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A Minimal, Compartmental Model for a Dendritic Origin of Bistability of Motoneuron Firing Patterns

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Abstract. Various nonlinear regenerative responses, including plateau potentials and bistable repetitive firing modes, have been observed in motoneurons under certain conditions. Our simulation results support the hypothesis that these responses are due to plateau-generating currents in the dendrites, consistent with a major role for a noninactivating calcium L-type current as suggested by experiments. Bistability as observed in the soma of low- and higher-frequency spiking or, under TTX, of near resting and depolarized plateau potentials, occurs because the dendrites can be in a near resting or depolarized stable steady state. We formulate and study a two-compartment minimal model of a motoneuron that segregates currents for fast spiking into a soma-like compartment and currents responsible for plateau potentials into a dendrite-like compartment. Current flows between compartments through a coupling conductance, mimicking electrotonic spread. We use bifurcation techniques to illuminate how the coupling strength affects somatic behavior. We look closely at the case of weak coupling strength to gain insight into the development of bistable patterns. Robust somatic bistability depends on the electrical separation since it occurs only for weak to moderate coupling conductance. We also illustrate that hysteresis of the two spiking states is a natural consequence of the plateau behavior in the dendrite compartment.

Keywords: motoneurons, dendrites, bistability, plateau potentials, compartmental modeling

1. Introduction

Under certain conditions, bistable repetitive firing behavior has been observed in vertebrate motoneurons, such as cat lumbar (Hounsgaard et al., 1988a) and turtle motoneurons (Hounsgaard and Kiehn, 1989). While the amplitudes of the two stable spiking states are similar, the frequencies can differ by as much as 10 Hz. When action potentials are suppressed by TTX, bistability is observed as a plateau potential that provides the cell with two stable steady states. Such bistable behaviors are present in intact animals (Eken and Kiehn, 1989) and can be induced in reduced preparations by application of pharmacological agents, such as serotonin (Hounsgaard et al., 1988a; Hounsgaard and Kiehn, 1989) or noradrenaline (Conway et al., 1988), or during fictive locomotion (Brownstone et al., 1994).

Schwindt and Crill (1984) originally suggested that a persistent, inward current, likely calcium-mediated, generated the plateau potentials they observed in cat motoneurons during penicillin-induced spinal seizures. Recently, Hounsgaard and Kiehn (1989) identified a nifedipine-sensitive, L-like calcium conductance that contributes to the serotonin-dependent plateaus in turtle spinal motoneurons.

The spatial distribution of the calcium conductance underlying the plateau potentials has not been determined. Studies have indicated the presence of active membrane properties in the dendrites of motoneurons (Fujita, 1989; Walton and Fulton, 1986). Hounsgaard and Kiehn (1993) investigated the dendritic properties of turtle motoneurons by invoking differ-

ential polarization of the cell membrane with applied electric fields. They found evidence that calcium conductances generating calcium spikes and calcium plateaus are located in the dendrites and are compartmentally separated from the ionic conductances in the cell soma.

Our simulation results support the hypothesis that the bistability observed in motoneurons is due to calcium current-mediated, bistable dynamics in the dendrites. In particular, the higher-frequency spiking states, or the depolarized plateaus under TTX, occur because the dendrites are in a depolarized stable state. To investigate this hypothesis, we construct an idealized model of a motoneuron that consists of two compartments. The soma and proximal dendrites are represented by one compartment that contains sodium-like repetitive spiking kinetics. The more distal dendrites are lumped into the second compartment with voltage-dependent outward and noninactivating inward currents, endowing this compartment with two stable steady states. Coupling current flows between the compartments through a conductance, thereby mimicking electrotonic spread. The behavior of this minimal model under typical experimental paradigms compares qualitatively with the bistable behavior experimentally observed in motoneurons. In addition, the model predicts qualitatively the dendritic voltage time courses, which have yet to be measured experimentally. This dendritic behavior in the model explains many of the phenomena observed experimentally in the soma and enables one to develop or further enhance one's biophysical intuition.

Our understanding continues to grow about the impact on firing properties contributed by cable properties and nonuniformly distributed voltage-dependent currents in a dendritic neuron (for example, Llinas and Sugimori, 1980; Huguenard et al., 1989; Stuart and Sakmann, 1994). In multi-compartmental models of neocortical pyramidal cells, spiking (Amitai et al., 1993) and plateau potential behavior (Reuveni et al., 1993) suggested that active conductances are located in dendrites distal to the cell soma. Some bursting behaviors (Traub et al., 1991; Rhodes and Gray, 1994) also appear to depend on differential distribution of sodium, calcium, and potassium currents. Pinsky and Rinzel (1994) developed a two-compartment model of a hippocampal CA3 pyramidal cell that exaggerates the segregation of active currents to analyze the dependence on spatial distribution of currents in obtaining bursting behavior. Gutman (1971, 1991) constructed a cable model of motoneuron dendrites that exhibits plateau behavior. With a spike-generating lumped soma at the cable's proximal end, he observed bistability at the soma if the cable was sufficiently long.

In this paper, following Pinsky and Rinzel (1994) by using a lumped model of a soma with dendritic-cable analog, we limit the number of electrotonic-like/structural parameters needed in the model's definition, and we study systematically the effects of electrically separating different regenerative properties, in this application to motoneurons, repetitive spiking and bistable plateaus. We apply the techniques of nonlinear dynamics and bifurcation theory to illuminate how the response to somatic current injection changes with the strength of the coupling conductance. By carefully considering behavior when the coupling strength is weak, we gain insight into the development of bistable patterns. We show that the nonuniform distribution of firing properties in proximal and distal compartments is an important factor in generating bistability; the multiple firing modes occur only for a certain range of coupling conductances.

2. Model

Our motoneuron model consists of two compartments, one representing the soma and proximal dendrites and the other the lumped distal dendrites (Fig. 1A). Each compartment contains a minimal number of active currents. The soma compartment has an inward sodium-like current, I_{Na}, and an outward potassium, delayed-rectifier current, I_{K-dr}; I_S is the applied current. These currents are sufficient to cause persistent spiking for some values of I_S. The dendrite compartment has an inward, noninactivating, calcium L-like current, I_{Ca}, and an outward potassium, delayed-rectifier-like current, I_K, which give it plateau potential behavior. The two compartments interact by current flow through the coupling conductance g_c. The model's equations are based on the dimensionless, conductance-based Morris-Lecar model (Morris and Lecar, 1981; Rinzel and Ermentrout, 1989) and are contained in the appendix along with the parameter values.

The left and right panels of Figs. 1B and 1C show the behavior of the isolated soma and dendrite compartments, respectively. The response of each compartment to an injected current ramp is shown in Fig.