendocardial P-to-VM electrical coupling is not continuous, but that discrete regions of P to VM propagation can be identified. In 11 of the 12 LV preparations and in all of the papillary muscles that we have studied (Veenstra et al., 1984; and unpublished observations), we have found discrete regions in which the P action potentials propagate from the subendocardial P layer into the VM layer. On only one septal preparation did P-to-VM propagation appear to be continuous, in that, using our criteria for Purkinje-ventricular muscle junction identification, we were unable to define any discrete Purkinje-ventricular muscle junctional regions within the mapped area. However, using our third criterion that the morphology of the extracellular VM waveform at a Purkinje-ventricular muscle junction be uniphasic and negative, we could identify several separate recording sites in the mapped area with this VM waveform morphology. We could also identify such sites on the other three preparations that had both well-coupled regions and relatively discrete junctional sites (as in Fig. 1), suggesting that even on well-coupled regions the junctional sites were discrete, but were below our spatial and/or temporal resolution.

This points up one possible limitation of these experiments. We made our measurements on the endocardial surface at 1-mm horizontal and vertical spacings. Perhaps with finer spatial resolution we could better identify and localize Purkinje-ventricular muscle junctional sites on preparations with well-coupled regions. There is an inherent problem in increasing the spatial resolution, however, as doing so requires more precise temporal resolution, which, for the VM signals, can be difficult due to the somewhat broad negative phase of the VM waveform.

The other form of conduction discontinuity we feel exists between the subendocardial P and VM layers is temporal; this refers to the time delay...
between local P cell and VM cell activation. On "well-coupled" preparations (such as in Fig. 1), there is a several-millisecond time delay between P activation and VM activation at each location. On preparations with discrete Purkinje-ventricular muscle junctions (e.g., Fig. 3), similar delays are found at the junctions; these delays appear to be related to a slowly rising depolarization of the VM cells (see Fig. 5).

Based on the above findings, we propose that the left ventricular distribution of subendocardial P-to-VM electrical coupling is inhomogeneous. This implies that there exists both a spatially inhomogeneous distribution of Purkinje-ventricular muscle junctional regions and that these junctional regions do not have uniform P-to-VM electrical coupling (leading to variable conduction delays or temporal discontinuities). Thus, on some LV areas (as in Fig. 3), P-to-VM electrical coupling is very poor except at discrete, localized sites. On other areas (e.g., Fig. 1), the regions of P-to-VM coupling are more closely spaced and of lower resistivity; these areas appear well-coupled. However, even on these areas, the junctional regions may differ in their relative degree of coupling, as shown by the existence of the Purkinje-ventricular muscle junction near the right end of Figure 1.

We feel this proposal extends the work of Myerburg et al. (1972, 1975, 1978) and Nagao et al. (1981). Myerburg et al. noted the existence of limited sites of subendocardial P-to-VM conduction, but did not define these in detail. Nagao et al. showed that on some RV areas, VM activation closely followed overlying P activation. However, perhaps because of a lack of spatial resolution, they did not further characterize the nature of the VM activation pattern—that is, they did not distinguish between a VM activation pattern in which VM activation uniformly follows P activation vs. one in which more discrete Purkinje-ventricular muscle junctions are present, with new VM activation fronts being initiated at each Purkinje-ventricular muscle junctional site. (For example, in our Figure 4, over the length of the mapped region, VM activation appears to follow P activation relatively closely, even though well-defined, discrete Purkinje-ventricular muscle junctional sites are present.)

**Ventricular Muscle May Electrically Load the Purkinje Layer**

The possibility that the VM layer electrically loads the P layer on the papillary muscle apex, a region thought to be devoid of P-to-VM inter-connections (Myerburg et al., 1972, 1978), is suggested by our P strand vs. P layer conduction velocity studies (Table 1). We found that the action potential conduction velocity in a P strand is about one-third faster than in a P layer overlying VM. Note that our mean P layer conduction velocity of 1.59 m/sec agrees well with the values of 1.62 m/sec determined by Myerburg et al. (1978), and that of 1.67 m/sec determined by Nagao et al. (1981) from the RV. Further, Nagao et al. also determined RV false tendon conduction velocity and obtained a mean value of 2.02 m/sec, which compares well to our mean value of 2.08 m/sec.

