Conduction of hyperpolarization along hamster feed arteries: augmentation by acetylcholine

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Emerson, Geoffrey G., Timothy O. Neild, and Steven S. Segal. Conduction of hyperpolarization along hamster feed arteries: augmentation by acetylcholine. Am J Physiol Heart Circ Physiol 283: H102–H109, 2002. First published February 28, 2002; 10.1152/ajpheart.00038.2002.—The conduction of vasodilation along resistance vessels has been presumed to reflect the electrotonic spread of hyperpolarization from cell to cell along the vessel wall through gap junction channels. However, the vasomotor response to acetylcholine (ACh) encompasses greater distances than can be explained by passive decay. To investigate the underlying mechanism for this behavior, we tested the hypothesis that ACh augments the conduction of hyperpolarization. Feed arteries (n = 23; diameter, 58 ± 4 μm; segment length, 2–8 mm) were isolated from the hamster retractor muscle, cannulated at each end, and pressurized to 75 mmHg (at 37°C). Vessels were impaled with one or two dye-containing microelectrodes simultaneously (separation distance, 50 μm to 3.5 mm). Membrane potential (E_m) (rest, approximately −30 mV) and electrical responses were similar between endothelium and smooth muscle, as predicted for robust myoendothelial coupling. Current injection (−0.8 nA, 1.5 s) evoked hyperpolarization (−10 ± 1 mV; membrane time constant, 240 ms) that conducted along the vessel with a length constant (λ) = 1.2 ± 0.1 mm; spontaneous E_m oscillations (~1 Hz) decayed with λ = 1.2 ± 0.1 mm. In contrast, ACh microiontophoresis (500 nA, 500 ms, 1 μm tip) evoked hyperpolarization (−14 ± 2 mV) that conducted with λ = 1.9 ± 0.1 mm, 60% further (P < 0.05) than responses evoked by purely electrical stimuli. These findings indicate that ACh augments the conduction of hyperpolarization along the vessel wall.

cable theory; length constant; microcirculation; endothelium; smooth muscle

THE MEMBRANE POTENTIAL (E_m) of smooth muscle cells is a key physiological determinant of vasomotor tone and reactivity (7, 16, 32, 34). Through electromechanical coupling (26), smooth muscle cells contract with depolarization and relax with hyperpolarization (17). Blood flow control involves the concerted interplay of vasomotor responses among the arteries and feed arteries that comprise vascular resistance networks (24). Under physiological conditions, these vessels display a high degree of spontaneous tone coincident with E_m of −30 to −40 mV (8, 32). From this resting condition, events that evoke hyperpolarization can produce relaxation and vasodilation within seconds. Once triggered, electrical signals can travel along constitutive vessel branches of the network through gap junction channels between endothelial cells and smooth muscle cells, though the precise nature of coupling can vary between vascular beds (8). In such a manner, the spread of hyperpolarization underlies the conduction of vasodilation along arterioles and feed arteries (8, 32).

Given the near-linear relationship between changes in E_m and changes in vessel diameter through the range of −45 to −5 mV (7, 32, 34), the ability of hyperpolarization to coordinate the simultaneous relaxation of multiple smooth muscle cells is determined in large part by the extent to which the amplitude of the signal is preserved with distance along the vessel segment. Such behavior is typically described in light of cable theory (13). The first studies (12) of electrical conduction in arterioles used low-intensity current injection (0.5 s, −1 nA) to minimize the activation of voltage-sensitive ion channels. Signals were found to decay electrotonically, i.e., in a manner that indicated a passive signaling system. More recently, through accounting for the effect of network branching on signal dissipation, the behavior of KCl-induced depolarizations has confirmed the passive nature of electrical signaling in arteriolar networks (25, 34).

