Quantification of the Factors That Influence Discharge Correlation in Model Motor Neurons

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Taylor, Anna M. and Roger M. Enoka. Quantification of the factors that influence discharge correlation in model motor neurons. J Neurophysiol 91: 796–814, 2004. The purpose of this study was to quantify the influence of intrinsic properties, active dendritic conductances, and background excitation and inhibition on measures of discharge correlation in the time and frequency domains with known levels and patterns of common synaptic input. The study involved a computer simulation of a population of neurons with a range of input resistances (0.54–3.7 MΩ) and surface areas (407,000–712,000 μm²). The neurons were simulated with no, moderate, or high levels of active dendritic conductances and were activated with either excitatory input only or excitatory and inhibitory inputs. The patterns of common input, either branched common input or common modulation, were tested with 0, 30, 60, and 90% common input. The results confirmed previous findings of an exponential relation between the level of common input and indexes of synchronization; only when the common input comprised ≥60% of the total excitatory input was there a significant effect on discharge correlation. Synchronization was greatest in models that had passive dendrites. Active dendritic conductances caused the discharge rate of the neuron to saturate and decreased motor-unit synchronization. However, the addition of 10% background inhibitory input increased synchronization in these models. In contrast, common rhythmic modulation of inputs at 24 Hz usually decreased synchronization. Significant coherence at the modulated frequency occurred in the commonly modulated neurons when ≥60% of the inputs were modulated. Furthermore, active dendritic conductances decreased coherence. Branched common input caused high levels of coherence across a broad spectrum and when combined with active dendritic conductances caused significant frequency peaks in the 30- to 50-Hz band. In conclusion, the level of inhibitory input and active dendritic conductances interact with the amount of common input to determine time- and frequency-domain discharge correlation.

INTRODUCTION

Similar discharge times for action potentials by a pair of neurons are typically taken to indicate a common influence on the activity of the neurons. This is proposed to take two forms: one, branched axonal projections from a presynaptic neuron (Bremner et al. 1991; Sears and Stagg 1976), or two, the modulation of presynaptic neuronal activity by a higher-order neuron (Farmer et al. 1993b; McAuley et al. 1997). Because correlated discharges can reflect the connectivity of neurons in the CNS (Datta et al. 1991; Farmer 1998; McAuley et al. 1997), such measures can provide a unique insight into functional connections within the human spinal cord.

To provide valid information about synaptic input patterns, it is crucial that the estimate of discharge correlation varies only as a function of the input pattern. The translation of correlated synaptic input to correlated discharge times depends on the two neurons responding in approximately the same manner to the input. The factors that could influence the transfer function of the neuron include membrane resistances, background activity, and active ionic conductances. Some studies on humans suggest that there may indeed be a tendency for neuronal properties to influence the degree of correlation in discharge times. For example, Datta and Stephens (1990) reported that motor units with similar thresholds tend to exhibit higher levels of correlated discharge than those with disparate thresholds. Furthermore, motor units with similar discharge rates and discharge variability often have higher indexes of synchronization (Schmied et al. 1994).

Data from respiratory motor neurons in cats indicated that there were differences in the pattern of short-term synchrony with different levels of anesthesia (Kirkwood et al. 1982). The authors inferred that these differences were due to different dominant sources of synaptic input. However, there is an alternate possibility. Because anesthesia depresses persistent inward currents that result from dendritic conductances, the different features of the central peaks and the pattern of oscillation in the cross-correlograms observed by Kirkwood and colleagues could reflect different levels of active dendritic conductances.

Variation in the level of synchronization that is observed experimentally could be explained either by nonuniform distribution of common projections from presynaptic neurons to motor neurons in a population or by variation in the intrinsic properties of the pairs of neurons, which would influence the response of each neuron to common input. Although previous studies have addressed some of these issues in single motor neurons with injected current (Binder and Powers 2001; Türker and Powers 2001), the range of intrinsic properties that were represented by the sample of neurons was relatively limited. Furthermore, motor-unit recordings obtained from humans are often restricted, due to technical reasons, to low-threshold motor units, which precludes the study of correlated activity between most motor units in the pool.

Another form of correlation between the discharge times of neurons is the presence of common periodicities in the times of discharge as assessed using coherence analysis. Common frequencies in the discharge times of two neurons are usually assumed to arise from oscillatory activity in second-order neurons. However, some network-simulation studies have shown that the presence of a calcium conductance in model

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neurons can lead to phase-locked oscillations among the neurons when activated by a constant source of excitation, such as injected current (Falcke et al. 2000). Although short-term synchrony and coherent oscillations have been observed to coexist (Semmler et al. 2002), it appears that common Poisson input does not evoke the same peaks in coherence functions that common periodic inputs do in simulated neurons that have the same intrinsic membrane properties (Halliday 2000).

The purpose of this study was to quantify the influence of intrinsic properties, active dendritic conductances, and background excitation and inhibition on measures of discharge correlation in the time and frequency domains with known levels and patterns of common synaptic input.

METHODS

To approximate the range of intrinsic properties that would be present in a motor neuron pool, such as the human first dorsal interosseous, neurons were simulated for every fifth motor unit of 120 virtual neurons. The model neurons were simulated using the GENeral NEural Simulation System (GENESIS; Bower and Beeman 1995).

The details of the neuron model are presented in the APPENDIX. Because experimental data suggest that there are many more motor neurons that innervate slow-contracting muscle fibers compared with those that innervate fast-contracting muscle fibers (Enoka and Fuglevand 2001), the properties for the model neurons were varied exponentially, with motor neuron 1 presumed to be the first recruited and motor neuron 120 presumed to be the last recruited. The general form of the relation between model neuron number (recruitment order) and motor neuron properties was

\[ P_k = P_1 \cdot e^{(\ln P_{120})/x} \]

where the parameter \( P \) for neuron \( k \) was a function of the parameter value for motor neuron 1 \( P_1 \) and varied exponentially as a function of motor neuron number over the range of parameter values, \( \text{RP} \).

The responses of the model neurons were tested under two conditions of common input: simultaneous input times and commonly modulated random inputs at 0, 30, 60, and 90% of total excitatory input. Furthermore, the neurons were tested in the presence of 10% inhibition was used to allow the investigation of the interaction between inhibitory inputs and dendritic conductances and common input without causing a significant change in discharge rate, which would have been a confounding factor when making comparisons between conditions. Three levels of active dendritic conductances (none, moderate, and high) were also examined.

Model morphology

The electrotonic structure of the model neurons was based on morphology data from Culheim et al. (1987). The dendritic structure of motor neurons was approximated using a compartmental equivalent cable, with four cylinders representing the dendrites (Fig. 1). The surface area of the model neurons varied inversely with threshold (Fleshman et al. 1988) and was within the range that has been observed experimentally. The diameters of the first dendritic compartments ranged from 25.6 \( \mu \text{m} \) for the lowest threshold motor neuron (motor neuron 1) to 45.1 \( \mu \text{m} \) for the highest threshold motor neuron (motor neuron 120) (Fleshman et al. 1988). The diameter of dendritic compartment 2 was 90% of the diameter of dendritic compartment 1, dendritic compartment 3 was 70% of the diameter of dendritic compartment 2, and dendritic compartment 4 was 50% of the diameter of dendritic compartment 3. The lengths of each compartment were the same in all models: 2,006, 951, 2,545, and 1,801 \( \mu \text{m} \) for dendritic compartments 1–4, respectively. Because there was not a clear trend in somatic surface area with motor neuron size in the data of Culheim et al. (1987), the soma of all models was represented as a sphere with a diameter of 51.7 \( \mu \text{m} \). The initial segment was modeled as a cylinder that was 125 \( \mu \text{m} \) in length, with a diameter that varied with motor neuron number. Thus motor neuron 1 had the lowest current threshold, smallest surface area (406,672 \( \mu \text{m}^2 \)), shortest electrotonic length (1.8 \( \lambda \)), and smallest diameter for the initial segment compartment (4.4 \( \mu \text{m} \)), and motor neuron 120 had the highest current threshold, largest surface area (712,379 \( \mu \text{m}^2 \)), longest electrotonic length (3.3 \( \lambda \)), and largest diameter for the initial segment (7.5 \( \mu \text{m} \)).

