Effects of K⁺ and K⁺-Induced Polarization on (dV/dt)_{max}, Threshold Potential, and Membrane Input Resistance in Guinea Pig and Cat Ventricular Myocardium

HIROSHI KISHIDA, BORYS SURAWICZ, AND LON TAI FU

SUMMARY We studied the non-membrane potential-dependent effect of K⁺ on (dV/dt)_{max} and threshold potential in guinea pig and cat ventricular myocardium. Membrane potential (MP) was changed uniformly in segments (length < 1.0 mm) of papillary muscles by applying extracellular polarizing current pulses across a single sucrose gap. Control [K⁺] was 5.4 mm and test [K⁺] values were 2.0, 10.0, 11.5, 13.0, 16.2, 20, 22, and 24.0 mm. Each muscle was studied under four conditions: (1) control [K⁺] and unaltered (control level) resting MP (E_r); (2) one of the test [K⁺] values and the unaltered (test level) E_r; (3) the same test [K⁺] and E_r held at the control level; (4) control [K⁺] and E_r held at the test level. At all [K⁺] > 11.5 mm, (dV/dt)_{max} showed a decrease significantly (P < 0.01) greater than the corresponding MP-dependent decrease in both guinea pig and cat myocardium. This non-MP-dependent decrease averaged 7.5% at 11.5 mm, 26.5% at 13.0 mm, 37.2% at 16.2 mm, and 22.7% at 20.0 mm. At [K⁺] > 20.0 mm, (dV/dt)_{max} was predominantly slow-channel-dependent; it was increased by hyperpolarization to -110 mV at [K⁺] = 20 and 22 mm but not at [K⁺] > 24 mm. Threshold potential became progressively less negative with increasing [K⁺], but this effect was dependent only on MP. The membrane input resistance (r_m) was determined by two opposing factors: at a given [K⁺], r_m increased with depolarization; and at a given MP, r_m decreased with increasing [K⁺]. Our study shows that non-MP-dependent depression of (dV/dt)_{max} in the ventricular myocardium occurs at [K⁺] concentrations that may be encountered in vivo.

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IN 1955, Weidmann showed that the rate of rise of the action potential of a sheep Purkinje fiber depolarized by 13.5 mm [K⁺] returned to the control value when the membrane potential (MP) was clamped to -92 mV (Weidman, 1955a). This experiment established that the effect of [K⁺] on the rate of rise was secondary to the effect on MP.

Imanishi and Surawicz (1976) found that high [K⁺], suppressed depolarization attributed to an inward current flowing through the slow channel in guinea pig ventricular myocardium, and they showed that this effect was due to a non-MP-dependent action of [K⁺]. These observations prompted Fu and Surawicz to study the non-MP-dependent effect of [K⁺] on rapid-channel-dependent (dV/dt)_{max} in guinea pig papillary muscles. The results of this study, published in an abstract, showed that the effect of high [K⁺] on (dV/dt)_{max} was greater than the effect of depolarization per se (Fu and Surawicz, 1975).

Since these findings were unexpected and contrary to the prevailing notions, we decided to repeat our experiments, using a sucrose gap instead of the vaseline gap employed in the first series of experiments (Fu and Surawicz, 1975). In the new series of experiments, described in this paper, we studied a wide spectrum of [K⁺], and used ventricular muscles from two animal species. This study confirmed the initial findings (Fu and Surawicz, 1975) and established that the non-MP-dependent depression of (dV/dt)_{max} was produced by values of [K⁺] that may be expected to occur in vivo.

The study also includes measurements of membrane input resistance (r_m) and previously unreported independent effects of MP and [K⁺] on the threshold potential in ventricular myocardium.

Methods

Right ventricular papillary muscles (3-5 mm long × 0.5-1.0 mm in diameter) were excised from the hearts of guinea pigs (200-250 g) killed by a blow on the neck, or from the hearts of cats (1.5-3 kg) anesthetized with pentobarbital (30 mg/kg, ip). The muscles were mounted in a single three-compartment sucrose gap chamber (gap width = 2 mm) of the type described by Reuter and Scholz (1988). The tip of the papillary muscle protruding into the proximal (test) compartment was ≈1 mm long. During the initial equilibration period, the preparation was stimulated for about 60 minutes by a Grass

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model S3GR stimulator (Si) at a constant rate of 0.5 Hz by rectangular pulses 2 msec in duration and twice threshold strength, through a pair of silver wire (diameter = 0.1 mm) electrodes that were insulated except at their tips and placed in the distal compartment close to the partition. All compartments were separately perfused at a rate of 3 ml/min initially for approximately 60 minutes with Tyrode's solution (composition in mm: NaCl, 126.0; KCl, 5.4; CaCl₂, 1.8; MgCl₂, 1.05; NaHCO₃, 24.0; NaH₂PO₄, 0.42; glucose, 5.0) gassed with 5% CO₂-95% O₂. Then the perfusing fluid in the middle compartment was replaced by isotonic sucrose solution (300 mm) containing 5 mm glucose and 1 x 10⁻⁵ m CaCl₂ and gassed with 100% O₂. The effectiveness of the sucrose gap as a seal between the proximal and the distal compartments was tested by adding dye to the solution perfusing the middle compartment and by replacing the Tyrode's solution in the distal compartment by isotonic KCl solution. We assumed an absence of leak when dye did not enter the proximal compartment and when the presence of KCl in the distal compartment did not change the MP in the proximal compartment. Changes in [K⁺]₀ (2.0, 10.0, 11.5, 13.0, 16.2, 20.0, and 24 mm) were made without adjusting for change in osmolality. We established in preliminary experiments that such adjustment was not necessary, because no measurable change in MP or (dV/dt)ₜₜₚ max occurred after the addition of sucrose, which produced the same increase in osmolality as the highest [K⁺]₀ (24.0 mm) used in the study. Bath temperature was 36.5-37°C, and the pH of the Tyrode's solution was 7.4.

MP was held at various chosen levels by the method described in a previous study in which a vaseline gap was used instead of a sucrose gap (Imanishi and Surawicz, 1976). In brief, after turning off the driving stimulus (Si), a Grass S-88 stimulator (S₁) delivered extracellular polarizing rectangular pulses of current of various strengths through a pair of spiral Ag-AgCl electrodes, one in each compartment. A resistor (270 kΩ) in series with the S₁ stimulator maintained the polarizing current nearly constant. Another Grass S-88 stimulator (S₂), connected in series with S₁, delivered polarizing current pulses, which altered the level of the holding potential. Two types of experiments were performed. In the first, the current required to maintain the holding potential (S₂) continued to flow during application of polarizing current pulses of 20-msec duration, and in the second, holding potential was maintained for 2 seconds, and then the current required to hold this potential (S₁) was turned off simultaneously (delay less than 1 μsec) with the application of a 1-msec depolarizing stimulus of the minimal strength required to elicit an action potential.

