

# Common Synaptic Input to Motor Neurons, Motor Unit Synchronization, and Force Control

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FARINA, D. and NEGRO, F. Common synaptic input to motor neurons, motor unit synchronization, and force control. *Exerc. Sport Sci. Rev.*, Vol. 43, No. 1, pp. 23–33, 2015. In considering the role of common synaptic input to motor neurons in force control, we hypothesize that the effective neural drive to muscle replicates the common input and is, thus, the main determinant of force production. Such a perspective argues against a significant role for motor unit synchronization in force control. **Key Words:** neural drive to muscle, motor unit, motor neuron, synaptic input, force control, synchronization

## INTRODUCTION

Despite the fact that the general neural mechanisms for muscle force generation are well known, several details on the way in which motor neurons transform synaptic input into a neural command signal to the muscles are less understood. One of the reasons for this limited knowledge is that our only window into the behavior of motor neurons *in vivo* in humans is very narrow. This consists of the analysis of motor neuron behavior by motor unit recordings, obtained from the innervated muscles (1). However, classic experimental methods allow for the analysis of only a few motor units concurrently, out of the hundreds of active units during a movement. This narrow view made it difficult to understand the relations between some of the characteristics of motor neuron behavior and the generated force.

In this focused review, we report the conclusions recently drawn from a series of studies that used a combination of theoretical analyses, computational modeling, and advanced techniques for investigating the activity of several concurrently active motor units. These studies mainly addressed the

transformation of synaptic input by the pool of motor neurons and the role of common synaptic input to motor neurons for force control. The detailed description of the role of common input to motor neurons for force generation also implies a re-examination of the classic concept of motor unit synchronization.

The approach we will follow is to extend the classic view in studying common input to motor neurons by defining a concept of motor unit synchronization for the entire motor neuron pool. In doing so, an extended view of the neural determinants of muscle force will emerge. Figure 1A represents the way in which motor unit synchronization usually is explained in relation to common synaptic input to motor neurons. In this view, a pair of motor neurons receive a proportion of common synaptic input and a proportion of independent input. Because of this source of common input, the trains of discharge timings of the two motor neurons are correlated, and the strength of this correlation is termed *motor unit short-term synchronization*. Accordingly, motor unit synchronization usually is measured from pairs of motor unit discharges by applying correlation analysis in the time or frequency domains (28). The values for synchronization obtained by this approach are relatively small, which is interpreted commonly as an indicator of a small proportion of common input to the motor neuron pair. We extend this view to the full motor neuron pool, as in the right panel of Figure 1, by conceptualizing a common synaptic input to all motor neurons, in a similar way as described by De Luca and Erim (5), as well as independent inputs to each motor neuron. It is worth noting here that the presence of a common and an independent input to the entire motor neuron pool is a simplified model. In this simplification, the common synaptic input has to be

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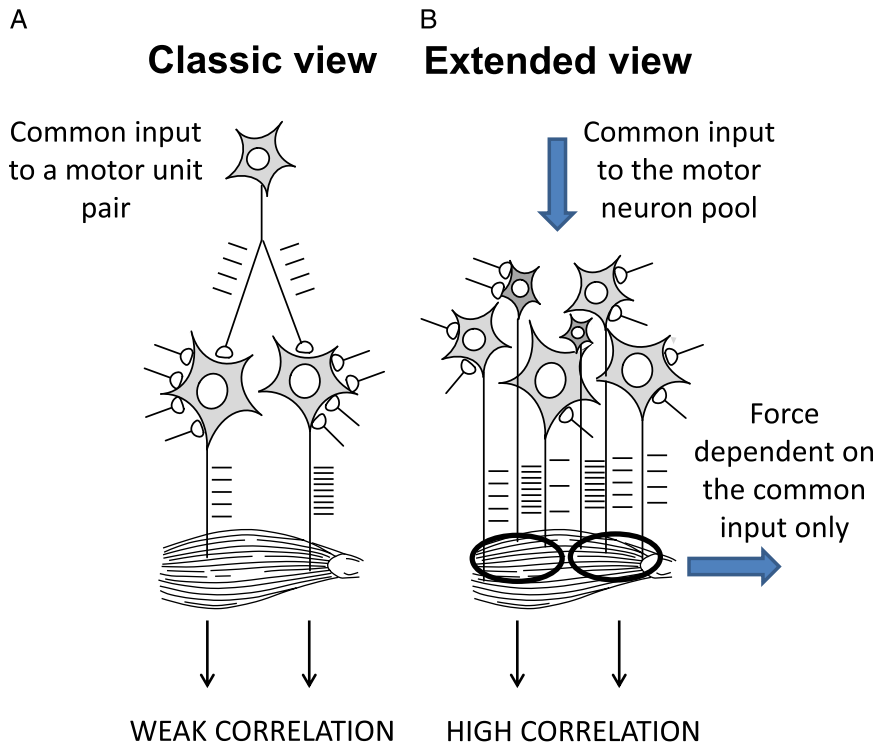
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**Figure 1.** A. The classic view of representing and quantifying correlation between motor neuron activities considers pairs of neurons that receive a proportion of common input and independent inputs. Because of the common input, their output trains of discharge times are partly correlated. The correlation levels usually are found to be small, especially when the full bandwidth is considered (motor unit synchronization). B. We extend the classic view by conceptualizing a common input to the entire motor neuron pool, as also proposed by De Luca and Erim (5). We expand this concept by determining its profound consequences. Specifically, we prove the hypothesis that such largely spread common input is actually the *only* relevant input for the determination of the neural drive to muscle and for force control. This result has consequences on the validity and functional significance of the classic correlation analysis of the output trains of discharge times of pairs of motor units, as in the classic view. One fundamental consequence of the presence of a shared common input to the pool of motor neurons that strongly affects the classic view is that the correlation between merged discharge timings of motor units increases for increasing number of units. This is a reflection of the fact that the merged discharged timings of all motor units (neural drive to the muscle) approximate very accurately the common input.