Another possible explanation for the change in P strand vs. P layer action potential conduction velocity is the changed geometry of the P system (strand vs. layer). The geometric transformation from a strand to a layer could result in changes in effective membrane capacitance and/or the coupling resistance between cells such that the P layer action potential conduction velocity is less (Matsuda 1960).

Although the change in geometry might explain the change in P strand vs. P layer action potential conduction velocity, this consideration would not explain the other two lines of evidence for electrical interconnections between the apical papillary muscle P layer and its underlying VM. (1) Apical P cell action potential duration (at 90% repolarization) has been shown to be significantly less than that of P strand cells (Veenstra et al., 1984), and surface P cell action potential duration decreases even further at the Purkinje-ventricular muscle junction. [Matsuda (1960) also found differences in action potential duration between P strand cells and P cells in the dog subendocardium.] (2) We have shown that with apical papillary muscle VM stimulation, VM-to-P propagation can occur at locations apical to, and separate from, basal Purkinje-ventricular muscle junctional sites (as defined from P stimulation) (Overholt et al., 1984).

**Advantage of Discrete Conduction Sites**

In our simulation studies, we were able to reproduce the experimentally observed phenomena using discrete regions of lowered junctional resistivity. These studies also suggested that, from a functional perspective, the presence of discrete subendocardial P-to-VM junctional regions, vs. "continuous" P-to-VM coupling, could be a very useful feature in the sense that the overall conduction velocity of both the P and VM layers in the plane of the endocardial surface will be increased by having a spatially inhomogeneous distribution of junctional sites. As shown by the simulations, if there is continuous electrical coupling between the P and VM layers, overall action potential conduction velocity in the P layer will be much slower due to its being electrically loaded by the VM layer. On the other hand, if discrete regions of P-to-VM coupling are present, then action potential conduction velocity in the P layer will be faster, as it is now electrically "unloaded" at areas outside the Purkinje-ventricular muscle junctions. In the VM layer, overall conduction velocity will vary with the spatial distribution of, and degree of electrical coupling present at, the discrete junctional regions. If these regions are relatively close together, and junctional resistivity is
Rawling et al. / LV Purkinje Ventricular Muscle Coupling

low, then VM layer activation will closely follow that of the P layer, with a relatively constant delay between them. If, however, the junctional regions are widely spaced, then the VM activation pattern will be one in which the VM activation front propagates at its intrinsic conduction velocity between junctional sites. Finally, if junctional resistivity is too great, propagation of the P layer activation front and of the VM layer activation front will appear to be independent of one another (as on the papillary muscle apex).

One consequence of having discrete sites of functional P-to-VM electrical coupling is that the subendocardial VM activation pattern could be abruptly changed by conditions which block junctional sites, even if conduction within the subendocardial P and VM layers remains nearly normal. Purkinje-ventricular muscle junctions have been shown to have a relatively low safety factor for action potential propagation (Alanis et al., 1961; Mendez et al., 1970; Veenstra et al., 1984; Evans et al., 1984). Further, we have recently shown that some Purkinje-ventricular muscle junctional sites can be reversibly blocked by elevation of the extracellular potassium concentration to only 8 mM (Overholt et al., 1984). This suggests that under the right conditions the subendocardial P-VM interface may be quite labile, and that significant changes in VM activation could occur. These changes could result in increased dispersion of VM activation, which could lead to conduction abnormalities and/or facilitate reentrant excitation (Sasyniuk and Mendez, 1971).

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D A Rawling, R W Joyner and E D Overholt

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