Both methods produced identical changes in (dV/dt)ₜₜₚ max, as is shown in Figure 5 (see below). This means that the currents applied to "hold" the MP had no effect on (dV/dt)ₜₜₚ max. However, as expected, these currents altered the MP during early repolarization, which was not the object of our study. We used the first method in all experiments in which we measured the threshold potential, and the second method predominately in the experiments in which we explored the effects of hyperpolarization (see below).

MP values were measured as potential differences between a pair of intra- and extracellular standard glass microelectrodes positioned close to each other near the partition. The resistance of the electrodes ranged from 10 to 20 MΩ. The measured membrane voltage was led to a differential DC preamplifier (Transidyne, model MPA 6). The MP (dV/dt)ₜₜₚ max and the amplitude of polarizing current were displayed simultaneously on the screen of a Tektronix 564B storage oscilloscope and photographed with a Polaroid camera.

The possible errors in the measurement of the MP stemming from the resistance of the solution and the extracellular electrode were minimized by the use of an extracellular voltage clamp (New and Trautwein, 1972), as described previously (Imanishi and Surawicz, 1976).

The fibers were identified as true ventricular muscle by the criteria used by Katzung (1975). Each complete experiment consisted of the following four steps: (1) control [K⁺]₀ (5.4 mm) and unaltered resting MP (Eₘ) (control level); (2) test [K⁺]₀ and unaltered (test level) Eₘ (3) test [K⁺]₀ and Eₘ held at control level; (4) control [K⁺]₀ and Eₘ held at test level. All measurements were made within 30-60 minutes after change to a new [K⁺]₀. Experiments were accepted only if a single-cell impalement was maintained throughout all four steps. Both the configuration of the action potential and the Eₘ were the same at the onset and at the end of each experiment. The non-MP-dependent effect of potassium was obtained from the difference between steps 2 and 4 and from the difference between steps 1 and 3; the [K⁺]₀-independent effect of MP was obtained from the difference between steps 1 and 4 and between steps 2 and 3.

**Method of Measurements**

Threshold potential was determined by the method used by Weidmann (1955b) and identified as the inflection point between the electrotonic potential (upward convex) and the foot of the action potential (upward concave). Since latency could alter the threshold potential, we aimed at obtaining in each experiment the same latencies of about 5, 10, and 15 msec by varying the strength of depolarizing pulses. Within this range of latencies the threshold potential value was usually the same, but in some experiments the threshold potential was less negative after the latency of 5 msec than after the latencies of 10 and 15 msec. Therefore, our results include only threshold potentials measured after latencies of about 10 or 15 msec.
in the duration of latency had negligible effects on the (dV/dt)_{max} (differences < 1%).

We calculated $r_m$ as the ratio of the difference between the holding potential and the threshold potential which elicited an action potential after latency of 10 msec to the strength of the corresponding current pulse. Statistical evaluation of results was performed with Student's t-test.

### Results

#### Steady State Conditions

A potassium-sensitive electrode (Hill et al., 1976) was used to monitor $[K^+]_o$ in the bath during changes of superfusing test solutions. At the rate of superfusion used in this study, steady state was achieved within 5-10 minutes, and no further changes were observed.

#### Table 1: Effect of $[K^+]_o$ and $E_m$ on Threshold Potential, (dV/dt)_{max}, and $r_m$ in Guinea Pig Papillary Muscle

<table>
<thead>
<tr>
<th>$[K^+]_o$ (mM)</th>
<th>5.4 and 2.0 mm (n = 5)</th>
<th>5.4 and 10.0 mm (n = 6)</th>
<th>5.4 and 11.5 mm (n = 7)</th>
<th>5.4 and 13.0 mm (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$Em$ (mV)</td>
<td>83.0 ± 0.3</td>
<td>99.4 ± 0.4</td>
<td>99.4 ± 0.4</td>
<td>83.0 ± 0.5</td>
</tr>
<tr>
<td>$Threshold$</td>
<td>65.1 ± 0.4</td>
<td>72.7 ± 0.4</td>
<td>70.2 ± 0.4</td>
<td>65.4 ± 0.5</td>
</tr>
<tr>
<td>(dV/dt)_{max}</td>
<td>219.2 ± 7.6</td>
<td>236.3 ± 10.6</td>
<td>225.3 ± 8.3</td>
<td>211.8 ± 9.2</td>
</tr>
<tr>
<td>$Percent$</td>
<td>100 ± 1.8</td>
<td>107.6 ± 10.2</td>
<td>102.8 ± 8.3</td>
<td>98.2 ± 0.4</td>
</tr>
<tr>
<td>$r_m$</td>
<td>128.9 ± 7.5</td>
<td>122.1 ± 6.2</td>
<td>81.6 ± 4.4</td>
<td>62.9 ± 5.2</td>
</tr>
</tbody>
</table>

All values are expressed as means ± SE; n = number of preparations.

**FIGURE 1** Simultaneous recording of MP and (dV/dt)_{max} of the action potential upstroke at opposite ends of a cat papillary muscle preparation during application of current pulses of 20-msec duration. From top to bottom: MP and (dV/dt)_{max} at one end, MP and (dV/dt)_{max} at the opposite end, and the current pulse. Note the similarity of both MP and (dV/dt)_{max} traces at both recording sites in each of the two panels. On the left, the muscle is depolarized to approximately -60 mV by $[K^+]_o = 13.0$ mm, and on the right, the same muscle is hyperpolarized to approximately -84 mV at the same $[K^+]_o$. 