Membrane properties

The intrinsic properties of the models also varied with threshold. Similar to the step model proposed by Fleshman et al. (1988) and the ratios of somatic-to-dendritic resistance estimated by Rose and Vanner (1988), the dendrites had a higher specific membrane resistance than the initial segment and soma. The soma and initial segment of motor neuron 1 had a specific membrane resistance of 600 \( \Omega \text{cm}^2 \), and the dendrites had a specific membrane resistance of 30,000 \( \Omega \text{cm}^2 \).

![Motor Neuron 1 and Motor Neuron 120](image)

FIG. 1. The structure of the model neurons. All models had 6 compartments, which are labeled in the top figure. Top: model motor neuron 1; bottom: the morphology for model motor neuron 120. The models between motor neurons 1 and 120 had dimensions that varied exponentially with motor neuron number from those for the smallest motor neuron (1) to the largest (120). The lengths of the dendritic compartments were the same for all models, but the diameters increased with motor neuron number. As a result, the electrotonic lengths of the models also increased with motor neuron number.
contrast, the specific membrane resistances for motor neuron 120 were 100 and 5,000 \( \Omega \text{cm}^2 \) for the soma-initial segment and dendrites, respectively. The specific axial resistance for all compartments and motor neurons was 70 \( \Omega \text{cm} \), and the specific membrane capacitance was 1.0 \( \mu \text{F/cm}^2 \). As a result of the dimensions of the models, the axial resistances to current flow in motor neuron 1 from dendrite 4 to 3, dendrite 3 to 2, dendrite 2 to 1, dendrite 1 to the soma, and the soma to the initial segment were 8.64, 1.58, 2.70, 0.02, and 3.68 \( \text{M} \Omega \), respectively. The axial resistances between the same compartments in motor neuron 120 were 7.97, 2.82, 0.52, 0.88, and 1.98 \( \text{M} \Omega \).

**Ion channels**

Action potentials were initiated in the initial segment. Both the initial segment and soma contained "fast" sodium and delayed-rectifier potassium conductances (\( g_{\text{Na-p}} \) and \( g_{\text{Kdr}} \)). However, the somatic sodium and potassium conductances (\( g_{\text{Na-s}} \) and \( g_{\text{Kdr-s}} \)) had higher thresholds for activation, and there was a lower density of sodium channels. The soma also contained a slow (presumed calcium-dependent) potassium conductance (\( g_{\text{Ks}} \)). Although the active dendritic conductances that contribute to synaptic amplification comprise multiple channel types (Carlin et al. 2000; Hounsgaard and Mintz 1988; Lee and Heckman 2001; Powers and Binder 2003), only four ionic conductances were used to represent the active properties of dendrites as in other modeling studies (Booth et al. 1997; Powers 1993). A persistent sodium conductance (\( g_{\text{Na-p}} \)) was located in the soma (Lee and Heckman 2001; Powers and Binder 2003). Furthermore, L- and N-type calcium conductances (\( g_{\text{CaL}} \) and \( g_{\text{CaN}} \)) and a calcium-dependent potassium conductance (\( g_{\text{KCa}} \)) were located in the second dendritic compartment. Dendritic compartment 2 was used as the location of the active dendritic conductances based on some previous experimental and modeling studies, which suggested that there is a high density of active dendritic conductances at \( \approx 0.5 \text{ A} \) from the soma (Bennett et al. 1998) or \( 180–360 \mu \text{m} \) from the soma for a region \( \approx 100 \mu \text{m} \) long (Rose et al. 2002). Excitatory and inhibitory conductances (\( g_{\text{Rin}} \) and \( g_{\text{Rinh}} \)) were located on all dendritic compartments with varying densities.

**SPIKE-GENERATING CONDUCTANCES.** The properties for activation and inactivation of the spike-generating conductances were similar to those used in previous neuron models (Booth et al. 1997; Jones and Bawa 1997; Traub 1977). The voltage at half-activation was 5 mV more depolarized in the soma than in the initial segment. The increased voltage for half-activation in combination with a lower density of the sodium conductance resulted in a higher threshold for action potential initiation in the soma compared with the initial segment. The afterhyperpolarization period was generated by a slow passive conductance in the soma (Coombs et al. 1955; Jones and Bawa 1997; Traub 1977). The voltage at half-activation was 5 mV more depolarized in the soma than in the initial segment.

**ACTIVE DENDRITIC CONDUCTANCES.** The L-type calcium channels had a lower threshold for activation, slower rate of activation, and could not be inactivated. In contrast, the N-type channels had a higher half-activation voltage, faster kinetics, and could be inactivated. The maximum densities of the L- and N-type calcium conductances for the moderate condition were 0.35 and 0.4 \( \text{mS/cm}^2 \). This corresponded to a total conductance for L-type calcium channels in motor neurons 1 and 120 of 0.57 and 0.99 \( \mu \text{S} \), respectively. The total conductances for N-type calcium channels were 0.65 and 1.1 \( \mu \text{S} \). In the high-active dendritic conductance state, the densities were 0.6 and 0.8 \( \text{mS/cm}^2 \) (motor neuron 1 total conductances of 0.97 and 1.3 \( \mu \text{S} \); motor neuron 120 L- and N-type conductances of 1.7 and 2.3 \( \mu \text{S} \)). The reversal potential for calcium was \( +80 \text{ mV} \). The maximal conductance density of the potassium channels was 0.34 \( \text{mS/cm}^2 \) in the moderate condition and 0.45 \( \text{mS/cm}^2 \) in the high condition. The total maximal conductance of potassium in the second dendritic compartment of motor neuron 1 was 0.55 and 0.73 \( \mu \text{S} \) in the moderate and high conditions, respectively. The maximal conductances for motor neuron 120 were 0.96 and 1.3 \( \mu \text{S} \).

The activation of the dendritic conductances produced persistent inward currents in the model neurons in response to a voltage-clamp ramp from \(-70 \) to \(-30 \text{ mV} \) and back in 8 s (Fig. 2). The magnitude of the persistent inward current for motor neuron 1 on the ascending phase of the ramp was \(-8.18 \text{nA} \) with moderate conductances and \(-11.92 \text{nA} \) with high levels of active dendritic conductances (Fig. 2A). The persistent inward current in motor neuron 120 with high levels of active dendritic conductances was \(-8.56 \text{nA} \) (Fig. 2B). Lee and Heckman (1998a) reported persistent inward current amplitudes of

![FIG. 2. The current-voltage relation for the model neurons. Both panels show the results of a somatic voltage-clamp ramp from \(-70 \) to \(-30 \text{ mV} \) and back to \(-70 \text{ mV} \) over 8 s under either the moderate (dashed line) or high (solid line) levels of active dendritic conductances that were used in the model. The ascending phase of the voltage ramp is depicted with the thick line, and the descending phase with the thin line. A: the current-voltage relation for motor neuron 1 showed evidence of a persistent inward current at both the moderate and high levels of active dendritic conductances. With increased activation of dendritic conductances, the threshold for onset of the current decreased and the persistent inward current was not inactivated within the range of the voltage ramp. B: motor neuron 120 did not show evidence of a persistent inward current with the moderate level of active dendritic conductances but did show evidence of a persistent inward current at the high level of active dendritic conductances. Furthermore, the threshold for the onset and offset of the persistent inward current was more depolarized than that for motor neuron 1.](http://jn.physiology.org/doi/fig)
18.9 ± 7.8 nA in fully bistable motor neurons obtained from a decerebrate cat preparation. In contrast, Powers and Binder (2003) showed that motor neurons in the rat hypoglossal nucleus exhibit inward currents during the ascending phase of a voltage ramp with an amplitude of −422.4 ± 352.6 pA. These two studies emphasize the differences between motor neurons in different species and anatomical locations. In keeping with our goal of modeling neurons with properties similar to cat motor neurons, the model neurons in this study had persistent inward currents within the range observed by Lee and Heckman.