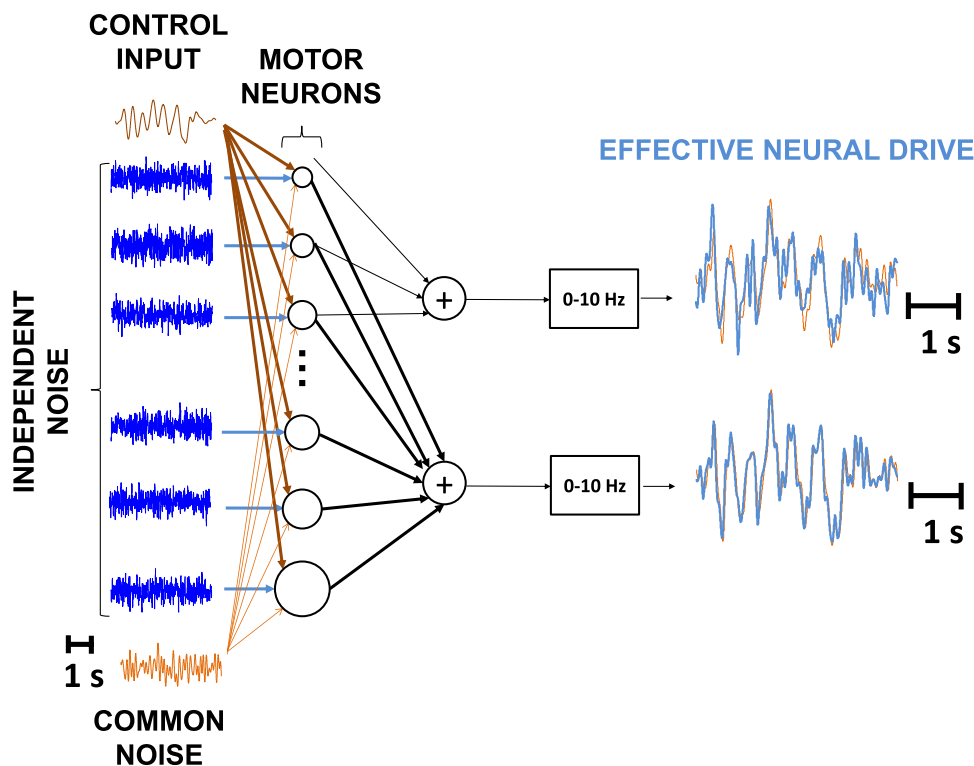
interpreted as the portion of the sum of inhibitory and excitatory inputs to each motor neuron that results in the same net input to all motor neurons, beside a potential scale factor. A similar interpretation holds for the independent input. In this review, we analyze the extended view presented in Figure 1B. With respect to the concept of common drive as correlated activity of motor unit pairs for low frequencies (5), we further analyze the consequences of the presence of common input to the motor neuron pool by discussing the hypothesis that the generated muscle force depends exclusively on this type of input. The demonstration of this hypothesis has consequences on the methods used for the study of correlated activity among motor neurons, such as the analysis of synchronization or of common drive, as performed classically from pairs of motor units.