Physiological signals often entail ligand-receptor interactions that can activate multiple signaling pathways. For example, acetylcholine (ACh) evokes pronounced hyperpolarization of endothelial cells through the activation of calcium-activated potassium channels (5). ACh also stimulates the release of autacoids from the endothelium that evoke smooth muscle cell hyperpolarization (4, 10, 31). In addition to ion channel activation, the elevation of intracellular calcium and release of autacoids may influence cell-to-cell coupling through gap junctions (15, 23). We therefore reasoned that hyperpolarization triggered by ACh might conduct differently than a signal from a purely electrical stimu-
In the present study, we tested this hypothesis with feed artery segments that spanned a range of "cable" lengths using a mathematical expression developed for this purpose (6).

**METHODS**

Procedures were approved by the Animal Care and Use Committee of The John B. Pierce Laboratory and performed in accord with the National Institutes of Health Guide for the Care and Use of Laboratory Animals.

**Surgical isolation.** Male Golden hamsters weighing 70–90 g (Charles River Laboratories; Kingston, NY) were anesthetized with pentobarbital sodium (65 mg/kg ip). While being viewed through a stereomicroscope, a 2-cm incision was made over the left scapula and the skin was reflected to expose the underlying retractor muscle (33). Exposed tissue was moistened with physiological saline solution (PSS) containing (in mmol/l) 148 NaCl, 4.7 KCl, 2.0 CaCl2, 1.17 MgSO4, 0.026 EDTA, 2.0 3-(N-morpholino)propanesulfonic acid, 5.0 glucose, and 2.0 pyruvate. Reagents were obtained from Sigma (St. Louis, MO) or Baker (Phillipsburg, NJ). The retractor muscle was reflected to expose 1–3 feed artery-collecting vein pairs leading to its ventral surface. Vessel pairs were excised by cutting each end and transferred to a chilled (4°C) dissecting dish containing calcium-free PSS with 1% albumin (catalog no. 10856, Amersham; Cleveland, OH). The hamster was then given an intraperitoneal overdose of pentobarbital sodium.

To preserve the integrity of the feed artery, the adjacent vein was pinned to a Sylgard (Dow Corning; Midland, MI) surface. Connective tissue was dissected away, with care taken to avoid touching the artery. The isolated artery was transferred to a custom-made vessel chamber (1 ml vol) filled with calcium-free PSS (containing 1% albumin) chilled to 4°C.

**Vessel cannulation.** Two cannulation pipettes (30 μm outer diameter) prepared from borosilicate glass capillary tubes (model GC150T-10; Warner Instruments; Hamden, CT) were filled with PSS (containing 2 mmol/l CaCl2 and 1% albumin) and lowered into the vessel chamber using micromanipulators. Each cannula was connected to a hydrostatic column filled with ACh (1 mol/l), and connected via an Ag/AgCl wire to a microiontophoresis current generator (model 260, World Precision Instruments; Sarasota, FL). The micropipette was moved by remote control of a hydraulic micromanipulator (model MX630R, Siskiyou Design; Grants Pass, OR) to minimize mechanical disturbance during subsequent electrophysiological recording. The tip was positioned within 5 μm of the vessel wall toward the downstream end (with respect to the direction of superfusion) of the cannulated segment and ACh was delivered as a brief pulse (500 nA, 500 ms). The intensity and duration of this stimulus were determined to be just sufficient to evoke maximal dilation at the site of stimulation. Responses were eliminated by withdrawing the micropipette >50 μm from the vessel, confirming that ACh stimuli were highly localized (7, 8).

**Current injection.** During dual cell impalements, current was injected into one electrode, while the electrical responses were monitored with both electrodes simultaneously (7, 12). The "criterion" stimulus (-0.8 nA; 1.5 s) for current injection was selected based on its evoking a robust response and being within linear range of our microelectrodes (7). Before impalement, the bridge balance of the electrometer was adjusted during current injections into the vessel bath. With stable impalement, the bridge was balanced during current pulses into the cell so that the charging of membrane capacitance at the onset of the pulse began smoothly from the baseline potential (20). Typically, several injections were necessary to obtain a balanced bridge; tachyphylaxis to these electrical stimuli was negligible (7, 9).

