Impulse Encoding Across the Dendritic Morphologies of Retinal Ganglion Cells

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Sheasby, Brent W. and Jurgen F. Fohlmeister. Impulse encoding across the dendritic morphologies of retinal ganglion cells. J. Neurophysiol. 81: 1685–1698, 1999. Nerve impulse entrainment and other excitation and passive phenomena are analyzed for a morphologically diverse and exhaustive data set (n = 57) of realistic (3-dimensional computer traced) soma-dendritic tree structures of ganglion cells in the tiger salamander (Ambystoma tigrinum) retina. The neurons, including axon and an anatomically specialized thin axonal segment that is observed in every ganglion cell, were supplied with five voltage- or ligand-gated ion channels (plus leakage), which were distributed in accordance with those found in a recent study that employed an equivalent dendritic cylinder. A wide variety of impulse-entrainment responses was observed, including regular low-frequency firing, impulse doublets, and more complex patterns involving impulse propagation failures (or aborted spikes) within the encoder region, all of which have been observed experimentally. The impulse-frequency response curves of the cells fell into three groups called FAST, MEDIUM, and SLOW in approximate proportion as seen experimentally. In addition to these, a new group was found among the traced cells that exhibited an impulse-frequency response twice that of the FAST category. The total amount of soma-dendritic surface area exhibited by a given cell is decisive in determining its electrophysiological classification. On the other hand, we found only a weak correlation between the electrophysiological group and the morphological classification of a given cell, which is based on the complexity of dendritic branching and the physical reach or “receptive field” area of the cell. Dendritic morphology determines discharge patterns to dendritic (synaptic) stimulation. Orthodromic impulses can be initiated on the axon hillock, the thin axonal segment, the soma, or even the proximal axon beyond the thin segment, depending on stimulus magnitude, soma-dendritic membrane area, channel distribution, and state within the repetitive impulse cycle. Although a sufficiently high dendritic Na-channel density can lead to dendritic impulse initiation, this does not occur with our “standard” dendrite densities and is not seen experimentally. Even so, impulses initiated elsewhere do invade all except very thin dendritic processes. Impulse-encoding irregularities increase when channel conductances are reduced in the encoder region, and the F/I properties of the cells are a strong function of the calcium- and Ca-activated K-channel densities. Use of equivalent dendritic cylinders requires more soma-dendritic surface area than real dendritic trees, and the source of the discrepancy is discussed.

INTRODUCTION

The impulse-encoding mechanism of intact retinal ganglion cells recently was explored on the basis of a series of models (Fohlmeister and Miller 1979a,b), the five nonlinear ion channels of which were identified from earlier voltage-clamp data (Kaneda and Kaneko 1991a,b; Lasater and Witkovsky 1990; Lipton and Tauc 1987; Lukasiewicz and Werblin 1988). Although the light-evoked impulse responses of individual retinal ganglion cells may be continuous (tonic) or it may consist of brief bursts (phasic responses) to light ON, OFF, or both ON/OFF (Baylor and Fettiplace 1979; Bellem et al. 1983), virtually all ganglion cells respond with tonic repetitive firing to depolarizing currents injected into the soma (Fig. 1). This relatively uniform response pattern among all ganglion cells allowed a systematic model development with regard to incorporating the effects of cell morphology on impulse entrainment. The development began with a single compartment model (Fohlmeister and Miller 1997a; Fohlmeister et al. 1990) and proceeded to a series of multicompartment models in which the dendritic tree was represented by an equivalent cylinder (Fohlmeister and Miller 1997b). The multicompartment models allowed for non-uniform distributions of the channels throughout the neuron and clearly showed that first-order encoding effects are due to the axial or “longitudinal” currents that naturally arise from the cell geometry. The present paper extends this analysis to realistic (traced) dendritic morphology (cf. Arkin and Miller 1988).

Experimental spike train records indicated that about half of all ganglion cells yield a tonic impulse rate of ~1 imp·s⁻¹·pA⁻¹ of constant stimulus current injected into the soma. The remaining cells responded with lower impulse rates (0.5–0.7 imp·s⁻¹·pA⁻¹), with the slowest cell responses showing various forms of irregularity in the spike train. This variability among ganglion cells was reproducible by adjusting the geometric parameters (specifically the diameter) of the dendritic equivalent cylinder, not, however, by manipulations of ion channel densities or distributions (cf. Eliasof et al. 1987). The real dendritic trees of the present study are not amenable to geometric manipulation. It is therefore remarkable that our data set of 57 traced cells yields a distribution in the impulse firing properties that closely matches that seen experimentally, with however, the notable addition of a new group of cells that respond with high impulse frequencies (called “superFAST” herein), which were apparently not recognized as a distinct group in the data collection process. The early subsections of RESULTS therefore explore details of the variety of the encoding phenomena on the basis of a single (fixed) distribution of ion channels, called “standard” herein. This channel distribution was deemed to represent the healthiest cells in the equivalent cylinder study. Modifications in the channel distribution subsequently are considered, leading to the conclusion that all retinal ganglion cells—irrespective of size or dendritic branch-
METHODS

Experimental methods for obtaining the impulse train records are given in Fohlmeister and Miller (1997a,b). Because virtually all ganglion cells responded with tonic repetitive firing to constant current injected into the soma, respond with tonic repetitive firing to constant current injected into the soma.

RESULTS

Impulse frequency versus stimulus current

Impulse trains of the set of realistic model neurons were obtained by numerical integration with simulated stimulation of 10–50 pA, in increments of 10 pA (e.g., Fig. 3). Populations of model neurons were found that correspond to the physiological classification of fast (≈1 imp · s⁻¹ · pA⁻¹), medium (≈0.7 imp · s⁻¹ · pA⁻¹), and slow (≈0.5 imp · s⁻¹ · pA⁻¹) cells (Fohlmeister and Miller 1997a). In addition to these groups, a population of cells was encountered with impulse frequencies that were substantially higher (60–124 Hz at 40 pA) than those of the aforementioned classifications (Tables...
2–4). The slope of the impulse frequency versus stimulus current (F/I) curve for the equivalent dendritic cylinder models (Fohlmeister and Miller 1997b) earlier was found to be a strong function of soma-dendritic membrane area, and we find that this group of superFAST" cells have an average soma-dendritic membrane area of less than half that of the remaining groups (Table 5). Small cells more readily take up HRP stain, and all stained cells were traced as they appeared (C. Toris, personal communication). SuperFAST cells therefore probably are over-represented in our morphological data set and may actually be somewhat rare in the Tiger Salamander retina (see DISCUSSION).

**Physiological and morphological classifications**

The simulated spike train records were subjected to a phase plot analysis in which the time rate of change (dV/dr) is plotted against the membrane potential (V). Phase plot analysis is a sensitive means of evaluating impulse wave-form in general (Fitzhugh 1969), and, for our immediate purposes, of determining the presence and details of an "initial segment-soma-dendritic (IS-SD) break," in particular. An IS-SD break sometimes is observed in impulses recorded at the soma, as an indication that these impulses were initiated on neighboring...
membrane with a lower threshold (Coombs et al. 1957). The IS-SD break appears as a feature in phase plots corresponding to the early rising phase of the impulses (Fig. 3, phase plot, \(\rightarrow\)). Although impulses in retinal ganglion cells do not uniformly exhibit the IS-SD break, its occurrence increases among the ‘slower’ cells and becomes characteristically related to the irregular firing of slow cells.

