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Research report

Structural mechanisms to produce differential dendritic gains

Dongchul C. Lee[a], Alicia L. Jensen[a], Matthew A. Schiefer[a], Charles W. Morgan[b], Warren M. Grill[c,*]

[a]Department of Biomedical Engineering, Case Western Reserve University, Cleveland, OH 44106, USA
[b]Clinical Investigation and Research Department, Naval Medical Center Portsmouth, Portsmouth, VA 23708-2197, USA
[c]Department of Biomedical Engineering, Duke University, Box 90281, Durham, NC 27708-0281, USA

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Abstract

The axons of sacral parasympathetic preganglionic neurons (PGNs) originate on a primary dendrite between 10 and 110 μm from the soma. Therefore, it was hypothesized that the location of the axon origin would impact the relative efficacy of ipsilateral and contralateral synaptic inputs. The morphology of two PGNs was reconstructed, and the transfer impedance was used to quantify the influence of synaptic inputs on the transmembrane potential at the axon initial segment. The ratio of ipsilateral transfer impedance to contralateral transfer impedance (termed the relative gain) was increased by 14–29% for axons originating from the dendrite vs. axons originating from the soma. The addition of 50 synchronized "gating" synapses on the proximal dendrites increased the relative gain by 17–38% when the axon originated from the dendrite, but only by 11–15% when the axon originated from the soma. The efficacy of synaptic inputs and the ability of proximal gating synapses to regulate synaptic efficacy were strongly influenced by the site of origin of the axon. The position of axon origin is an effective structural mechanism to regulate the relative efficacy of synaptic inputs arriving at different locations on the dendritic tree.

Theme: Endocrine and autonomic regulation
Topic: Gastrointestinal and urogenital regulation

Keywords: Preganglionic; Computational neuroscience; Neural model; Axon; CNS

1. Introduction

The primary structure of a neuron–dendrites, a soma, and an axon–has resulted in the view that neuronal elements and their functional roles align to produce a polarized structure–function relationship: inputs arrive at the dendrites, are integrated at the soma, and the output signaling occurs in the axon. However, this generalization of neuronal structure and function is being challenged by recent findings; for example, dendritic voltage-dependent ionic channels [47], initiation of action potentials in the dendrites [42], release of neurotransmitter from dendrites [40], and neurons in which the axon originates from a dendrite [13]. The objective of the analysis presented here, performed on an atypical neural structure where the axon originates from a root dendrite, was to determine the impact of the position of axon origin on the synaptic efficacy of inputs to different regions of the dendritic tree.

Neurons with the axon originating from a root dendrite have been documented throughout the central nervous system, but the impact of this structure on processing of synaptic inputs into axonal outputs has not been quantitatively determined in a morphologically realistic model. The axon originates from a dendrite in parasympathetic preganglionic neurons (PGN) of cat spinal cord [29,30], considered in the present study, as well as dopaminergic neurons in cat [19], rat substantia nigra neurons [13], hypothalamic neurons of the bison [35] and guinea pig [10], hippocampal interneurons of the rat [26], and spinal cord neurons of the rat [5] and human [37]. The axon-from-dendrite morphology raises questions regarding the functional properties of

* Corresponding author. Fax: +1 919 684 4488.
E-mail address: warren.grill@duke.edu (W.M. Grill).

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the dendritic structure [25], the axon origin, and their role in neural excitability [36].

Sacral parasympathetic preganglionic neurons (PGNs) innervate the bladder, urethra, colon, and sex organs. The PGNs of the lateral band of spinal lamina VII innervate the urinary bladder and, when viewed in the transverse plane, have bipolar or tripolar dendritic fields oriented dorsally and ventrally along the lateral border of the grey matter and laterally toward the central canal in laminae IV and V. PGN axons originate as a branch from a dendrite without a detectable axon hillock at distances from the soma ranging from 10 μm to 110 μm (average 34 μm) (Fig. 1) [29]. Following an initial segment of 15–40 μm, PGN axons contain a 59–630 μm long unmyelinated segment and are then myelinated with internodal distances that average 93 μm [28]. Similar soma-to-axon distances are observed in dopaminergic neurons in cat substantia nigra (55% < 30 μm and 45% > 30 μm) [19] and hippocampal interneurons (~100 μm) [26], while in the rat substantia nigra the soma-to-axon distance can be as large as 240 μm [13].

