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Intersymbol interference in axonal transmission

Patrick Crotty*, William B Levy

Department of Neurosurgery, University of Virginia, Charlottesville, VA, USA

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Abstract

The relative refractory period of an action potential affects any second closely following impulse. Starting with the constraining conjecture that consecutive action potentials produce minimal interference with each other, we investigate the twin-pulse maximum frequency. Using an updated version of the Hodgkin–Huxley squid giant axon, this constrained maximum firing frequency varies with transmembrane conductance density and diameter. Using the twin-pulse constraint and keeping velocity constant, smaller, higher-conductance density axons are generally preferred to larger, lower-conductance density ones.

Keywords: Interspike interval; Information processing; Refractory period

1. Introduction

Neurons transmit information by means of action potentials (APs), which can encode information in many different ways, e.g., by the presence or absence of a spike during some fixed time interval (a binary code), or in the distribution of intervals between successive action potentials (an interspike interval (ISI) code). More complex coding schemes which use groups of action potentials, or frequency codes, are also possible.

Although some suppose that noise limits axonal signaling (e.g., [10,13]), here we consider another possible intrinsic limit on information transmission rates in axons, the minimum ISI determined by the relative refractory period. The absolute refractory period has a substantial effect on the channel capacity of the axon [1]. The relative refractory period also has an effect but it is more challenging to quantify in terms of biophysical parameters. During the relative refractory period, a new action potential can be generated, but the local electrical properties of the axon differ from their usual values because of the previous action potential. Conceptually, a second closely following action potential is traveling in the "wake" of the first one, and as a result, the first AP affects the second AP's speed [3]. When the speeds differ, the initial interval between the APs is not preserved, and the ISI can either increase or decrease. In this way, information which is encoded by the timing of the spikes is corrupted.

This phenomenon, which is called "intersymbol interference" in engineering, is not a stochastic process and so does not strictly qualify as noise. Assuming that the axon is not too long, there is a one-to-one correspondence between the initial ISI and its value at one particular subsequent point. However, this value is different for different points so without distance knowledge the signal is corrupted. (If the axon is too long, as we will show below, then ISIs under a certain length can converge to a single value.)

In this study, we calculate the maximum AP firing frequency, which is the inverse of the total (absolute plus relative) refractory period. We assume that pairs of action potentials are minimally interfering. If the biological nervous system is indeed able to correct for deterministic ISI distortion, then this would be the frequency at which the corrections start to occur. If the nervous system does not make such a correction, then this is the maximum firing frequency which does not lead to information loss due to the ISI distortion. In either case, it is of significance for understanding the functioning of the nervous system.

2. Methods

Our computer simulations were constructed using the NEURON and NMODL programming languages [5]. Our

*Corresponding author.
E-mail address: prc9m@virginia.edu (P. Crotty).

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model uses a 10 cm long axon at 18.5 °C. The differential equation for the membrane potential was solved numerically using a second-order Crank–Nicholson method with a 1 μs time step, and with the axon divided into 1000 isopotential segments. Smaller time steps and more segments did not substantially alter our results.

The biophysics of the axon were modeled after the Hodgkin–Huxley study of the squid giant axon [6]. We used their models for voltage-activated Na^+ and K^+ channels, with the addition of a time-dependent membrane capacitance component which is proportional to the fraction of sodium gating particles in the open position and to the sodium channel density (see [11] for details). We also used Hodgkin and Huxley's values for the ionic equilibrium potentials, with the resting potential set at −65 mV. The leak channel was considered to be composed of separate sodium and potassium leak channels. No additional ionic currents were included. Whenever the maximum conductance densities were varied, all of them were varied by the same factor in order to keep the resting potential unchanged. The time-varying capacitance component was also varied by this factor.

Action potentials were produced by means of simulated 100 mA, 1 μs current injections into one end of the axon. An important, initial question was whether the degree of interference between successive action potentials depended significantly on the characteristics of the stimulation. To study this, we varied the stimulus amplitude and duration over several orders of magnitude and found no significant influence on our major results (see below). We took the interval between the onsets of the current injections as the initial ISI, T_0.

