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Noise-driven adaptation: in vitro and mathematical analysis☆

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Abstract

Variance adaptation processes have recently been examined in cells of the fly visual system and various vertebrate preparations. To better understand the contributions of somatic mechanisms to this kind of adaptation, we recorded intracellularly in vitro from neurons of rat sensorimotor cortex. The cells were stimulated with a noise current whose standard deviation was varied parametrically. We observed systematic variance-dependent adaptation (defined as a scaling of a nonlinear transfer function) similar in many respects to the effects observed in vivo. The fact that similar adaptive phenomena are seen in such different preparations led us to investigate a simple model of stochastic stimulus-driven neural activity. The simplest such model, the leaky integrate-and-fire (LIF) cell driven by noise current, permits us to analytically compute many quantities relevant to our observations on adaptation. We show that the LIF model displays "adaptive" behavior which is quite similar to the effects observed in vivo and in vitro.

Keywords: Adaptation; Noise; Integrate-and-fire; Fokker–Planck

It is widely understood that sensory neurons adapt to the prevailing statistics of their inputs [10]. Fairhall et al. [5] recently reported one such adaptation process in the fly visual system; they described a motion-sensitive neuron that appears to scale its input–output function to adapt its firing rate to the variance of the observed motion signal. However, the mechanisms underlying this type of contrast-dependent adaptation are unknown; specifically, it is unclear whether the observed phenomena arise from network

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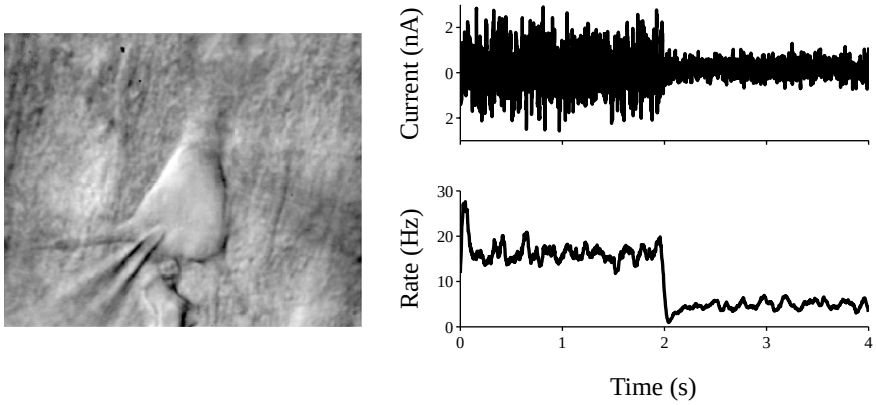

Fig. 1. Experimental details. Sagittal slices were prepared from adolescent and adult rats (P14-P24) as described in [8]. Briefly, slices were maintained at 30°C in artificial cerebrospinal fluid consisting of (in mM): 125 NaCl, 2.5 KCl, 25 glucose, 25 $NaHCO_3$, 1.25 NaH_2PO_4, 2 $CaCl_2$, and 1 $MgCl_2$. Cells were visualized using infrared differential interference contrast microscopy with a 40× water immersion objective. Dual-electrode whole-cell recordings were made using pipettes with 5–15 M resistance when filled with (in mM): 100 K-gluconate, 20 KCl, 4 ATP-Mg, 10 phosphocreatine, 0.3 GTP, and 10 HEPES, pH 7.3 (310 mOsm). Recordings were performed in current clamp using Axoclamp 2B amplifiers (Axon Instruments, Foster City, CA), and stimulus presentation and data acquisition was managed using IGOR (Wavemetrics, Lake Oswego, OR). Gaussian white noise current stimuli were delivered through one electrode, while voltage was recorded through the other electrode and processed on- and off-line. Left panel shows a photograph of a cell with the recording and stimulating electrodes partially visible; right panel shows a sample trace of the current input (including a jump between two values of noise variance), and the corresponding peri-event time histogram (note that the noise current was not "frozen," that is, a new noise current was drawn i.i.d. for each trial).

dynamics or from dendritic or somatic mechanisms in individual neurons. We hypothesized that (1) somatic mechanisms could account for at least part of the observed adaptation phenomena, and that (2) these somatic effects are general in the sense that they depend only weakly on the biophysical parameters governing a given neuron's behavior. To test hypothesis (1), we recorded intracellularly from layer V pyramidal neurons in sensorimotor cortex in vitro (see Fig. 1 for details), while stimulating with a noise current whose standard deviation (or "contrast") was varied parametrically. Hypothesis (2) will be addressed mathematically below.