The conceptual representation in Figure 1B can be represented with the block diagram of Figure 2. The pool of motor neurons receives independent inputs as well as common inputs — inputs that are the same for all neurons — to generate the neural drive to the muscle, that is, the cumulative train of discharge times of the active motor neurons. The common input comprises components needed for force control (control input) and noise components (common noise) that determine oscillations of the neural drive to muscles around the target level. In this figure and in the remainder of the review, we focus on synaptic inputs in the frequency bandwidth below

the average discharge rate of the motor neurons, which approximately corresponds to the frequency bandwidth of the generated force. Under this assumption, we postulate that the motor neuron pool is designed as an extremely effective *linear* filter that cancels the independent components and transmits, approximately unaltered, the common input components of the neural signal for muscle control, as in Figure 2. Because force control depends *only* on these common input components and not on the independent noise, the classic notion of synchronization (17), and in general of the strength of correlation between motor unit discharges, requires a reexamination. In Figure 2, we further introduce the concept of effective neural drive to the muscle, with a similar meaning as in Farina *et al.* (12) and Negro *et al.* (20), to indicate the neural drive to the muscle in the bandwidth relevant for force generation (<10 Hz). The analysis of Figure 2 that will follow provides an extended view on the way motor neurons integrate their inputs and on the meaning of correlations between the discharge timings of motor neurons.

## LINEARITY OF THE MOTOR NEURON POOL

In this section, we will analyze the linearity property of individual motor neurons and of the pool of motor neurons.



**Figure 2.** Generation of the effective neural drive to the muscle. A pool of 112 simulated motor neurons receives three sources of input. The control input (37% of the variance of the total synaptic input in this example; bandwidth, 0–4 Hz) is common to all motor neurons and is the input used by the central nervous system for force control. The control input is superimposed by a common noise (13% of the variance of the total synaptic input; bandwidth, 0–10 Hz), also distributed to all motor neurons. In addition, each motor neuron also receives an input that is independent from that of the other motor neurons (independent noise) (50% of the variance of the total synaptic input; bandwidth, 0–50 Hz). The pool of motor neurons processes the three inputs. In this figure, the motor neurons are simulated as compartment systems according to a described model (4,22). The cumulative train of discharge times of three (upper trace) and 112 (full population, lower trace) motor neurons is shown in the effective bandwidth for force generation (0–10 Hz; effective neural drive to the muscle) in the two cases (blue traces) as compared with the sum of the control input and common noise (total common input; red traces). The pool of motor neurons filters the independent noise so that the neural drive to the muscle exactly corresponds to the total common synaptic input that the motor neurons receive.

For this analysis, we will not consider the independent synaptic inputs to motor neurons, shown in Figure 2, but only the common inputs. Independent input components will be discussed in the next section. A system is linear if the sum of two inputs, each scaled by a constant factor, determines the same output as the sum of the outputs determined by the two inputs separately, scaled by the same factors. An important property of linear (and time-invariant) systems is that a sinusoidal oscillation fed to the system is undistorted at the system output, that is, the response of the system to a sinusoid is a pure sinusoid at the same frequency, without addition of components at other frequencies.

Motor neurons receive synaptic input from afferents and presynaptic neurons and supraspinal centers. Their action can be assimilated well to an integration of the net synaptic input and a discharge of an action potential when the integrated input surpasses an excitation threshold. This operating principle is a sampling process: the time interval between a motor neuron discharge and the preceding one is associated with the strength of the synaptic input in that interval of time. The sampling is rather slow for individual motor neurons, which *in vivo* in humans discharge at rates of up to only 30 to 40 pulses per second (pps) for most muscles (15). As for any sampling process, the sampled input signal is represented accurately if the sampling rate — the discharge rate for motor neurons — is

sufficiently large with respect to the frequency bandwidth of the input signal (18). A single motor neuron usually undersamples its synaptic input because of its low operating discharge rate (22). Therefore, the information contained in the synaptic input to individual motor neurons is distorted when transformed in the output train of action potentials. For example, a cortical oscillatory input at 20 Hz to a motor neuron determines an output train of action potentials whose discharge rate is not exactly modulated at 20 Hz but contains other components (2). This distortion of the input information can be viewed as caused by undersampling — and therefore, it is stronger for high than lower input frequencies — or, equivalently, to the nonlinear nature of motor neurons caused by their threshold-based discharges. The fact that a motor neuron is a nonlinear system can be explained by a simple example. Two synaptic currents fed to the soma of a motor neuron separately may not determine discharges if each of them is below the activation threshold. Nonetheless, the sum of the two synaptic currents may cause the motor neuron to generate action potentials because it may pass the threshold. The two inputs separately determine two null outputs, thus, the sum of the two outputs is still null contrary to the output determined by the sum of the two inputs.