Because impulse frequency response, an IS-SD break, and/or irregular firing are readily apparent features, we established a classification based on the following defining characteristics: group 1, impulse frequency >55 Hz at 40 pA (23 cells); group 2, impulse frequency <55 Hz at 40 pA and no IS-SD break at 10 pA (11 cells); group 3, regular impulse firing, with IS-SD break at 10 pA (14 cells); and group 4, irregular impulse train at 10 pA of constant current stimulus (9 cells).

Group 1 consists of the observed super-\(\text{FAST}\) cells, and the cutoff criterion of 55 Hz (at 40 pA) was chosen because this value falls in the center of a substantial gap in the observed \(F/I\) slopes among the traced cells of our data set. Note in Table 3 that the averages of the impulse frequency responses of groups 2–4 correspond closely to those of \(\text{FAST}\), \(\text{MEDIUM}\), and \(\text{SLOW}\) cells of the earlier physiological classification (Fohlmeister and Miller 1997a, Fig. 11) and that the behavior of group 1 cells, with an average \(F/I\) slope that is double that of the group 2 (\(\text{FAST}\)) cells, suggests that this is a distinct population with perhaps a distinct signaling function.

The degree of correspondence with the morphological classification (Toris et al. 1995) is substantially more diffuse with group 1 containing small simple through medium complex cells and group 4 containing medium simple through large cells. Indeed, medium simple and medium complex cells are represented in every group. On the other hand, the bulk of small simple cells (13 of 14) fall into group 1, and groups 3 and 4 contain no small cells of either complexity. Table 2 gives the full distribution by group and morphological classification.

### Soma-dendritic membrane area

Contrary to the diffuse correspondence between morphological and electrophysiological classifications, a much stronger correlation was found between our physiological classification and the total soma-dendritic surface area of a given cell. The immediate corollary is that the morphological classification—based on profuseness of dendritic branching and on the length of dendrites—is correlated only weakly with their total membrane surface area. The only substantial exceptions to this rule appear to be the morphologically small simple cells, which are also predominantly group 1, super-\(\text{FAST}\) cells.

To quantify these statements, we tabulated the surface areas of our data set of cells for the somas, dendrites, and soma-plus-dendrites by both morphological and physiological classifications and computed their averages and standard deviations (Table 5). One immediately striking feature in this tabulation is the great variation in soma and dendritic surface areas within a given morphological group, particularly among the medium simple and medium complex cells, and that somatic and dendritic-membrane areas of individual cells are not correlated. Note, for example, that the soma surfaces of large cells range from 384 to 1,384 \(\mu\text{m}^2\), typically smaller than those of medium complex and small complex cells, whereas their dendritic surface areas are typically much larger than those of medium complex and small complex cells.

The primary result of this subsection is, however, the narrow range of surface areas of the dendrites and dendrites-plus-soma found for our electrophysiological group 2 and group 3 cells. This finding shows that the primary determinant for the impulse discharge rate of retinal ganglion cells to soma stimulation is the total amount of membrane present on the dendrites and soma. (Dendritic stimulation, on the other hand, affects the pattern of discharge, see following text.) This result implies that virtually all dendritic membrane is involved in the charging process during interspike intervals and is consistent with

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### Table 1. Distribution of ionic channels

<table>
<thead>
<tr>
<th>Rev. Pot.</th>
<th>Channel</th>
<th>Dendrites, mS/cm²</th>
<th>Soma, mS/cm²</th>
<th>Initial Segment, mS/cm²</th>
<th>Narrow Segment, mS/cm²</th>
<th>Axon, mS/cm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>+35 mV</td>
<td>Na</td>
<td>25</td>
<td>80</td>
<td>150</td>
<td>100–400*</td>
<td>70</td>
</tr>
<tr>
<td>Variable</td>
<td>Ca</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>–75 mV</td>
<td>K</td>
<td>12</td>
<td>18</td>
<td>18</td>
<td>0–18*</td>
<td>18</td>
</tr>
<tr>
<td>–75 mV</td>
<td>A</td>
<td>36</td>
<td>54</td>
<td>54</td>
<td>0–54*</td>
<td>0</td>
</tr>
<tr>
<td>–75 mV</td>
<td>K(_{\text{Ca}})</td>
<td>0.001</td>
<td>0.065</td>
<td>0.065</td>
<td>0.065</td>
<td>0.065</td>
</tr>
<tr>
<td>–62.5 mV</td>
<td>Leak</td>
<td>0.008</td>
<td>0.008</td>
<td>0.008</td>
<td>0.008</td>
<td>0.008</td>
</tr>
</tbody>
</table>

**A. Standard**

**B. Weakened**

Distributions of ionic channels throughout the model neurons in units of milliSimens/square centimeter. Left column lists the equilibrium potentials (Rev. Pot.) used in the simulations. A gives our standard channel distribution (called “EC2.5” in Fohlmeister and Miller 1997b). B represents our weakened cells (“EC1”) with lower channel densities in the encoder region. The Na-channel density on the dendrites may range between 15 and 25 mS/cm²; dendritic K channels are required (cf. Fohlmeister and Miller 1997b, Fig. 6). * Viable range of Na- and K-channel densities on the axonal narrow segment (see text) (Wollner and Catterall 1986).
the observation that the length of dendrites of retinal ganglion cells is only a fraction of their electrotonic space constants.

To refine this result, we undertook a further subdivision of our group 2, the 11 cells of which contain a subset of 4 that show, in phase plots with 10 pA of stimulus current, a slight tendency toward an IS-SD break. IS-SD break is most pronounced with low stimulus currents and vanishes for higher levels of stimulus; this indicates a change in the location at which the impulses are initiated (see Fig. 4).

<table>
<thead>
<tr>
<th>Group</th>
<th>SS</th>
<th>SC</th>
<th>MS</th>
<th>MC</th>
<th>L</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>—</td>
<td>23</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>2</td>
<td>6</td>
<td>2</td>
<td>—</td>
<td>11</td>
</tr>
<tr>
<td>3</td>
<td>—</td>
<td>—</td>
<td>3</td>
<td>10</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>—</td>
<td>—</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>1–4</td>
<td>14</td>
<td>8</td>
<td>14</td>
<td>17</td>
<td>4</td>
<td>57</td>
</tr>
</tbody>
</table>

Distribution of our data set (n = 57) of cells grouped by morphological classification (SS, small simple; SC, small complex; MS, medium simple; MC, medium complex; L, large) and physiological response classification (1–4). We find that this classification has the following correspondence with an earlier physiological classification: Group 1 = superfast; 2 = fast; 3 = medium; 4 = slow (Fohlmeister and Miller 1997a). Note that members of MS and MC cells occur for every physiological group.