The presence of active dendritic conductances caused a slight increase in discharge rate of motor neurons 1 and 120 at lower levels of injected current. Furthermore, motor neuron 1 exhibited a “secondary range” (Kernell 1965) in the frequency-current relation in the presence of active dendritic conductances (Fig. 3A) at higher levels of injected current. The model neurons could also produce self-sustained firing (Fig. 3B), a classic behavior associated with persistent inward currents (Heckman 2003).

SYNAPTIC CONDUCTANCES. The maximum conductance and time constants for rise and decay of the excitatory synaptic conductance (g_{max}, τ_1, and τ_2) were 5 nS, 2 ms, and 3.8 ms, respectively, with a reversal potential of 4.6 mV (Finkel and Redman 1983). The inhibitory synaptic conductance had g_{max}, τ_1, and τ_2 values of 9 nS, 4 ms, and 8.2 ms, with a reversal potential of −80.7 mV (Stuart and Redman 1990). The distribution of excitatory and inhibitory synapses was generalized from experimental data (Brannstrom 1993), which indicate that the density of excitatory synapses decreases at the most distal extent of the dendrites and decreases to a greater extent in motor neurons that innervate fast-twitch muscle fibers compared with those that innervate slow-twitch fibers. Similarly, the density of inhibitory synapses was highest close to the soma and also decreased more in motor neurons that innervate fast-twitch fibers. The density of excitatory and inhibitory synapses for motor neuron 1 and motor neuron 120 for each dendrite compartment are shown in Table 1.

The models were activated for 60 s at each of 10 levels of excitation, which were ~0.75, 1.5, 2.5, 4, 7, 12, 20, 35, 60, and 100% of the maximum excitation for motor neuron 1 and at four levels of common input (0, 30, 60, and 90%). A greater number of low excitation levels were tested to facilitate comparison with human data, which largely involve low-force contractions. Furthermore, a sensitivity analysis was performed to test the influence of the proportion of the inward current due to the N- and L-type calcium channels. In these simulations, the excitation level was fixed at the 35% level, there was 10% background inhibition, and the potassium conductance density was maintained at 0.34 mS/cm² (moderate active condition). The combined conductance density for g_{Ca,L} and g_{Ca,N} was fixed at 0.75 mS/cm² (moderate conductance level) and the density of g_{Ca,L} and g_{Ca,N} were varied inversely between 0.1 and 0.65 mS/cm². Each ratio of conductances was tested at the four levels of branched common input (0, 30, 60, and 90%). The Crank-Nicholson integration method and a time step of 0.01 ms were used for all simulations.

**FIG. 3.** Discharge behavior of the models in response to injected and synaptic current. A: the frequency-current relations are shown for motor neurons 1 and 120 (●, ○, and ■, □, respectively) in the absence (●, ○) and presence (■, □) of high levels of active dendritic conductances. Each data point shows the frequency of discharge of the model neuron in response to a 2-s current pulse injected to the soma. In some cases, the data points are overlapping so that only 1 symbol is visible. The current threshold for motor neuron 1 was 0.5 nA and the current threshold for motor neuron 120 was 19 nA. B: an example of self-sustained firing evoked in motor neuron 1 with high levels of active dendritic conductances by a 40-nA current pulse (trace at the bottom of the figure). The thick line (top trace) shows the membrane potential in the 2nd dendritic compartment. The thin line shows the membrane potential measured at the initial segment. The onset of the persistent inward current is reflected by the rapid depolarization of the membrane potential in the 2nd dendritic compartment after the beginning of the current pulse. After the current was removed, the neuron continued to discharge due to the inward current generated in the dendrites. C: an example of the action potentials initiated at the initial segment of motor neuron 1 with passive dendrites in response to synaptic input at 12% of maximal excitation. The amplitude of the fluctuations in the membrane potential during the afterhyperpolarization period was similar to the values measured experimentally by Calvin and Stevens (1968).
The two forms of synaptic input in this study were tested for motor neuron 1 when discharging at a rate of ~10 Hz. The composite input model with an average rate of 100 Hz had a mean amplitude for synaptic noise of 2.2 mV (maximum of 9.78), a time constant of 3.2 ms, and a CV for discharge rate of 10.8% (Fig. 3C). In contrast, the simulations in which each input was individually represented (292 inputs each with a mean rate of 100 Hz) had a mean amplitude for membrane noise of 0.35 mV (maximum of 1.25), a time constant of 15.6 ms, and a CV for discharge rate of 1.25%. It is also possible that a larger number of individual inputs could arrive at a lower rate for the same net input (29,200 EPSPs/s). Therefore the membrane noise for a simulation with 1,168 inputs discharging at 25 Hz each was also analyzed. This input structure had a mean amplitude for synaptic noise of 0.57 mV (maximum of 2.44 V), a time constant of 16.0 ms, and a CV for discharge of 0.93%. The composite input method probably provided a more accurate approximation of the experimental levels of synaptic noise due to the equivalent cable structure of the model neurons. The equivalent cable had a local input resistance that was ~3.5 times lower than a morphologically realistic model for the same number of synaptic neurons each second. To simulate these inputs, it is necessary to generate individual spike trains for each of the input sources. Because of the high rate of inputs, however, there will often be more than one excitatory postsynaptic potential (EPSP) occurring in the dendrites at the same time. These individual inputs can be simulated as composite inputs that represent the EPSPs due to several presynaptic inputs occurring simultaneously by chance (Jones and Bawa 1997; Murthy and Fetz 1994). To ascertain if this simplification could produce the same postsynaptic effects as simulating the individual synaptic inputs, we compared the characteristics of membrane noise for the two simulation methods with the data reported by Calvin and Stevens (1968).

To quantify membrane noise, the action potentials were removed from the membrane voltage records before any further analysis. The mean slope of each section of data was removed, and the peak-to-peak amplitude of each fluctuation in membrane voltage was measured. The sampling rate for the simulated membrane voltage was 5 kHz, and the duration of each trial was 60 s. The time constant of the synaptic noise was assessed with autocorrelation functions.

Calvin and Stevens (1968) reported that, on average, the amplitude of the fluctuations in membrane voltage was 2 mV, but sometimes it reached 8 mV. The autocorrelation of the membrane noise was exponential and had a time constant of 4 ms (their Fig. 1). The coefficient of variation (CV) for discharge rate in their recordings was ~10%.

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There were two components to the input received by all motor neurons. One was a random component that represented synaptic activation from multiple sources, and the other was a common component that was designed to represent the source of common input. The random component had a frequency of 100 Hz and was different for each compartment within a motor neuron and between motor neurons. The input times had a Poisson distribution, and the random number generator was re-seeded before calculating each set of input times. In the absence of common input, the amplitude of the random activation was adjusted by varying the number of synapses that were activated at that level of excitation. In the presence of common input, the amplitude of the common input was calculated as a percent of the total number of synaptic inputs, and the amplitude of the random component corresponded to the number of synapses that were not activated by the common component.

Branched common input was modeled as a set of synaptic inputs that were applied simultaneously to all dendritic compartments of every model neuron. Thus this component of synaptic input was exactly the same for all simulated neurons. The frequency of activation of the common input was set at 50 Hz so that any possible influence of discharge rate on coherence could be differentiated from both the background frequency of activation and the periodic input frequency in the common modulation trials.

Common modulation of random inputs was achieved by imposing a sinusoidal oscillation on a separate set of random input times (Poisson distributed and 50-Hz mean rate) for every dendritic compartment of each model neuron. The frequency of the oscillations was 24 Hz for all the inputs, thus representing an in-phase, high-frequency oscillation of random inputs. The frequency was set to 24 Hz because the frequency-domain correlation in discharge times of human motor units has been observed to have a peak between 16 and 32 Hz (Farmer et al. 1993a). The amplitude of the oscillatory drive was 10% of the instantaneous discharge rate of the random inputs (5 Hz). The power spectra and autocorrelations for the random and branched common input showed no evidence of periodicities in the inputs. As intended, there was a peak at 24 Hz in the power spectrum for the modulated common inputs, and the modulated frequency was also evident in the autocorrelations for these inputs.