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**TABLE 1** Effect of $[K^+]_o$ and $E_m$ on Threshold Potential, (dV/dt)_{max}, and $r_m$ in Guinea Pig Papillary Muscle

<table>
<thead>
<tr>
<th>$[K^+]_o$ (mM)</th>
<th>5.4 and 13.0 mm (n = 5)</th>
<th>5.4 and 16.2 mm (n = 5)</th>
<th>5.4 and 20.0 mm (n = 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$Em$ (mV)</td>
<td>83.0 ± 0.4</td>
<td>60.7 ± 0.2</td>
<td>60.4 ± 0.2</td>
</tr>
<tr>
<td>$Threshold$</td>
<td>65.0 ± 1.0</td>
<td>41.9 ± 1.4</td>
<td>44.2 ± 1.2</td>
</tr>
<tr>
<td>(dV/dt)_{max}</td>
<td>209.1 ± 9.4</td>
<td>102.7 ± 7.0</td>
<td>158.0 ± 7.0</td>
</tr>
<tr>
<td>$Percent$</td>
<td>100 ± 1.7</td>
<td>49.1 ± 3.3</td>
<td>75.6 ± 3.3</td>
</tr>
<tr>
<td>$r_m$</td>
<td>51.6 ± 2.0</td>
<td>61.7 ± 3.7</td>
<td>113.3 ± 3.7</td>
</tr>
</tbody>
</table>

All values are expressed as means ± SE; n = number of preparations.
obtained within less than 20 minutes in all experiments.

In 15 preliminary experiments, MP was measured every 15 minutes after a change from control Tyrode's solution to a different test solution while the microelectrode remained inserted in the same cell. Steady state was approached within 15-30 minutes, and the difference between MP after 30 and 60 minutes always was less than 1 mV. Therefore, all experiments were made within 30-60 minutes after the change of [K+]o.

Longitudinal Homogeneity of MP

The voltage homogeneity during application of depolarizing and hyperpolarizing currents of various strength was tested in two fibers by comparing transmembrane potentials recorded simultaneously at opposite ends of the preparation with the use of two pairs of microelectrodes, as described in a previous study (Imanishi and Surawicz, 1976). Application of depolarizing and hyperpolarizing currents of a strength comparable to that used in most experiments produced MP changes that differed at the two sites by less than 1 mV at [K+]o = 2.0 and 5.4 mM and less than 3 mV at [K+]o ranging from 11.5 to 16.2 mM. Figure 1 shows an example of homogeneous MP and similar (dV/dt)m values at both ends of the preparation at a [K+]o of 13.0 mM both before and during hyperpolarization to approximately −84 mV.

MP-Dependent and Non-MP-Dependent Effects of [K+]o

Table 1 summarizes the effects of [K+]o and of resting (or holding) MP on the threshold potential, (dV/dt)max, and rm in guinea pig papillary muscles, and Table 2 shows the statistical significance of these results. In each set of experiments summarized in Table 1 the results are compared to values obtained at control [K+]o and control Em. The results for the cat papillary muscles were the same as for the guinea pig and are not included in the tables.

**Threshold Potential (Table 1 and Fig. 2)**

The control threshold potential averaged approximately −65 mV. It became progressively less negative with increasing [K+]o and more negative at [K+]o = 2.0 mM. However, Figure 2 shows that the differences between the threshold potential at [K+]o = 5.4 mM (solid line) and those at different test [K+]o values (broken line) were significant only at [K+]o = 20 mM. This suggests that the threshold potential for rapid-channel-dependent depolarization was dependent exclusively on MP but not on

<table>
<thead>
<tr>
<th>[K+]o (mM)</th>
<th>Difference between</th>
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<tbody>
<tr>
<td>2.0 and 5.4 at −83 mV</td>
<td>2.0 and 5.4 at −99 mV</td>
</tr>
<tr>
<td>5.4 and 2.0</td>
<td>TP</td>
</tr>
<tr>
<td>(n = 5)</td>
<td>(dV/dt)max</td>
</tr>
<tr>
<td></td>
<td>r m</td>
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<tr>
<td>10 and 5.4 at −83 mV</td>
<td>10 and 5.4 at −66 mV</td>
</tr>
<tr>
<td>5.4 and 10.0</td>
<td>TP</td>
</tr>
<tr>
<td>(n = 6)</td>
<td>(dV/dt)max</td>
</tr>
<tr>
<td></td>
<td>r m</td>
</tr>
<tr>
<td>11.5 and 5.4 at −83 mV</td>
<td>11.5 and 5.4 at −63 mV</td>
</tr>
<tr>
<td>5.4 and 11.5</td>
<td>TP</td>
</tr>
<tr>
<td>(n = 7)</td>
<td>(dV/dt)max</td>
</tr>
<tr>
<td></td>
<td>r m</td>
</tr>
<tr>
<td>13 and 5.4 at −83 mV</td>
<td>13 and 5.4 at −63 mV</td>
</tr>
<tr>
<td>5.4 and 13.0</td>
<td>TP</td>
</tr>
<tr>
<td>(n = 5)</td>
<td>(dV/dt)max</td>
</tr>
<tr>
<td></td>
<td>r m</td>
</tr>
<tr>
<td>16.2 and 5.4 at −83 mV</td>
<td>16.2 and 5.4 at −55 mV</td>
</tr>
<tr>
<td>5.4 and 16.2</td>
<td>TP</td>
</tr>
<tr>
<td>(n = 5)</td>
<td>(dV/dt)max</td>
</tr>
<tr>
<td></td>
<td>r m</td>
</tr>
</tbody>
</table>

**Table 2 Statistical Significance of the Results in Table 1**

TP = threshold potential; rm = membrane input resistance; n = number of preparations; NS = not significant.
Figure 2. Relation between the MP (abscissa) and the threshold potential expressed as percent of control value at $[K^+]_o = 5.4$ mM (ordinate). The filled circles connected by the solid line and the corresponding vertical bars represent average ± SE at $[K^+]_o = 5.4$ mM; the unfilled circles connected by the broken line and the corresponding vertical bars represent average ± SE at seven different values of $[K^+]_o$ ranging from 2.0 (far left, MP = approximately −99 mV) to 20.0 mM (far right, MP = −50 mV). The values represented by filled circles were obtained by holding MP at the same level as the unaltered (test) resting MP at the test $[K^+]_o$. The difference between the values marked by the filled circles and those marked by the unfilled circles at each MP represents the non-MP-dependent effect of $[K^+]_o$, which is significant only at $[K^+]_o = 20.0$ mM. See text.

$[K^+]_o$, whereas the threshold potential for slow-channel-dependent depolarization appeared to be $[K^+]_o$-dependent.

$(dV/dt)_{max}$ (Table 1 and Figs. 3-11)

The control average $(dV/dt)_{max}$ in different groups of experiments varied from approximately 209 to approximately 232 V/sec; $(dV/dt)_{max}$ increased slightly but significantly at $[K^+]_o = 2.0$ mM. This increase was due to both lowering $[K^+]_o$ and hyperpolarization. There was a progressive decrease in $(dV/dt)_{max}$ with increasing $[K^+]_o$.