Fig. 3. Left, top 3 records: simulated repetitive firing responses to soma stimulation (10, 20, and 40 pA) of a typical group 3, medium complex ganglion cell modeled with the standard channel density distribution and \( g_{\text{Na}} = 100 \text{ mS/cm}^2 \) on the axonal narrow segment (Table 1). Bottom: very-low-frequency repetitive firing generated by a superfast small simple cell stimulated with 1.55 pA into the soma. This cell yielded an impulse frequency of 0.19 imp/s with 1.54 pA, a nominal interspike interval of 25 s with 1.53 pA, and remained subthreshold for smaller stimuli. Right: phase plots of \( \Delta V/\Delta t \) vs. \( V \) of 2 records (10 and 40 pA) on the left and of a physiologically recorded medium cell with 20 pA. Phase plot cycle advances clockwise around the closed loop once for every impulse with the plotted points spaced by 0.2 ms and superimposed by successive impulses. Horizontal segment at the left represents the interspike interval; top of the plots, peak rate of rise of the impulses; extreme right of the plots, impulse peak; bottom, repolarization phase. 1, occurrence of an initial segment-soma-dendritic (IS-SD) break. IS-SD break is most pronounced with low stimulus currents and vanishes for higher levels of stimulus; this indicates a change in the location at which the impulses are initiated (see Fig. 4).

Table 2. Distribution of retinal ganglion cells

<table>
<thead>
<tr>
<th>Group</th>
<th>SS</th>
<th>SC</th>
<th>MS</th>
<th>MC</th>
<th>L</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>—</td>
<td>23</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>2</td>
<td>6</td>
<td>2</td>
<td>—</td>
<td>11</td>
</tr>
<tr>
<td>3</td>
<td>—</td>
<td>—</td>
<td>3</td>
<td>10</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>—</td>
<td>—</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>1–4</td>
<td>14</td>
<td>8</td>
<td>14</td>
<td>17</td>
<td>4</td>
<td>57</td>
</tr>
</tbody>
</table>

Distribution of retinal ganglion cells grouped by morphological classification (SS, small simple; SC, small complex; MS, medium simple; MC, medium complex; L, large) and physiological response classification (1–4). We find that this classification has the following correspondence with an earlier physiological classification: Group 1 = superfast; 2 = fast; 3 = medium; 4 = slow (Fohlmeister and Miller 1997a). Note that members of MS and MC cells occur for every physiological group.

Table 3. Impulse frequencies of retinal ganglion cells

<table>
<thead>
<tr>
<th>Group</th>
<th>10 pA</th>
<th>20 pA</th>
<th>40 pA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>22.74 (13.2–37.0)</td>
<td>48.26 (28.6–73.8)</td>
<td>88.86 (59.9–124.2)</td>
</tr>
<tr>
<td>2</td>
<td>9.81 (8.1–11.8)</td>
<td>21.37 (17.5–25.5)</td>
<td>44.48 (37.0–52.2)</td>
</tr>
<tr>
<td>3</td>
<td>6.90 (5.9–8.1)</td>
<td>14.47 (12.0–17.5)</td>
<td>30.70 (25.2–37.6)</td>
</tr>
<tr>
<td>4</td>
<td>— irregular</td>
<td>10.38 (9.0–11.7)</td>
<td>21.16 (17.2–24.8)</td>
</tr>
</tbody>
</table>

Frequencies are in impulses per second. Averages, and ranges (in parentheses), of impulse frequencies in response to 10, 20, and 40 pA of stimulus current grouped by physiological response type (1–4).
and charging time constants ($t$ and Table 2).

The greater surface area required of an equivalent cylinder is due to the fact that the equivalent cylinder cable equation involves a monotonically decreasing space constant with distance from the soma (Rall 1961). Thus electrotonic distance increases more rapidly than the geometric distance from the soma to the periphery of the tree, and this is simulated by a longer geometric equivalent cylinder which then yields the greater surface area.

### Resting state and charging parameters

The systematically larger surface area of the equivalent cylinder requires the lower leakage channel density of $g_L = 5 \mu S/cm^2$ to yield input resistance homology with experiment (Coleman and Miller 1989) as well as with the realistic models, which employ $g_L = 8 \mu S/cm^2$ (Fohlmeister and Miller 1997b, Table 1). Table 4 lists the averages and ranges of input resistances ($R_i$ in gigaohms) and charging time constants ($\tau$ in milliseconds) of the simulated cells as determined by hyperpolarizing current steps of $-1 \mu A$ injected into the soma of the resting model neurons.

A noteworthy result of our simulations of realistic models is the finding that the charging times, $\tau$, agree with physiological experiment (Fohlmeister and Miller 1997a, Table 2), but both are invariably $\sim 20\%$ smaller (shorter) than those determined for the equivalent dendritic cylinder models, an observation already noted earlier (Fohlmeister and Miller 1997b). Unlike input resistance, charging times reflect more closely the membrane RC, and the smaller time constants of the realistic models are due to the larger leakage conductance (i.e., smaller resistance) per unit area of membrane, relative to that for the equivalent cylinder models.

### Site of impulse initiation

In general, longitudinal (electrotonic) currents dominate over membrane current during the interspike intervals, and membrane current dominates locally during the impulse phase (i.e., where the membrane is in a state of excitation), thus ensuring the sharpness of spikes (Fohlmeister and Miller 1997b). Relatively small stimulus currents ($\leq 10 \mu A$) lead to relatively slow subthreshold depolarization rates, which allow for relatively extensive electrotonic spread during the latency between current-onset and the first impulse and during the interspike intervals. This spreading of stimulus current causes action potentials to be initiated on the highly excitable membrane of the axonal narrow segment (cf. Ringham 1971) or even on the proximal axon beyond that segment because of geometric effects (Fig. 4, top). As a result, a pronounced IS-SD break is seen in action potentials recorded at the soma (Fig. 4, top). As the level of stimulus current is increased, the local depolarization rate at the site of current injection (the soma) also is increased, allowing less time for lateral current spread, with the result that the soma is nearer to threshold when the axonal narrow segment activates (Fig. 4, middle), and any IS-SD break becomes less pronounced. Sufficiently large stimulus currents ($\geq 40 \mu A$) can bring the soma membrane to threshold so rapidly (during the interspike interval), that electrotonic spread of the stimulus current becomes relatively unimportant, and impulses are initiated almost simultaneously on the soma membrane, the initial segment, and the proximal narrow segment (Fig. 4, bottom). Thus with increasing levels of orthodromic (soma) stimulation, the impulse initiation site moves to locations more proximal to the soma.