For a control system, distortion of the command inputs because of nonlinearity usually is detrimental. For a nonlinear

system, the sum of two sources of input will not result in the same output signal as the sum of the outputs to each input separately. For example, in a single motor neuron, which is nonlinear, the convergence of descending drive and afferent input determines an output spike train that cannot be predicted by knowing the response to the two inputs separately. Interestingly, the neuromuscular system copes with the distortion and nonlinearity of individual motor neurons in a simple and effective way (22).

The distortion introduced by the nonlinearity of the individual motor neurons can be represented by an additive noise term. The output of each motor neuron therefore comprises the sum of a component linearly related to the input and additional nonlinear components. Therefore, if the *same* input — common input — is shared across several motor neurons, all the output trains of action potentials will contain the same information about the common input — the linear part of the output. Moreover, under the physiological condition that motor neurons in the pool have different intrinsic properties, each train additionally will contain an *independent* distortion component not caused by an input signal but generated by the nonlinearity of motor neurons. The muscle receives a neural signal from the motor neuron pool that can be assimilated to the cumulative train of action potentials of the active motor neurons, and which we refer to as the *neural drive to the muscle*. The neural drive is a sum (or average) of all output trains of discharge times, so that the common input components (present in all discharge trains) are enhanced with respect to the distortion components (different for each train). Although the individual motor neurons distort the input signal they receive (Fig. 3A), a pool of many motor neurons (population processing) provides as output an accurate representation of the common inputs (2,12,13,21) (Fig. 3B).

Figure 3B shows the properties of a pool of motor neurons when transmitting the sum of two common inputs and an independent input with respect to the properties of an individual motor neuron (Fig. 3A). The system made by the pool of motor neurons transform the input  $I_1$  into the output  $O_1$  and  $I_2$  into  $O_2$  when they are applied separately. When the sum  $I_T$  of  $I_1$  and  $I_2$  is applied to the system, it is transformed into  $O_T$ , which corresponds to the sum of the two outputs when the inputs are applied separately. This linearity property, which does not hold for individual motor neurons (Fig. 3A), is well approximated by the pool of motor neurons (Fig. 3B).

The approximated linearity of the motor neuron pool explains why it is possible to investigate neural connectivity between muscles or between supraspinal areas and muscles with linear techniques, that is, correlation methods (11,12,22,24). Finally, we should note that, because an effective cancellation of the distortion components requires the sum of the activity of a sufficient number of motor neurons, there is a force threshold below which the generation of the neural drive is nonlinear. This force threshold depends on the recruitment strategy of the muscle as well as on the frequency bandwidth in which the neural drive is analyzed (6,20). For frequencies of the neural drive that corresponds to force generation (<10 Hz), the force threshold may be extremely small (few percent of the maximal force) because low

frequencies of the synaptic input are sampled accurately at relatively low sampling rates.