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Fluctuations in membrane potential

To determine how different common input conditions and levels of dendritic active conductances were influencing the transfer of current along the dendrites to the soma, membrane voltage was recorded with the spike-generating conductances (g_{Na}, g_{Kdr}, g_{Na},_s, g_{Ks}) blocked in the soma and initial segment. The mean depolarization and SD of the membrane voltage were quantified for the soma and second dendritic compartment (where the dendritic active conductances were located) for motor neurons 1, 40, 50, and 120. Furthermore, the membrane voltage at the soma was cross-correlated for comparison with the correlation between discharge times. This subset of model neurons was chosen to reflect the properties of the neurons with highest and lowest input resistances as well as two neurons that had more similar and relatively low thresholds for discharge.

Data analysis

All analyses used custom programs written in Matlab version 6.1 (The Mathworks, Natick MA). First, the mean discharge rates and coefficient of variation for discharge rate were calculated. Second, the models with a mean rate >6 Hz were analyzed for synchronization at
every level of excitation and degree of common input. Each set of discharge times was correlated with every other set for that condition.

ASSESSMENT OF SHORT-TERM SYNCHRONIZATION. Correlation was quantified using cross-correlation histograms of the discharge times that occurred within 100 ms of each other (Datta and Stephens 1990). After constructing the cross-correlation histogram (bin size: 1 ms) between the discharge times for a pair of motor neurons, a cumulative sum (Ellaway 1978) of the counts in the histogram was used to detect the peak in the cross-correlation histogram within the 20 ms surrounding the time of the reference discharge. The baseline number of counts was taken from the mean of the bins of the cross-correlation histograms that were ±50 ms from time 0. If the mean bin count in the baseline region was <4, the correlation analysis was not continued. Three indexes of correlation were computed from the size of the peak in the cross-correlation histogram: index $E$ was calculated as the counts in the peak above chance divided by the number of counts in the train with a lower discharge rate (Datta and Stephens 1990); index Common Input Strength (CIS) was calculated by dividing the counts in the peak above chance by the duration of the trial (Nordstrom et al. 1992); and index $k$ was the ratio of extra counts in the peak to the baseline number of counts (Ellaway and Murthy 1985). Correlations were determined for every motor neuron relative to every other motor neuron in the same condition.

ASSESSMENT OF COHERENCE BETWEEN MOTOR NEURON DISCHARGES. Frequency-domain correlation was quantified using coherence analysis (Farmer et al. 1993a; Rosenberg et al. 1989). First, the discharge times of the each of the motor neurons were converted to bins of ones or zeros depending on whether a discharge had occurred in that time (sampling rate of 300 Hz). Next, the pooled coherence (Amjad et al. 1997) for all pairs of discharges in each condition was computed as

$$C_{xy} = \frac{\sum_{i=1}^{n} P_{x,y}(f) |L|}{\left( \sum_{i=1}^{n} P_{x,y}(f) |L| \right) \left( \sum_{i=1}^{n} P_{y,y}(f) |L| \right)}$$

where the pooled coherence ($C_{xy}$) between the two signals $x$ and $y$ is a function of the sum of the autospectra ($P_{xx}$ or $P_{yy}$) for each pair of discharges ($i$) as a function of frequency ($f$) multiplied by the number of disjoint segments ($L$) used to construct the spectrum and the sum of the cross-spectra of the signals ($P_{xy}$) and the number of segments in each. The window size for the power spectra was 512 points with no overlap, and all analyses were run using custom-written Matlab programs.

Statistical differences between levels of synchrony were assessed using one-way ANOVAs with model condition, level of excitation, and degree of common input as factors. One-way ANOVAs were also used to detect significant peaks in the pooled coherence spectra. For these tests, the pooled coherence functions were separated into 5-Hz bins, and 0–100 Hz were tested. Tukey’s post hoc tests were used to identify the location of statistical differences. Regression analysis was used to determine significant linear correlations between motor unit synchronization, discharge properties, and input resistance within each model condition. The alpha level was $P < 0.05$.

RESULTS

The results comprised the characteristics of membrane voltage for a subset of the model neurons, the discharge characteristics (mean and variability) for the population of model neurons, and the effects of the model parameters on the amounts of motor-unit synchronization and pooled coherence.

Membrane voltage

The structure of the membrane voltage was similar for the soma and second dendritic compartment of all models. The dendritic compartment, however, was more depolarized and had greater variability (Fig. 4D and Table 2). The amplitude of voltage fluctuations, or membrane noise, increased logarithmically with excitation in all model neurons (Fig. 5). The amplitude of the voltage fluctuations for motor neuron 1 was greater than for motor neuron 120 with both passive and active dendrites ($P < 0.001$; Table 2). In addition, inhibitory input increased membrane noise, especially in cells with active dendritic conductances (Fig. 4, E and F).

Fluctuations in membrane potential in the model neurons were similar ($P > 0.3$) in response to branched common input and modulated common input (Table 2). However, there was a peak in the cross-correlation of the membrane voltage for cells that received 60 and 90% branched common input (Fig. 6). Furthermore, the presence of 90% common modulation resulted in a periodic, low-amplitude correlation between the membrane voltage signals for each pair of model neurons (Fig. 6).

Discharge characteristics

A motor neuron was classified as recruited when it discharged action potentials at a rate ≥6 Hz. For the ease of comparison, excitation was expressed as a percentage of the maximum excitation that was tested ($E_{max}$), which depended on the surface area and density of synapses on the model neurons. The level of excitation, amount of common input, presence of inhibitory inputs, and amplitude of dendritic active conductances all influenced the discharge characteristics of the model neurons. Furthermore, the discharge pattern of the neurons depended on input resistance. The discharge characteristics of the models with moderate and high densities of active dendritic conductances were statistically similar; therefore these results were combined and compared with discharge characteristics of motor neurons in the absence of dendritic active conductances.

PASSIVE MODEL WITH NO INHIBITION. Motor neurons 1–15 were recruited to discharge at >6 Hz with an excitation level of 1.37% $E_{max}$. The highest threshold motor neuron (120) was recruited at 12% $E_{max}$. Although discharge rate increased with excitation, most motor neurons exhibited rate limiting of discharge rate, especially low-threshold motor neurons. The maximal rate for motor neuron 1 (17.0 Hz) was attained by 34% $E_{max}$, whereas the rate for motor neuron 120 (23.2 Hz) continued to increase up to 100% $E_{max}$ (Fig. 7A). The discharge rate of all motor neurons across all levels of activation decreased with the imposition of 90% branched common input and modulated common input. The recruitment threshold for motor neuron 1 increased to 2.5% $E_{max}$ with 90% branched common input, whereas the threshold for discharge of motor unit 120 was only increased with common modulation (20%). The discharge characteristics for motor neuron 1 and motor neuron 120 are shown in Table 3 for each of the model conditions.

The coefficient of variation for discharge rate (CV = (SD/mean) · 100) across all levels of excitation was lower, on average, for motor neuron 1 compared with motor neuron 120 (13.8 and 29.6%, respectively). The CV for discharge rate
increased as the level of branched common input increased, reaching values of 20.6 and 38.4% for motor neurons 1 and 120, respectively, with 90% common input. The effect of modulated common input on discharge-rate variability was similar to that of branched input.

PASSIVE MODEL WITH 10% INHIBITION. The addition of background inhibitory input had no effect \((P = 0.14)\) on the discharge rates of the motor neurons (Fig. 7A). The maximal rate for motor neuron 1 was 17.5 Hz, and the maximal rate for motor neuron 120 was 23.2 Hz in the presence of inhibition. Both branched common input and modulated common input tended to depress the discharge rate of model neurons similarly across levels of excitation. For example, the mean discharge rates of motor neurons 1 and 120 were decreased by 11 and 14% with 90% common input (branched and modulated). Discharge variability increased in the presence of 90% modulated common input, and further increased with 90% branched common input (Table 3).

ACTIVE DENDRITIC CONDUCTANCES WITH NO INHIBITION. At recruitment threshold, a number of the low- and mid-threshold motor neurons (up to motor neuron 90) discharged at high rates in the presence of active dendritic conductances (motor neuron 1; 20.4 Hz). Rate increased modestly over the range of input levels; for example, the discharge rate of motor neuron 1 was 26.3 Hz at maximal excitation (Fig. 7B). The high-threshold motor neurons were recruited at lower levels of synaptic input compared with the passive condition, began discharging at elevated rates, and reached greater maximal rates compared with the passive condition (range: 10.8 at recruitment to 46.3 Hz at maximal excitation for motor neuron 120). The maximal rate of motor neuron 120 was 26% lower at the highest level of common input (branched and modulated). In contrast, the discharge rate of the low-threshold models did not change with high levels of common input (Table 3).