### Axonal doublet spiking and active propagation failure

It has been established for some time that the presence of the morphologically narrow segment, which follows an initial segment of some $30-60 \mu m$, can cause impulse propagation

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### Table 4. **Charging characteristics**

<table>
<thead>
<tr>
<th>Group</th>
<th>$R_{in}$, GΩ</th>
<th>$\tau$, ms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.97 (1.65–2.32)</td>
<td>57.9 (47–67)</td>
</tr>
<tr>
<td>2</td>
<td>1.36 (1.24–1.56)</td>
<td>73.4 (69–77)</td>
</tr>
<tr>
<td>3</td>
<td>1.12 (0.97–1.25)</td>
<td>79.4 (77–81)</td>
</tr>
<tr>
<td>4</td>
<td>0.90 (0.79–1.05)</td>
<td>83.0 (81–84)</td>
</tr>
</tbody>
</table>

Averages, and ranges of the resting potentials (Rest), input resistances ($R_i$), and charging time constants ($\tau$), grouped by physiological response type (1–4). Parentheses enclose ranges.

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### Table 5. **Membrane surface areas (µm²)**

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Soma</th>
<th>Dendrites</th>
<th>Soma + Dendrites</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Electrophysiological classification</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>23</td>
<td>711 ± 228 (287–1,120)</td>
<td>1,383 ± 793 (291–2,191)</td>
<td>2,094 ± 855 (969–4,474)</td>
</tr>
<tr>
<td>2</td>
<td>11</td>
<td>1,222 ± 294 (908–1,838)</td>
<td>2,927 ± 515 (2,087–3,722)</td>
<td>4,149 ± 525 (3,154–4,871)</td>
</tr>
<tr>
<td>3</td>
<td>14</td>
<td>1,109 ± 340 (384–1,403)</td>
<td>4,618 ± 853 (3,712–6,681)</td>
<td>5,727 ± 648 (4,764–7,064)</td>
</tr>
<tr>
<td>4</td>
<td>9</td>
<td>1,270 ± 406 (796–2,196)</td>
<td>6,623 ± 1,185 (5,239–8,372)</td>
<td>7,893 ± 1,176 (6,206–9,272)</td>
</tr>
<tr>
<td><strong>Morphological classification</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SS</td>
<td>14</td>
<td>681 ± 225 (287–1,000)</td>
<td>1,020 ± 559 (291–2,179)</td>
<td>1,701 ± 679 (969–3,154)</td>
</tr>
<tr>
<td>SC</td>
<td>8</td>
<td>978 ± 310 (659–1,651)</td>
<td>1,971 ± 518 (1,220–2,899)</td>
<td>2,949 ± 607 (2,021–3,807)</td>
</tr>
<tr>
<td>MS</td>
<td>14</td>
<td>1,075 ± 327 (298–1,403)</td>
<td>3,701 ± 1,191 (1,828–5,409)</td>
<td>4,776 ± 1,358 (2,126–6,743)</td>
</tr>
<tr>
<td>MC</td>
<td>17</td>
<td>1,213 ± 401 (603–2,196)</td>
<td>4,479 ± 1,478 (1,825–7,345)</td>
<td>5,692 ± 1,598 (1,999–8,603)</td>
</tr>
<tr>
<td>L</td>
<td>4</td>
<td>930 ± 416 (384–1,384)</td>
<td>7,566 ± 819 (6,681–8,372)</td>
<td>8,495 ± 1,023 (7,065–9,272)</td>
</tr>
</tbody>
</table>

Surface areas of cell somas, dendrites, and their sum grouped by physiological and morphological classifications. Note the large range (in parentheses) and ±SD in membrane areas of medium simple and medium complex cells, which are responsible for their wide ranges of electrophysiological responses (see text and Table 2).
difficulties that can be ameliorated to some extent by increasing the Na-channel density on the membrane of the narrow segment (Carras et al. 1992; Fohlmeister and Miller 1997b). Because it is structurally thin in comparison with its neighboring axon, the narrow segment also contributes to an electrical impedance mismatch that occurs at the junction of the axon and the soma. This impedance mismatch manifests itself in impulse propagation delays as well as active propagation failures under certain circumstances (cf. also Antidromic stimulation).

Axial (electrotonic) current flowing from the axon into the soma encounters two additive effects: reduced axial resistance due to the increase in cross-sectional area and increased membrane surface area per unit length in the axial direction. Both effects require the electrical charge carried by the axial current to depolarize a large increase in membrane area on entering the soma. That charge is sometimes insufficient to bring the soma to threshold, or, if sufficient, the soma spike occurs with a latency which is manifested by a pronounced IS-SD break. These effects are most pronounced for large soma-dendritic surface areas and are exacerbated by the presence of the axonal narrow segment that further restricts axial current flow from the axon.

One manifestation of the impedance mismatch between the narrow segment and the soma is the occurrence of more-or-less closely spaced spike doublets propagating on the axon for impulses that are recorded singly in a spike train at the soma (Fig. 5, A and B). The axonal spike doublets may occur for every soma spike, or they may occur for every second or third impulse with the intervening spikes propagating singly on the axon. The corresponding low-frequency impulse trains recorded at the soma show small (1–2 ms) irregularities in the durations of their interspike intervals.

Axonal spike doublets invariably are initiated with an impulse generated on the axon some 100–150 μm beyond the narrow segment. This impulse propagates on the axon, whereas its electrotonic (axial) current in the antidromic direction causes a brief, relatively abrupt depolarization in the soma-axon hillock region. The abrupt depolarization represents the rising phase of an IS-SD break as seen in the phase plot of the difficulties that can be ameliorated to some extent by increasing the Na-channel density on the membrane of the narrow segment (Carras et al. 1992; Fohlmeister and Miller 1997b). Because it is structurally thin in comparison with its neighboring axon, the narrow segment also contributes to an electrical impedance mismatch that occurs at the junction of the axon and the soma. This impedance mismatch manifests itself in impulse propagation delays as well as active propagation failures under certain circumstances (cf. also Antidromic stimulation).

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soma in Fig. 5A’ (↓). This depolarization, like a threshold shock depolarization, causes an impulse to be generated in the soma, axon hillock, and proximal narrow segment almost simultaneously but with a delay (1–2 ms) that allows the axon to recover sufficiently from the refactoriness of the first impulse to also propagate this second member of the doublet. Because the soma-narrow segment impedance mismatch is more pronounced for the larger cells, this phenomenon is most prominent for group 4 cells and occurs more readily at lower stimulus intensities in smaller cells. The effect therefore enhances the signal by doubling the number of propagated spikes for the larger cells and at low stimulus levels in general.

A more extreme form of the axonal spike doublet phenomenon—seen among cells with the largest soma-dendritic membrane area—involves one or more “failed spikes” in the soma followed by a full-blown impulse recorded in the soma (Fig. 5D). The occurrence of this phenomenon we term “irregular,” and it defines our group 4 (i.e., slow cells in Fohlmeister and Miller 1997a). In these records, all impulses, including the failed soma spikes, are initiated on the axon some 30–150 μm beyond the narrow segment and propagate orthodromically on the axon (Fig. 5D). Antidromically, these impulses propagate into the distal end of the narrow segment (peak to +22 mV), then widen throughout the narrow segment and decay in amplitude (+18 mV at midpoint, −20 mV at proximal end), finally reaching peaks of −40 mV (initial segment) and −55 mV (soma). After one or more failed spikes, a full-blown impulse occurs in the soma: electrotonic charge from the repeated axonal discharges, in combination with the maintained stimulus current, ultimately being sufficient to bring the soma to threshold. Similar phenomena also have been observed in mammalian (rabbit) ganglion cells (Fig. 5E), indicating that this effect may possibly be quite general.