These anatomical observations lead to the hypothesis that an axon branching from a dendrite will bias the efficacy of synaptic inputs arriving on the ipsilateral parent (or sister) dendrites over inputs arriving on the contralateral dendrites [13,29]. Further, synapses impinging on the proximal dendrite between the site of axon origin and the soma, termed "gating synapses", could regulate the relative efficacy of other synaptic inputs arising from different regions of the dendritic tree.

The role of the site of axon origin was addressed through computer simulation of synaptic integration in cat PGNs. Specifically, the effects of the location of axon origin on synaptic efficacy and gating properties were investigated in three-dimensional cable models of cat PGNs. The transfer impedance (Z_c) was used to quantify the efficacy of synaptic inputs from different positions on the dendritic tree for axons originating from the soma or from a dendrite. The transfer impedance [6,17]

$$Z_c = \left(V_{Axon\_origin}/I_{Syn}\right) \quad (1)$$

describes how a current applied at one location (I_{syn}, synaptic input on the dendrites) affects the transmembrane potential at the axon origin (V_{Axon_origin}) where action potential initiation occurs [13,26,42].

2. Methods

Three-dimensional cable models of parasympathetic preganglionic neurons (PGN) from cat sacral spinal cord were implemented to study the effect of the location of the axon origin on synaptic efficacy. Two morphologically typical cells were selected from 25 PGNs filled with horseradish peroxidase or neurobiotin and reconstructed using the Neurolucida (Microbrightfield) tracing program from serial 50-μm sections [29,31]. The tracing was done with a 40× objective lens and the image displayed on a computer screen. The software recorded the data points as three-dimensional coordinates (x, y, z). The system was calibrated to yield a precision of 0.1 μm, no corrections were made for tissue shrinkage, and to remove any sampling artifacts of reconstruction, such as sudden changes of diameter, entire segments were examined before any analysis [21]. The first modeled neuron (Cell-541, Fig. 1A) had an average axon-to-soma distance (~30 μm), and the second modeled neuron (Cell-641, Fig. 1B) had a long axon-to-soma distance (~71 μm). The axon-to-soma distance was defined as the distance from the axon to the outer boundary of the soma determined from neurons in adjacent Nissl-stained sections where the soma border is

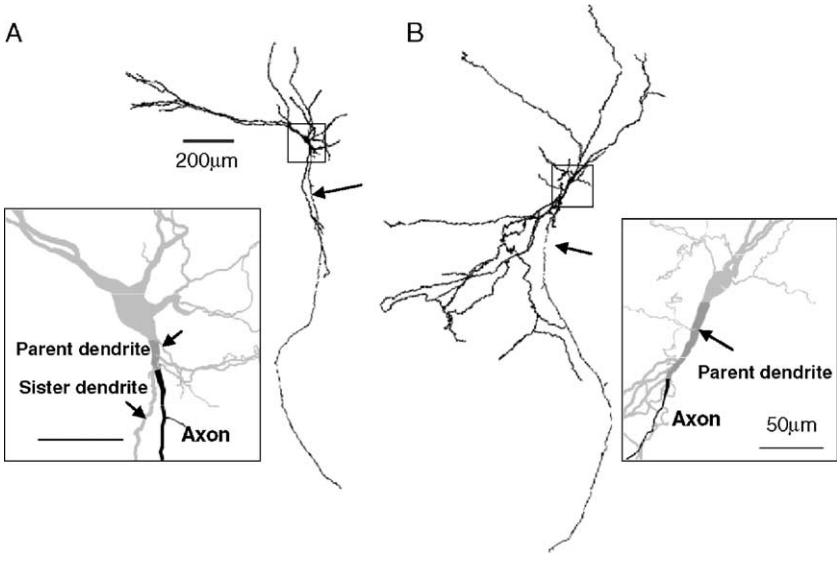

Fig. 1. Morphology of preganglionic parasympathetic neurons from the cat spinal cord. (A) In Cell-541, the axon originated from a ventral dendrite 30 μm from the soma. (B) In Cell-641, the axon originated from a ventral dendrite 71 μm from the soma. Axons are indicated by arrows in low magnification images.