For ease of comparison, we analyzed our data using the basic framework utilized in [5] (see also, e.g., [4]). For each neuron, we estimated a separate spike-triggered average (STA) at each current standard deviation [3], using data acquired after the neuron had reached a steady-state firing rate. We then projected our stimulus onto the normalized STA function (this operation is equivalent to a time-reversed convolution, or filtering), and estimated, via a nonparametric histogram approach, the conditional probability of a spike given each observed value of the projected current. These conditional firing rate functions (termed N-functions, for nonlinearity, in keeping with convention) will be the main object of our analysis (see Fig. 2 for an example).

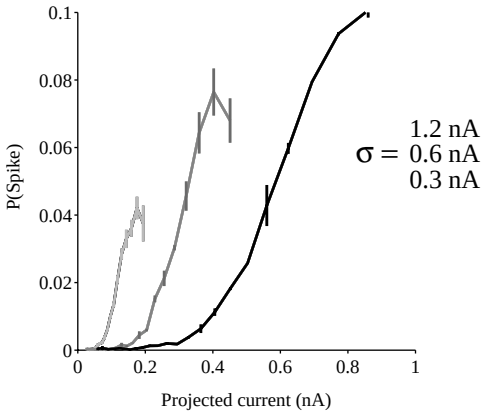

Fig. 2. Examples of N-functions for a single pyramidal neuron. Each curve represents data for a particular standard deviation of input current.

Our main observations are as follows: first, the STA (which is often thought of as a linear prefilter for the cell, the stimulus dimension to which the neuron is most sensitive) changed with the standard deviation of the injected current. As σ was increased, we observed a systematic reduction in the time-to-peak as well as the half-width of the STA, consistent with results seen in vitro [3] and in vivo [1]. We also observed changes in the N-functions (Fig. 2). If we define "gain" as the slope of the N-function, we have that the gain of the observed cortical cells was consistently inversely proportional to the standard deviation of the injected current; this result is strikingly similar to those of Fairhall et al. [5].

What could explain the gain changes described above? One common model for gain changes in cortical cells requires the presence of some channel whose conductance is dependent on the firing rate of the cell; it has been shown, for example, that calcium-dependent potassium channels can lead to changes in the input-dependent firing rate of the cell (see e.g. [11]). It seems plausible that such macroscopic changes in the firing rate could manifest themselves in changes at the more detailed level of the N-function (although, to our knowledge, these effects have not been studied in detail). However, we believe that an even simpler phenomenon is (at least partially) responsible here. Our hypothesis is that much of the "adaptation" phenomenon described above can be explained by the basic spiking dynamics of the cell, even in the absence of nonlinear ion channels. (See also [9], where a similar idea was proposed using different methods.)

To explain our results, we introduce some tools from the theory of stochastic dynamical systems. We start with perhaps the simplest widely-used neural model, the leaky integrate-and-fire (LIF) cell, described by the following equation:

$$\frac{dV}{dt} = \frac{1}{\tau_m}(V_L - V + R_m I) - (V_{th} - V_{reset})\delta(V - V_{th}),$$

where V denotes voltage, τ_m the membrane time constant, R_m the membrane resistance, V_L the leak reversal potential, V_{th} and V_{reset} the threshold and reset potential, respectively, and I is an input current which in our case is given by a standard white noise process of stationary mean μ and standard deviation σ.