Antidromic stimulation

Antidromically propagating impulses, initiated on the distal axon, can lead to three types of phenomena: including the classical phenomenon of impulse invasion of the soma followed by electrical silence, impulse invasion of the soma followed by an orthodromically propagating “echo-spike,” and failure of the impulse to invade the soma.

Except for group 4 (slow) cells, the second and third types of phenomena occur only in the presence of the morphological narrow axonal segment, which we conclude to be the proximal cause of these phenomena. As a general trend, in any given cell, a sufficiently thin narrow segment invariably leads to failure of antidromic invasion of the soma. As the diameter of the narrow segment is increased, antidromic spikes begin to invade the soma and to generate an echo-spike in response to that invasion. Both phenomena are related to the propagation delays leading to the failed soma spikes or axonal spike doublets discussed in the last three paragraphs of the previous subsection. Finally, for a narrow segment of sufficiently large diameter, spike invasion of the soma invariably occurs and the echo-spike fails to develop. Group 4 cells form an exception for which antidromic spikes fail to invade the soma even with a “narrow segment” diameter equal to that of the general axon (1 μm).

The range of diameters of the narrow segment for which the echo-spike occurs shifts to larger values for cells with greater soma-dendritic surface area or, alternatively, as one advances from superfast (group 1) to slow (group 4) cells. Commonly, this diameter range shifts to lower values when the narrow segment is made more highly excitable. For example, a typical medium simple group 2 cell with standard channel densities throughout ($\overline{g_{Na}} = 100 \text{ mS/cm}^2$ on the narrow segment) showed no impulse invasion for narrow segment diameters ≤0.53 μm. The invasion plus echo-spike range occurred for narrow segment diameters of 0.54–0.63 μm, and invasion with no echo-spike for narrow segment diameters ≥0.64 μm. With $\overline{g_{Na}} = 200 \text{ mS/cm}^2$ on the narrow segment, the range of echo spiking in this same cell occurred for narrow segment diameters of ~0.1 μm smaller and occurred for diameters of 0.36–0.47 μm when $\overline{g_{Na}}$ was increased to 400 mS/cm² on the narrow segment. With $\overline{g_{Na}} = 400 \text{ mS/cm}^2$ on a sufficiently large diameter narrow segment, antidromic impulses invade the soma even for group 4 cells, but these invariably are accompanied by an echo-spike. The sequence of the three panels of Fig. 6 give an indication of the transition across the three types of antidromic phenomena (noninvasion, invasion plus echo, invasion alone) that occur with increasing diameter (or increasing excitability) of the narrow segment.
On the other hand, we found a much weaker correlation between Na-channel density on the initial segment and the type of antidromic invasion (or lack of invasion) phenomenon exhibited by a given cell. Absence of Na channels on the initial segment (or the narrow segment) invariably leads to invasion failure. However, soma invasion does occur with $g_{Na} = 25 \text{ mS/cm}^2$ on the initial segment for the smaller cells and with $g_{Na} \approx 70 \text{ mS/cm}^2$ for all cells. It appears therefore that the excitability properties of the soma and the narrow segment are more decisive for determining antidromic invasion than those of the initial segment.

The phenomenon of the echo-spike (Fig. 6, middle) arises as follows: an impulse of normal amplitude (peak to about +27 mV) propagates antidromically on the axon. This impulse increases in amplitude (peak to about +30 mV) on entering the narrow segment, but declines in amplitude (peak about −18 mV) in crossing the narrow segment. The initial segment almost simultaneously peaks at about −40 mV, at which time the rising phase of a pronounced IS-SD break occurs in the soma. After a delay of 1.5−2 ms, during which time the soma continues to slowly depolarize, a full-blown spike arises simultaneously in the soma (to +22 mV), the initial segment (to +20 mV), and the proximal portion of the narrow segment (to +17 mV). This impulse propagates across the narrow segment and into the axon yielding the orthodromically propagating echo-spike. The membrane potential waveform at the location of the junction of the narrow segment and axon, although clearly an active response sufficiently large to be considered an impulse (peak about +7 mV), nevertheless shows an inflection in its rising phase, a kind of axonal IS-SD break, due to a combination of the low grade refractoriness remaining from the antidromic impulse and to some impedance-mismatch at that junction.

Modifying the channel densities

The magnitude of the membrane capacitance ultimately sets the scale for the magnitudes of the ionic conductances (cf. Fohlmeister and Miller 1997b, Fig. 6); the charging requirements for the membrane capacitance therefore restricts modifications of the standard channel density distribution to about ±30%, except for electrotonically coupled regions with little membrane area such as the axonal narrow segment. The Ca current and the associated $I_{K_{Ca}}$ are not essential to spiking but strongly control the interspike intervals. Their magnitudes are determined in relation to the spiking current magnitudes. We therefore evaluate the effects of reducing channel densities (“weakening” the cells) in the encoder region, modifying channel densities on the narrow segment of the axon, and varying the calcium channel densities in the soma and dendritic regions.

Consider the weakened channel densities (Table 1) with the narrow segment $g_{Na} = 100 \text{ mS/cm}^2$, which is the minimum value required to insure reasonably faithful propagation of action potentials under most conditions of excitation. This modification results in two principal effects: impulse frequencies are reduced for all stimulus levels and for all classifications of cells and irregular firing patterns increase substantially among the cells of our morphological data set.

The percentage change in impulse frequency was least for our group 1 (superFAST) cells (7% at 40 pA) and increased systematically to 17% (group 2) and 31% (group 3), reaching 35% at 40 pA for group 4 (SLOW) cells. The percentage change in the F/I slope for group 1 cells is insufficient for them to be reclassified in a slower category (i.e., group 1) with this reduction in channel densities. Because irregularities in the impulse encoding also increase beyond those observed experimentally, thus making further reductions in the conductances untenable, this supports our new superFAST category as constituting a real population of ganglion cells.

The firing irregularities (i.e., intermittent or periodic spike failures in the soma) were a defining feature for our group 4 (SLOW) cells and occurred almost exclusively for low stimulus currents (≤20 pA). With the reduced channel densities, irregularities spread to group 3, and occasional group 2 cells for low stimuli, and to all stimulus levels of the group 4 (SLOW) cells. This spreading in firing irregularities for weakened cells is reversed by increasing the Na-channel density on the narrow segment of the axon alone to $g_{Na} = 300 \text{ mS/cm}^2$, and impulse firing frequencies also recover the values determined for the standard channel densities. However, antidromic invasion does not recover with this modification; a typical medium simple group 2 cell with weakened channel densities and $g_{Na} = 300 \text{ mS/cm}^2$ on the narrow segment requires a minimum narrow segment diameter of 0.7 μm for invasion. We consider this to be an unacceptable result because the axonal narrow segments of ganglion cells have diameters in the range of 0.3–0.6 μm, and the majority of cells do show antidromic spike invasion of the soma experimentally, sometimes followed by an echo-spike (Fohlmeister and Miller 1997b).

