Relationship Between EPSP Shape and Cross-Correlation Profile
Explored by Computer Simulation for Studies on Human Motoneurons

P. Ashby and D. Zilm
Playfair Neuroscience Unit, University of Toronto, and Addiction Research Foundation, Toronto, Canada

Summary. We used a computer model (making several simplifying assumptions) to explore the relationship between the characteristics of an excitatory postsynaptic potential (EPSP) and the profile of the change in firing probability that occurred when that EPSP was delivered to a rhythmically discharging neuron. In circumstances applicable to studies on human motoneurons we found that the magnitude of the period of increased firing probability in the cross-correlation (produced by the rising phase of the EPSP) was related to the number of stimuli and to the proportion of the interspike interval that the EPSP was within reach of threshold. The interstimulus interval and the statistical distribution of the motoneuron interspike intervals were of little consequence. For this model the subsequent period of reduced firing probability was proportional to the amplitude of the EPSP and not to the duration of its falling phase.

Key words: EPSP – Cross correlation

Introduction

It is likely that some of the characteristics of postsynaptic potentials in single neurons can be derived from cross-correlations between the timing of afferent volleys and the discharges of the neuron when it is firing rhythmically. The relationship between EPSP shape and cross-correlation profile will depend on the circumstances. For cat motoneurons, when both the interspike and interstimulus intervals are longer than the EPSP, the rising phase of the EPSP makes the greatest contribution to the probability change (Fetz and Gustafsson 1980). It is not clear whether the cross-correlation profile is best described by the first derivative of EPSP shape (Knox 1974; Knox and Poppele 1977) or the derivative plus a direct component (Kirkwood 1979; Gustafsson and McCrea pers. communic.). In cross-correlograms obtained from human motoneurons the period of increased firing probability is much shorter than the total duration of the responsible EPSP and may also represent its rising phase (Ashby and Zilm 1982). If cross-correlations are to be used to explore the synaptic connections to single motoneurons in man we need to know how variables such as EPSP amplitude, the interstimulus intervals and the mean and statistical distribution of the interspike intervals affect the estimation of EPSP amplitude or shape from the cross-correlogram.

We used a computer model (that makes several simplifying assumptions about human motoneurons) to determine, empirically, how the relationship between EPSP shape and cross-correlation profile might be influenced by these variables. In order to reproduce the circumstances of human experiments as closely as possible, the model was designed so that series of interspike intervals recorded from real human motoneurons could be used in simulations.

Methods

Basis of the Model

In a typical human experiment the spike train of a single, voluntarily activated, motoneuron is obtained by inserting a needle electrode into a muscle and recording each occurrence of a given motor unit action potential. The interspike intervals generally lie between 50 and 500 ms and are roughly Gaussian in distribution.

While the subject maintains this motoneuron discharge afferent volleys (regular or random, but always random relative to the motoneuron discharges), elicited by natural stimulation or by electrical stimulation of peripheral nerves are delivered to the spinal cord, usually at rates between 1/s and 3/s.
If the afferent volley (which arrives at the motoneuron after a delay due to the conduction time in the afferent fibers) gives rise to an excitatory postsynaptic potential (EPSP) in the neuron, and if this occurs at an appropriate time in the interspike interval, the EPSP will bring the membrane potential to threshold and cause the motoneuron to discharge. This event will be visible at the muscle electrode after an afferent delay representing the conduction time of the motor axon, muscle fiber, and the neuromuscular delay. The event will thus appear in the cross-correlation at a time after the spike equal to the sum of the afferent and efferent delays (which we call the “peripheral latency”).

In order to model the essentials of this interaction between EPSPs and a rhythmically discharging neuron several simplifying assumptions were made:

1. It was assumed that there is linear summation of EPSP and membrane potential voltages as in cat motoneurons (Brock et al. 1952).

2. When a part of an EPSP reaches threshold, the generation of a spike was assumed to extinguish the remainder of the EPSP (Coombs et al. 1955).

3. It was assumed that the essentials of the interaction between EPSPs and a rhythmically discharging neuron can be modeled by constructing trajectories representing the effective “distance” of an EPSP from threshold at any time during the interspike interval.

4. For cat motoneurons this “distance” is governed by a number of factors:

3.1. The trajectory of the membrane potential during the interspike interval. In adapted cat motoneurons discharging with their primary range (less than 35 impulses/s) the trajectory of the membrane potential can be described by a “scope”, whose depth is proportional to the interspike interval, followed by a ramp of constant gradient (Schwindt and Calvin 1972; Schwindt 1973; Calvin 1975).

3.2. Changes in threshold during the interspike interval. In cat motoneurons threshold falls during the early part of the interspike interval and rises during the latter half (Calvin 1974).

3.3. Changes in membrane conductance during the interspike interval. Conductances, responsible for the after-hypopolarization, are maximum immediately after a spike and, although complex in the first 20 ms, fall in a roughly exponential manner (Baldissera and Gustafsson 1970; Schwindt and Calvin 1973; Baldissera and Gustafsson 1974; Mauritz et al. 1974). The changes in conductance following spikes in rhythmically firing neurons are essentially similar (Schwindt and Calvin 1973; Mauritz et al. 1974). These conductance changes probably account for the reduction in the amplitude of EPSPs delivered in the first 30 ms after a spike (Coombs et al. 1955).

3.4. Voltage dependent alterations in membrane conductance. The membrane conductance is also voltage dependent (Nelson and Frank 1967), but this conductance is probably overwhelmed by the after-hypopolarization conductance immediately after a spike (Baldissera and Gustafsson 1974).

3.5. Variations in EPSP amplitude with changes in membrane potential. As a general rule depolarization of the membrane potential reduces the amplitude of EPSPs, but there may be very little change in the subthreshold region (Coombs et al. 1955; Werman and Carlen 1976; Edwards et al. 1976).

All of these factors (but mainly the first three) contribute to the effective “distance” of an EPSP from threshold at any instant during the interspike interval. The trajectory representing this “distance” during the interspike interval (especially in the first 30 ms after the spike) cannot be easily predicted. In the later part of the interspike interval, however, these effects are either small or linear so that this trajectory may be described by a simple ramp.

4. It is assumed that the variability of the interspike of a rhythmically discharging motoneuron can be represented by using series of variable intervals (from human recordings or from standard statistical distributions) to construct interspike trajectories. The variability of the interspike trajectories is thus “built in”. The ramps do not have random activity on top of them, but the way in which the randomness is introduced should be of little consequence at the instant of the encounter between the rising phase of an EPSP and the membrane potential trajectory (especially if the EPSP has a short rise time and a large amplitude). This method was chosen because we wanted to use series of interspike intervals recorded from real human motoneurons in our simulations in addition to series of intervals from standard statistical distributions.

The Computer Simulation

A computer was used to model the interaction between EPSPs and a rhythmically discharging motoneuron (Fig. 1). The “grain” of the simulation (the smallest unit of time simulated) was 1 ms.

Each simulation required:
1. A series of up to 600 “interspike intervals”. The series were obtained from standard statistical distributions and from recordings from human tibialis anterior motoneurons. The intervals could be from 1 to 2,000 ms in duration, but were typically within the range 40–400 ms. These interspike intervals were used to construct trajectories representing the effective distance of an EPSP from threshold during the interspike interval. Based on the considerations discussed above the trajectories were constructed so that immediately after a spike the “distance” from threshold in “units” (the scoop) was set equal to the duration of the next interspike interval in ms. The trajectory then rose at 1 “unit” per ms to intersect threshold at the end of the interval.