Figure 3 shows that at $[K^+]_o = 10.0$ mM the $(dV/dt)_{max}$ was dependent only on MP and not on $[K^+]_o$. In this figure, the effects of $[K^+]_o = 5.4$ and 10.0 mM are compared at holding potentials of approximately −83 mV (A,B) and −67 mV (C,D). It can be seen that $(dV/dt)_{max}$ is lower at −67 mV than at −83 mV (A vs. C and B vs. D) but is the same at both $[K^+]_o$ levels (A vs. B and C vs. D). Similar results were obtained in other experiments (Table 1).

Figure 4 shows results of a typical experiment in which we compared the effects of $[K^+]_o = 5.4$ and 11.5 mM at two different holding potentials of approximately −83 mV (A,B) and −63 mV (C,D). It can be seen that $(dV/dt)_{max}$ decreased due to both depolarization (A vs. C and B vs. D) and increase in $[K^+]_o$ (A vs. B and C vs. D). Other experiments produced similar results (Table 1). The non-MP, $[K^+]_o$-dependent decrease in $(dV/dt)_{max}$ averaged 7.5% and was significant ($P < 0.01$) (Table 2).

Figure 5 shows results of a typical experiment in which we compared the effects of $[K^+]_o = 5.4$ and 13.0 mM at holding potentials of approximately −82 mV (a,b) and −60 mV (c,d) using two different
methods of current applications. In part A, depolarizing pulses of 20 msec are delivered during maintenance of the holding potential, and in part B, depolarizing stimuli of 1-msec duration are delivered virtually simultaneously with turning off the current applied to hold the MP. It can be seen that (dV/dt)$_{max}$ is identical for each of the four pairs of panels, and that (dV/dt)$_{max}$ decreased due to both

**FIGURE 4** Effects of $[K^+]_o = 5.4$ and 11.5 mM at the resting or holding MP of −83 mV (A, B) and at the holding or resting MP of −63 mV (C, D) in guinea pig papillary muscle. Note that the (dV/dt)$_{max}$ is slightly higher in A than in B, and slightly higher in C than in D. Note also that in each panel the threshold potential is less negative after 5 msec than after the 10- and 15-msec latency periods.

**FIGURE 5** Comparison of the results obtained by two methods used in the study of the non-MP-dependent effect of $[K^+]_o$ in guinea pig papillary muscle. All data in both A and B were obtained during the same cell impalement, the resting or holding potential = −82 mV in all four upper panels and −60 mV in all four lower panels. In part A, depolarizing current pulses of 20-msec duration are delivered during application of constant polarizing current pulses required to hold the MP. Note that at each of the two holding potentials the (dV/dt)$_{max}$ is lower at $[K^+]_o = 13.0$ mM than at $[K^+]_o = 5.4$ mM, and that at each of the two $[K^+]_o$ values, the (dV/dt)$_{max}$ is lower at the holding potential of −60 mV than at −82 mV. Note also that in each panel in part A the threshold potential is the same after both a shorter and a longer latency period. In part B, single action potentials are elicited simultaneously with turning off the current required to hold the potential. Note that the (dV/dt)$_{max}$ in each panel in part B is identical to that in the corresponding panel in part A.
depolarization (a vs. c and b vs. d) and increase in 
[K+]o (a vs. b and c vs. d). Other experiments on 
guinea pig (Table 1) and cat papillary muscles (Fig. 
6) produced similar results. The non-MF, [K+] o- 
dependent decrease in (dV/dt)max averaged 26.55% 
and was significant (P < 0.001) (Table 2).

Figure 7 shows results of a typical experiment in 
which we compared the effects of [K+]o = 5.4 and 
16.2 mM at two different holding potentials of ap-
proximately -84 mV (A,B) and -55 mV (C,D). It 
can be seen that (dV/dt)max decreased due to both 
depolarization (A vs. C and B vs. D) and increase in

Figure 6  Non-MF-dependent effect of [K+]o = 13.0 mM on (dV/dt)max in cat papillary muscle studied by the method 
used in panel B in Figure 5. [K+]o = 5.4 mM in A and G, and 13.0 mM in the remaining panels. Note that the (dV/dt)max is higher during hyperpolarization than at MP = -57 mV. The increase is greater at -90 mV than at -80 mV but 
there is no further increase at -100 and -110 mV. Note further that the (dV/dt)max is lower at [K+]o = 13.0 mM at all MP values than at [K+]o = 5.4 mM at MP = -80 mV.
NONMEMBRANE POTENTIAL K⁺ EFFECT ON (dV/dt)max/Kishida et al.

Figure 8 Effects of [K⁺]₀ = 20.0, 22.0, and 24.0 mM on the upstroke of the action potential in guinea pig papillary muscle (single-cell impalement). In A, control at [K⁺]₀ = 5.4 mM. In B, C, and D, holding potential is approximately −84 mV, and in E, F, and G, resting MP is unaltered (test). Note that at [K⁺]₀ = 20.0 and 22.0 mM hyperpolarization causes a slight increase in (dV/dt)max (B vs. E and C vs. F), but at [K⁺]₀ = 24.0 mM the upstroke velocity is the same at both MP values and is apparently too slow to produce a differentiated signal of measurable amplitude (D and G).

Figure 9 Relation between MP (abscissa) and (dV/dt)max (ordinate) expressed as percent of control value ([K⁺]₀ = 5.4 mM). The filled circles connected by the solid line and the corresponding vertical bars represent average ± SE at [K⁺]₀ = 5.4 mM, whereas the unfilled circles connected by the broken line and the corresponding vertical bars represent average ± SE at nine different [K⁺]₀ values ranging from 2.0 mM (far left, MP = −99 mV) to 24 mM (far right, MP = −45 mV). The values represented by filled circles were obtained by holding MP at the same level as the unaltered (test) resting MP at the test [K⁺]₀. The difference between the values marked by the filled circles and those marked by the unfilled circles represents the non-MP-dependent effect of [K⁺]₀ at a given MP. Asterisks show the statistical significance of these differences. In this and in the subsequent diagrams, the numbers in parentheses designate the number of papillary muscles. See text.
levels of approximately -83 and -99 mV. Hyperpolarization to approximately -99 mV increased (dV/dt)_{max} by less than 6% at eight different test [K⁺]₀ values ranging from 2.0 to 24.0 mM without altering the shape of the curve relating (dV/dt)_{max} to [K⁺]₀. At less negative E_m levels only two [K⁺]₀ were tested, and the slopes of lines connecting (dV/dt)_{max} at each E_m reflect the magnitude of the [K⁺]₀-induced decrease in (dV/dt)_{max}. The slope is flat at MP = -66 mV but becomes progressively steeper as the E_m declines from -63 to -55 mV. This means that the non-MP-dependent contribution of [K⁺]₀ to the decrease in (dV/dt)_{max} reached maximum at E_m = -55 mV. At E_m = -50 and -48 mV the depressing effect of [K⁺]₀ became less pronounced, but at these E_m the rapid Na⁺ inward current probably was largely inactivated, and the (dV/dt)_{max} was predominantly slow-channel-dependent.