A fundamental consideration in adjusting the Na-channel density on the narrow segment is the maintenance of a stable resting state for the neuron as a whole. With standard channel densities elsewhere, the Na-channel density on the narrow segment can be increased to $g_{Na} = 1,000 \text{ mS/cm}^2$ while maintaining a stable neural resting state. However, such large values of $g_{Na}$ convert the neuron into a bistable system in that it will not recover from the excited state once threshold is crossed. The bifurcation point leading to a bistable system depends somewhat on the total surface area of soma and dendrites of a given neuron, but is approximately $g_{Na} = 500 \text{ mS/cm}^2$. The corresponding value for the (otherwise) weakened channel densities is approximately $g_{Na} = 400 \text{ mS/cm}^2$. Because the model neuron must be monostable, we consider $g_{Na} = 300 \text{ mS/cm}^2$ to be a reasonable upper limit for the Na-channel density on the narrow segment with a sufficient safety margin, although this value may be as high as ~400 mS/cm² for the healthiest cells. The transition from mono- to bistable is quite sharp. For example, one group 2 neuron with otherwise standard channel densities is monostable with $g_{Na} \leq 498.069 \text{ mS/cm}^2$ and bistable with $g_{Na} \geq 498.070 \text{ mS/cm}^2$ on the narrow segment. The same neuron weakened is monostable with $g_{Na} \leq 396.087 \text{ mS/cm}^2$ and bistable with $g_{Na} \geq 396.088 \text{ mS/cm}^2$ on the narrow segment.

With the standard channel densities and low stimulus levels (~10 pA), increasing $g_{Na}$ from 100 mS/cm² to ≥200 mS/cm² on the narrow segment moves the orthodromic impulse initiation point from the proximal axon beyond the narrow segment onto the narrow segment itself. Propagation delays between the narrow segment and the soma thereby are reduced, and this is the principal reason for the reduced degree of firing irregularities, as noted in the preceding text. The effect is most pro-
nounced for group 4 and 3 cells and does not apply to the highly regular firing group 1 (superFAST) cells. On the other hand, the presence or absence of the potassium currents, $I_K$ and/or $I_A$, on the narrow segment show little effect on impulse entrainment or other excitation phenomena in the bulk of cells with standard channel densities. This picture changes quite dramatically with the weakened channel densities (and with $g_{Na} = 300 \text{ mS/cm}^2$ on the narrow segment), as follows.

### Spike doublets recorded in the soma

Removing the delayed rectifier and A-type K channels from the axonal narrow segment introduces spike doublets in impulse trains recorded at the soma for many, but not all, cells (Fig. 7). This occurrence of spike doublets is more prevalent with lower levels of stimulus current ($\leq 20 \text{ pA}$). Impulse bursts may replace the doublet spiking in some cells, and this bursting can go over to continuous high-frequency firing under certain stimulus conditions. This last phenomenon is not stable, and we observed no systematic pattern of it among our grouping of cells. As an example, one group 4 cell showed bursting with 20 and 50 pA of constant stimulus current (Fig. 8) and yielded continuous high-frequency firing with 40 pA of stimulus. A short impulse burst also can occur immediately after the "break" of current of a rectangular depolarizing stimulus pulse, during which a regular low-frequency impulse train was generated.

During the burst, the membrane potential of the axonal narrow segment fluctuates erratically within the relatively depolarized range of $-30$ to $0 \text{ mV}$ (Fig. 8, bottom). This fluctuation decouples the soma firing pattern from that of the axon, with the result that the number of spikes in the soma, and those propagating on the axon, may not be equal. Note in Fig. 8 that the fluctuation on the narrow segment undergoes a depolarizing upswing in response to every spike generated in either the soma or on the axon. The depth of the subsequent downswing depends on the degree of synchronization between the soma and axonal spikes; when the soma and axonal spikes are coincident, the encoder region undergoes hard reset of the narrow segment, and termination of the burst. Right: impulse invasion into 2 dendrites, and the propagating impulses on the axon $5 \text{ mm distal}$ from the soma.

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**FIG. 8.** Bursting exhibited by some neurons with the weakened channel densities (Table 1B with $g_{Na} = 300 \text{ mS/cm}^2$ and $g_{K} = 0$ on the narrow segment). Example shown is a group 4, large cell. Burst duration can vary with stimulus level. Impulse initiation differs between the 1st and subsequent spikes within a burst indicating distinct and separate impulse initiation sites as expressed by the differential forms of the IS-SD break in the phase plots. **Bottom:** expanded view of membrane potentials during a single burst at several locations on the neuron. **Left:** soma, midnarrow segment, and proximal axon; note the coincidence of the final spikes of the burst on the soma- and proximal axon-membranes leading to the hard reset of the narrow segment, and termination of the burst. Right: impulse invasion into 2 dendrites, and the propagating impulses on the axon $5 \text{ mm distal}$ from the soma.
those cases, it may be that the long experimental protocol has caused a fraction of the channels to become nonfunctional (i.e., to ‘‘weaken’’ the cell). Nevertheless, it is interesting to note that impulse trains consisting of spike doublets are commonly recorded in W ganglion cell somas of the cat retina (Fig. 7C) (Rowe and Palmer 1995; Rowe, personal communication; cf. also Caldwell and Daw 1978). In that case, doublet spike trains appear to be recorded only in cells with thin axons, as determined from the impulse propagation velocity on the axon.

**Calcium system**

The calcium current is the only current modeled with a variable reversal potential because the cytoplasmic Ca concentration can vary substantially in response to Ca influx during action potentials. In addition to its effect on the reversal potential, the cytoplasmic Ca-concentration also gates the Ca-activated K current (Barrett et al. 1982; Cannel et al. 1987; Chad et al. 1987; Gorman and Thomas 1978; Hernandez-Cruz et al. 1990; Latorre et al. 1989; Marty 1981; Meech 1978; Pallotta et al. 1995; Rogawski 1989). The Ca-activated K-current \( I_{K,\text{Ca}} \) acts to strongly suppress spontaneous excitation and therefore strongly contributes to the existence of a stable resting state in our model ganglion cells (cf. Fohlmeister and Miller 1997b). The effect is uniform across all morphological classes. These model neurons fire spontaneously in a broad range \(-10\) imp/s when \( I_{K,\text{Ca}} \) is blocked and increase their impulse-frequency rates by some 30–80% relative to those with \( I_{K,\text{Ca}} \) intact (Hugues et al. 1982) for all nonzero stimulus levels. Despite these effects in the \( F/I \) properties, \( I_{K,\text{Ca}} \) contributes little to the shape of action potentials and is too small to be recognized in phase plots.