A noise-driven dynamical system can, in general, be described either in terms of the pathwise (single-trial) behavior of the system or in a distributional (ensemble) sense. The pathwise behavior of the noise-driven LIF cell is easily understood: below threshold, the cell is a one-dimensional Ornstein–Uhlenbeck process [7]; at threshold, the voltage is reset instantaneously to V_{reset}. This system is clearly one-dimensional and strong Markov; that is, its behavior in the future depends on its past only through V at the present time. The distributional description of the noise-driven LIF model—that is, the equations governing the behavior of the probability distribution on voltage, $P(V)$, as a function of time—turns out to be most useful. The following Fokker–Planck equation completely characterizes the distributional behavior of the system, given initial conditions [7]

$$\frac{\partial P}{\partial t} = \frac{\sigma_0^2}{2}\,\frac{\partial P^2}{\partial^2 V} + \frac{1}{\tau_m}\,\frac{\partial[(V - V_0)P]}{\partial V} + R(t)(\delta(V - V_{reset}) - \delta(V - V_{th}))$$

with $R(t)$ the time-dependent mean firing rate of the cell, $\sigma_0 \equiv R_m\sigma/\tau_m$, and

$$V_0 = R_m\mu + V_L$$

the steady-state rest potential. The PDE above is a perturbed diffusion equation: the first term corresponds to diffusion (the effect of the injected noise on the voltage at time t), the second is a drift term (corresponding to the V-dependent steady-state driving force back towards the rest potential V_0), and the third corresponds to the voltage probability flux resulting from spiking activity, which is subtracted from $P(V)$ at V_{th} and added at V_{reset}. This equation has been introduced by several authors [2,6] as an approximation to the behavior of the LIF cell under a barrage of random synaptic currents. Note that since we are injecting Gaussian white noise and not a simulated superposition of PSPs, the above equation is *exact* within the LIF framework.

Surprisingly, many of the quantities of interest turn out to be analytically computable for this model. Most of what we need can be read directly from the following steady-state solution to the PDE:

$$P(V) = \frac{2R}{\sigma_0^2}\int_{\max(V,V_{reset})}^{V_{th}} dV' e^{[(V'-V_0)^2-(V-V_0)^2]/\tau_m\sigma_0^2},$$

where $P(V)$ denotes the invariant density and R is the equilibrium firing rate; note that $P(V)$ is in a sense a perturbed Gaussian, as expected of the solution to a perturbed diffusion equation with linear drift. We plot $P(V)$ for a few different values of noise in Fig. 3: when the injected noise is small (σ near zero), $P(V)$ looks like a Gaussian centered at V_0. However, as σ grows, $P(V)$ develops a kink at V_{reset}, dives nearly linearly to zero at V_{th}, and develops a large negative tail. We will see below that the

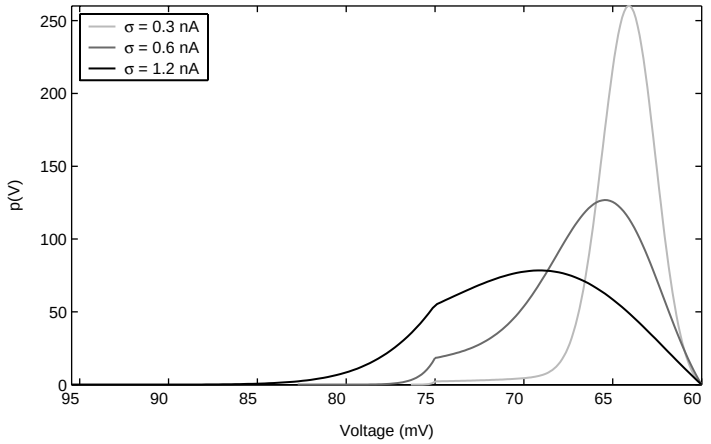

Fig. 3. Three examples of invariant densities, $P(V)$, for three different values of noise variance σ^2. $V_{\rm th}$ is -60 mV and $V_{\rm reset}$ is -75 mV here.

size of this negative tail—the probability that the Ornstein–Uhlenbeck process will have wandered into a highly hyperpolarized state—has a critical effect on the "gain" of the neuron, according to several reasonable definitions of gain.

Recall the definition of the N-function introduced above: this quantity is a conditional firing rate, given some filtered version of the recent stimulus. It is difficult to approach this gain function analytically when this filter is chosen by cross-correlation methods, as in the preceding section, because the STA of the LIF cell turns out to be a rather poorly behaved mathematical object (for example, it is not hard to show that this function depends rather strongly on the time step $\mathrm{d}t$ of the numerical simulation, with no well-defined limit in the continuous limit as $\mathrm{d}t \to 0$). Even when the filter is chosen to be a step function, detailed analysis of this conditional firing rate function seems to require a rather complicated analysis of the conditional pathwise behavior of the Ornstein–Uhlenbeck process, which has in our hands not yet led to any interesting conclusions. However, we can derive useful information about certain limits of the gain function, as the support of the step filter shrinks to zero or goes to infinity.