**Experimental protocols.** To test the hypothesis that ACh can augment the spread of hyperpolarization, responses to ACh were compared with those to current injection (8). For "short" vessel segments (2–2.5 mm long), a single microelectrode was impaled into a cell ~0.1 mm from the upstream end. An ACh stimulus was applied at 0, 0.5, 1.0, or 2.0 mm downstream of the microelectrode and then repeated with the micropipette positioned at each of the other sites (in random order); a 2-min rest occurred between stimuli and tachyphylaxis to ACh was negligible (8). "Intermediate" (3.5–4.5 mm) and "long" (7.0–8.5 mm) ves-
similarly over distance for intermediate (Fig. 3) and impalements, an ACh stimulus was applied 500 μm beyond the downstream microelectrode.

**Data analysis.** Electrical responses (resolution ±0.5 mV) were acquired at 400 Hz, the time constant of the recording system was <10 ms. Representative tracings were selected to demonstrate typical responses. At defined locations along vessel segments, the magnitude of each response (V) was calculated as (peak − resting) values. Assuming electrotonic conduction along a finite vessel segment with sealed end (6), V(x) can be expressed mathematically as shown in Fig. 1. As detailed in Figs. 3–6, variations of this expression were fitted to the data using a least-squares method in Excel 97 (Microsoft) to calculate λ for each vessel segment. Summary data are presented as means ± SE.

**RESULTS**

On pressurization, vessels (n = 23) first dilated to their maximal diameter (85 ± 5 μm) and then developed tone spontaneously (resting diameter, 58 ± 4 μm). When fully equilibrated, E_m of endothelial cells (−28 ± 1 mV, n = 84) was not different from that of smooth muscle cells (−29 ± 1 mV, n = 73), as previously reported (7). All vessels were studied from this initial resting condition. Because endothelial cells and smooth muscle cells are electrically coupled to each other in these vessels (7), and the electrical behavior of smooth muscle cells was not different from that of endothelial cells under the conditions of these experiments (Figs. 3, 4, and 6), data were pooled for our analyses of cable properties.

Injection of −0.8 nA into an endothelial cell or a smooth muscle cell near the center of a long segment evoked hyperpolarization (−7 ± 1 mV) of the impaled cell (Fig. 2). During current injection, E_m hyperpolarized to 84% of a new steady-state level in 240 ms; this value was taken as τ_m (13).

Dual-cell recordings were obtained in 17 vessel segments at separation distances of 50 μm to 3.5 mm. Across these experiments, current-induced hyperpolarization (−10 ± 1 mV; range −3 to −30 mV) decayed similarly over distance for intermediate (Fig. 3) and long segments (Fig. 4), with λ = 1.3 ± 0.1 and 1.0 ± 0.2 mm, respectively (Table 1). In contrast, ACh-induced hyperpolarization (−14 ± 2 mV; range −2 to −35 mV) conducted along short (Fig. 5), intermediate (Fig. 6), and long (n = 1; not shown) segments significantly further (λ = 1.9 ± 0.2 mm) than hyperpolarization induced by current injection (P < 0.05, Student’s unpaired t-test; Table 1). Our calculation of λ based on hyperpolarization to ACh was independent of vessel segment length and thereby confirmed the validity of the expression in Fig. 1 (6). In seven vessels, λ was determined for both stimuli; responses to current injection (λ = 1.2 ± 0.1 mm) were significantly different (P < 0.05; Student’s paired t-test) than those to ACh microiontophoresis (λ = 1.9 ± 0.2). Furthermore, λ was independent of the amplitude of hyperpolarization for both current injection (Fig. 7A) and for ACh microiontophoresis (Fig. 7B), with values clustered around 1 and 2 mm, respectively (P < 0.05).

