Published in final edited form as:

Neural Comput. 2005 May ; 17(5): 991–995.

Gain Control by Concerted Changes in I_A and I_H Conductances

Denis Burdakov

Neurosciences Division, Biological Sciences, University of Manchester, Manchester M13 9PT, U.K.

Abstract

Stability of intrinsic electrical activity and modulation of input-output gain are both important for neuronal information processing. It is therefore of interest to define biologically plausible parameters that allow these two features to coexist. Recent experiments indicate that in some biological neurons, the stability of spontaneous firing can arise from coregulated expression of the electrophysiologically opposing I_A and I_H currents. Here, I show that such balanced changes in I_A and I_H dramatically alter the slope of the relationship between the firing rate and driving current in a Hodgkin-Huxley-type model neuron. Concerted changes in I_A and I_H can thus control neuronal gain while preserving intrinsic activity.

1 Introduction

Maintaining stable intrinsic activity patterns in the absence of relevant stimuli is thought to be important for proper information processing in neurons and neural circuits (Turrigiano & Nelson, 2000; Davis & Bezprozanny, 2001; Marder & Prinz, 2002). But the ability of neurons to change gain, that is, to alter the slope of the relationship between driving stimulus and firing response, is also critical for computation in diverse neural systems (Salinas & Thier, 2000; Salinas & Sejnowski, 2001). It is therefore of interest to define biologically plausible parameters that allow the gain of a neuron to be modulated without changes in its intrinsic (stimulus-independent) activity. It was recently demonstrated, using biological and model neurons, that one of the ways to achieve such “silent” modulation of gain is by covarying the frequencies of excitatory and inhibitory background synaptic input currents (Chance, Abbott, & Reyes, 2002). Another recent report indicated that biological neurons can intrinsically covary the magnitudes of certain excitatory and inhibitory ionic currents: increasing the expression of the transient outward current (I_A) led to proportional increases in hyperpolarization-activated inward current (I_H) in lobster somatogastric neurons (MacLean, Zhang, Johnson, & Harris-Warrick, 2003). This biological coregulation of I_A and I_H did not result in significant changes in intrinsic firing properties (MacLean et al., 2003). Therefore, this note addresses the question of whether the concerted changes in I_A and I_H can act as a cellular mechanism for “silent” gain modulation.

2 Results and Discussion

To explore the effects of concerted changes in I_A and I_H on neuronal gain, a recently published model of lobster somatogastric neurons (Prinz, Thirumalai, & Marder, 2003) was used. This is a Hodgkin-Huxley-type, single-compartment model that comprises seven membrane currents (I_{Na} , I_{CaS} , I_A , I_{KCa} , I_{Kd} , I_H , and I_{leak}) and an intracellular calcium buffer, and exhibits tonic intrinsic firing (Prinz et al., 2003). All maximal conductances (except those for I_A and I_H , which were varied as indicated) were as in Prinz et al., and simulations were performed using MATLAB stiff systems numerical integrator ode15s, at time resolution of 25 μ s.

The maximal conductances (g) of I_A and I_H were changed from the values in Prinz et al. (10 and 0.05 mS/cm², respectively) in such a way so as to keep the intrinsic firing characteristics (tonic pattern and firing frequency) unaltered. The relationship between the two conductances for the latter condition is shown in Figure 1C. Changes in g_A and g_H markedly altered the firing responses of the model neuron to a tonic excitatory current: balanced increases in g_A and g_H decreased the firing response (see Figures 1A and 1B). This implies that the concerted changes in g_A and g_H selectively altered the gain, since the tonic nature of firing and the firing frequency remained unaffected.

To quantify the changes in gain in a simplified but plausible way, the firing rate (f) was plotted against the driving excitatory current (I) for a range of combinations of g_A and g_H that resulted in the same intrinsic firing rate. The balanced increases in g_A and g_H led to progressive decreases in the gain (slope) of the f - I relationship (see Figure 1D). The gain was altered most steeply when the sum of g_A and g_H was below 100 mS/cm² (see Figure 1E); this conductance range is consistent with physiological g_A and g_H values in lobster somatogastric neurons (MacLean et al., 2003; Prinz et al., 2003). Decreases in gain saturated when the sum of g_A and g_H exceeded about 100 mS/cm² (see Figure 1E).

These results indicate that concerted changes in I_A and I_H may allow neurons to vary gain while preserving intrinsic activity patterns. To the best of my knowledge, such cellular mechanism of gain control has not been previously reported. This mechanism is biologically plausible (MacLean et al., 2003), and could potentially be of general physiological importance considering that I_A and I_H are expressed together in many types of biological neurons and are under the control of a variety of neuromodulators (Yang et al., 2001; Ramakers & Storm, 2002; Schweitzer, Madamba, & Siggins, 2003; Frere & Luthi, 2004).

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Figure 1.

(A, B) Examples of simulations illustrating that concerted changes in I_A and I_H affect neuronal gain without changes in unstimulated firing rate or pattern. (A) Neuron with a small I_A and I_H (g_A and g_H are 10 and 0.05 mS/cm², respectively) responds to a tonic excitatory current with a large increase in firing rate. (B) Increasing I_A and I_H in a balanced manner that leaves unstimulated firing unaltered (here, g_A and g_H are 50 and 1 mS/cm², respectively) leads to a marked reduction of the firing response to the same excitatory current. Simulation protocols used to elicit I_A , I_H , and firing responses in A and B are shown

schematically below the corresponding traces. (C) The relationship between g_A and g_H that satisfies the condition of unaltered intrinsic firing characteristics. (D) Examples of f-I relationships of neurons with different balanced combinations of g_A and g_H (respectively, in mS/cm²: black circles = 10 and 0.05, white squares = 20 and 0.18, black triangles = 50 and 1, white diamonds = 100 and 6). (E) Gain values (the slopes of f-I relationships such as those shown in *D*) plotted against the sum of g_A and g_H for combinations of g_A and g_H that do not alter intrinsic firing characteristics.