For example, we have an exact expression for the "transient gain function"

$$F_0(x,\sigma) \equiv \lim_{T\to 0} P\left(\text{spike} \in (-T,0] \,\middle|\, \int_{-T}^{0} I(t)\,\mathrm{d}t = x\right) = \int_{V_{\rm th}-\frac{xR_{\rm m}}{\tau_{\rm m}}}^{V_{\rm th}} P(V)\,\mathrm{d}V$$

and the counterpart "long-time" gain function

$$F_\infty(x,\sigma) \equiv \lim_{T\to\infty} P\left(s \in (-\mathrm{d}t,0] \,\middle|\, \int_{-T}^{0} I(t)\,\mathrm{d}t = xT\right)$$

$$= -\frac{\sigma_0^2}{2}\,\frac{\partial P_{\mu+x}(V)}{\partial V}\,\bigg|_{V=V_{\rm th}} \mathrm{d}t + o(\mathrm{d}t),$$

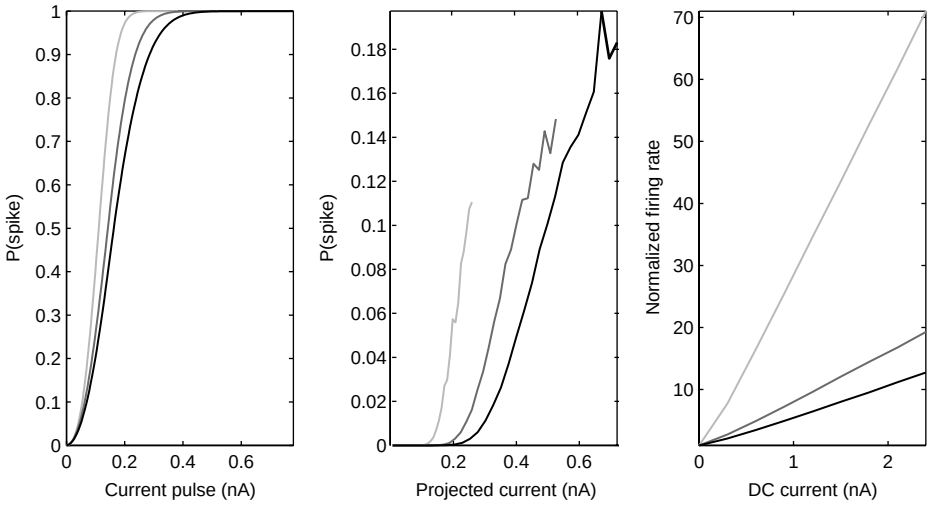

Fig. 4. Three "gain functions" for integrate-and-fire cell: middle panel shows N-function, computed by Monte Carlo; left panel is "transient" function $F_0(x,\sigma)$, and right is "long-time" function $F_\infty(x,\sigma)/F_\infty(0,\sigma)$, both computed analytically. (Note that $F_\infty(x,\sigma)/F_\infty(0,\sigma)$ is normalized so that the y-axis is a dimensionless ratio.)

where the subscript in the last expression indicates the dependence of the invariant density on the DC input current. The variable x in the two expressions above corresponds to the projected current (the x-axis in Fig. 2). The σ-dependence of these functions (computed analytically) is shown in Fig. 4; also shown are some sample N-functions, computed via Monte-Carlo. These gain functions are all σ-dependent, indicating strong adaptive phenomena in the standard LIF cell.

We have two related main conclusions. First, a very simple preparation displays "adaptation" to noise current input over a time scale of hundreds of milliseconds; this adaptation phenomenon must be independent of any "upstream" (e.g., synaptic) processes, since currents were injected and voltages measured directly at the same soma. Second, perhaps more surprisingly, a very simple model, devoid of any interesting dynamics save the (instantaneous) spiking process itself, adapts strongly to changing stimulus distributions; we can describe this behavior exactly, and it turns out to match the in vitro data qualitatively. The fact that a model as generic as the LIF cell displays adaptation so similar to that observed in vitro and in vivo seems to indicate that variance-dependent adaptation is, in fact, a general feature of spiking cells in the nervous system.

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