Unlike \( I_{K,\text{Ca}} \), the Ca current, \( I_{\text{Ca}} \), can be blocked with virtually no effect on the resting cell because of its high threshold for activation. The rising phase of impulses is dominated by \( I_{\text{Na}} \) as clearly identified and expressed in phase plots (Fig. 9). Thus Ca current comes into play—substantially—only as the impulse approaches its peak, at which point \( I_{\text{Ca}} \) adds some 10 mV to that peak value due to its large, positive reversal potential. This increased peak voltage causes a substantial increase in Na inactivation as well as K-channel activation, leading to a relatively deep afterhyperpolarization and prolonged subsequent interspike interval. When the Ca-channels are blocked, impulse amplitude therefore is reduced at both extremes (peak and afterhyperpolarization), followed by a more rapid return to threshold. Thus impulse frequencies increase by some 50–100% for all levels of constant current stimulation, and this agrees quantitatively with experiment (Fohlmeister and Miller 1997a,b).

The Ca current imparts a unique ‘‘signature’’ to the latter part of the falling phase of action potentials, clearly expressed in phase plots, which allows the relatively precise determination of its magnitude. As \( g_{\text{Ca}} \) is increased, the phase plot trajectory shows an increasing downward bulge (increasing rate of repolarization) located about \(-30\) to \(-40\) mV (Fig. 9). For sufficiently large \( g_{\text{Ca}} \) (\( \geq 6 \text{ mS/cm}^2 \)), this bulge is preceded by a decrease in the rate of repolarization (at \(-0\) mV, Fig. 9C), which indicates a tendency to generate plateau action potentials.

**FIG. 9.** Effect of changing the density of Ca channels on the dendrites and soma. Records shown are of a group 2, medium simple cell stimulated with 25 pA. A: standard channel densities with \( g_{\text{Na}} = 100 \text{ mS/cm}^2 \) on the axonal narrow segment and all Ca channels blocked; note the negative Ca signature for this case. B: weakened channel densities with \( g_{\text{Na}} = 300 \text{ mS/cm}^2 \) on the axonal narrow segment and doubled Ca current. \( g_{\text{Ca}} = 2 \text{ mS/cm}^2 \) (dendrites and soma); C: standard channel densities with \( g_{\text{Na}} = 300 \text{ mS/cm}^2 \) on the axonal narrow segment and with tripled Ca current and reduced Na current in the soma-dendritic region, specifically \( g_{\text{Na}} = 6 \text{ mS/cm}^2 \), \( g_{\text{Ca}} = 0 \) (dendrites), and \( g_{\text{Ca}} = 4.5 \text{ mS/cm}^2 \), \( g_{\text{Na}} = 40 \text{ mS/cm}^2 \) (soma). In general, increasing the Ca current causes a reduction in impulse frequency (cf. Fohlmeister and Miller 1997a,b), which the increased value of \( g_{\text{Na}} (= 300 \text{ mS/cm}^2) \) on the axonal narrow segment in B and C has only partially reversed. Equally dramatic is the effect on the shapes of the phase plots that reflect the impulse waveforms. Note the calcium signature (Ca-sign.) during the falling phase of impulses and the increased peaks of action potentials due to Ca current. Note also the pronounced IS-SD break due to the reduced Na-channel densities in the soma, and reflecting the effect of impulse initiation on the more highly excitable axonal narrow segment.
potentials (similar to those of cardiac Purkinje fibers). Increasing the Ca current also leads to strong suppression of impulse frequencies (Fig. 9, top) and failed spiking in the soma, effects that are only partially ameliorated by increasing the Na-channel density to 300 or 400 mS/cm² on the axonal narrow segment. These effects are uniform across all morphological classes. The calcium signature is sufficiently large, sensitive and channel specific to allow the mean Ca-channel density in the dendrite-soma region to be determined accurately from phase plots (cf. Fohlmeister and Miller 1997a,b).

Dendritic stimulation

The number of active synaptic locations in a given dendritic tree was determined by dividing the total dendritic membrane area (in square micrometers) by 250, which yields a count that closely approximates the number of active ribbon-synapses to light stimulation (R. F. Miller, personal communication). This number ranged from 5 for a group 1 cell to 30 for a group 4 cell. Dendritic sites were stimulated singly or variously distributed with total excitation (depolarizing) currents in the range of 15–320 pA. In all cases, the resulting impulses or impulse trains were initiated similar to those with soma stimulation (Fig. 10A), namely in the narrow segment-initial segment-soma region, with all impulses faithfully propagated on the axon. With 320 pA of total “synaptic” current divided equally among the active sites, impulse frequencies ranged from ~50 Hz for the slowest of group 4 (slow) cells to ~200 Hz for the group 1 (superfast) cells. Localized stimulation near a distal end of the dendritic tree increases the latency to first spike and reduces the impulse frequency relative to localized stimulation near the soma for equal levels of synaptic current. This effect increases with increasing levels of stimulus is largest for group 4 and almost nonexistent for group 1 (superfast) cells. For example, the latency difference in a relatively slowly firing group 2 (medium complex) cell stimulated at 20 and 80% along a typical dendrite is 1.4 ms with 30 pA and 8.1 ms with 150 pA of synaptic current. The corresponding increases in impulse frequency are 2.3 and 41.5%, respectively. Substantial though these timing effects are, a treatment of subunit (Hochstein and Shapley 1976) or transient directional hyperacuity phenomena (Grzywacz et al. 1994) across morphological classes are beyond the present scope, primarily because they involve signal processing throughout the retina.

Impulses initiated as described above invade almost all branches of the dendritic trees (cf. Stuart and Sakmann 1994); they fail only to invade very thin branches, analogous to propagation failures across the axonal narrow segment noted in earlier sections (cf. Fig. 5). Spike failure to invade some dendritic branches appears to be restricted to a small subset of morphologically medium complex cells that are also group 1 (superfast), and therefore of necessity exhibit many thin dendritic processes. When such thin processes are stimulated with sufficiently large depolarizing currents (~10 pA), they remain depolarized (in the range of ~30 to ~10 mV) and interact with the spiking in the soma to produce complex phase-locking patterns (Fig. 10, C and C’). This phase locking reflects the fact that membranes endowed with both regenerative (Na) and recovery (K) channels represent oscillators that are coupled electrotonically through the dendritic morphology. In the particular neuron shown, only two of five dendritic recording sites