The coefficients of variation for low-threshold motor neurons were extremely low at recruitment (1.3% at 0.8% of \(E_{\text{max}}\))...
TABLE 2. Characteristics of somatic and dendritic membrane voltage with spike-generating conductances blocked

<table>
<thead>
<tr>
<th>Condition</th>
<th>0% Common Input</th>
<th>90% Branched Common Input</th>
<th>90% Common Modulation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Soma</td>
<td>Soma</td>
<td>Soma</td>
</tr>
<tr>
<td>Passive</td>
<td>Avg $V_m$</td>
<td>SD $V_m$</td>
<td>Avg $V_m$</td>
</tr>
<tr>
<td>No inhibition</td>
<td>Neuron 1</td>
<td>Neuron 120</td>
<td>Neuron 1</td>
</tr>
<tr>
<td></td>
<td>$-50.1 \pm 9.9$</td>
<td>$-61.2 \pm 3.7$</td>
<td>$-62.3 \pm 2.5$</td>
</tr>
<tr>
<td>10% inhibition</td>
<td>Neuron 1</td>
<td>Neuron 120</td>
<td>Neuron 1</td>
</tr>
<tr>
<td></td>
<td>$-53.4 \pm 9.0$</td>
<td>$-62.7 \pm 2.4$</td>
<td>$-63.5 \pm 1.5$</td>
</tr>
<tr>
<td>Active</td>
<td>No inhibition</td>
<td>Neuron 1</td>
<td>Neuron 1</td>
</tr>
<tr>
<td></td>
<td>$-32.0 \pm 1.8$</td>
<td>$-50.8 \pm 1.8$</td>
<td>$-40.0 \pm 2.9$</td>
</tr>
<tr>
<td>10% inhibition</td>
<td>Neuron 1</td>
<td>Neuron 120</td>
<td>Neuron 1</td>
</tr>
<tr>
<td></td>
<td>$-1.8 \pm 1.4$</td>
<td>$-1.4 \pm 1.4$</td>
<td>$-1.9 \pm 2.3$</td>
</tr>
<tr>
<td></td>
<td>$-2.7 \pm 1.2$</td>
<td>$-5.1 \pm 4.7$</td>
<td>$-5.4 \pm 3.3$</td>
</tr>
<tr>
<td></td>
<td>$10.6 \pm 5.0$</td>
<td>$6.8 \pm 4.8$</td>
<td>$7.3 \pm 5.9$</td>
</tr>
</tbody>
</table>

The mean depolarization (Avg $V_m$) and standard deviation (SD $V_m$) of the membrane potential in the soma and second dendritic compartments (Dend2) during activation is reported as the mean ± SD for all 10 levels of excitation with 0% common input, 90% branched common input, and 90% common modulation for motor neurons 1 and 120 in the absence (Passive) or presence of dendritic active conductances (Active) with and without inhibitory input.

**FIG. 5.** The change in mean membrane potential with increases in excitation. The mean somatic voltage during simulations in which the spike-generating conductances were blocked is plotted for motor neurons 1 and 120. The error bars indicate the SD of the membrane potential at each level of excitation. A: the model neurons with passive dendrites exhibited a plateau in membrane depolarization and membrane voltage variability at higher levels of excitation. The addition of 10% background inhibition hyperpolarized the membrane. B: the membrane potential of model neurons with active dendrites was more depolarized than the passive models and saturated rapidly with increasing amounts of synaptic input. The addition of background inhibition reduced the inward-current induced depolarization of the somatic membrane potential and increased variability of the membrane potential.

for motor neuron 1 in the presence of active dendritic conductances. At higher discharge rates, however, the CV for discharge rate for low-threshold motor neurons was the same as the average discharge variability in the passive condition (13.8%). In contrast, the CV for discharge rate of the high-threshold motor neurons was increased compared with the passive condition.

ACTIVE DENDRITIC CONDUCTANCES WITH 10% INHIBITION. The presence of inhibition increased the maximal discharge rate of motor neuron 1 (from 27.0 to 31.8 Hz), but had little effect on the maximal rate of motor neuron 120 (Fig. 7B). Furthermore, inhibition increased the CV for discharge compared with the active dendritic conductance models that lacked inhibitory input, especially for low-threshold neurons (motor neuron 1 had a twofold greater CV for discharge). Discharge variability declined by 19% for motor unit 1 with 90% common input. However, the CV for discharge of motor unit 120 was not different for any of the levels or patterns of common input (Table 3).

**Synchronization**

The level of motor-unit synchronization did not increase proportionally with the amount of branched common input for any of the model neurons. Under all model conditions, there was a significant association ($P < 0.001$) between increased excitation and the indexes of synchronization. The CIS, E, and $k^i$ indexes were similarly influenced by common input, active dendritic conductances, and inhibitory input. Furthermore, the synchronization indexes were influenced by the presence of inhibition and active dendritic conductances. Increased amounts of common modulation either decreased short-term synchronization or had no effect.

**BRANCHED COMMON INPUT.** In the passive model with no inhibition, the indexes of synchronization at 60 and 90% common input were significantly greater ($P < 0.001$) than all other levels of common input (Fig. 8). However, this was due in part to the positive correlation between the level of excitation and indexes of synchronization (Fig. 9). The correlations between the amount of common input and synchronization were similar.
common input levels were significantly different from all other levels of common input ($P < 0.001$).

The amount of synchronization progressively decreased in the presence of active dendritic conductances (Fig. 8). Nonetheless, synchronization was significantly increased at 60 and 90% branched common input ($P < 0.037$ for 60% and $P < 0.001$ for 90%). The CV for discharge rate had lower correlations with synchronization when there were active dendritic conductances. The presence of background inhibition increased the responsiveness of the models with dendritic active conductances to common input, especially in the model with moderate dendritic active conductances (Fig. 8). In addition, there was a stronger correlation with the CV for discharge. With inhibition, both the 60 and 90% common-input conditions were significantly greater ($P < 0.001$) than the 0 and 30% conditions. However, the amount of synchronization was still lower than either of the passive models. Unlike the passive model, there was a positive association between common input

**FIG. 6.** Cross-correlations of the somatic membrane potential with sodium and potassium channels blocked. All cross-correlations are for *motor neurons* 40 and 50 at 10% of maximum excitation. The cross-correlations were similar for model neurons with passive (A) and active (B) dendrites. With 0% common input (dashed line), there was little correlation between the neurons. However, there was a strong correlation in the presence of 90% branched common input (thin solid line). Low-amplitude, positive correlation was evoked by 90% common modulation (thick solid line) with peaks occurring regularly at the modulated frequency (24 Hz).

**FIG. 7.** The discharge rate for the active and passive models at different levels of activation. *A*: the discharge patterns of *motor neurons* 1 and 120 are depicted for the passive condition. *Motor neuron* 1 initially discharged at a higher rate than *motor neuron* 120, but reached a lower maximal rate than *motor neuron* 120 at high levels of excitation. The presence of 10% background inhibition did not have a significant effect on the discharge rates for both motor neurons. With inhibition, the maximal rate for *motor neuron* 1 was increased, whereas the maximal discharge rate of *motor neuron* 120 was decreased. The data are plotted as mean discharge rate ± SD of discharge rate for each level of excitation.
The presence of active dendritic conductances and inhibition influenced the peaks and magnitude of the pooled coherence. Increases in branched common input caused greater coherence across a broad range of frequencies. In contrast, common modulation at 24 Hz resulted in a single distinct peak at that frequency. Peaks at 24 Hz, however, only occurred reliably at the 90% level of common modulation.

**Coherence**

The presence of active dendritic conductances and inhibition influenced the peaks and magnitude of the pooled coherence. Increases in branched common input caused greater coherence across a broad range of frequencies. In contrast, common modulation at 24 Hz resulted in a single distinct peak at that frequency. Peaks at 24 Hz, however, only occurred reliably at the 90% level of common modulation.