Membrane Input Resistance (r_m) (Table 1 and Fig. 12)

Levels of r_m were expressed as percent of control r_m at [K⁺]₀ = 5.4 mM and MP = approximately -83 mV. 

![Figure 10](image.png)

**Figure 10** [K⁺]₀-independent effect of MP (unfilled bars) and non-MP-dependent effect of K⁺ (striped bars) on (dV/dt)_{max}, expressed as percent of control (dV/dt)_{max} at [K⁺]₀ = 5.4 mM and MP = -83.2 ± 0.2 mV. See text.

![Figure 11](image.png)

**Figure 11** Non-MP-dependent effect of [K⁺]₀ on the (dV/dt)_{max} at several MP levels. The points represent the average values from Table 3 and the results of single experiments during hyperpolarization to -99 mV (not included in Table 3). On the abscissa log [K⁺]₀ is represented, and on the ordinate (dV/dt)_{max} is expressed as percent of control values at [K⁺]₀ = 5.4 mM. Note that at MP = approximately -83 mV the slope approximates a straight line within the range of [K⁺]₀ = 11.5-20.0 mM. Note further that the slope is nearly flat at -66 mV, and that it becomes progressively steeper at -63, -60, and -55 mV. See text.

![Figure 12](image.png)

**Figure 12** Effects of MP at [K⁺]₀ = 5.4 mM (filled circles) and at various test [K⁺]₀ (unfilled circles) on r_m expressed as percent of control ([K⁺]₀ = 5.4 mM; MP = approximately -84 mV). Each symbol represents average value, and the corresponding vertical bar represents SE at seven different [K⁺]₀ levels ranging from 2.0 to 20.0 mM. The values represented by filled circles were obtained by holding MP at the same levels as the unaltered (test) resting MP at the corresponding test [K⁺]₀. The difference between the filled and the unfilled circle at each MP represents the non-MP-dependent effect of [K⁺]₀. Asterisks show statistical significance of the differences at the following [K⁺]₀: 2.0 and 10.0 (P < 0.01), 11.5, 13.0, and 16.2 mM (p < 0.001). See text.
mV. In the absence of any voltage control, \( r_m \) increased at \([K^+]_o = 2.0 \text{ mM}\) and decreased progressively with increasing \([K^+]_o\) as the membrane was depolarized.

The \( r_m \) decreased at any given \([K^+]_o\) within the 10.0–20.0 mM range when MP was shifted to approximately −83 mV and also at any MP held within a range of from approximately −70 to −43 mV when \([K^+]_o\) was increased. Figure 12 shows that at MP levels negative to approximately −80 mV the difference between \( r_m \) in test \([K^+]_o\), and \( r_m \) at \([K^+]_o = 5.4 \text{ mM}\) increased progressively with increasing \([K^+]_o\).

### Discussion

#### Critique of the Method

All experiments were performed during steady state of both \([K^+]_o\) and MP, and all spontaneous changes of MP and \((dV/dt)_{max}\) were in agreement with the expected effects of tested \([K^+]_o\). We found that at \([K^+]_o = 5.4 \text{ mM}\) the \(V_m\) for \((dV/dt)_{max}\) was −54.5 mV (see below), close to the value −55.7 ± 2.5 mV for half-inactivation of the rapid sodium system found by Beeler and Reuter (1970) in canine ventricular myocardium. Similarly, the curve relating \((dV/dt)_{max}\) to changes in RMP induced by changing \([K^+]_o\) (broken line in Fig. 9) had nearly the same shape as in the study of Gettes and Reuter (Fig. 7 in Gettes and Reuter, 1974).

The most important experimental error in our results can be due to the nonuniform longitudinal and/or radial voltage control during applications of depolarizing current pulses at \([K^+]_o\) of 2.0 and 5.4 mM and of hyperpolarizing current pulses at \([K^+]_o\) ranging from 11.5 to 24 mM. We have established that our method produced an adequate longitudinal voltage control, but we have not measured the MP below the surface.

We postulate that the use of the bath-clamp diminishes errors stemming from that part of series resistance \((r_s)\) that is caused by the bathing solution and the extracellular microelectrode. Yet this probably represents only a small portion of the total \(r_s\) expected to influence the radial voltage control. Other components of this \(r_s\) include the epithelial layer surrounding the bundle and the clefts within the bundle (Attwell and Cohen, 1977). Beeler and Reuter (1970) estimated that \(r_s\) was about 600 \(\Omega\) in dog ventricular trabeculae 1 mm long and 0.7 mm in diameter. Using their method of calculating \(r_s\), we found it to range in our acceptable experiments from 112 to 320 \(\Omega\), although in some of our records \(r_s\) was not evident because the voltage deflection lacked the initial sharp spike (e.g., in Fig. 3). However, it has been stated that the \(r_s\) measured by the method of Beeler and Reuter probably does not include the more deeply situated resistance of the clefts (Attwell and Cohen, 1977). To estimate the latter, Beeler and Holland passed the electrode through a myocardial trabecula that was 900 \(\mu\text{m}\) in diameter and found that the \(r_s\) in the middle of the bundle was almost 600 \(\Omega\), of which 175 \(\Omega\) was attributed to the surface epithelium and about 25 \(\Omega\) to the bath and the microelectrode (Beeler and McGuigan, in press). Recently, Reuter and Scholz reported a detailed study of voltage control in the ventricular muscle in the sucrose gap. Using a dual microelectrode method that directly compares the time courses of the applied current and the membrane current, Reuter and Scholz (1977) showed that the longitudinal distribution of potential can be regarded as uniform. These authors also inserted an electrode into the bundle and measured a voltage drop across the \(r_s\) of only 2–4 mV, which indicated reasonable homogeneity of the voltage in the radial direction during the slow inward current (Reuter and Scholz, 1977). These experiments show that the membrane potential during the flow of slow inward current can be adequately controlled both longitudinally and radially in a single sucrose gap (Beeler and McGuigan, in press).

