Encoder Adaptation Modulates the Visual Responses of Crayfish Interneurons

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Submitted 12 January 2004; accepted in final form 7 March 2004

Glantz, Raymon M. and John P. Schroeter. Encoder adaptation modulates the visual responses of crayfish interneurons. J Neurophysiol 92: 327–340, 2004. First published March 17, 2004; 10.1152/jn.00035.2004. The responses of sustaining and dimming fibers were characterized by the time varying firing rates elicited by extrinsic current and flashes of light. These data were simulated by an adaptive integrate-and-fire model. A postimpulse shunt conductance simulated spike-frequency adaptation. The correlation between observed and model current-elicted impulse rates was 0.94–0.98. However, except for a difference in input resistance (both measured and simulated), the voltage to impulse encoders of the two cell groups was similar and exhibited comparable degrees of spike-frequency adaptation (40 to 45%). The encoder model derived from current-elicted responses (with fixed parameters) was used to simulate visual responses elicited by light flashes. These simulations included a synaptic current derived from the time course of the postsynaptic potential (PSP). The sustaining fiber visual response consisted of a large excitatory PSP and high-frequency transient burst that adapted (by ~80%) to a low-frequency plateau discharge. The simulations indicated that spike-frequency adaptation had no effect on the transient discharge but reduced the plateau firing rate by ~60%. Encoder adaptation enhances the sustaining fiber response to the time derivative of the stimulus. In dimming fibers, the light flash elicits an inhibitory PSP that interrupts the “dark discharge” and an OFF response following the end of the flash. The simulations indicated that spike-frequency adaptation reduces the firing rate of both the dark discharge and the OFF response. Thus the model suggests that different effects of encoder adaptation on the two cell types arise from the same encoder mechanisms, but different actions are determined by differences in impulse rate and the time course of the discharge.

INTRODUCTION

A critical feature of many sensory systems is the capacity to detect change in the environment. This capacity is expressed in a disproportionately higher neuronal sensitivity to fast temporal variations in stimuli. In visual systems, it is well established that light adaptation in photoreceptors and the properties of the peripheral lateral inhibitory network contribute to the response adaptation observed in higher order cells (Glantz and Bartels 1994; Naka and Nye 1970; Sakai 1992). In several systems, the firing rate of higher order visual neurons appears to be linearly related to the magnitude of the suprathreshold postsynaptic potential (PSP) (Carandini and Ferster 2000; Korenberg et al. 1989; Sakai 1992). Thus the firing rate may be controlled by light adaptation in photoreceptors and the properties of the afferent pathways that generate the PSP. In crayfish visual interneurons (i.e., sustaining fibers and dimming fibers, Glantz et al. 1995; Kirk et al. 1983; Pfeiffer and Glantz 1989) and a number of other interneurons (Fohlmeister et al. 1977; Galarreta and Hestrin 2001; Poliakov et al. 1997; Powers and Binder 1996), the time course of the discharge may be quite distinct from that of the PSP, and the discharge may exhibit a higher temporal frequency response than the PSP (French et al. 2001; Glantz et al. 1995; Knight et al. 1970). Following an illumination increment (or decrement for dimming fibers), response adaptation in the sustaining fiber PSP is on the order of 15–50%, while the concurrent sustaining fiber discharge may decline by ≤95 or 100%. The difference may reflect the impulse threshold, the properties of the spike generating mechanism (i.e., the voltage to impulse encoder) (Kretzberg et al. 2001; Mainen and Sejnowski 1995; Wang 1998), dynamic properties of the synaptic current (Dobrunz et al. 1997), voltage-dependent conductances in the dendrites (Magee et al. 1998), or some combination of these. A substantial body of theoretical work suggests that self-inhibition (Fohlmeister et al. 1977; Knight et al. 1970) or spike-frequency adaptation (Benda and Herz 2003; Ermentrout 1998; Liu and Wang 2001; Wang 1998) may contribute to the time-dependent decline of the sustaining fiber visually elicited step response. The extent of that contribution, however, is not accessible to simple inspection because the adaptation is dynamically determined by the recent history of impulse activity (Benda and Herz 2003; Liu and Wang 2001). Furthermore, encoder adaptation may be based on any of several ionic channels (Benda and Herz 2003; Sah 1996; Schwarz et al. 1997), with different dependence on voltage, intracellular [Ca2+], or the recent history of impulse activity. Variations in channel distribution can produce substantial differences in the time course of the discharge (Wang and McKinnon 1995) among otherwise similar cells.

Sustaining fibers have several features that can facilitate the analysis of integrative mechanisms. Dendritic recordings (Kirk et al. 1983; Waldrop and Glantz 1985) reveal PSPs of ±40 mV associated with impulses of only 5–10 mV. Thus the PSPs can be separated from the spike trains (French et al. 2001) while preserving most of the details of the time-varying membrane potential. Furthermore, the impulses appear to be passively conducted from the spike initiating zone (where the action potential amplitude is 70–80 mV) to the dendritic tree. TTX blocks the sustaining fiber action potential but has no observable influence on the magnitude or time course of the PSP (Waldrop and Glantz 1985). In the presence of TTX, the current-voltage functions principally reveal a leakage conductance. This implies that the voltage-dependent conductances are not present in high density in the dendrite. If voltage-dependent dendritic currents are minimal, the relationship between the PSP and the firing rate is principally governed by the time course of the synaptic current and the dynamical proper-
ties of the spike generating mechanism. Here we formulate a minimal adaptive integrate-and-fire model that uses synaptic currents to generate impulses at rates controlled by spike-frequency adaptation (Koch 1999; Liu and Wang 2001). The analysis and model are implemented for two cell classes (sustaining fibers and dimming fibers) arising in the crayfish second optic neuropile. The cells have complementary visual responses (on vs. off discharges), but they discharge at substantially different rates.

Extrinsic current was used to characterize impulse generation (i.e., the voltage to impulse encoders). We found that spike-frequency adaptation diminished the current-elicited firing rate by 35–45% in 50–200 ms in both cell classes. The time varying firing rates were simulated by an adaptive integrate-and-fire encoder model. Spike-frequency adaptation was simulated by a shunting conductance. For each cell, the same model with fixed parameters and supplemented by a model of the synaptic current was used to describe the visually elicited response. Because the simulated visual responses contain the adaptive characteristics of the encoder, they provide a theoretical measure of the influence of encoder adaptation on the visually elicited discharge. The simulations indicate that spike-frequency adaptation contributes to the time-dependent decline of the sustaining fiber visually elicited discharge, and it influences both the dark discharge and decremental responses of dimming fibers.

METHODS

Physiological preparation

Adult crayfish, Pacifastacus leniusculus, of both sexes were prepared as in Glantz et al. (1995). The eyestalks were decapsulated into their sockets with cyanoacrylate adhesive and chilled to 8°C. Hemolymph was replaced with oxygenated crayfish saline buffered with 5.0 mM HEPES at pH 7.5. During the experiments, the animal was clamped in a lucite chamber and submerged in buffered saline that was continuously oxygenated and slowly warmed to 15°C. The optic lobe was exposed by removal of the dorsal eyestalk cuticle, and the optic neuropile was visualized by removing portions of an overlying sheath. The results are based on studies of 48 neurons in 34 animals. Twenty-nine of these neurons met several constraints, and they are the focus of this report. These 29 cells exhibited repeatable responses to both current and light, and they were differentially responsive to a range of stimulus magnitudes. Furthermore, in each of these cells, the PSPs were large enough so that the PSP time course could be extracted (see PSP extraction) from the complex physiological waveform that also included action potentials.