**BrancHed COMMON INPUT.** In the branched common input models, there was an increase in coherence across a broad spectrum with 60 and 90% common input (Fig. 11). The passive model with no inhibition did not exhibit distinct peaks at 0 and 30% common input. At 60 and 90% common input, however, the coherence at 0–10 Hz was significantly lower ($P < 0.001$) than the rest of the frequencies. With the addition of 10% inhibition, the coherence from 5 to 10 Hz was significantly greater than any other frequency ($P < 0.001$) in the absence of common input. As the amount of common input increased, however, the peak at 5–10 Hz decreased, and at 60 and 90% common input, only the 0- to 5-Hz bin had significantly lower coherence than the other frequencies.

**Active dendritic conductances decreased the magnitude of the coherence between motor neurons.** The models with moderate conductances did not display any significant peaks at 0 or 30% common input levels. The model with moderate conductances had a small but significant peak at 35–40 Hz. The addition of inhibition resulted in a significant peak at 30 Hz and greater overall coherence at both 60 and 90% common input compared with the model that had no inhibition (Fig. 11, middle). Furthermore, the models with moderate active conductances in the dendrites also had significant amount of coherence at 0–5 Hz with 90% common input.

With no common input, the greatest coherence for the models with high densities of active dendritic conductances and no inhibitory input occurred at 0–5 Hz. However, as the amount of common input increased, the coherence at 0–5 Hz decreased, and a significant peak at 45 Hz developed progressively (Fig. 11, bottom). Inhibition attenuated the low-frequency coherence that occurred in the absence of common input as well as the peak at 45 Hz, which also became broader.

**M O D U L A T E D COMMON INPUT.** Modulation of 90% of the inputs at 24 Hz produced significant peaks ($P < 0.001$) in the coherence spectra for all conditions except the high conductance model with no inhibition (Fig. 12). The passive model with no inhibition had the highest coherence value at 90% common
modulation (0.14). Inhibition in the passive model modestly decreased the peak magnitude of the pooled coherence (0.12). The passive models with 60% common modulation also had significant peaks at 24 Hz, although they were lower. There were no significant peaks in the passive models with 0 and 30% common modulation.

As with branched common input, active dendritic conductances decreased the amount of coherence between motor neurons that were commonly modulated. However, inhibition increased coherence between model neurons with active dendritic conductances. In the model with moderate conductances and no inhibition, the peak at 24 Hz (0.002) was only significant at the 90% level of common modulation. With 10% inhibition, the peak at the 20- to 25-Hz bin was only significantly different from the 0- to 5-, 25- to 30-, and 40- to 45-Hz bins for 60% common modulation, and the coherence at 24 Hz (0.03) was significantly different from all other frequencies with 90% common modulation.

The high-conductance model without inhibition or common modulation had greater amounts of coherence between 60 and 65 Hz and below 5 Hz, but this did not reach statistical significance. There were no significant peaks with 30% common modulation. With 60% common modulation, however, the 65- to 70-Hz bin had significantly greater coherence than the 10- to 20- and 85- to 90-Hz bins (P < 0.046). With 90% common modulation, the peak at 24 Hz was not significant. The presence of inhibition in the high-conductance model resulted in a peak at the 35- to 40-Hz bin with 0 and 30% common modulation but not with 60% common input. Thus it appears that a sufficient amount of common modulation at 24 Hz negated the frequency contribution from 35 to 40 Hz due to the combination of inhibition and high levels of active dendritic conductances. The coherence at 24 Hz (0.005) was significantly greater than all other frequencies when 90% of the input was modulated in common.

Proportion of calcium conductances

The relative contribution of the different types of calcium conductances had a significant effect on the amount of synchronization between model neurons. There was an increase in the indexes of synchronization with increased densities of the N-type calcium conductance (Fig. 13A). This was paralleled by an increase in the CV for discharge with an increase in the N-type conductance (Fig. 13A). Although the mean discharge rate was modestly lower with an increased density of N-type conductances, this difference was not significant.

The increase in synchronization that occurred with the higher densities of the N-type conductance caused greater coherence across a broad spectrum (Fig. 13B). There was a significant peak between 25 and 40 Hz as well as greater coherence at 0–10 Hz compared with the coherence between...
10 and 25 Hz in the model with an N-type conductance density of 0.65 ms/cm². In contrast, the coherence was lower overall with a lower density of N-type calcium conductance (higher density of L type), and there were significant peaks at 30–50 Hz and 65–75 Hz in the model with N-type conductance density of 0.1 mS/cm².

**DISCUSSION**

The results from this study indicate that similar to previous reports (Binder and Powers 2001), the level of short-term synchronization between a pair of neurons was not linearly related to the amount of common input. In addition, the present findings suggest that active dendritic conductances and background inhibition have a significant influence on the amount of motor-unit synchronization and the coherence of motor neuron discharges. The CV for discharge rate covaried with all three indexes (CIS, E, and k') of motor-unit synchronization. Higher discharge rates and lower input resistances of the motor neurons were also associated with greater indexes of synchronization.

**Discharge patterns**

The mean and CV for discharge rate provide details about the organization of synaptic inputs onto the motor neuron (Calvin and Stevens 1968; Laidlaw et al. 2000; Matthews 1996). The mean and CV for discharge rate in the model neurons were generally within the range that is observed in human motor units. Similar to data from human motor units (Gydikov and Kosarov 1974), the low-threshold model neurons initially increased discharge rate at a faster rate but then reached a lower maximal discharge rate than high-threshold motor neurons. A previous simulation study found that differential distributions of input could produce rate-limiting effects on discharge rate (Heckman and Binder 1993). The results from the current study suggest that rate limiting can also be caused by the electrotonic properties of the neuron. Although a linear increase in discharge frequency with injected current at the soma has been observed (Kernell 1965), the model neurons exhibited rate limiting with synaptic input. As the level of synaptic input increased, the dendritic compartments of the model neurons were depolarized to the equilibrium potential for excitatory input (4.6 mV), which decreased the driving potential for the flow of synaptic current across the membrane.

The one exception to the similarity of discharge variability between the model and human data was for low-threshold neurons with dendritic active conductances. At low levels of synaptic input, the dendritic compartments of the model neurons were depolarized to the equilibrium potential for excitatory input (4.6 mV), which decreased the driving potential for the flow of synaptic current across the membrane. The mean and CV for discharge rate provide details about the organization of synaptic inputs onto the motor neuron (Calvin and Stevens 1968; Laidlaw et al. 2000; Matthews 1996). The mean and CV for discharge rate in the model neurons were generally within the range that is observed in human motor units. Similar to data from human motor units (Gydikov and Kosarov 1974), the low-threshold model neurons initially increased discharge rate at a faster rate but then reached a lower maximal discharge rate than high-threshold motor neurons. A previous simulation study found that differential distributions of input could produce rate-limiting effects on discharge rate (Heckman and Binder 1993). The results from the current study suggest that rate limiting can also be caused by the electrotonic properties of the neuron. Although a linear increase in discharge frequency with injected current at the soma has been observed (Kernell 1965), the model neurons exhibited rate limiting with synaptic input. As the level of synaptic input increased, the dendritic compartments of the model neurons were depolarized to the equilibrium potential for excitatory input (4.6 mV), which decreased the driving potential for the flow of synaptic current across the membrane.

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**FIG. 9.** The relation between synchronization indexes k' and CIS and level of excitation. The indexes of synchronization were significantly correlated with the level of excitation. The panels are arranged as in Fig. 8. The data in each plot represent the mean of all pairs of discharges across all levels of common input for each of the branched common input models. The data are plotted as means ± SEs.
than one that fluctuated substantially. Indeed, the variability of the somatic membrane voltage increased as the amount of synaptic input increased. The narrow range of discharge rates displayed by the low-threshold neurons is consistent with previous observations on stretch-induced discharge in motor neurons with dendritic active conductances (Lee et al. 2003). The presence of low levels of background inhibitory input actually increased the mean discharge rate of low-threshold motor neurons with active dendritic conductances. Others have reported a similar phenomenon in motor neurons with dendritic active conductances (Heckman et al. 2002). Inhibition may hyperpolarize the neuron, which somewhat decreases the amplitude of dendritic currents and allows synaptic input to have a larger effect on the discharge rate of the neuron. A higher discharge rate is possible with the addition of synaptic input because the amplitude of the persistent inward current is not equivalent to the maximal synaptic input current to the neuron. This mechanism was clearly demonstrated by the additional depolarization and increased variability of the somatic membrane potential in the presence of inhibitory input.