In the Appendix, we have calculated the possible consequences of the voltage drop across the maximal observed \(r_s\) of 320 \(\Omega\). These calculations show that a systematic error due to the \(r_s\) of this magnitude would not explain the observed \((dV/dt)_{max}\) values during hyperpolarization at high \([K^+]_o\) and during depolarization at \([K^+]_o\) values of 2.0 and 5.4 mM.

If we had to ascribe our results following depolarization at \([K^+]_o\) of 5.4 mM to a series of systematic errors, we would have to postulate that: (1) the depolarizations from the level of approximately −84 to −66 mV were always accurate; (2) the depolarizations to −63 mV and less negative membrane potentials were always inaccurate; and (3) the inaccuracies increased progressively when depolarizations increased to −63, −60, and −55 mV. Such findings would not be likely without some obvious differences between the \(r_m\) value within the region between −66 and −55 mV. Yet this was not the case, because the average current strength required to depolarize from approximately −84 mV to −66 or −55 mV was nearly the same (Table 3 in the Appendix), a finding compatible with an inward-going rectification within this region of MP. These observations confirm the recent studies of McDonald and Trautwein, who showed a region of reduced conductance between −80 and −40 mV in the cat papillary muscle (McDonald and Trautwein, 1978) and an even more pronounced inward-going rectification in guinea pig papillary muscle (Trautwein and McDonald, 1978). The presence of anomalous rectification contributes to the improvement of voltage control (Beeler and McGuigan, in press) and thereby diminishes the likelihood of an experimental error in this portion of our study.

A more likely possibility of introducing serious errors is the voltage control in the hyperpolarizing direction, particularly at higher \([K^+]_o\) levels, at which one may expect higher conductance and decreased space constant. However, within the \([K^+]_o\)
range from 10.0 to 16.2 mM we cannot attribute the observed differences in \((dV/dt)_{max}\) to any consistent or significant differences between \(r_m\) levels during hyperpolarizations. For example, \(r_m\) levels during the hyperpolarization from \(-66\) to \(-84\) mV at \([K^+]_o\) of 10.0 mM and from \(-55\) to \(-83\) mV at \([K^+]_o\) of 16.2 mM were of similar magnitude. However, the hyperpolarization at \([K^+]_o\) of 10.0 mM restored \((dV/dt)_{max}\) to the control value, and that at \([K^+]_o\) of 16.2 mM to only 57% of the control value. In this example, changes in membrane conductance cannot explain the coincidence of an absent experimental error at \([K^+]_o\) of 10.0 mM and a systematic 14-mV error at \([K^+]_o\) of 16.2 mM. Other examples in the Appendix show that equally large, unexplained differences in the magnitude of systematic errors in polarization would be required to invalidate the observed effects of high \([K^+]_o\), on \((dV/dt)_{max}\).

Perhaps the most important argument against a systematic experimental error in the \((dV/dt)_{max}\) measurement in the fibers hyperpolarized to \(-84\) mV is the very small additional effect on \((dV/dt)_{max}\) following hyperpolarization to \(-99\) mV (Fig. 11) or to more negative MP (Fig. 8). If the depression of \((dV/dt)_{max}\) in fibers hyperpolarized to \(-84\) mV were due to an experimental error, we would expect such errors to be corrected more decisively by further increases in hyperpolarization.

One additional source of evidence in support of reasonable voltage homogeneity is the small standard error in the measurements of the threshold potential in different types of experiments (Table 1). Increasing in small steps the amplitude of subthreshold depolarization revealed small differences between the maximal subthreshold and the threshold potentials. This means that there was no evidence of a propagated action potential during 20 msec of sustained depolarization to a potential that was only a few millivolts more negative than the threshold potential. Similarly, the identical threshold potentials after the 10- and 15-msec latencies in each preparation suggest that the action potentials after longer durations of latency were elicited by the depolarizing currents and not by the uncontrolled action potentials spreading from prematurely depolarized regions within the bundle.

In conclusion, the available evidence indicates that the non-MP-dependent depression of \((dV/dt)_{max}\) by high \([K^+]_o\) is a biological phenomenon, and not an artifact resulting from a series of very large systematic experimental errors. However, without the full knowledge of the magnitude and the consequences of radial voltage nonhomogeneity, quantitative inaccuracies of our data cannot be ruled out. In particular, confirmations will be needed to validate the critical value of \([K^+]_o = 11.5\) mM at which the MP-independent effect of potassium became manifest, and the critical value of \([K^+]_o = 24.0\) mM at which the depolarization was suppressed at all levels of MP.

Non-MP-Dependent Effect of \([K^+]_o\) on \((dV/dt)_{max}\)

Few studies of the non-MP-dependent effect of \([K^+]_o\) on \((dV/dt)_{max}\) in cardiac tissues have been reported in the literature. Chen et al. (1975) found that the effect of \([K^+]_o = 9.4\) mM on \((dV/dt)_{max}\) in guinea pig papillary muscle was due exclusively to depolarization. This finding is in agreement with our results, which showed a significant non-MP-dependent effect of potassium at \([K^+]_o \geq 11.5\) mM but not at \([K^+]_o = 10.0\) mM.

Our results differ from the findings of Weidmann (1955a), who found that in sheep Purkinje fibers the depression of the rate of rise of action potential by \([K^+]_o\) of 13.5 mM could be restored to control value by hyperpolarization to \(-92\) mV. The difference between our results and those of Weidmann may be due to the difference in the fiber type, but there is another previous observation by Dudel and his coworkers (Dudel et al., 1967) that differs from the findings of Weidmann (1955a). These investigators studied current-voltage relations in short sheep Purkinje fibers at a constant speed of depolarization of 200 V/sec and reported that in an unspecified number of experiments a small excitatory sodium current that was present in Tyrode's solution at \([K^+]_o = 2.7\) mM disappeared at \([K^+]_o = 10.8\) mM (Dudel et al., 1967). Although Dudel et al. commented that "An increase in \([K^+]_o\), seems to depress the excitatory sodium system" (Dudel et al., 1967), they did not discuss this finding further in the text.

Mechanism of Non-MP-Dependent Effect of \([K^+]_o\) on \((dV/dt)_{max}\)

It has been customary to relate the magnitude of the \((dV/dt)_{max}\) of the cardiac action potential to the magnitude of the rapid inward sodium current. A simulation by Beeler and Reuter showed an excellent correlation between the measured \((dV/dt)_{max}\) and the theoretical sodium inactivation curve in the ventricular muscle (Fig. 5 in Beeler and Reuter, 1977). Thus it appears reasonable to attribute the depression of \((dV/dt)_{max}\) by \([K^+]_o\) to the depression of rapid inward sodium current. Such interpretation is consistent with the effect of \([K^+]_o\) on the rapid inward sodium current studied by Adelman and Palti in the voltage-clamped squid axon (Adelman and Palti, 1969). These authors found that the steady state "initial transient membrane conductance" decreased progressively with increasing \([K^+]_o\), and that this effect could not be explained solely on the basis of membrane depolarization induced by \([K^+]_o\) (Adelman and Palti, 1969).