Recording and data acquisition

Sustaining and dimming fibers were impaled in the second-optic neuropile (medulla externa) with sharp micropipettes filled with 3.0 M K+-acetate. Electrodes had 80- to 100-Mohm resistances and 0.2- to 0.4-ms time constants (after capacity compensation). Signals were fed to an Axoclamp (Axon Instruments, Foster City, CA) IB amplifier. The neurons were identified by their location and their characteristic responses to a flash of light. The voltage, current, and stimulus signals (see Visual stimuli) were digitized at 1,000 Hz/channel with a National Instruments (Austin, TX) A/D card running under a Pentium computer and LABVIEW software.

Visual stimuli

Light flashes were produced with a green (λ = 532 nm) solid state laser diode (MWK Industries, Pomona, CA) with maximum intensity of 1.2 mW/mm² at the eye. The laser beam was positioned with galvanometer mirrors. Stimulus intensity was controlled with a neutral density wedge with optical density spanning 6.0 log₁₀ units and with the optical density increasing by a factor of 10 over each 2.5 cm of wedge length. The laser diode was operated with a relay circuit and pulse generator. Contrast flashes were derived from a Hitachi display oscilloscope driven by a Picasso Image Synthesizer (Innesfree, Cambridge, UK). A stimulus patch subtending 10–20° was superposed on a background subtending a 120° on a side. Stimulus flashes were of 0.5- to 1.0-s duration presented at 0.2 Hz or 5.0-s duration presented once per 30 s. The 5.0-s stimuli were used in the earliest studies to determine the time course of adaptation. Since most cells approach steady state in 0.5–1.0 s, ~90% of the data were obtained with the shorter flashes.

Current injection protocols

Impulse trains were elicited with rectangular pulses of 0.02–4.5 nA. The pulses were 0.5- to 4.0-s duration and delivered at a repetition rate of 0.2–0.05 Hz. The magnitudes and durations were set to generate a wide range of impulse rates and of sufficient duration to measure the spike-frequency adaptation. To minimize long-term or cumulative adaptation, the current pulses were delivered in blocks of 10–20 stimuli separated by 30–60 s. Test pulses of fixed magnitude were inserted throughout the stimulus sequence to assess nonstationarity. The injected currents were monitored at a port on the Axoclamp IB amplifier.

Spice train isolation

The light- and current-elicited impulse trains were separated from the PSP or slowly varying potential by wavelet denoising (Johnson et al. 2000). In this nonlinear method, the wavelet transform was computed using the Daubechies-6 (Daubechies 1992) wavelet. Wavelet coefficients less than an adjustable threshold were set to zero, and the result was inverse-transformed to give the raw spike train.

PSP extraction

For the light-elicited responses, the PSP was separated from the superposed spike train by digital subtraction of the previously identified spikes (French et al. 2001). The binarized spike train (a train of 1s and 0s) produced by wavelet denoising was first used to locate the spike positions. The spike foot was found using the known spike width, adjusted for PSP-dependent variations. The spike was removed from the baseline potential by interpolation. This method yielded a potential comparable to that in the raw data, and, except for the small regions spanned by the spike foot, the high-frequency membrane noise was left intact. A possible difficulty is that some of the spike foot is inevitably included in the voltage record. To evaluate this artifact, we hyperpolarized cells with sufficient current to block impulse generation during the light response and then compared the time course of the PSP isolated by hyperpolarization (as in Fig. 1B, continuous line) to those derived by spike subtraction (as in Fig. 1B, broken line) from responses elicited at rest potential shown in Fig. 1A. In general, we found that with intradendritic recordings the PSPs were large (~35 mV), the impulses were small (5-10 mV), and the averaged PSP isolated by subtraction was nearly indistinguishable from that isolated by hyperpolarization. Conversely, recordings nearer the spike initiating zone exhibited 40- to 80-mV impulses superposed on 2- to 5-mV PSPs. Four of the 21 sustaining fibers and 6 of 18 dimming fibers had these features. In these cells, the PSPs isolated by spike subtraction contained large artifacts, and the data could not be used to compute the synaptic currents in the second phase of this study.

Specification of the stimulus

For the current injection experiments, a square-wave current trajectory was obtained by appropriate scaling of the voltage represen-
FIG. 1. Comparison of sustaining fiber postsynaptic potentials (PSPs) derived by spike subtraction and isolated by hyperpolarization. A: response to a 0.5-s flash at log intensity ~3.5. B: isolated PSPs. Broken line is average of 16 PSPs following spike subtraction. Continuous line is the average of 6 responses to the same stimulus and in the presence of a 1.8-nA hyperpolarizing current. Hyperpolarization produced an increase in PSP amplitude.

Characterization of the response for model and data

The response of the cell and of the model was the current derived from the PSP with Eq. 3. Because the simulations are sensitive to the recent history of activity (e.g., impulses), computations initiated at the start of a stimulus sequence can generate large artifacts. To avoid these artifacts, the beginning of each data set was lengthened by two stimuli and associated with two average responses for model input and these stimulus-response pairs were discarded at the end of the computation.

Adaptive leaky integrate-and-fire model

The adaptive leaky integrate-and-fire encoder is given by

$$I_i + I_e + I_b = (\tau_m R_m) dV/dt + (G_{adapt} + I R_m) V$$

(1)

where $I_i$ is the extrinsic current, $I_e$ is the synaptic current (set to 0 for noise-free extrinsic current studies), $I_b$ is a steady background current that drives spontaneous impulse activity, $V$ is the membrane potential above resting potential ($V_{rest} = 0$), $\tau_m$ is the membrane time constant, and $R_m$ is the input resistance. When $V$ reaches the impulse threshold, $V_{th}$, an impulse is produced and $V$ is set to $V_{rest}$. $G_{adapt}$ is the postimpulse conductance (the adaptive mechanism) that is initially zero and incremented after each impulse by $G_{inc}$. $G_{adapt}$ decays exponentially with time constant $\tau_{adapt}$

$$dG_{adapt}/dt = -G_{adapt}/\tau_{adapt}$$

(2)

$G_{adapt}$ is a shunting conductance (Koch 1999). It gates the currents of $V_{rest}$ but it is not specifically linked to a potassium equilibrium potential.

Previous studies (Fohlmeister and Miller 1997; Liu and Wang 2001) indicate that an adaptive mechanism based on a calcium-activated potassium conductance will be delayed due to the time required for Ca$^{2+}$ to accumulate in the cytoplasm. Furthermore, we found that the hyperpolarizing afterpotential associated with each impulse typically required about 20 ms to attain maximum amplitude. We simulated this delay by requiring a succession of two impulses above a specified impulse rate threshold for activation of $G_{adapt}$ following onset of a current pulse or light flash. The threshold rate was set just below the peak rate of the smallest transient response in each series.