Motor-unit synchronization

The three indexes of synchronization were similarly related to the level of common input and increased at high excitation levels, presumably due to the higher discharge rates, as observed by Türker and Powers (2002). All of the indexes were significantly correlated with the CV for discharge rate, especially in the passive models and those with inhibition. Matthews (1996) suggested that heightened levels of synaptic noise would increase discharge variability and increase the probability that two neurons would respond to a simultaneous input. However, this was not corroborated by the current measurements of membrane variability as the presence of branched common input had only a minor influence on the SD of membrane voltage.

Active dendritic conductances. The presence of active dendritic conductances decreased motor-unit synchronization, which may have been due to the saturation of discharge rate of the neurons. Interestingly, the activation of dendritic conductances reduced the depolarization of the second dendritic compartment as shown in Table 2. The levels of depolarization in the second dendritic compartment reached 10 mV in some model neurons. Because it is not possible experimentally to measure dendritic membrane potential during synaptic activation, these model data cannot be compared with experimental data. However, the model predicts that one of the results of active dendritic conductances is to increase membrane conductance, which effectively shunts synaptic input current. This results in a lower sensitivity of the neuron to the timing of
synaptic inputs as indicated by the lower indexes of synchronization obtained in the presence of dendritic conductances.

Obviously, the translation of these model data to human observations depends on whether there are persistent inward currents present in the motor neurons that are monitored during motor unit experiments. Although the data from experimental animals suggest that active dendritic conductances are relatively ubiquitous in motor neurons, the results in the human literature have been mixed (Collins et al. 2002; Gorassini et al. 1998, 2002; Keen et al. 2002; Kiehn and Eken 1997; Zijdewind and Thomas 2001). This may be due to the difficulty in finding an unambiguous method of assessment or perhaps due to the focus on overt signs of large inward currents, such as self-sustained firing, despite the significance of dendritic active conductances for the input-output function of the neuron, such as rate modulation and synaptic amplification (Binder and Powers 1999; Heckman and Lee 1999; Lee and Heckman 2000; Lee et al. 2003; Prather et al. 2001).

Most human studies of plateau potentials have been performed on the tibialis anterior and triceps surae muscles because the activation of inward currents is mediated, at least in part, by serotonergic ion channels (Hounsgaard and Kiehn 1989), which are often found in neurons that innervate postural muscles. The literature on synchronization indicates that although many muscles show some level of discharge correlation, the amount of synchronization in postural muscles is typically weaker (Datta et al. 1991) than in muscles used for manual dexterity. These findings, in combination with the current results, suggest that one factor influencing variations in the level of synchronization may be the activation of dendritic conductances. However, it is possible that the effect of dendritic active conductances depends on the specific conductances that are contributing to the persistent inward current.

\( L \)-type calcium channels have slow gating kinetics and may tend to saturate the response of the cell. Conversely, \( N \)-type conductances have faster kinetics and may increase the likelihood that the neuron will respond to the timing of synaptic input. We evaluated the influence of different ratios of “fast” to “slow” calcium conductances while maintaining the same net density of dendritic calcium conductances. As predicted, an increase in the \( N \)-type (fast) conductance significantly increased the CV for discharge as well as indexes of synchronization.

**Inhibitory Input.** Voluntary contractions in human subjects involve inhibitory input from various sources. The findings from this study indicate that inhibition increases synchrony.
between motor neurons with active dendritic conductances. At high excitation levels, inhibition does not influence synchrony in neurons with passive dendrites, but in these neurons, inhibition can have a desynchronizing effect at low levels of excitation.

These results may explain the apparent discrepancy between previous modeling and experimental data. Maltenfort et al. (1998) used a model of Renshaw inhibition to show that the presence of inhibition in a pool of motor neurons had a decorrelating effect on neuronal discharge. In contrast, a recent human study showed that pharmacological enhancement of recurrent inhibition resulted in greater synchrony in a muscle that is known to have Renshaw cell input compared with a muscle that does not (Mattei et al. 2003). Our results for low excitation levels in passive models were similar to the findings of Maltenfort and colleagues, whereas our results for models with dendritic active conductances were more similar to the experimental findings of Mattei et al. Thus it is possible that the human data reflect the influence of both inhibitory inputs and active dendritic conductances.

**Modulated Common Input.** The rhythmic modulation of random input times at 24 Hz did not have a significant influence on the short-term synchronization of motor units. A frequency-domain analysis is often paired with a time-domain analysis to address patterns of neural connectivity. Previous studies have found correlations between time- and frequency-domain measures of synchronization (Farmer et al. 1993a; Kilner et al. 2002; Semmler et al. 2002). One inference from these relations is that the mechanisms responsible for frequency-domain synchrony also contribute to time-domain synchrony, especially in the 16- to 32-Hz range. However, the results from the current study suggest that the presence of correlation in the time domain cannot be induced by modulation of independent inputs when the amplitude of the modulation is 10% of the mean input rate.

**Motor neuron coherence**

The presence of coherence between the discharges of motor neurons is assumed to reflect oscillatory drive of the inputs to the motor neurons (Farmer 1998; Farmer et al. 1993a; Halliday 2000; Halliday and Rosenberg 2000; McAuley et al. 1997), with the peaks in the spectra reflecting the frequency of modulation. Similar to previous modeling results (Halliday 2000), our findings on motor neuron coherence suggest that the features of the coherence spectra with branched common input...
The coherence function. The novel modulation. The presence of active dendritic conductances also altered the coherence spectra for both branched common input and common modulation. The coherence spectra for the models with the highest N-type calcium conductance (0.65 mS/cm²; thick line) compared with the pooled coherence for the models with the lowest density (0.1 mS/cm²; thin line). Both spectra are for the condition with 90% branched common input.

BRANCHED COMMON INPUT. The pattern of coherence with branched common input involved a greater magnitude of coherence across a wide range of frequencies as the amount of common input increased. This was likely due to the convergence of discharge patterns with increases in common input. Therefore the frequency content would also have been similar; although the passive models had attenuated coherence at lower frequencies.

Dendritic conductances generated significant peaks in the coherence spectra, especially with greater levels of branched common input. The frequency of the peak at 60 and 90% common input increased from the 25- to 30-Hz bin to the 40- to 45-Hz bin between the moderate and high levels of active dendritic conductances, which may be attributable to a cycle in the dominant (inward or outward) dendritic current. Over time, the inward conductance causes a gradual membrane depolarization, which in turn increases the outward potassium conductance, eventually leading to a repolarization of the membrane. However, once the drive for the outward potassium conductance is decreased, the inward (calcium) conductances again gradually depolarize the membrane. This cycle between the balance of conductances across the membrane likely imparts a rhythmicity to the excitability, which is reflected as a dominant coherent frequency. As more inputs are delivered simultaneously to the pair to neurons, the overall coherence between the neurons increases and accentuates the peak due to the dynamics of the ionic conductances. Furthermore, a higher density of ionic conductances could increase the rate at which the balance of conductances is cycled, causing the increase in the dominant frequency for the high compared with moderate active dendritic conductance models.

It is notable that the peaks in the coherence spectra in the models with active conductances occurred within a range that has been observed in human motor-unit discharges (McAuley et al. 1997). Because cortical gamma oscillations are presumed to be involved in sensory binding and processing, frequency peaks around 40 Hz have been interpreted to reflect cortical rhythms (Brown 2000). However, the simulation data suggest that rhythms in this frequency band can also arise from the properties of the neurons themselves.