## THE MOTOR NEURON POOL AS A FILTER TUNED ON COMMON INPUT

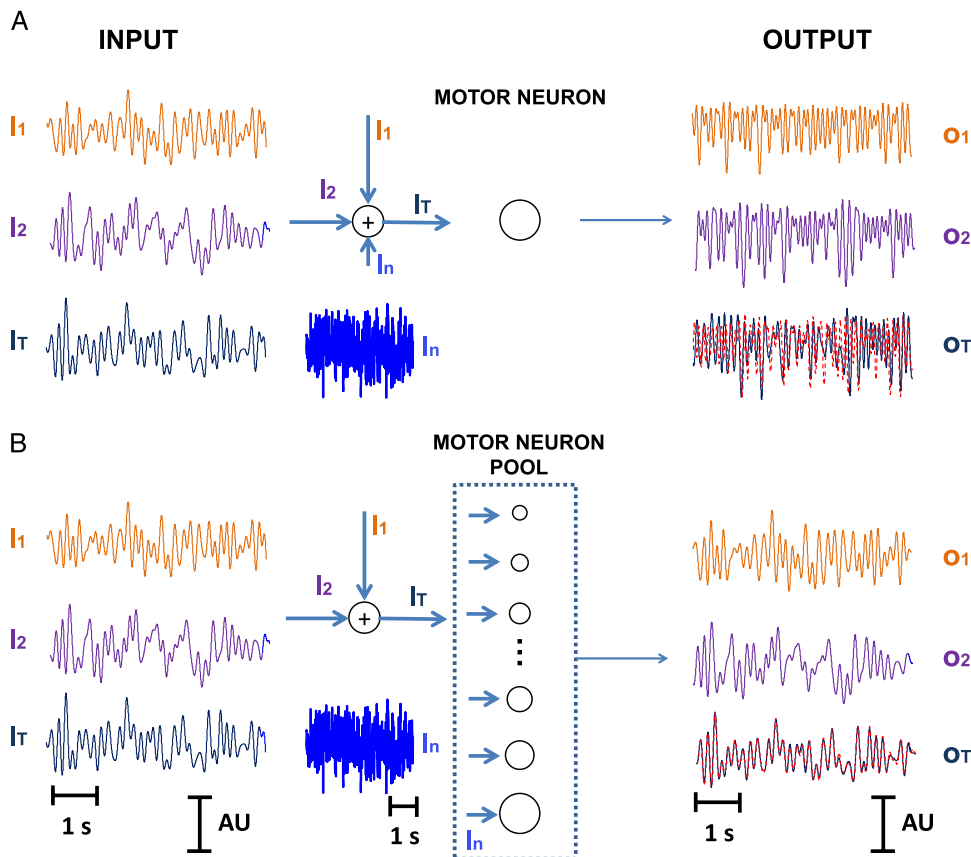
The spread of common input to several motor neurons determines the linearity of the motor neuron pool for the generation of the neural drive to the muscle (Fig. 3). However, the averaging process occurring when generating the neural drive to muscles acts not only on the distortion components, but also on any source of synaptic input that is independent, for each motor neuron. Thus, the motor neuron pool not only acts as a linear system but also as a very selective filter that eliminates the synaptic input components that are not common to all motor neurons (9,12). With careful analysis of Figure 3B, it indeed can be noted that the output to each common input almost exactly reproduces the common input itself, despite the presence of an independent input. This requires again a sufficient number of active motor neurons (Fig. 2) that depends on the relative amount of independent versus common input (20) (see section on Motor Unit Synchronization). Above this threshold of active motor neurons, the motor neuron pool transfers the common synaptic input to the output with high accuracy and cancels all other input components.

The observation that the neural drive to the muscle is the common synaptic input to motor neurons because independent components are filtered out has consequences relevant for the concept of correlated motor unit activity (24,27) as well as for force control. The main observation in this respect is that any control signal necessarily has to be *common* to the motor neuron pool (or to a sufficient number of motor neurons if the muscle is compartmentalized) to effectively regulate force.

## MOTOR UNIT SYNCHRONIZATION

The observation that discharges of pairs of motor units are not independent but show a degree of correlation has led to the introduction of the concept of motor unit (short-term) synchronization (27) (Fig. 1A). Synchronization is quantified classically by time or frequency domain linear methods of correlation, for example, cross histogram of a pair of motor unit discharge times. The concept of motor unit synchronization has been associated with a deliberate strategy of neuromuscular activation with specific functional roles (28). For example, it has been speculated that motor unit synchronization may increase the rate of force development during rapid contractions (28).

It is relevant to note that the classic concept of motor unit synchronization, as well as that of common drive, is associated with the trains of discharge times of motor units, that is, to the motor neuron outputs and *not* to the synaptic inputs to motor neurons. This perspective is not fully appropriate because it does not relate motor unit synchronization to a causal physiological mechanism directly but rather to the final effect of this mechanism. In this perspective, we should ask the