The impulse rate is also constrained by the refractory period, $t_{ref}$. $V$ is held at $V_{rest}$ following each impulse at $t_i$ so long as $t - t_i < t_{ref}$.

Currents derived from the membrane potential or PSP

The extracted potential provided the basis for computing the synaptic current by assuming that the potential is constrained by the same variables that define the encoder. Thus $I_i$ is given by

$$I_i = (\tau_m R_m) dV/dt + [V_G(V_{th} - V)]$$

(3)

Here, the synaptic conductance $G_s(V)$ was previously shown to be a fixed sigmoidal function of the instantaneous synaptic potential (V) (Waldrop and Glantz 1985). As the potential varies from 0 to 40 mV, $G_s$ normalized by the resting input conductance, $G_{inc}(R_m^{-1})$, varies from 0 to 1.5. $G_s$ acts in parallel with $G_{adapt}$. $k$ represents the ratio between the synaptic resistance and the input resistance, $R_m$ at the spike initiating zone, and $\tau_m$ is the membrane time constant. For the visual stimuli, $I_i$ was calculated from the PSP using Eq. 3 for input to Eqs. 1 and 2.

Optimization of model parameters

Equations 1 and 2 specify a seven-parameter ($I_i$, $G_{inc}$, $\tau_{adapt}$, $V_{th}$, $t_{ref}$, $\tau_m$, $R_m$) model that generates firing times given the extrinsic ($I_e$) and synaptic ($I_s$) currents. To describe the response to current stimuli, $I_i$ is set to zero. To describe the response to light flashes, $I_i$ is set to zero, and $I_s$ is calculated from Eq. 3. In this case, the model has eight parameters, including the resistance ratio, $k_b$. In practice, the refractory period ($t_{ref}$) was fixed to a value slightly smaller than the shortest interspike interval (ISI; 4 or 5 ms) and was not varied during optimization. For each cell, an optimum fit of the model response to the observed response was discovered for the current step stimuli. The parameters so determined were used to describe the model response to light flashes, varying only the background current $I_b$ and the resistance ratio $k_b$. It was necessary to vary $I_i$ between the two simulations because the background discharge often varied between sets of measurements and was usually suppressed by repeated flashes of light.

To find the best fit of model responses to stimulus-elicted responses, the step current input or the extracted PSP input was discretized with a time interval of 0.5 ms (one-half the digitization interval). This time step reduced aliasing artifacts to a few percent and allowed reasonably rapid calculation times. Selection of optimum parameters for the fit was performed using the Nelder-Mead methods in the MATLAB optimization toolkit. Software was produced in-house to start the optimization from a particular set of parameters and to specify the parameter dimensions used. Discovery of the true optimum was difficult due to the “stair-step” nature of the optimization.
tion surface, which in some cases had many nonminimal but relatively flat regions. These regions were avoided by requiring the optimizer to restart many times at regions distant from an apparent minimum. The best fitting parameters found by this procedure were taken to be the true optimum.

The fit of the model to the data were evaluated by the root mean square error (RMSE) and the linear correlation coefficient. The RMSE = \( \sum \{ \sqrt{(F_d - F_m)^2} \} / n \), where \( F_d \) is the observed instantaneous impulse rate, \( F_m \) is the model instantaneous rate, and \( n \) is the number of data points in the optimized data set. Optimization was always performed on a family of responses (5–13) associated with variations in extrinsic current. The tabulated results indicate the RMSE normalized by the average SD of the measured data set.

RESULTS

Our current injection studies were carried out on 21 sustaining fibers and 18 dimming fibers. Our overall strategy had two phases. In the first, we characterized the spike generator by analysis of the time-varying discharge elicited by current pulses and simulation of the discharge by Eqs. 1 and 2. The optimized model provided good approximations of the peak and steady-state firing rates and the magnitude of spike-frequency adaptation in every neuron. In the second phase, we examined the visual responses of 29 of the same neurons and simulated these responses as an interaction between the synaptic current (derived from the PSP) and the identical model (same parameter values) derived from responses elicited by extrinsic current.

Sustaining fiber’s current-elicited discharge

At suprathreshold currents, the characteristic response pattern consists of a brief high-frequency transient followed by adaptation to a lower frequency plateau rate (as in Fig. 2, A–D). Adaptation reduces the firing rate by \(-40\%\) as described.

![FIG. 2. Sustaining fiber current-elicited and simulated impulse trains. A–D: samples of responses to the indicated 0.5-s current pulses. Stimulus timing is indicated by the bar at bottom E–H. Average firing rate vs. time for current magnitudes indicated in adjacent panels. Shaded areas indicate \( \pm \)SD of the instantaneous firing rate. Each function is the average of 10 responses. Solid line superposed on firing rate functions is the model response for the same currents. Model parameters are in Table 1, column 2.](http://jn.physiology.org/)

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below. The peak transient rate (estimated from the 1st 1 or 2 ISIs as in the firing rate functions of Fig. 2, E–H) is occasionally quite variable (average CV is 0.18) while the plateau discharge is both regular and less variable (CV is 0.11) as shown by the shaded areas (±SD) of Fig. 2, E–H. The average CV for the whole population was 0.06 for the transient and 0.08 for the plateau discharge. In spontaneously active neurons, the termination of the current pulse is typically associated with a hyperpolarization and silent period in the discharge of up to several hundred millisecond duration as in Fig. 2, A–D. Similar responses in other cells have been attributed to the cumulative effects of a slow hyperpolarizing afterpotential (Schwarz et al. 1997; Wang and McKinnon 1995). We estimated the speed of adaptation by fitting a single exponential (by least squares) or the sum of two exponentials to the firing rate functions between the peak and the end of the plateau. At peak firing rates \( <25 \text{ im/s} \), the firing rates of nearly all cells decline as a single exponential with a time constant \((\tau_1)\) of 100–250 ms. For about one-half the cells, the same holds for rates \( \leq 60 \text{ im/s} \), and the time constants were weakly dependent [correlation coefficient \((r = 0.55)\) on the inverse of the peak impulse rate; data not shown. At the highest firing rates, adaptation evolves in two stages (as in Figs. 2, G and H, and 3, F–H for dimming fibers) as previously described in other neurons (Sawczuk et al. 1995; Wang 1998). The initial phase is rapid \((\tau_{a1} = 21.7 \pm 11.1 \text{ ms})\) and accounts for 70% of the total adaptation. In the second stage, \(\tau_{a2}\) is 100–300 ms. The two time constants were relatively insensitive to the peak impulse rate but the component of adaptation associated with \(\tau_{a1}\) increased as the peak firing rate increased.