Spontaneous oscillations in membrane potential (~1 Hz; amplitude 10–15 mV; Fig. 8) were seen in five vessels. Oscillations were simultaneous and similar in both shape and magnitude when the separation distance was small (Fig. 8A). However, as separation distance increased, oscillations at the second electrode became smaller, smoother, and delayed relative to oscillations at the first electrode (Fig. 8B). The ratio of oscillation amplitudes in this vessel decayed with a λ of 1.3 mm (Fig. 8C). At a separation distance of 2,200 μm, the peak of the oscillations at the downstream electrode was delayed (relative to oscillations at the proximal electrode) by 48 ± 6 ms, indicating an effective conduction velocity of ~45 mm/s. Length constants of 1.1, 1.1, 1.2, and 2.9 mm were calculated for the other four vessels using the equation in Fig. 3A. The vessel with λ = 2.9 mm was not included in our analysis (Table 1) as explained in the discussion.

With the use of τ_m (Fig. 2) and λ based on current injection (Fig. 3 and 4), additional parameters were

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**Fig. 2.** Input resistance (R_m) and membrane time constant (τ_m) of feed arteries. Single responses to injection of −0.8 nA for 1.5 s conducted during n = 30 impalements from n = 6 vessels were measured at the injecting electrode and averaged to generate this record. Long segments (7.0–8.5 mm) were used to approximate infinite cables. Responses were similar in endothelial cells and smooth muscle cells and therefore pooled. Current injection resulted in a hyperpolarization of −7 ± 1 mV (R_m = 9 MΩ) that reached 84% amplitude in 240 ms (=τ_m).

**Fig. 1.** Feed artery segment of finite length is impaled simultaneously with an electrode for injecting current (I) and an electrode for recording voltage (V). l, Vessel length; y, distance between downstream end of vessel and stimulus electrode; x, distance between downstream end of vessel and recording electrode; λ, length constant; r_a, axial resistance.
calculated (Table 2) as follows. Input resistance ($R_{in}$) was calculated using the equation

$$R_{in} = \frac{V_1}{I}$$

where $V_1$ is the change in voltage at the injected site and $I$ is the injected current. The intracellular resistance per unit length of vessel to axial current flow ($r_m$) as well as the membrane resistance per unit length of vessel ($r_a$) were calculated by solving two equations simultaneously (12)

$$\lambda = \frac{r_m}{r_a}$$

$$R_{in} = \sqrt{\frac{r_m}{r_a}}$$

In feed arteries of the hamster retractor muscle, conduction spreads along the vessel via the endothelial cell layer (8). The cross-sectional area ($A$) of this layer is calculated from the expression

$$A = \pi[(D/2 + q)^2 - (D/2)^2]$$

where $D$ is the resting internal diameter and $q$ is the average thickness of the endothelial cell layer ($0.5 \mu m$) (21). This expression simplifies to

<table>
<thead>
<tr>
<th>Segment length, mm</th>
<th>Current Injection</th>
<th>$n$</th>
<th>Oscillations</th>
<th>$n$</th>
<th>$\lambda$ ACh</th>
<th>$n$</th>
</tr>
</thead>
<tbody>
<tr>
<td>2–2.5</td>
<td></td>
<td>9</td>
<td>1</td>
<td>2</td>
<td>2.0 ± 0.3</td>
<td>6</td>
</tr>
<tr>
<td>3.5–4.5</td>
<td></td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1.8 ± 0.3</td>
<td>11</td>
</tr>
<tr>
<td>7–8.5</td>
<td></td>
<td>6</td>
<td>1</td>
<td>2</td>
<td>2.3 ± 0.3</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>15</td>
<td>1</td>
<td>4</td>
<td>1.9 ± 0.2</td>
<td>18</td>
</tr>
</tbody>
</table>

Values are means ± SE; $n$ = no. of vessel segments. ACh, acetylcholine; $\lambda$, length constant (mm). For each vessel segment, $\lambda$ was calculated with the expressions in Figs. 3–6 by using responses to current injection, spontaneous oscillations, or to ACh microiontophoresis. The value for $\lambda$ was significantly greater for ACh stimuli than for current injection or oscillations and was independent of segment length. *$P < 0.05$, analysis of variance.
\[ A = \pi q(D + q) \]

The resistivity of the cytoplasm \((R_i)\) was calculated by using the equation (25)
\[ R_i = r_a q \pi (D + q) \]

The membrane resistance \((R_m)\) was calculated from the equation
\[ R_m = \frac{\tau}{C_m} \]

where membrane capacitance \((C_m)\) is assumed to be 2 \(\mu\)F/cm² (28).