The effects of inhibition depended on the level of active dendritic conductances. With no common input, the models with passive dendrites and inhibition had low-amplitude significant peaks. However, the presence of background inhibition did not change the characteristics of the coherence spectra across different levels of common input. The effect of inhibition was different for moderate and high densities of dendritic conductances. Inhibition increased the coherence at the dominant frequency with moderate conductances, whereas the coherence at the dominant frequencies with high levels of dendritic active conductances was decreased by inhibition. Modeling work has shown that both intrinsic conductances and inhibitory circuits can produce oscillatory activity in populations of neurons (Falcke et al. 2000; Pauluis et al. 1999; Traub et al. 2001). Furthermore, a recent study in humans showed that cortical oscillations ~20 Hz are increased after a pharmacological intervention that increases the size of inhibitory postsynaptic currents in cortical neurons (Baker and Baker 2003). Our results suggest that phase-locked oscillatory activity is differentially influenced by both intrinsic conductances and inhibitory input.

COMMON MODULATION. Similar to the findings of Halliday (2000), large amounts of common modulation (≥60% with passive dendrites and 90% with dendritic active conductances) were necessary to produce distinct peaks at the modulated frequency. Despite the clear distinction between the coherence at the modulated frequency (24 Hz) and the other frequencies in the spectra, the magnitude of the coherence due to common modulation was always lower than the magnitude of the co-
herence due to branched common inputs. In addition, the peaks due to common modulation were much narrower than any of the coherence peaks in the branched input models.

As with the findings for branched common input, dendritic active conductances progressively decreased the magnitude and distinction of the peak at the modulated frequency. The findings for branched common input showed that dendritic active conductances probably caused oscillations in the discharge of the model neurons, which could have interfered with the frequency component due to the oscillating modulation of the inputs. The high-conductance model with no inhibition was the only model that did not exhibit a peak at the modulated frequency for any level of common modulation. Therefore when the magnitude of the inward dendritic current is large enough, coherence analysis appears to be insensitive to common modulation of the inputs to neurons.

Interestingly, the presence of inhibition in the passive model decreased the magnitude of coherence, whereas background inhibition increased the coherence between model neurons with active dendritic conductances. Inhibition decreased the magnitude of the inward current from the dendrites and thus enhanced the relative influence of the modulated frequency. In the passive model, inhibition did not have any beneficial effect in this sense because there were no other correlating influences.

The peak magnitudes of coherence in human studies are often in the range 0.2–0.4 (Farmer et al. 1993a; Halliday et al. 1999; Semmler et al. 2002). Although a direct comparison cannot be made, the coherence spectra for the simulations used in this study suggests that only very large amounts of common input (>90%) could produce these magnitudes of coherence. Furthermore, branched common input is more effective at producing this level of coherence than is modulated common input. One clear limitation of the current results is that multiple amplitudes of the oscillating modulation were not tested.

In conclusion, a source of common input is necessary to evoke correlated discharges by a pair of motor neurons. However, the amount of discharge correlation between the pair varies with the level of excitation, the presence of inhibitory input, and the presence of active dendritic conductances. Thus indexes of synchronization in neurologically healthy subjects may be better suited to monitor the level of active dendritic conductances and amount of inhibition that may be present during a task or in an individual subject. The mechanisms that lead to short-term synchronization likely do not include low-amplitude, common-rhythmic modulation of inputs. Coherence analysis has a different structure for branched common input compared with common modulation of randomly timed inputs. Broader peaks occur with branched input than with modulated inputs. Furthermore, the peaks in coherence spectra can also reflect the activation of dendritic conductances and are modified in the presence of background inhibition. Both time- and frequency-domain measures of discharge correlation will be differentially influenced by the pattern of common input and the interaction between the level of dendritic conductances and inhibitory input.

APPENDIX

The balance of current across the membrane was modeled as an equivalent circuit

$$I_m = C_m \frac{dV_m}{dt} + \sum g_i(V_m - E_i) + I_{app}$$

where the net current ($I_m$) was the sum of 1) the current required to charge the membrane capacitance ($C_m$) with a change in membrane potential ($V_m$), 2) individual ionic currents, which were the product of the ionic conductance ($g_i$) and the difference between the membrane and ionic reversal potential ($E_i$, for each ion k), and 3) any external current ($I_{app}$). In addition, each ionic conductance was modeled as

$$g_{Na} = \tilde{g}_{Na} m^h(V_m - E_{Na})$$
$$g_{Ks} = \tilde{g}_{Ks} q^p(V_m - E_{Ks})$$
$$g_{CaL} = \tilde{g}_{CaL} m^r(V_m - E_{CaL})$$
$$g_{CaN} = \tilde{g}_{CaN} n^s(V_m - E_{CaN})$$

where $\tilde{g}$ is the maximal conductance for an ion k, and the exponential terms are the state variables, which represent the kinetics of activation and inactivation of the ionic conductances (Hodgkin and Huxley 1952). The values for $\tilde{g}_{Na}$ and $\tilde{g}_{Ks}$ were initially based on those used by Jones and Bawa (1997). These values were then adjusted and balanced with $g_{Na}$ and $g_{Ks}$ to produce action potentials with an appropriate threshold, amplitude, and time course. The somatic conductances were adjusted so that there was a higher threshold for discharge at the soma than at the initial segment. The dendritic conductances ($g_{CaL}$, $g_{CaN}$, and $g_{Ks-Ca}$) were tested with a sensitivity analysis to find those conductances that would evoke a similar amplitude of inward current in motor neuron 1 with moderate dendritic conductances and motor neuron 120 with high levels of active den-

<table>
<thead>
<tr>
<th>Ionic Conductance</th>
<th>State Variable</th>
<th>$V$, mV</th>
<th>$s$, mV</th>
<th>$\tau$, ms</th>
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<tbody>
<tr>
<td>Na</td>
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<td>0.09</td>
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<tr>
<td>Na</td>
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<td>30/[15]</td>
</tr>
<tr>
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<td>Ca</td>
<td>$f$</td>
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</tr>
</tbody>
</table>

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dritic conductances and have an offset threshold that was more depolarized than −70 mV.

The steady state for each of the state variables ($v$) depends on membrane potential ($V_{m}$) and has the form (Booth et al. 1997; Powers 1993)

\[ v = \frac{1}{1 + \exp(V_{m} - X)/\delta} \]

where $X$ is the voltage at half-activation (inactivation) and $\delta$ defines the sensitivity of the change in conductance with voltage. The values of $X$ and $\delta$ and the time constants ($\tau_v$) for activation and inactivation were based on those used in previously published models (Booth et al. 1997; Carlin et al. 2000; Jones and Bawa 1997; Powers 1993; Traub 1977) and adjusted to produce reasonable behavior in the model (Table A1).

This form for describing the gating kinetics of ion channels relates to the Hodgkin-Huxley activation ($\alpha$) and inactivation ($\beta$) rate constants as

\[ v_0 = \frac{\alpha}{\alpha + \beta} \]
\[ \tau_v = \frac{1}{\alpha + \beta} \]

The potassium conductance ($g_{k-cs}$) was determined solely by the concentration of calcium in the second dendrite compartment due to activation of the two calcium conductances. Therefore it was implicitly related to voltage

\[ g_{k-cs} = g_{k-cs} \left[ \frac{[Ca^{2+}]}{[Ca^{2+}]} \right] + K \]

where $[Ca^{2+}]$ is the intracellular calcium concentration, and $K$ is the concentration at half-activation, with a value of 350 nM. The change in intracellular calcium with time was

\[ \frac{d[Ca^{2+}]}{dt} = B_{cis} - \frac{[Ca^{2+}]}{\tau} \]

where $B$, which is a constant that converts the calcium current ($I_{Ca}$) to a concentration, was 8.68 mol C$^{-1}$ m$^{-3}$. The constant $B$ describes the rate of ion flux resulting from $I_{Ca}$ per unit volume. The decay in calcium concentration over time is governed by the time constant of decay ($\tau_v$), which was 50 ms.

The synaptic conductances were modeled as dual-exponential functions (Rall 1967)

\[ g_{syn} = \frac{g_{max}}{\tau_1 - \tau_2} (e^{-t/\tau_1} - e^{-t/\tau_2}) \]

where the synaptic conductance ($g_{syn}$) rose to a maximum value of $g_{max}$ with a rising time constant $\tau_1$ and time constant for decay given by $\tau_2$.

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REFERENCES