Simulation of the sustaining fiber response to extrinsic current

The firing rates simulated by the adaptive integrate-and-fire model are shown by the continuous line superposed on the shaded areas of Fig. 2, E–H. The model captures the principal features of the observed response including 1) the timing of the peak impulse rate; 2) the current-dependence of both the peak and plateau firing rates (details in Fig. 4); and 3) the suppression of the discharge following the termination of the current pulse. The correlation between the measured and simulated
the peak rate and 0.99 and 48.6 imp/s/nA for the plateau rates, respectively. The dimming rate. Model peak and steady-state rates are indicated by X and ●, respectively. The correlation coefficient ($r$) and regression slopes ($m$) are 0.95 and 20.3 imp/s/nA for the peak rate and 0.96 and 11.8 imp/s/nA for the plateau response, respectively. B: as in A, for the dimming fiber described in Fig. 3, $r$ and $m$ are 0.97 and 83.0 imp/s/nA for the peak rate and 0.99 and 48.6 imp/s/nA for the plateau rates, respectively.

instantaneous firing rates (elicited by 7 current magnitudes) was 0.96 (the RMSE/SD was 0.91 SD; Table 1, column 1). Similar results were obtained for a population of 17 sustaining fibers (Table 1, column 2). We estimated the temporal accuracy of the model by comparing the observed and simulated latencies to 90% of the maximum impulse rate. For the cell described in Fig. 2, at the lowest three current magnitudes, the model latencies deviated from observed values by 6–22 ms. At the higher currents tested, the average deviation was <1.0 ms.

For the population as a whole, the average deviation at the highest currents was 4.8 ± 3.6 ms. It is possible that the underlying mechanisms of $G_{\text{inc}}$ and $\tau_{\text{adapt}}$ might vary systematically with the firing rate. We examined this possibility by optimizing the model, one response at a time, for each response in a series. We found no evidence for systematic variations. In general, $G_{\text{inc}}$ and $\tau_{\text{adapt}}$ optimized for single responses fell within a few percent of the values obtained for the entire response population. This result implies that wide variations in the magnitude of adaptation can be produced by variations in the current-elicited firing rate and an invariant adaptive mechanism.

For the entire sustaining fiber data set, the simulated $\tau_{\text{adapt}}$ was 99 ± 77 ms, and it provided a reasonable estimate of the time course of adaptation in most responses. The responses that exhibited two decay time constants during adaptation were also approximately by $\tau_{\text{adapt}}$ (as determined in the optimization routine), and these simulations were less precise. For these data the simulated responses generally decayed more slowly than the observed responses as shown in the dimming fiber response in Fig. 3H and the discrepancy contributed to the RMSE. The optimized value of $\tau_{\text{adapt}}$ was typically between $\tau_{\text{r1}}$ and $\tau_{\text{r2}}$.

We also found that $\tau_{\text{adapt}}$ is similar to the decay time constant of the hyperpolarizing afterpotential (as in Table 1). The significance of this similarity is that $\tau_{\text{adapt}}$ is the theoretical decay time constant of the postimpulse conductance and this time constant should be reflected in the time course of the hyperpolarizing after-potential.

Dimming fiber current-elicited response

Dimming fibers are characterized by an off response following a decrement in illumination and inhibition of a tonic discharge following an increment of illumination. The dimming fiber-elicited discharge, shown in Fig. 3, A–D, is similar to that of sustaining fibers with a short latency transient discharge followed by rapid adaptation to a lower frequency plateau rate. The speed of the initial phase of adaptation can be ascertained from the firing rate plots in Fig. 3, E–H. At the highest currents (as in Fig. 3H), the peak rate persists for no more than two ISIs.

Simulation of the dimming fiber response to extrinsic current

The integrate-and-fire simulation of the dimming fiber discharge was comparable to that for sustaining fibers. The model response (as in Fig. 3, E–H, solid line through the shaded area) captured the timing of the peak rate and provided good approximations of the transient and plateau firing rates. The model parameters for dimming fiber simulations (Table 1, columns 4 and 5) were generally similar to those of the sustaining fiber simulation but for the input resistance (Table 1, $R_{\text{in}}$), which was 100–200% larger for the dimming fibers. For the cell described in Fig. 3, we simulated the responses to nine current magnitudes (model parameters in Table 1, column 4) and the correlation between observed and model responses was 0.98 (RMSE was 0.49 SD).

Sensitivity and robustness of the integrate-and-fire model

As noted in METHODS, the optimization surface has a “stair-step” nature that implies that changes in one parameter (e.g.,


Predictive power of the integrate-and-fire model

When spike trains are elicited by ramp or sinusoidal currents, the timing of the response (data not shown) is sensitive to the slope or frequency as well as the magnitude of the current trajectory (Fohlmeister et al. 1977; Knight et al. 1970). Small deviations in the timing of simulated responses can produce large increases in the RMSE compared with model descriptions of the responses to current pulses. When the parameters of Eqs. 1 and 2 are optimized for these responses, the RMSE is typically 20–30% larger than that for comparable current pulse responses. We examined the predictive power of the model for different current waveforms in 19 cells. In each case, the model was optimized for responses to current pulses, and we determined the RMSE of the model (with fixed parameters) for a population of responses to sine wave currents of varied frequency or ramp currents with varied depolarizing slope. The RMSE for the pulse-elicited responses was equivalent to about 0.68 SD relative to the measured responses. In 10 of the 19 cases, the RMSE of the simulated ramp- or sine wave-elicited response was about 20–30% larger than that for the pulse responses. For these cells, the model derived for the responses to current pulses was about as good as an unconstrained simulation of the same data. In another four cells the principle deviation was a shift in the level of spontaneous activity between the two stimulus protocols. For these cells, an adjustment of $I_b$ brought the RMSE of the simulation to within 20–30% of that for the pulse responses. For the remaining five cells, the RMSE of the model response was about 200% larger than that for the pulse-elicited responses. The principle source of the discrepancy was an apparent reduction in the neuron’s sensitivity to current when subjected to continuous sinusoidal current. The sensitivity shift may indicate a nonstationarity in the spike generator. Alternatively, the reduced sensitivity may reflect the activation of a slow and persistent form of spike-frequency adaptation (Sawczuk et al. 1995) elicited by the continuous impulse activity during sine wave stimulation.

**Frequency–current functions**

The frequency–current ($f$–$I$) functions are an important feature of the voltage to impulse encoder and also provide useful