**DISCUSSION**

In the present study, the biophysical properties of hamster feed arteries as conductors of hyperpolarization were analyzed using cable theory. Our analysis reveals that the length constant of these vessels was ~60% longer \((P < 0.05)\) when hyperpolarization was induced by ACh than when induced by current injection. In a purely passive system, the decay of an electrical signal should be similar irrespective of the initial

![Fig. 5. Acetylcholine (ACh)-induced hyperpolarization in short segments of feed arteries.](image)

**Fig. 5.** Acetylcholine (ACh)-induced hyperpolarization in short segments of feed arteries. \(A\): vessel segments \((l = 2.0 \text{ to } 2.5 \text{ mm})\) were isolated and impaled with a microelectrode at a defined distance \((y = 100 \mu\text{m})\) from the upstream (with respect to flow of physiological saline solution along the vessel) end of the segment. ACh was applied by microiontophoresis (500 nA, 500 ms) to the microelectrode while electrical responses \(V_1\) and \(V_2\) were recorded. \(B\): magnitude of hyperpolarization \((V)\) was plotted vs. \(D\). \(C\): for each recording from 2 EC, 2 SMC, or 1 EC and 1 SMC, the ratio of \(V_2/V_1\) was plotted vs. \(D\). To calculate \(\lambda\) for each vessel segment \((2-4\) recordings each), a least-squares fit of the equation in \(A\) was performed. A composite curve (solid line) based on the average \(\lambda\) for all vessels \((n=11)\) is shown. Dotted line indicates the expected decay based on data from current injection (Table 1).

![Fig. 6. ACh-induced hyperpolarization in feed artery segments of intermediate length.](image)

**Fig. 6.** ACh-induced hyperpolarization in feed artery segments of intermediate length. \(A\): vessel segments \((l = 3.5 \text{ to } 4.5 \text{ mm})\) were isolated and impaled with 2 microelectrodes separated by a variable \(D\). An ACh micropipette was positioned at \(a = 500 \mu\text{m}\) downstream from microelectrode 1. ACh was applied by microiontophoresis (500 nA, 500 ms) while electrical responses \(V_1\) and \(V_2\) were recorded from microelectrodes 1 and 2, respectively. \(B\): representative traces showing \(V_1\) and \(V_2\) when microelectrodes were separated by \(D = 3.5 \text{ mm}\). \(C\): for each recording from 2 EC, 2 SMC, or 1 EC and 1 SMC, the ratio of \(V_2/V_1\) was plotted vs. \(D\). To calculate \(\lambda\) for each vessel segment \((2-4\) recordings each), a least-squares fit of the equation in \(A\) was performed. A composite curve (solid line) based on the average \(\lambda\) for all vessels \((n=11)\) is shown. Dotted line indicates the expected decay based on data from current injection (Table 1).

stimulus. Therefore, the behavior revealed by the present experiments indicates that the properties that define \(\lambda \) \((r_a \text{ and } r_m)\) can change according to the stimulus or that an active mechanism contributes to the conduction of hyperpolarization triggered by ACh.

We estimated \(\lambda\) with a single recording electrode by examining the decay in the electrical signal with distance from the triggering stimulus. A similar approach has been used with depolarizing stimuli (25). A more rigorous estimate of \(\lambda\) involves measurement of membrane potential simultaneously at two points along an electrical pathway and was found here to give similar results (Table 1). Simultaneous current injection and recording from submucosal arterioles of the guinea pig small intestine found \(\lambda = 1.1 \text{ to } 1.6 \text{ mm}\) (12). Our experiments with current injection yield \(\lambda = 1.2 \text{ mm}\), which
agrees well with the original measurements. Similar values have also been obtained for isolated vascular smooth muscle cells (0.9 mm) (29) and guinea pig vas deferens (0.9 mm) (3). In strips of porcine coronary arteries, was not different between electrical- and kinin-induced hyperpolarization (19). In contrast, our experiments with ACh-induced hyperpolarization generated 1.9 mm, which was significantly longer than for current injection. This outcome was independent of vessel segment length or the number of microelectrodes used for recording, confirming the validity of the model used for analysis (6).