**Figure 3.** Nonlinearity of individual motor neurons versus linearity of the motor neuron pool. A. A motor neuron, simulated with the same compartment model used in Figure 2, receives two generic sources of input ( $I_1$  and  $I_2$ ; bandwidth, 0–10 Hz) and a third source of input of larger bandwidth ( $I_n$ ; bandwidth, 0–50 Hz). The result of the processing of these inputs by the motor neuron is shown in the effective bandwidth for force generation (as in Fig. 2). The outputs  $O_1$  and  $O_2$  are the outputs of the motor neuron when it receives the input  $I_1$  or  $I_2$  separately, respectively. The output  $O_T$  (blue line) is the output of the motor neuron when it receives the sum of the two inputs  $I_1 + I_2$ . This output is compared with the sum of the outputs  $O_1$  and  $O_2$  (dashed red line) obtained when receiving the two inputs separately. There is a large difference between the sum of the responses of the system to the two inputs separately and the response of the system to the sum of the two inputs. This indicates the nonlinearity of the individual motor neuron. Moreover, the input  $I_n$  also is transmitted to the output.  $I_1$  and  $I_2$  can be seen as two sources of synaptic input for force control (e.g., supraspinal and afferent) and  $I_n$  as synaptic noise because of the excitatory and inhibitory inputs at the thousands of synaptic connections to the motor neuron. In this case, the transmission of the common input is distorted (nonlinear) and noisy. B. The same situation as in (A) is now shown by substituting a single motor neuron with a pool of 112 active motor neurons as the transmission system. All the inputs are the same and the system output is shown, as for the case in (A). The inputs  $I_1$  and  $I_2$  are now common inputs distributed to the entire motor neuron pool whereas  $I_n$ , representing synaptic noise, is an independent component, different for each motor neuron. When using a large population of motor neurons as a transmission system, the sum of the outputs  $O_1$  and  $O_2$ , obtained when processing the two common inputs  $I_1$  and  $I_2$  separately, exactly corresponds to the response of the system to the sum of the two inputs  $I_1 + I_2$ . The system, thus, acts linearly, that is, it acts on individual components of input in the same way as they are processed when they are applied to the system in combination with other inputs. Moreover, with the pool of motor neurons, the independent noise  $I_n$  is completely canceled out. Contrary to the individual motor neuron, which acts nonlinearly and noisy, the pool of motor neurons is a system that linearly reproduces the sources of common input and attenuates all sources of independent input. AU indicates arbitrary units.

question on which physiological or anatomical properties are revealed from the correlation between motor unit trains of discharge times. This question is best addressed by considerations derived from the previous discussion on the types of input to motor neurons and their effect on the neural drive to muscles.

We should first notice that motor neurons *must* receive common input for force control to be possible, as previously discussed. Indeed, inputs that are not distributed to the full pool of motor neurons commonly (or to a compartment) are cancelled out effectively by the averaging process that leads to the generation of the neural drive to the muscle and therefore do not have an effect on force control. Force control can only be achieved by those motor neurons that receive a common input (experimental evidence indicate that these motor neurons are the entire pool) by means of that common input.

This observation implies that trains of discharge times of motor units *cannot be* independent; if they were, force could not be modulated by the central nervous system. Synchronization, as correlation between motor unit action potential trains, is therefore *necessarily* present, independently of any potential functional role it may have.

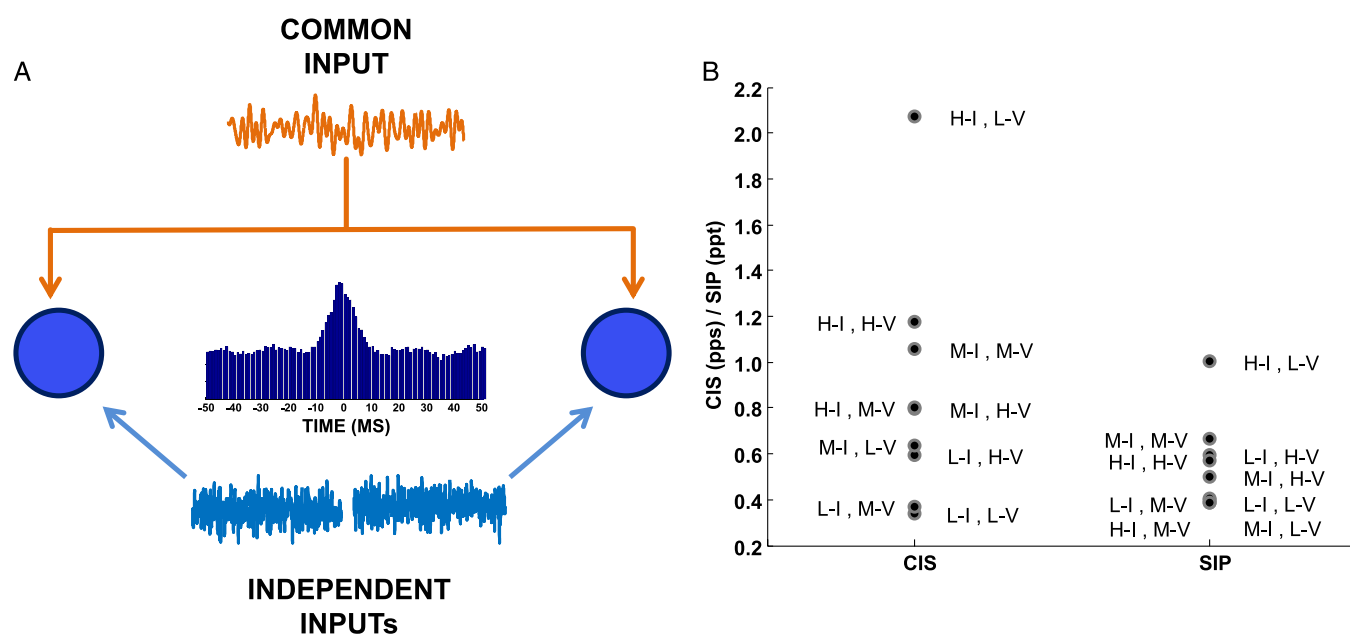
Another relevant concept when discussing motor unit synchronization is that the correlation between two trains of motor unit discharges, classically used for quantifying synchronization, is associated poorly with the correlation between the synaptic inputs of the two corresponding motor neurons (25,29). This is caused by the nonlinearity previously described that distorts the two inputs when transferred to the output trains of action potentials. Indeed, it is the pool of motor neurons that is approximately linear but not the individual