### Table 1. Parameters of the adaptive integrate and model

<table>
<thead>
<tr>
<th>SusF 1</th>
<th>SusFs</th>
<th>Observed SusF</th>
<th>DimF 1</th>
<th>DimFs</th>
<th>Observed DimF</th>
</tr>
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<tbody>
<tr>
<td>$N$</td>
<td>1 (7)</td>
<td>17 (8)</td>
<td>17</td>
<td>1 (9)</td>
<td>12 (12)</td>
</tr>
<tr>
<td>$I_b$ ($I_b$: nA)</td>
<td>1.44</td>
<td>0.59 ± 0.37</td>
<td>0.28</td>
<td>0.14 ± 0.17</td>
<td>0.15</td>
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<tr>
<td>$G_{inc}$ ($10^{-7}$ S)</td>
<td>1.3</td>
<td>1.8 ± 1.6</td>
<td>89 ± 47°</td>
<td>142</td>
<td>80 ± 45</td>
</tr>
<tr>
<td>$\tau_{adap}$ (ms)</td>
<td>70</td>
<td>99 ± 77</td>
<td>24.7 ± 21.7</td>
<td>29.0</td>
<td>39.2 ± 25.2</td>
</tr>
<tr>
<td>$V_{th}$ (mV)</td>
<td>9.0</td>
<td>6.1 ± 2.9</td>
<td>5.2</td>
<td>4.5 ± 2.1</td>
<td>5.0</td>
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<tr>
<td>$t_{ref}$ (ms)</td>
<td>5.5</td>
<td>5.1 ± 1.6</td>
<td>9.6 ± 4.2</td>
<td>19.5</td>
<td>24.1 ± 1.5</td>
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<tr>
<td>$R_m$ (MO)</td>
<td>12.5</td>
<td>8.6 ± 5.0</td>
<td>0.95</td>
<td>1.07 ± 0.19</td>
<td>0.29</td>
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<tr>
<td>$k$</td>
<td>1.05</td>
<td>0.92 ± 0.45</td>
<td>0.49</td>
<td>0.75 ± 0.19</td>
<td>0.60</td>
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<tr>
<td>$I_b$ ($I_b$: nA)</td>
<td>0</td>
<td>0.29 ± 0.47</td>
<td>0.29</td>
<td>0.19 ± 0.25</td>
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<tr>
<td>RMSE/SD</td>
<td>0.91</td>
<td>0.59 ± 0.20</td>
<td>0.49</td>
<td>0.75 ± 0.19</td>
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<tr>
<td>RMSE/SD</td>
<td>0.84</td>
<td>0.89 ± 0.26</td>
<td>0.26</td>
<td>0.19 ± 0.25</td>
<td></td>
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</table>

Values are mean ± SD. SusF 1, sustaining fiber shown in Figs. 2, 4, and 6; DimF 1, dimming fiber shown in Figs. 3, 4, and 7; SusFs and DimFs, whole population of each of the two cells types; RMSE/SD, root mean square error normalized by the average SD of the firing rate. For the first row ($N$), the first entry is the number of cells, the parentheses contain the typical number of extrinsic current magnitudes per cell. The columns labeled Observed contain directly measured values derived from the cells in the adjacent columns. *The observed values in the $\tau_{adap}$ row indicate the decay time constant of the hyperpolarizing afterpotential. In the row headings (first column) $f$ or $L$ indicates values for the current or light models respectively, when they differed.

$V_{th}$, if accompanied by changes in other parameters (e.g., $I_b$, $R_m$), may produce no change in the RMSE. In this respect, any particular model (i.e., a specific set of parameter values) should be viewed as a global description (Goldman et al. 2001). Although the model approximates the behavior of the neuron (in a least squares sense), the particular parameter values of the model are only meaningful in the context of the entire set.

It is significant, however, that the fit of the model to the data are not equally sensitive to variations in the several parameters. We determined the percent change in each of the parameters that is necessary to increase the RMSE by 50%. The relative sensitivities (inversely related to the percent change) were $V_{th}$ (11%) > $R_m$ (16%) > $\tau_{adap}$ (18%) > $G_{inc}$ (20%) > $I_b$ (46%) > $t_{ref}$ (82%). The sensitivity analysis also revealed that reductions of parameter values were generally more effective than increases vis a vis a an increase in the RMSE. Furthermore, the relative significance of a parameter can vary between cells, and different parameters typically influence different aspects of the response. Thus the sensitivity to variations in $\tau_{adap}$ is high in strongly adapting cells and low in weakly adapting cells. The peak firing rate is sensitive to $V_{th}$ and $R_m$ but relatively insensitive to $G_{inc}$ and $t_{adap}$: The reverse holds for the simulation of spike-frequency adaptation. If two variables are changed simultaneously such that the changes have opposing effects on the firing rate (e.g., a reduction in $V_{th}$ and a reduction in $R_m$), it requires about twice as large a percentage change (compared with single variable changes) to produce the same increase in RMSE.

To measure the robustness of the model, we determined the extent to which variations of the entire set of parameters could compensate for a large change in any one of them (e.g., $V_{th}$). We reduced one parameter value sufficiently to increase the RMSE by 50% and optimized the remaining six parameters to minimize RMSE. Invariably, the RMSE of the new parameter set was within 1–2% of the original minimum. If the initial condition involved two parameters jointly offset (by 20–40%) to produce a 50% increase in RMSE, optimization of the five remaining parameters could reduce the RMSE to within 10% of the original value. These results imply that the ability of the model to describe the neural responses as defined by the RMSE is a robust feature of the structure of the model and not a reflection of particular parameter values.
estimates of spike-frequency adaptation. The open circles in Fig. 4A indicate the peak firing rates versus extrinsic current, and the squares are the steady-state rates for the sustaining fiber responses shown in Fig. 2. The vertical lines are ±SD. Similarly, the circles and squares in Fig. 4B are peak and steady-state rates, respectively, versus current for the dimming fiber in Fig. 3. A common feature of $f-I$ functions that is not shown in Fig. 4 is a relatively steep rise in the transient impulse rate between 0 and threshold current (Ermentrout 1998). This initial segment is better described by $f \propto \sqrt{I}$ (Ermentrout 1998) than $f \propto I$. To examine the generality of this description, we computed the best linear fit (in a least squares sense) for $f = m_1I + b_1$ and the best linear fit to the square root of the current $(f = m_2\sqrt{I} + b_2)$ for the transient impulse rates of each of 37 cells. When the results are evaluated by the correlation between observed and computed firing rates, the accuracy of the linear and square root models were indistinguishable for most cells. Thus the average correlation between observed and computed peak rates was $0.946 \pm 0.041$ (SD) for the linear model and $0.933 \pm 0.060$ for the square root model. In most instances, the correlation coefficient was $0.94 - 0.99$, but the averages are diminished by one or two more variable cells. For the plateau firing rates, the $f-I$ relationship was approximately linear in all cells (Fig. 4A, A and B).

For a linear regression, the slope of the least-square function provides an estimate of the encoder’s sensitivity to current (imp/s/nA), and the difference between the regression slopes for peak transient responses (Fig. 4, A and B, solid lines) and steady-state responses (Fig. 4, A and B, broken lines) is a measure of spike-frequency adaptation. For the sustaining fiber described in Fig. 4A, the adaptation calculated by this method is 37%, while for the dimming fiber (Fig. 4B), it is 41%. Similar results were obtained for the two cell populations. The average adaptations were $42.5 \pm 16.4\%$ for sustaining fibers and $45.1 \pm 17.3\%$ for dimming fibers.

In general, the simulated peak and steady-state firing rates (Fig. 4, A and B, X and $\Delta_x$, respectively) closely approximated the observed rates. The correlations between observed and model peak and steady-state rates were about 0.95, and the regression slopes varied between 0.9 and 1.0. Furthermore, the spike-frequency adaptation of the simulated discharge (derived from the slopes of the $f-I$ functions, 38–42%) was similar to that of the neuronal responses (43-45%). Thus estimates of spike-frequency adaptation from $f-I$ functions suggest 40–45% decline in rate between the peak and steady-state discharge.