![Fig. 10. Excitation of ganglion cells with simulated dendritic (synaptic) stimulation. Results from 2 model neurons are shown (cell types are given at the top). Standard channel densities with $g_{Na} = 200, g_K = 0$ mS/cm² on the axonal narrow segment were employed, and all records were obtained with 70 pA distributed equally and arbitrarily among 18 (~3.9 pA per stimulation site, A), and 5 dendritic locations (14 pA per stimulation site, B and C) throughout the dendritic trees. A: although the impulses invade the dendrites, they are triggered on the initial segment of the axon. B–D: impulse train recorded in the soma, and dendritic membrane oscillations observed at 2 dendritic stimulation sites of thin diameter; the remaining 3 dendritic stimulation sites (not shown) were invaded by the back-propagating impulses from the soma, as in A. Phase locking or other dendritic oscillations (phase plots of panels C’ and D’) was observed only in superfast, morphologically medium complex cells on thin dendritic processes (the bulk of cells show simple dendritic invasion of soma impulses). Quasiperiodic dendritic oscillations of C indicate a phase-locked response (C’), although the nonperiodic dendritic oscillation observed in D and more clearly in the phase plot D’, indicate that this neural response may be an example of nonlinear dynamic chaos (see text).]
responded with complex oscillations; the remaining three were
driven by the back-propagating impulses from the soma (like
those in Fig. 10A). Although one of the “oscillating” dendrites
(Fig. 10C) is phase-locked to the soma, it is evident from the
corresponding phase plot (C’) that this dendritic oscillation is not periodic, and that this is due to small jitter in the spike train
at the soma. The records plotted in Fig. 10, B–D, are of the 100 ms segment between 400 and 500 ms after stimulus onset; the jitter is therefore not a transient property. Instead, the jitter appears to be a manifestation of dynamic chaos (i.e., deterministic nonperiodic oscillations), and this is most clearly seen in the second oscillating dendrite (Fig. 10D) and the corresponding phase plot (D’). Chaotic neural responses also were noted in Fohlmeister and Miller (1997b) for the dendritic equivalent cylinder models, where channel density ranges for this type of behavior are discussed.

**Discussion**

Retinal ganglion cells respond with a wide variety of impulse-encoding phenomena to electrode stimulation in the soma. A representative set of traced neurons will reproduce the range and distribution of impulse frequency versus stimulus current (F/I) responses seen experimentally, as well as certain special features (e.g., various forms of IS-SD break, spike doublets, bursting, and other spiking “irregularities”) and of passive charging parameters (input resistance and charging times). Electrophysiological impulse response rates are correlated strongly with the total membrane (surface) area of the dendritic processes and soma but (perhaps surprisingly) (cf. Mainen and Sejnowski 1996) only weakly correlated with morphological complexity of dendritic branching or the physical reach of the dendritic trees (Table 2). These conclusions are drawn from a modeling study of a set of ganglion cells (n = 57) traced in three dimensions and classified by size (small, medium, and large) and complexity (simple and complex) of the dendritic tree (Toris et al. 1995). The traced cells were supplied with five voltage- or ion-gated channels (plus leakage) that were distributed throughout the model neuron membrane according to the pattern determined for earlier models of retinal ganglion cells that employed equivalent dendritic cylinders (Fohlmeister and Miller 1997b).

The five-channel model had been developed in connection with a whole cell recording study, which found that ganglion cells of the tiger salamander retina could be classified into FAST, MEDIUM, and SLOW cells on the basis of their frequency versus stimulus discharge rate (Fohlmeister and Miller 1997a). In this connection, perhaps the most important result is the description of a group of superFAST cells (group 1 in Table 2), which are typically small simple but include small complex as well as medium simple and medium complex cells morphologically. This group has an average F/I slope twice (namely 2 imp · s⁻¹ · pA⁻¹) that of FAST cells and as a group clearly is separated from the FAST group. These superFAST cells were found to be remarkably robust with regard to both impulse frequency stability as well as stability in the site of impulse initiation. These neurons tolerate wide excursions (50% in either direction) from the standard channel density distribution with only small effects on impulse frequency, and all impulses are initiated in the axon-hillock region, except for near-threshold stimulus levels, for which the impulse trigger zone expands to encompass the axonal narrow segment and even the proximal axon beyond the narrow segment, a total distance of some 300 µm. SuperFAST cells (as well as cells of other groups) exhibit a large dynamic range (<0.2 to >200 imp/s at 22°C). The larger soma-dendritic surface areas of the FAST, MEDIUM, and SLOW cells (Table 5) cause greater delays between the spike on the narrow segment and that in the soma even for stimuli well above threshold (10–20 pA, cf. Fig. 4), and these large delays are responsible for the various more complex encoding phenomena noted earlier.

Group 1 (superFAST) cells are probably overrepresented in our morphological data pool (given in Table 2) due to small cell staining bias and may be more rare in the retina. However, small cells also are damaged easily by the electrode in the eyecup preparation, which may cause perhaps 50% of the current passed through the electrode to be shunted across the giga-seal, leading to lower impulse frequencies and measured input resistances. Experimentally they therefore may have been counted among the FAST cells. Table 2 of Fohlmeister and Miller (1997a) gives the proportion of 18 FAST cells to 10 MEDIUM cells. If we combine the number of our present group 1 and group 2 cells, the corresponding proportion is 34 (group 1 + group 2) to 14 (group 3) cells. However, if we scale the number of our group 1 cells according to their reduced soma surface area (cross-sectional area presented to the electrode) of ~711 µm² relative to the average area of ~1,200 µm² for cells of groups 2–4 (Table 5), the proportions of our group 1 + 2/group 3/group 4 are 25:14:9 cells. This is in remarkably close agreement with the experimentally found proportions of FAST: MEDIUM:SLOW = 18:10:7 cells (Fohlmeister and Miller 1997a, Table 2). It is reasonable therefore to identify our model groups 1–4 with the electrophysiological groups superFAST through SLOW, respectively, which renders our numeric classification redundant.

Viewing all aspects of this study, including the degree of prevalence of spiking irregularities across our data set of cell morphologies as well as antidromic soma invasion, it appears that 
\[ g_{Na} = 300 \text{ mS/cm}^2 \] may be the best (or most typical) value for the membrane of the axonal narrow segment. It is also possible that the narrow segment contains few or no delayed rectifier or A-type potassium channels. Reductions (by up to one-third) in the Na-, Ca-, K-, and KA-channel densities in the remainder of the encoder region (our weakened model, Table 1) are permissible; orthodromic impulse trains then are modified somewhat but remain within observational limits. Antidromic impulses, however, do not then readily invade the soma. Therefore we do not consider the weakened model to represent the “healthiest” cells but rather to represent the lower bound of a safety margin within which the cells remain viable.

The large variety of observed impulse entrainment phenomena was found to be due to the process by which some portion of the encoder region leads neighboring membrane in reaching threshold. Any instantaneous membrane potential profile along the neural “encoder” region (which extends from the dendrites to the proximal axon beyond the narrow segment) therefore can be highly variable and fluctuating in time, which is the primary cause of the irregularities in impulse frequency seen in some spike train records. However, impulse initiation never was observed on the dendrites (where \[ g_{Na} = 25 \text{ mS/cm}^2 \]), even with dendritic stimulation, although the dendrites contain the highest density of calcium channels. This is in agreement with the results of Velte and Maslund (1997), who observed dendritic invasion by impulses in rabbit ganglion cells but not dendritic
impulse initiation (T. Velte, personal communication). As the stimulus current is increased, impulse frequencies increase and the physical size (or extent) of the effective encoder region declines and with it the occurrence of spiking irregularities.

Given the absolute constraints on cell morphology (i.e., absence of free geometric parameters), in conjunction with the diversity of electrophysiological responses and their homology with experimental observation and classifications, and finally their homology with the observed passive responses of the neurons, we conclude that the five-channel model of retinal ganglion cells represents a realistic, first-order encoder for these cells. A single channel-density distribution (standard in Table 1) likely prevails across all morphological and electrophysiological classifications of the cells.

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