Assuming that the mechanism of \([K^+]_o\) action in our study is similar to one operating in the squid axon, we have expressed our results in the form of the inactivation curve of steady state \((dV/dt)_{max}\) at seven different values of \([K^+]_o\), (Fig. 13). The specific
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FIGURE 13  Steady state sodium inactivation curve of (dV/dt)_{max} at different [K⁺], in guinea pig papillary muscle. On the abscissa, log of MP is represented, and on the ordinate the inactivation variable h. The value \( h = 1.0 \) expresses the maximal value of (dV/dt)_{max} obtained during hyperpolarization to -99 mV at \([K⁺]₀ = 5.4 \text{ mM}\). See text.

The slope factor \((s)\) was obtained from the equation used by Hodgkin and Huxley (1952):

\[
h^{*} = \frac{1}{1 + \exp (V_{r} - V_{h})/s},
\]

where \( h^{*} \) is the maximal value of (dV/dt)_{max}, \( V_{r} \) the resting membrane potential, and \( V_{h} \) the potential at which \( h \) is half-maximal.

The \( V_{h} \) shown by arrows was: -54.5 mV at \([K⁺]₀ = 5.4 \text{ mM}\), -64.0 mV at 16.0 mM, and -68.0 mV at 20.0 mM. The value of \( s \) was: 3.5 mV at \([K⁺]₀ = 5.4 \text{ mM}\), 2.3 mV at 16.2 mM, and 1.1 mV at 20.0 mM. At other \([K⁺]₀\) levels, the number of points was not sufficient to estimate \( s \). The progressive decrease in \( s \) with increasing \([K⁺]₀\) is compatible with a progressive reduction of the total number of sodium channels per unit of membrane (decrease of maximal sodium conductance, \( g_{Na} \)). However, the same effects could be due to altered kinetics of activation or inactivation of the sodium system (Hodgkin and Huxley, 1952).

In the squid axon study of Adelman and Palti (1969), the inactivation of the excitatory current was not complete even at \([K⁺]₀ = 100 \text{ mM}\). In our study, hyperpolarization to -99 and -110 mV failed to increase (dV/dt)_{max} to a value greater than approximately 30 V/sec when \([K⁺]₀ \) exceeded 20.0 mM. This result suggests that the rapid inward Na⁺ current is suppressed at lower \([K⁺]₀\) in the ventricular myocardium than in the squid axon. Adelman and Palti attributed the inactivation of the rapid inward sodium current by \([K⁺]₀\) to one of the following mechanisms: an alteration in membrane structure, a noncompetitive inhibition, or a competitive inhibition of sodium carriers, but they acknowledged that “until further information is obtained as to the physical nature of the initial transient conductance mechanism, it remains extremely difficult to choose among the possible mechanisms for the role played by potassium in the inactivation process” (Adelman and Palti, 1969).

The suppression of (dV/dt)_{max} by increased \([K⁺]₀\) may be due to mechanisms other than the “inactivation” of rapid inward sodium current. Thus Weidmann pointed out that during normal propagation of cardiac action potential the timing of (dV/dt)_{max} does not correspond to the membrane potential at which the inward current is maximal (see Fig. 30 in Weidmann, 1956). This discrepancy indicates that (dV/dt)_{max} reflects the contribution of currents other than rapid inward sodium current. More recently, Cohen and Strichartz (1977) have criticized the use of (dV/dt)_{max} as an estimate of the inward sodium current by pointing out that the use of (dV/dt)_{max} can lead to misleading conclusions in situations in which the outward potassium and leakage currents are comparatively large relative to the inward sodium current.

We cannot rule out the possibility that the observed effects of \([K⁺]₀\) on (dV/dt)_{max} were due to the change in the relative ratio of the inward and outward conductances rather than to the inactivation of rapid inward sodium current. However, the contribution of high potassium conductance would be expected only during hyperpolarization to potentials negative to the K⁺ equilibrium potential but not during \([K⁺]₀\)-induced depolarization. The reasons for this are as follows. (1) In heart muscle in which anomalous rectification of the potassium channel is present the background outward current is less than 2% of the sodium current during the upstroke of the action potential at \([K⁺]₀ = 5.4 \text{ mM}\) (references in Beeler and Reuter, 1977). (2) Recently, McDonald and Trautwein (1978) studied the current-voltage relations of both the total steady state outward current and its time-independent background component in the cat papillary muscle and found that both currents displayed inward-going rectification. Raising \([K⁺]₀\) from 3 mm to 10, 20, and 30 mm increased conductance, but the K⁺-induced increases in conductance were offset by the stronger inward-going rectification, which resulted in nearly superimposable current-voltage relations for all four \([K⁺]₀\) levels at MP positive to K⁺ equilibrium potential (Fig. 5 in McDonald and Trautwein, 1978). (3) In keeping with the above effects of \([K⁺]₀\) on the current-voltage relation in the ventricular myocardium, we found no MP-independent current suppressed at lower \([K⁺]₀\) in the ventricular myocardium than in the squid axon. Adelman and Palti attributed the inactivation of the rapid inward sodium current by \([K⁺]₀\) to one of the following mechanisms: an alteration in membrane structure, a noncompetitive inhibition, or a competitive inhibition of sodium carriers, but they acknowledged that “until further information is obtained as to the physical nature of the initial transient conductance mechanism, it remains extremely difficult to choose among the possible mechanisms for the role played by potassium in the inactivation process” (Adelman and Palti, 1969).
effects of [K+], on the threshold potential (Fig. 2).

Although we have no evidence that the depolarizing effect of high [K+] within the studied range caused a net increase in K+ outward current, we cannot dismiss the possibility that the observed decrease in (dV/dt)max and the suppression of action potential upstroke by [K+], was produced by a mechanism postulated by Cohen and Strichartz (1977).

Another mechanism for the decrease in (dV/dt)max could result from a decrease in the driving force for the sodium ions, i.e., shift of the sodium equilibrium potential to more negative potentials. The marked sensitivity of (dV/dt)max to small changes in [K+], within the range of 11.5-16.2 mM makes this possibility unlikely. Moreover, we have not carried out any interventions that would be expected to increase intracellular sodium concentration and decrease the driving force for the sodium ions.