The magnitude of the observed adaptation (i.e., the change in impulse rate from peak to steady state, $\Delta F$) is related to the peak impulse rate ($F_p$). The relationship is approximately linear, and the regression slope $\Delta F/F_p$ provides an alternate estimate of spike-frequency adaptation. For sustaining fibers, the two measures ($f-I$ slopes and $\Delta F/F_p$) yielded similar results (i.e., ~40% adaptation). For dimming fibers, $\Delta F/F_p$ appears to exhibit a somewhat larger (53.6%) adaptation, but the difference is well within the SD of the estimate derived from the $f-I$ functions. It is possible, however, that when a population of adaptation measurements is scaled by the peak firing rate (and independent of the particular cell of origin), it may vary from that scaled by current and evaluated on a cell by cell basis. We have more confidence in estimates of adaptation based on the $f-I$ functions because each measurement is based on the responses to 6–10 stimuli, and the regression slopes were typically associated with high correlation coefficients.

**ISIs**

The ISI statistics of the current-elicited responses exhibit a predictable relation to the stimulus current. At the lowest suprathreshold currents, the discharge is irregular. Spontaneous fluctuations in membrane current and ion channel noise (White et al. 2000) contribute to the variability of the firing pattern. At rates below 10 imp/s, the CV of the ISIs is about 0.6. As the current increases, the firing pattern becomes more regular. At the highest currents, the mean ISI of the plateau discharge is $20-40$ ms, and the average CV is about 0.2. The serial correlation of successive ISIs has particular relevance for cells exhibiting spike-frequency adaptation. Wang (1998) has shown (in numerical simulation) that steady-state responses with mean ISI near or just larger than $\tau_{adapt}$ should exhibit a small (approximately $-0.2$) negative serial correlation due to the operation of the adaptive mechanism. Much of our data were not appropriate for these measurements because the firing rates were too high or the responses did not quite reach steady state (and thus contain a positive bias in the serial correlation). In general, we found that the serial correlations were close to zero (between $\pm0.05$) in most responses at constant mean rates exceeding 20 imp/s, and negative serial correlations exceeding $-0.1$ were not observed in these conditions. However, at lower firing rates of 5–12 imp/s, 10 of 13 cells exhibited significant ($P < 0.05$) serial correlation coefficients of $-0.17$ to $-0.5$ (Fig. 5).

**Sustaining fiber visual response**

Sustaining fiber excitation by an increment of illumination entails a rapid depolarization (the initial phase of the PSP) accompanied by a transient discharge as in Fig. 6A (solid trace). The PSP then declines toward a plateau phase, and the time course of the decay can vary from <100 ms to 0.5 s. The decay phase is often associated with a silent period in the discharge, while the plateau phase elicits a sustained discharge. Variations in stimulus intensity or contrast may be expressed in the response latency, the transient or plateau response phases, or all three. For the cell shown in Fig. 6, the transient phase of the PSP and the peak firing rate were nearly independent of

![FIG. 5. Steady-state discharge pattern is modified by spike-frequency adaptation. Serial correlation coefficient of successive interstimulus intervals (ISIs) vs. the mean current-elicited firing rate. Correlations were measured during the plateau discharge of responses to 4.0-s current pulses, 10 repetitions per current magnitude. Arrow indicates $\tau_{adapt}^{-1}$. *Significant correlations ($P < 0.05$).](http://jn.physiology.org/content/jn/92/3/634/F5.large.jpg)
stimulus intensity, but the response latency, the PSP plateau, and the sustained discharge all varied systematically with light intensity.

The firing rate functions in Fig. 6, E–H, indicate that the adaptation of the light-elicited response can be both profound (approaching 100% in Fig. 6E) and rapid (time constant of about 50 ms). These features are characteristic of most cells. The average response adaptation was 72 ± 18% (n = 102), and the adaptation time constant was about 50 ms.

The firing rate variability (shaded areas in Fig. 6, E–H, are ±SD of the mean rate) was typically about 20% (CV = 0.2) of the mean instantaneous rate throughout the response. Because the firing rate functions are derived from the reciprocal of the ISIs, a CV of 0.2 for a peak rate of 100 imp/s implies that the ISIs at the peak of the transient discharge are about 10.0 ± 2.0 ms.

**Simulation of the sustaining fiber light response**

The simulation of the visual response (Fig. 6, E–H, solid line superposed over shaded areas) is based on a current derived from the PSP (Fig. 6, A–D, dotted traces, inward currents are positive), and the parameters of the adaptive integrate and fire model derived from the responses to extrinsic current injection (Table 1, column 1, for the cell shown in Fig. 6). The correlation between observed and simulated impulse rates for this cell is r = 0.95 (for 6 stimulus intensities, RMSE = 0.84 SD). For the whole sustaining fiber population (17 cells, 6 or 7 light-elicited responses/cell), the average r = 0.91 ± 0.04, and the average RMSE was 0.89 SD.

The performance of the model can be appreciated by examining some of the details in Fig. 6, D and H. In this response, the PSP declines from its peak by 16% in 90 ms, and the concurrent firing rate declines by 85%. Underlying the change in firing rate is a steep change in synaptic current (dotted trace in Fig. 6D) as dV/dt goes from positive to negative and the similarly steep initial phase of spike-frequency adaptation. The model simulates this rate change with high fidelity as shown in Fig. 6H.

Because the firing rate function is in part derived from the time course of the PSP, an examination of the degree of
linearity between the PSP and firing rate provides a useful framework to evaluate the model. The cross-correlation function estimates the linear relationship between the PSPs and firing rate functions. For the cell shown in Fig. 6, the cross-correlation function (data not shown) exhibited maximum intensity at a time lag of 5 ms (i.e., within 1 ISI at peak rate) and a correlation coefficient $(r)$ of 0.72 at that time lag. This implies that the linear relationship between the PSP and the firing rate describes about 52% $(0.72^2)$ of the variance in firing rate. Conversely, the optimized model describes 90% of firing rate variance. The PSP versus firing rate correlations were similar for the entire sustaining fiber population $(r = 0.725 \pm 0.195, n = 17$ cells).

We also examined a more complex model in which the firing rate, $F = [k_1(V - V_{th}) + k_2(dV/dt)]$ (Poljakov et al. 1997; Stein 1980), more closely reflects the synaptic current. Although the results were a little better than those obtained with cross-correlation $(r = 0.8$ for observed vs. computed firing rates), they were substantially inferior to the nonlinear adaptive model.

The transient peak discharge is the most difficult to simulate because it is strongly influenced by variations in capacitative currents associated with fluctuations in the rising and decay phases of the peak of the PSP (as in Fig. 6, A–D, dotted line). Errors of 10–20% in the computed peak rates are not uncommon (Fig. 8A, solid line). Conversely, the plateau discharge is largely governed by a slowly varying potential (with minimal capacitative current), and the computed rates more faithfully reflect the observed response as shown in Fig. 8A (broken line). For the entire sustaining fiber population, the correlations between observed and model peak and plateau firing rates were 0.91 and 0.95, respectively.

There are two variants of the sustaining fiber response to a light flash that are not represented in Fig. 6. In one, the transient discharge is followed by a silent period of 100–150 ms before the onset of the plateau phase. In the second, there is no plateau discharge. Both of these response variants are well described by the model. The strong adaptations are associated with large values of $G_{inc}$ or $\tau_{adapt}$.