Along infinite cables, electrotonic signals decay to zero with distance, as shown by the expression (13)

\[ V = k e^{-D/\lambda} \]

However, for finite systems, the length of the cable may be sufficiently short so that an electrotonic signal does not have adequate distance to decay to zero. For example, in Figs. 3 and 6, the curves approach an asymptote that can be predicted by taking the limit of the mathematical expression as distance goes to infinity, which is \( e^{-1/\lambda} \). This limit predicts that a larger \( \lambda \) will have a higher asymptote, which is consistent with our findings.

### Table 2. Cable properties of feed arteries

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \lambda ), mm</td>
<td>1.1</td>
</tr>
<tr>
<td>( \tau ), s</td>
<td>0.240</td>
</tr>
<tr>
<td>( R_{in}, \Omega )</td>
<td>( 8.8 \times 10^6 )</td>
</tr>
</tbody>
</table>

Calculated parameters:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( r_a, \Omega \cdot \text{cm}^{-1} )</td>
<td>( 1.6 \times 10^8 )</td>
</tr>
<tr>
<td>( r_m, \Omega \cdot \text{cm} )</td>
<td>( 1.9 \times 10^6 )</td>
</tr>
<tr>
<td>( R_i, \Omega \cdot \text{cm} )</td>
<td>140</td>
</tr>
<tr>
<td>( R_m, \Omega \cdot \text{cm}^2 )</td>
<td>( 1.2 \times 10^5 )</td>
</tr>
</tbody>
</table>

Length constant \( (\lambda) \), time constant \( (\tau) \), and input resistance \( (R_{in}) \) were measured (Figs. 2–4; Table 1). From these values, axial resistance \( (r_a) \), resistivity of the cytoplasm \( (R_i) \), membrane resistance \( (r_m) \), and specific membrane resistance \( (R_m) \) were calculated using equations given in text.
The hyperpolarization evoked by ACh averaged 4 mV greater than for current injection \((P < 0.05)\), raising the possibility of a threshold potential beyond which the system exhibits nonlinear (i.e., regenerative) behavior. However, analysis of the ranges of hyperpolarization evoked by respective stimuli fails to indicate such a threshold (Fig. 7). Rather, \(\lambda\) was significantly different between current injection and ACh microiontophoresis throughout similar hyperpolarizing responses that spanned a range of \(-30\) mV. The variation in the amplitude of hyperpolarization in response to constant levels of current injection and ACh microiontophoresis (Fig. 7) can be explained by differences in any parameter that influences \(r_m\) or \(r_n\), including segment length, vessel diameter, and total wall cross-sectional area. For example, responses to current injection in intermediate segments \((-10 \pm 1\) mV) were significantly greater \((P < 0.05)\) than responses in long segments \((-7 \pm 1\) mV).

The overall value of \(\lambda\) depends on the ratio of \(r_m\) to \(r_n\) along the vessel wall. Our finding that ACh is augmented \(\lambda\) by \(-60\%\) may therefore reflect up to a 2.5-fold change in either of these biophysical properties. For example, in addition to the opening of potassium channels to produce hyperpolarization (5), the elevation in intracellular calcium triggered by ACh (1) can stimulate endothelial cells to produce NO and to form products of arachidonic acid. In turn, these downstream signaling events may alter \(r_m\) and/or the gating properties of gap junction channels (15) and thereby alter \(r_n\) (23). Alternatively, the augmented response to ACh may reflect an active signaling process. An outward potassium current that produces regenerative afterpotentials (2) and inward rectifier potassium channels may contribute to the conduction of vasodilation in arterioles of the coronary circulation (22). Whether these or additional mechanisms underlie the actions of ACh awaits further study.

