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Signal-dependent noise in premotoneuronal commands is necessary to explain the interspike interval variability of spinal motor neurons

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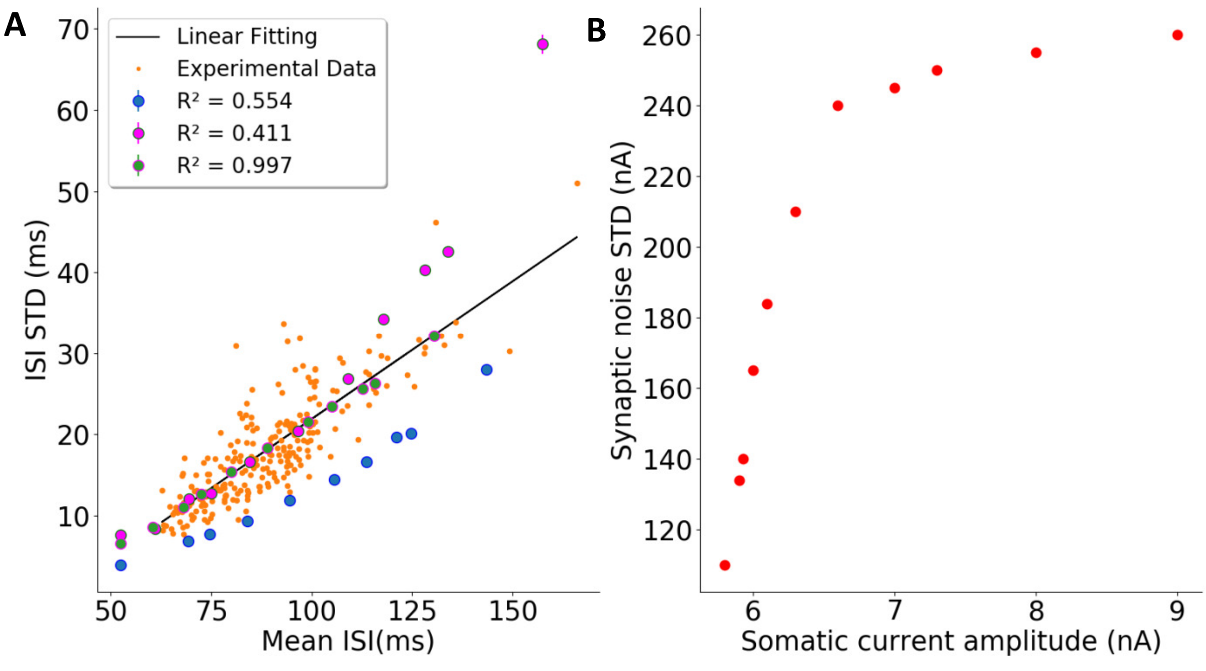
Background, Motivation and Objective. Spinal motor neurons (MNs) receive signals from descending pathways and sensory afferents. These premotoneuronal commands encompass both common and independent stochastic inputs, which yield random fluctuations in MN's membrane potential (synaptic noise). Previous animal studies have shown that the synaptic noise influences the variability of the interspike intervals (ISIs) of MNs. Additionally, data from human motor units (MUs) exhibit an increasing scaling of ISI standard deviation (STD) with the mean ISI. At least two possible mechanisms might influence the behavior of MU ISI variability: *i)* the intrinsic properties of MNs; and *ii)* the scaling of the synaptic noise with the mean excitation received by the MNs (the so-called signal-dependent noise, SDN). SDN was observed in the muscle force during isometric contractions, and in the discharge rate of cortical neurons. However, there is no definite evidence that the SDN occurs at the membrane potential of spinal MNs. In the present study, human experiments and computer simulations were combined to investigate the role of each putative mechanism described above on the behavior MU ISI variability.

Methods. Experiments were carried out on ten healthy human subjects (age: 27±3). All procedures were approved by the Ethics Committee of the University of Campinas (CAAE 59961616.8.0000.5404). The experimental protocol consisted of visually-guided force-marching tasks with the abduction of the index finger at 2.5% of the maximum voluntary contraction. High-density surface electromyogram signals were recorded from the first dorsal interosseous (FDI) muscle. These signals were decomposed into MU spike trains. Mean and STD of ISIs were computed for each recorded MU spike train. Computer simulations were performed using a two-compartment MN model implemented in Python programming language with the libraries of Neuron simulator. The MN model encompasses HH-like ionic channels into the soma (Na+, persistent Na+, K+, and slow K+) and a passive dendrite. MNs were parameterized and validated using data from anaesthetized cats. A step current was injected into the soma to produce rhythmic discharges at different rates. A white gaussian noise was injected into the dendrite to provide the synaptic noise. Three scenarios were evaluated: i) the synaptic noise was maintained constant across the simulations and its STD was adjusted to match subthreshold fluctuations of the membrane potential recorded from cat MNs; ii) the synaptic noise was maintained constant and its STD was increased as compared to the previous condition (i); and iii) the synaptic noise was varied across the simulations so that its STD depended on the mean depolarization produced by the step somatic current. Ten independent simulations were performed for eleven different mean excitations, and ISI statistics (mean and STD) were calculated.

Results. Experimental data from 240 MUs exhibited a linear relationship between ISI STD and ISI mean (Figure 1A, black line, R^2 = 0.842). Irrespective of the scenario, data from computer simulations shown a scaling between ISI STD and the mean ISI (Figure 1A, colored circles). Scenarios (i) and (ii) did not completely match the experimental outcomes (R^2 = 0.554 and R^2 = 0.411, respectively). Conversely, simulations from the third scenario (iii) were able to reproduce the average behavior of experimental data (R^2 = 0.997). The matching between computer simulations and experiments was achieved when the relationship between the somatic current amplitude and the synaptic noise STD followed an exponential saturation function (Figure 1B).

Discussion and Conclusions. Here we show that ISI STD and the mean ISI of a population of MUs from the FDI muscle followed a linear function, which is similar to other experimental findings reported in the literature. Moreover, computer simulations were able to reproduce the experimental data only when the synaptic noise STD and the mean MN excitation followed an exponential saturation function, i.e., when the SDN behavior is present at the MN membrane potential. The present findings suggest that the intrinsic properties of MNs is not sufficient to account for MU ISI variability. Also, we provided additional evidence that SDN is ubiquitous to the neuromuscular system.

Figure 1. (A) Relationship between ISI STD and mean ISI. Experimental data from 240 FDI MUs exhibit a linear scaling between ISI STD and mean ISI (black line, $ISI_{STD} = 0.34 \cdot ISI_{mean} - 12$). Colored circles represent data from computer simulations in three different scenarios (blue: scenario i; magenta: scenario ii; green: scenario iii; see Methods for details). (B) Relationship between synaptic noise STD and the mean excitation (injected current at MN soma).



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