**Dimming fiber visual response**

Dimming fibers respond to a flash of light with an inhibitory PSP (IPSP) and cessation of the dark discharge (Fig. 7, A–D, solid lines). At the lowest intensities, the IPSP decays, and the discharge resumes during the light flash (Fig. 7A). At higher light intensities (Fig. 7, B–D), the discharge is totally inhibited by the IPSP. At the termination of the flash, there is a rapid repolarization toward the “dark” potential. The repolarization is followed by a delayed depolarizing overshoot (typically of 5–10 mV) accompanied by the off discharge. Thus dimming fiber impulse trains exhibit three distinct phases; the dark discharge (typically 5–10 imp/s), the inhibited phase associated with increments of light (typically 0–3 imp/s), and the transient off response at the end of the light flash (peak rates $\leq 50$ imp/s). In addition to the reversal of the sign of the light response, dimming fibers differ from sustaining fibers in three other respects: 1) they generally exhibit higher firing rates in the dark and much lower transient impulse rates; 2) the off transient in both potential and impulse rates is slower; and 3) the dimming fiber input resistance is two to three times that of sustaining fibers (Table 1).

**Simulation of the dimming fiber light response**

Because dimming fiber potentials vary more slowly, the variable capacitative currents (Fig. 7, A–D, dotted line) are smaller, and the simulations of the peak rates have higher fidelity. This can be seen in the model firing rate functions of Fig. 7, E–H (dark lines superposed on shadowed areas), and in Fig. 8B. Although the dark discharge is variable (shaded area of Fig. 7, E–H, 1st 200 ms) due to spontaneous fluctuations in membrane potential (i.e., PSPs), the model provided a good approximation of these rates in most cells (as in Fig. 8). The firing rates shown in Fig. 8B (broken line) are typical of the impulse rates of dimming fibers during the interval between the off response and the beginning of the steady dark discharge. Most of the failures in model performance were associated with cells firing at rates $<5.0$ imp/s. In these conditions, spontaneous fluctuations in membrane current are substantial compared with the light-elicited currents.

**Adaptation of the visual response**

The magnitude of adaptation in sustaining fibers (i.e., the change in impulse rate from peak to plateau, $\Delta F$) is linearly related to the peak impulse rate in both the neuronal and model responses $(r = 0.95$ and 0.98, respectively), and $\Delta F$ is about 82% of the peak rate. In simulated responses, the average adaptation is 84% of the peak rate.

Our model focuses on three factors that predict a decline in firing rate between the peak transient rate $(F_p)$ and the plateau discharge: 1) the time course of the PSP; 2) the contributions of capacitative currents, which are much larger during the transient discharge; and 3) spike-frequency adaptation. We will assume that these three factors are additive.

The current injection studies indicate that the measured encoder’s output declines by $\sim 40%$ under conditions in which spike-frequency adaptation is the exclusive basis of the decline in rate. We can estimate the contribution of spike-frequency adaptation to the decline of the visual response firing rate by computing the model response with adaptation removed $(G_{adapt} = 0; \text{Fig. 9A, dotted line})$. Removing $G_{adapt}$ from this simulation has very little influence on the peak rate, but it doubles the plateau rate at 1.0 s after stimulus onset. The average effect for 17 sustaining fibers is a $121 \pm 75%$ increase in the plateau rate, and on average, $G_{adapt}$ is responsible for 38% of the adaptation of the model light response.

A second source of light response adaptation is the decline of the PSP from peak $(V_p)$ to plateau $(V_s)$. We can estimate the magnitude of this contribution $(\Delta F_{pvp})$, assuming that the decline in impulse rate is linearly proportional to the decline of the PSP normalized to the model peak impulse rate, $F_p$. That is, $\Delta F_{pvp} = F_{pvp}(V_p - V_s)/V_p$. The contribution of $G_{adapt}$ to adaptation of the model light response $(\Delta F_g)$ is derived from the difference between the plateau impulse rates with and without $G_{adapt}$. The sum of $\Delta F_{pvp}$ and $\Delta F_g$ provide an estimate of total adaptation $(F_a)$; as in Fig. 9C) that omits only the contribution of the capacitative current. The high correlation (and regression slope) between $F_a$ and model adaptation implies that $G_{adapt}$ and the adaptation of
the PSP are jointly responsible for most of the adaptation of the model’s visual response. The assumed linearity and additivity, however, may be contrary to the operation of the neuronal encoder.

In dimming fibers, the OFF response also exhibits adaptation. Although not shown by the cell in Fig. 7, the dimming fiber OFF discharge typically decays more rapidly than the corresponding PSP. The magnitude of the firing rate adaptation is a function of the peak impulse rate as in sustaining fibers. Removing $G_{\text{adapt}}$ from the dimming fiber model increases all of the rates by 120–150% (Fig. 9B). This result implies that a major effect of spike-frequency adaptation is to control the impulse rates at all frequencies exceeding about $\tau_1$ response. Because the dimming fiber OFF response typically evolves more slowly than the sustaining fiber ON response, there is sufficient time for encoder adaptation to control the OFF response. In exceptionally fast dimming fibers, the OFF response resembles the sustaining fiber ON response, and removing $G_{\text{adapt}}$ from the model produces results similar to that in Fig. 9A, i.e., no influence on the transient but a large increase in the plateau phase of the OFF response.

**DISCUSSION**

Except for a difference in input resistance, the sustaining and dimming fiber voltage-to-impulse encoders are very similar. The magnitude of spike-frequency adaptation is similar in both cell classes, as is the firing rate dependence of adaptation. In both cell types, the observed adaptation time constant is long (100-300 ms) at low firing rates, and this is preceded by a more rapid phase (of $-22$ ms) at higher impulse rates. The main consequence of the difference in $R_{\text{in}}$ (and a small difference in $V_{\text{th}}$) is that the dimming fiber firing rate is three to four times more sensitive to current than that of sustaining fibers. The magnitude and speed of spike-frequency adaptation that we observe is within the ranges of values previously noted in both crayfish (Fohlmeister et al. 1977) and mammalian neurons (Sawczuk et al. 1995; Schneider 2003). Furthermore, there is
extensive evidence that encoder adaptation may exhibit several phases operating over different time scales (Fohlmeister et al. 1977; Sah 1996; Sawczuk et al. 1995; Schneider 2003; Schwarz et al. 1997) and based on different ionic mechanisms (Benda and Herz 2003; Schwarz et al. 1997).

The adaptive integrate-and-fire model approximates the principal features of the encoders in both cell types, including the timing of the peak discharge, the $f$-$I$ functions, the magnitude of adaptation, and the dependence of adaptation on the peak firing rate. Furthermore, the simulations incorporate input resistances and membrane time constants that are not far removed from the measured values for the two cell populations (Table 1). Although we have no direct evidence that the spike-frequency adaptation we observe is connected to the time course of the hyperpolarizing afterpotential (Table 1, observed $\tau_{\text{adapt}}$) such an association has been noted previously (Sawczuk et al. 1995), and the relationship is also suggested by numerical simulations (Fohlmeister and Miller 1997; Liu and Wang 2001; Wang 1998). We interpret the similarity between $\tau_{\text{adapt}}$ and the decay time constant of hyperpolarizing afterpotential as further evidence that encoder adaptation may exhibit several phases operating over different time scales.