Threshold Potential

Dominguez and Fozzard (1970) reported that in short Purkinje fibers the threshold potential was less negative with short than with long current pulses but became quite constant with currents of 1 msec or longer. In our study, the threshold potential was constant after latencies of 10-15 msec but was sometimes less negative after 5 msec than after 10-15 msec. This suggests that in our preparation the duration of latency at which the threshold potential became constant was longer than in short Purkinje fibers. This difference may be attributed to the differences in size, architecture, and space constant between the Purkinje and ventricular fibers (Johnson and Tille, 1961; Kamiyama and Matsuda, 1966; Sakamoto, 1969). The threshold potential in Tyrode’s solution was —64.7 ± 0.6 mV, a value similar to the threshold potential reported by others in canine ventricular myocardial fibers studied in a baseline (Kamiyama and Matsuda, 1966; Sakamoto, 1969) or in a sucrose (Beeler and Reuter, 1970) gap.

The effect of [K+], on the threshold potential in the ventricular fibers has not been studied previously. In Purkinje fibers the threshold potential became less negative following increase in [K+], from 2.7 to 5.0 mM (Spear and Moore, 1974) or from 2.7 to 7.0 mM (Dominguez and Fozzard, 1970). In our study, threshold potential became more negative when [K+], was lowered from 5.4 to 2.0 mM. Conversely, the threshold potential became progressively less negative with increasing [K+],. These changes in threshold potential paralleled changes in Em and were not dependent on [K+],.

Potassium exerted a non-MP-dependent effect on threshold potential only at a concentration of 20.0 mM, but at this [K+],, the threshold potential of approximately —33 mV was close to the activation threshold of the slow inward current (New and Trautwein, 1972).

Membrane Input Resistance (rm)

Membrane resistance at the resting potential increased when [K+], was lowered from 5.4 to 2.0 mM and the fibers became hyperpolarized. Conversely, when [K+], was raised above 5.4 mM, membrane resistance decreased in keeping with the reported effects of [K+], on membrane K+ conductance in Purkinje fibers (Dominguez and Fozzard, 1970; Spear and Moore, 1974; Vassalle, 1965; Carmeliet, 1961). When MP was kept constant within a range of from approximately —70 to —43 mV, the increase in [K+], decreased rm. This effect can be attributed to the decreasing difference between Em and K+ equilibrium potential. Figure 12 shows that, at a fixed [K+],, rm decreased on membrane hyperpolarization and increased progressively with membrane depolarization. These voltage-dependent changes probably reflect the inward rectification of the membrane K+ conductance in ventricular myocardium (Fig. 1A in Beeler and Reuter, 1977).

Clinical Implications

We have shown that the K+-induced depolarization to a MP less negative than approximately —63 mV will depress (dV/dt)max of the ventricular myocardium due to two effects: a MP-dependent and a non-MP-dependent effect of [K+],. This means that at any [K+],, that exceeds approximately 10-11 mM the depression of (dV/dt)max may be expected to exceed the depression resulting from depolarization alone in the absence of an increase in [K+],. The non-MP-dependent effect of [K+], on (dV/dt)max may be expected to influence the conduction velocity in the ventricular myocardium in the presence of severe hyperkalemia. Plasma K+ concentrations in excess of 10.5 mM have been reported in patients with renal insufficiency (Finch et al., 1946; Keith and Burchell, 1949; Merril et al., 1950; Bull et al., 1953; Hopper et al., 1953). Recent studies using K+-sensitive electrodes have demonstrated that occlusion of coronary artery in pigs consistently increased [K+], above 10.0 mM in the extracellular fluid.
fluid within the ischemic myocardium (Hill and Gettes, 1977).

Appendix

(In collaboration with Dr. Jack W. Buchanan, Jr.)

Series resistance (r,) was calculated in from two to six records from each group of experiments. The model of ventricular muscle fiber membrane circuit with r, was proposed by Beeler and Reuter (1970), who measured r, by applying a voltage clamp and analyzing the upstroke of the current trace. We performed the same analysis by applying a square current pulse and analyzing the upstroke of the MP step. The tracings were magnified and the ascent of the MP was retracted to identify the initial rapid portion attributed to voltage drop across r, and the subsequent slower portion attributed to the charge of membrane capacity across membrane resistance. We assumed that r, was represented by the ratio of the amplitude of the rapid portion of the MP change to the strength of current applied across the gap. The r, calculated in this manner ranged from 112 to 320 Ω. The r, tended to be higher at lower [K+], but the number of experiments was not sufficient to test the significance of possible differences between r, at different levels of [K+]o. Table 3 shows the error in MP that could be attributed to the calculated r,.

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References


Hopper J Jr, O'Connell BP, Fluss HR: Serum potassium patterns...
Johnson EA, Tille J: Investigations of the electrical properties of cardiac muscle fibers with the aid of intracellular double-barreled electrode. J Gen Physiol 44: 443-467, 1961
Katzung B: Electrically induced automaticity in ventricular myocardium. Life Sci 14: 1133-1140, 1975
McDonald TF, Trautwein W: The potassium current underlying delayed rectification in cat ventricular muscle. J Physiol (Lond) 274: 217-246, 1978
Reuter H, Scholz H: A study of the ion selectivity and the kinetic properties of the calcium dependent slow inward current in mammalian cardiac muscle. J Physiol (Lond) 264: 17-47, 1977
Spear JF, Moore EN: Supernormal excitability and conduction in the His-Purkinje system of the dog. Circ Res 35: 782-792, 1974
Trautwein W, McDonald TF: Current-voltage relations in ventricular muscle preparations from different species. Pfluegers Arch 374: 79-89, 1978
Vassalle M: Cardiac pacemaker potentials at different extra- and intracellular K concentrations. Am J Physiol 208: 770-775, 1965
Weidmann S: The effect of the cardiac membrane potential on the rapid carrying availability of the sodium system. J Physiol (Lond) 127: 213-224, 1955a
Weidmann S: Effects of calcium ions and local anaesthetics on electrical properties of Purkinje fibres. J Physiol (Lond) 129: 568-582, 1955b
Weidmann S: Elektrophysiologie der Herzmuskelfaser. Bern, Hans Huber, 1956
Effects of K+ and K+-induced polarization on (dV/dt)max, threshold potential, and membrane input resistance in guinea pig and cat ventricular myocardium.

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