During a voltage step applied to an infinite cable, the voltage \((V)\) response at the injected electrode follows the equation

\[
V = V_1 \text{erf} \left(\frac{t}{\tau_m}\right)
\]

where \(V_1\) is the steady-state change in voltage at the injected electrode, \(t\) is time, \(\tau_m\) is the membrane time constant, and erf is the error function \((13)\). Accordingly, we obtained a value of 240 ms for \(\tau_m\) (Fig. 2), which is similar to values in arterioles \((260–500\) ms) (12) and vas deferens \((260\) ms) (3) of guinea pigs. Average input resistance \((8.8 \text{ M}\Omega; \text{Table 2})\) was similar whether recording from smooth muscle or endothelium and nearly three orders of magnitude less than the input resistance for an individual smooth muscle cell \(8 \text{ G}\Omega\) (14)). Our values are similar to those previously measured for guinea pig submucosal arterioles \((5–20\) M\Ω\) (12)) and hamster feed arteries (7). This difference between isolated cells and intact vessel segments reflects robust gap junctional coupling among smooth muscle cells and endothelial cells within the vessel wall (7).

Spontaneous oscillations that conduct along the vessel length and decay electrotonically with distance (Fig. 8) imply the existence of pacemaker cells that act as a point source for electrical current. In our analysis of these oscillations, we assumed that pacemaker cells were located outside of the region spanned by the pair of recording electrodes. In four vessels, \(\lambda = 1.2 \pm 0.1\) mm, which was not different from \(\lambda\) obtained with intracellular current injection. However, \(\lambda = 2.9\) mm in the fifth vessel, which was inconsistent with values for \(\lambda\) obtained in any of our other experiments. This discrepancy could be explained by the pacemaker site being located between the two electrodes. The spontaneous oscillations in membrane potential were \(>15\) mV yet were not associated with changes in vessel diameter (not shown). In contrast, current injection evoked robust vasodilation with \(-10\) mV hyperpolarization (7). To explain this discrepancy, we suggest that the greater duration of hyperpolarization during current injection \((>1.5\) s) compared with spontaneous oscillations \(<1\) s) was more effective in producing vasodilation. With either current injection or ACh microiontophoresis, the mechanical response lags behind the electrical response by 1–2 s (7). This delay likely reflects the time required to sequester intracellular calcium and deactivate the contractile machinery. Therefore, spontaneous oscillations in membrane potential may have been too brief and too frequent to evoke corresponding vasomotor activity.

On the basis of the time required for vasodilatation initiated in contracting hindlimb muscle to “ascend” into the femoral artery, the velocity of conduction along the arterial wall was first estimated to be \(-100\) mm/s (11). However, the electrical events underlying this response were not apparent. In previous studies using simultaneous dual cell recording (7, 12), a delay in electrical responses to applied stimuli was not resolved. In the present study, by measuring the delay between oscillations in smooth muscle cells separated by a known distance, our estimate of conduction velocity \((-45\) mm/s) is similar to previous values obtained for guinea pig ureter \((23\) mm/s) (30) and small intestine \((77–88\) mm/s) (27) and is clearly sufficient to coordinate smooth muscle cell relaxation within and among branches of vascular resistance networks.

In summary, this is the first study to determine cable properties of isolated microvessels at physiological transmural pressure and membrane potential. We demonstrate that hyperpolarization induced by current injection, as well as spontaneous oscillations in membrane potential, conducted along feed arteries with \(\lambda = 1.2\) mm. In contrast, hyperpolarization triggered by ACh conducted \(-60\%\) further, with \(\lambda = 1.9\) mm. This significant difference in \(\lambda\) was independent of vessel segment length and indicates that the nature of the stimulus can influence the effectiveness of the conducted response in promoting tissue blood flow.
REFERENCES