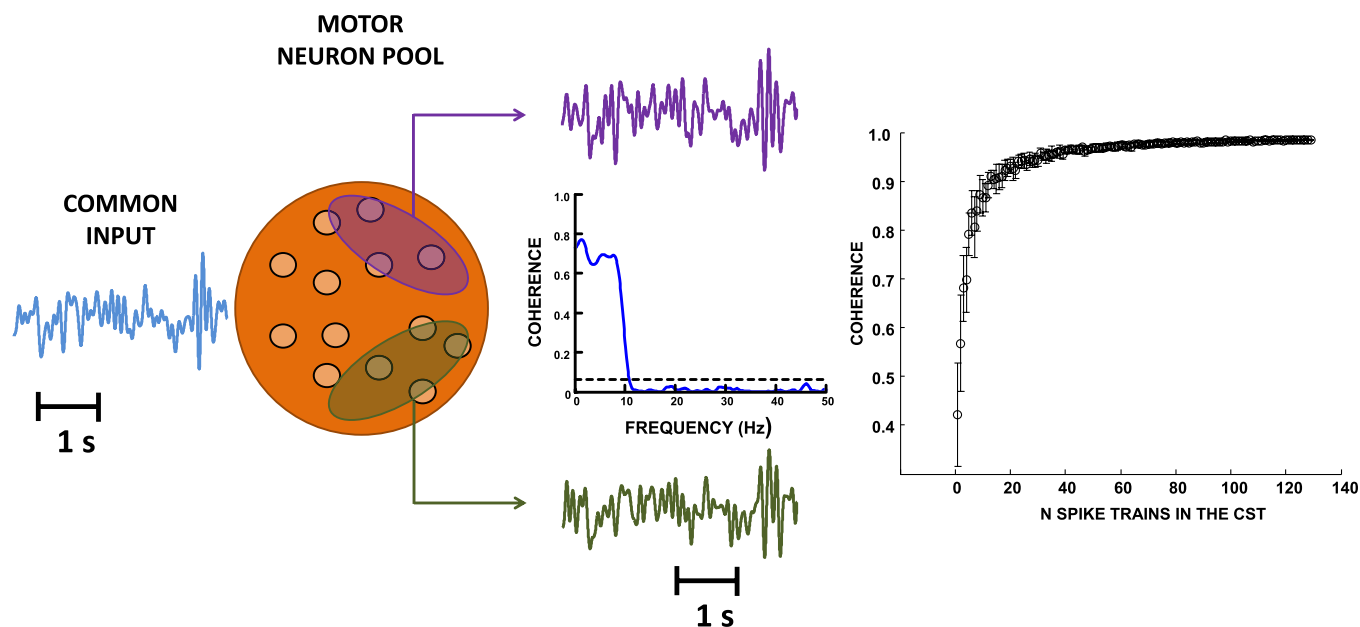
motor neurons (Fig. 3). For this reason, even if the two inputs would be identical, the trains of discharges generated by two different motor neurons would not be correlated perfectly. This conclusion explains the relatively low experimental values observed for synchronization between motor unit pairs. It has been long noted for correlated trains of action potentials of cortical neurons that the correlation of synaptic inputs and the correlation of the generated action potential trains for two neurons are associated in a complex manner that depends on the discharge rates and on intrinsic properties of the motor neurons (25,29). This is the reason why, for example, motor unit synchronization has been observed experimentally to depend on discharge rate (26). This experimental observation cannot be associated with a specific change in the strength of common input to the two motor neurons because the observation also is compatible with an unchanged common input. For example, Figure 4 represents simulations with two motor neurons that receive common and independent inputs in the same relative proportion. Despite in all cases the ratio between the strength of the two inputs is the same (40%), the total input (sum of the two inputs) was varied by changing its mean value across three levels (L, 4 nA; M, 6 nA; H, 8 nA) as well as its standard deviation (L, 0.5 nA; M, 1 nA; H, 1.5 nA). The changes in total input properties (but not in the relative contribution of the common input that remained 40% of the total input in all conditions) determined a large variability in classic indexes for the estimation of synchronization between pairs of motor units. For example, common input strength (CIS)