The interval between the action potentials was measured at the location 8 cm down the axon by recording the arrival times there defined as the voltage level increased above −10 mV. The change in the interval (i.e., activation minus arrival differences), labeled δT, is the difference of the second ISI, T_f, with the initial ISI, i.e., $\delta T \equiv T_f - T_0$. A positive value of δT means the ISI has increased with distance traveled, and a negative value means that it has decreased; the implication is that the second action potential is, respectively, slower or faster than the first one. The maximum firing frequency was determined by choosing an upper limit on $|\delta T|$ in the range of the ISI distortion produced by other noise sources (see below) and then finding the smallest initial ISI such that it and all larger ones had errors under this limit; the frequency was then the reciprocal of this ISI, $1/T_0$.

3. Results and discussion

The amplitude and duration of the current pulse which activated each action potential did not have substantial influence on the intersymbol interference, so long as the current pulse duration was small compared to the action potential duration. We established this by measuring the ISI changes at 8 cm using stimulus durations ranging from 1 to 100 μs and amplitudes ranging from 100 to over 10,000 mA. Over these ranges the change in ISI varied by only 61 μs. We also investigated how the larger current injections altered the maximum firing frequencies such that the ISI change at 8 cm was under 10 μs (see below), and we found that the maximum frequencies were at most 2 Hz different from their values with a 100 mA injection. We therefore conclude that the results are essentially independent of the details of the stimulation current over a wide range of experimentally reasonable values.

Fig. 1 illustrates the voltage at the 8 cm point along the axon for three pairs of action potentials with differing initial ISIs. For the longest initial ISI, 15 ms, the two action potentials are essentially identical and independent of each other, and the ISI is preserved. When the initial ISI is reduced to 7 ms, the second action potential is generated during the last phase of the wake of the first one, and its size and velocity are affected: its peak is 2 mV higher, and it moves about 0.61 m/s faster. Accordingly, the ISI at 8 cm is smaller than the initial ISI by 131 μs, and it continues to shrink as the APs move down the axon. When the initial ISI is reduced to just above the absolute refractory period, 1.77 ms, the interference is more pronounced. The second AP is now generated well inside the period of hyperpolarization following the peak of the first AP, and its peak is 1.6 mV lower. The velocity difference is now substantial: the second AP is more than 5 m/s slower than the first one,

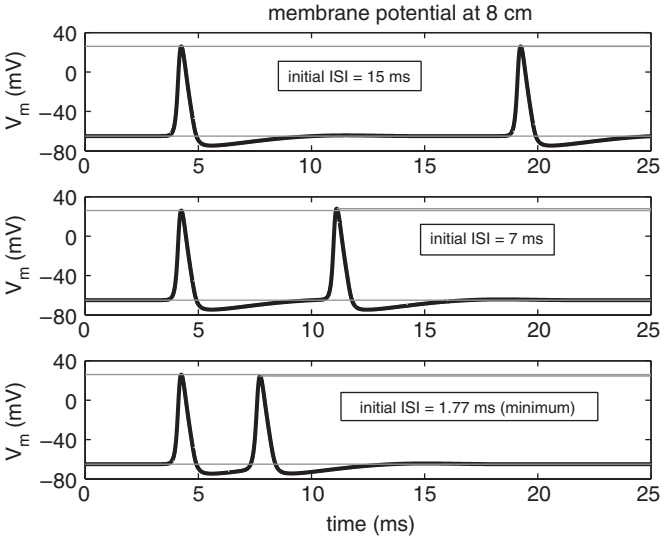

Fig. 1. For pairs of action potentials, the amplitude and velocity of the second action potential is affected by the first one if the interspike interval is too small. The graphs show the simulated voltage traces 8 cm from the point at which the action potentials are evoked by a pair of brief current pulses. The first action potential always has an amplitude of 91 mV and a velocity of 18.98 m/s. Top: with an initial interspike (i.e., interstimulation) interval of 15 ms, the second action potential is virtually identical to the first one. Middle: when the second action potential is generated 7 ms after the first one, it is 2 mV larger and 0.61 m/s faster at the 8 cm point, and the ISI has shrunk by 131 μs. Bottom: when the second action potential is generated just after the absolute refractory period of the first one (1.77 ms), it is 1.6 mV smaller and 5.28 m/s slower, causing the ISI to grow as the APs travel. By 8 cm, the ISI has increased to 3.39 ms.