**FIG. 8.** A: Sustaining fiber peak (○) and steady-state (■) light-elicited impulse rates vs. log stimulus intensity. Data from cell shown in Fig. 6. Vertical bars are ±SD. Solid and broken lines are peak and steady-state model rates, respectively. B: Dimming fiber peak (○) and steady-state (■) impulse rates vs. log stimulus intensity. Data are from same cell shown in Fig. 7. Solid and broken lines are model peak and steady-state rates, respectively.

**FIG. 9.** Influence of spike-frequency adaptation on the time course of sustaining and dimming fiber light-elicited responses. A: Sustaining fiber response (thin solid line), model-sustaining fiber response (dash-dot line), and model response with $G_{\text{adapt}} = 0$ (dotted line). Model parameters in Table 1, column 1. B: Dimming fiber light responses as in A. Model parameters in Table 1, column 4. C: Model adaptation in sustaining fibers as a function of $F_a$, which is the sum of adaptations produced by $G_{\text{adapt}} (\Delta F_g)$ and the adaptation of the PSP ($\Delta F_{\text{PSP}}$).
support of this relationship. A key feature of the simulated adaptation is contained in $G_{\text{mem}}$ (Eq. 3, Table 1), which stipulates that, following each action potential, the input resistance declines by $\sim 61\%$ in sustaining fibers and $\sim 66\%$ in dimming fibers. Although seemingly large, these decrements are smaller than those in some mammalian neurons (Schwarz et al. 1997). The conductance increase implies that currents just above threshold at rest potential will be substantially below threshold for some fraction of $\tau_{\text{adapt}}$. If two spikes occur in rapid succession, $G_{\text{adapt}}$ is augmented, and the stimulus current will be below threshold for a longer interval. This is consistent with explanation of the patterning of impulse trains (and the negative serial correlation) by spike-frequency adaptation by Wang (1998).

The adaptive model formulated here has several limitations. The first is that the simulation is prone to error when the mean ISI is substantially less than $\tau_{\text{adapt}}$. A second is that, at the highest impulse rates, the neurons adapt in two phases (with $\tau_{a1}$ and $\tau_{a2}$), while the model contains only one adaptation time constant. As a consequence, the simulated response often exhibits a decay time constant that is between $\tau_{a1}$ and $\tau_{a2}$. A third limitation arises from our decision to model encoder adaptation with a shunting conductance ($G_{\text{adapt}}$) rather than a potassium current [$G_{\text{adapt}}(V - V_k)$]. This approach is consistent with measurements indicating that $G_{\text{adapt}}$ is the controlling variable during the ISI (Fohlmeister and Miller 1997; Schwarz et al. 1997). If the hyperpolarizing current is substantial, however, the optimized model will exaggerate the magnitude of $G_{\text{adapt}}$ to compensate for the absence of the current.

Many neurons exhibit spike-frequency adaptation derived from $Ca^{2+}$ currents associated with the impulse and $Ca^{2+}$-dependent $K^+$ currents associated with the hyperpolarizing afterpotential (Benda and Herz 2003; Fohlmeister and Miller 1997; Liu and Wang 2001; Wang 1998; Wang and McKinnon 1995). In several of these neurons, the adaptation ($F_{\text{adapt}}$), expressed as a percent change in the peak rate ($F_p$), is proportional to $F_p$ and inversely related to the adaptation time constant, $\tau_{\text{adapt}}$ (Wang 1998). In sustaining and dimming fibers, the absolute magnitude of the rate change ($\Delta F$) is related to $F_p$, but $F_{\text{adapt}}$ (as a percent change) varies very little. The high correlations between $\Delta F$ and $F_p$ and the slopes of the $f$-$I$ functions (Fig. 4) all support this relationship. Our results do, however, support the contention that the speed of adaptation is related to $F_p$, but the relationship is not monotonic. The quantitative relationship is complicated by the fact that high firing rates are associated with two phases of adaptation. The two time constants might imply a role for two ionic mechanisms or the same mechanism (e.g., $g_{K(Ca)}$) regulated by a two phase process (e.g., regulation of $[Ca^{2+}]_{\text{in}}$).

An important difference between the current- and light-elicited response is that the latter is driven by a synaptic current, $I_s$. $I_s$ varies substantially during the stimulus period and also introduces variance between trials of the same stimulus. Thus the sustaining fiber visual response exhibits greater adaptation, and the CV is three to four times that of the current-elicited response. Our simulations indicate that the adaptation of $I_s$ plays a major role in the adaptation of the visual response.

When the influence of spike-frequency adaptation is evaluated for the sustaining and dimming fiber visual responses, the results appear to be quite distinct. To interpret our findings, it is essential to make two assertions explicit. The first is that the model produces a good approximation of the visual response. The second is that spike-frequency adaptation operates (at least in part) by increasing the input conductance of the spike generator. If these assertions are valid, the effect of setting $G_{\text{adapt}}$ to zero in the simulation is equivalent to eliciting the visual response following a selective pharmacological block of the spike-frequency adaptation mechanism (Fohlmeister and Miller 1997; Schwarz et al. 1997; Wang and McKinnon 1995). The results suggest that spike-frequency adaptation has little or no influence on the sustaining fiber dark discharge (mean ISI $> \tau_{\text{adapt}}$) or on the peak incremental impulse rate (which evolves too quickly). Encoder adaptation reduces the model firing rate during the simulated plateau phase by $\sim 60\%$. By reducing the plateau impulse rate, encoder adaptation enhances the response to the temporal derivative of the stimulus. In simulated dimming fibers, both the dark discharge and the peak of the OFF response are substantially diminished by encoder adaptation. Since the operational features of the encoders are much the same in the two cells types, we can infer that the different effects of adaptation are due to the differences in the time course and firing rates between the two cell classes.

The above results are related to two broader aspects of visual neuron function. Because the sustaining fiber’s transient discharge is tightly coupled to the onset of local increments in illumination, the firing rate is particularly sensitive to visual motion (Glantz et al. 1995). As a complex scene traverses the sustaining fiber receptive field, the passage of each element of positive contrast is reflected in a distinct burst (Miller et al. 2003). The bursts are separated by silent periods that are in part due to spike-frequency adaptation. The structure of the sustaining and dimming fiber discharges also have a bearing on crayfish behavior. These interneurons are connected to optomotor neurons (Glantz et al. 1984; Okada and Yamaguchi 1988) and participate in the control of ocular reflexes (Miller et al. 2002, 2003). Both the motoneurons and the behavior exhibit strong transient and weaker steady-state responses following rapid shifts in the distribution of illumination in the dorsal visual field. Our results suggest that spike-frequency adaptation may participate in this behavioral bias.

ACKNOWLEDGMENTS

We thank the staff at the Hatfield Marine Science Center, Newport, OR, and the Friday Harbor Laboratories, Friday Harbor, WA, for support and the use of facilities. We also thank S. Rabinowitz for assistance in preparing the text.

GRANTS

This project was supported by National Institute of Mental Health Grant MH-60861.

REFERENCES