ranged between less than 0.4 pps and more than 2 pps across the simulated conditions even if the relative strength of common input was unchanged. It is worth noting here that the variability in synchronization indexes shown in Figure 4 is caused by factors other than the relative strength of common input, for example, to the mean value of the total input; therefore, observations of differences in these indexes among subject groups (28) do not have the only possible explanation of a functional role of synchronization.

Synchronization is a population concept and can be inferred poorly from the analysis of pairs of neurons (21). When studying the population of motor neurons, one should consider that the neural drive to the muscle comprises only the common input components to the motor neurons. For example, if instead of using pairs of motor units for correlation analysis, we merge the discharge times of groups of motor units (so-called *cumulative discharge timings*), the correlation level monotonically increases with the number of units (21). In this view, for a certain number of motor units, the correlation approximates the maximum value of 1 because the oscillatory components of the cumulative discharge times of any sufficiently large number of units tend to be the same irrespective of the group of units and to be equal to the common input that the motor neurons receive. This concept is represented in Figure 5, where a common input is distributed to a motor neuron pool and the output of two sets of motor neurons is compared. When the number of motor neurons in each set increases, the oscillations in the output



**Figure 4.** Quantification of motor unit short-term synchronization by analysis of the cross histogram of a pair of motor neurons. A. Two motor neurons receive a proportion of common input and independent input. The motor neurons are simulated with a compartment model, as in the previous figures. The ratio between the power of the common input and that of the independent input is fixed for all the simulations. However, the properties of the total synaptic input to the two motor neurons (mean value and variance) are changed across three levels (high, medium, and low) within a physiological range. A cross histogram is computed from the discharge times of the two motor neurons and used to estimate the common input strength (CIS) and the synchronous impulse probability (SIP), which are indexes commonly used for quantifying the strength of motor unit synchronization. B. For both CIS and SIP, the values obtained by varying the motor neuron properties are reported. Despite that in all cases the relative strength of common input is the same, the estimates of CIS vary between approximately 0.3 and approximately 2 pps (pulses per second) and the estimates of SIP between approximately 0.4 and approximately 1 ppt (pulses per trigger). H-I indicates high input; M-I, medium input; L-I, low input; H-V, high variance; M-V, medium variance; L-V, low variance. Note that, in all conditions, the ratio between common and independent inputs is the same.



**Figure 5.** Any set of motor neurons sufficiently large enough generates the same cumulative output in the effective bandwidth. A pool of 120 simulated motor neurons receive a common input (bandwidth, 0–10 Hz) and independent inputs (not shown; bandwidth, 0–50 Hz) (power ratio, 50%). The outputs in the bandwidth 0 to 10 Hz of two sets of four motor neurons each are shown. The coherence functions between the two outputs also are shown, demonstrating that, in the signal bandwidth used for these simulations, the outputs of the two sets of motor neurons are similar. The peak of the coherence between the outputs of two sets of motor neurons is represented in the graph on the right as a function of the number of motor neurons in each set. The standard deviation bars indicate the variability obtained by randomly choosing any two separate sets with the given number of motor neurons. The coherence tends to 1 for increasing number of motor neurons and is above 0.9 when less than 20 motor neurons are used. The curve can be seen as an estimate of synchronization between cumulative trains of discharge times of an increasing number of motor units. Rather than the individual values, the rate of increase and saturation (reaching the level 1) of this curve depends on the ratio between the common and independent input. CST indicates cumulative spike train.

cumulative trains of discharge times of the two sets become similar to each other and, as a consequence, their coherence tends to 1.

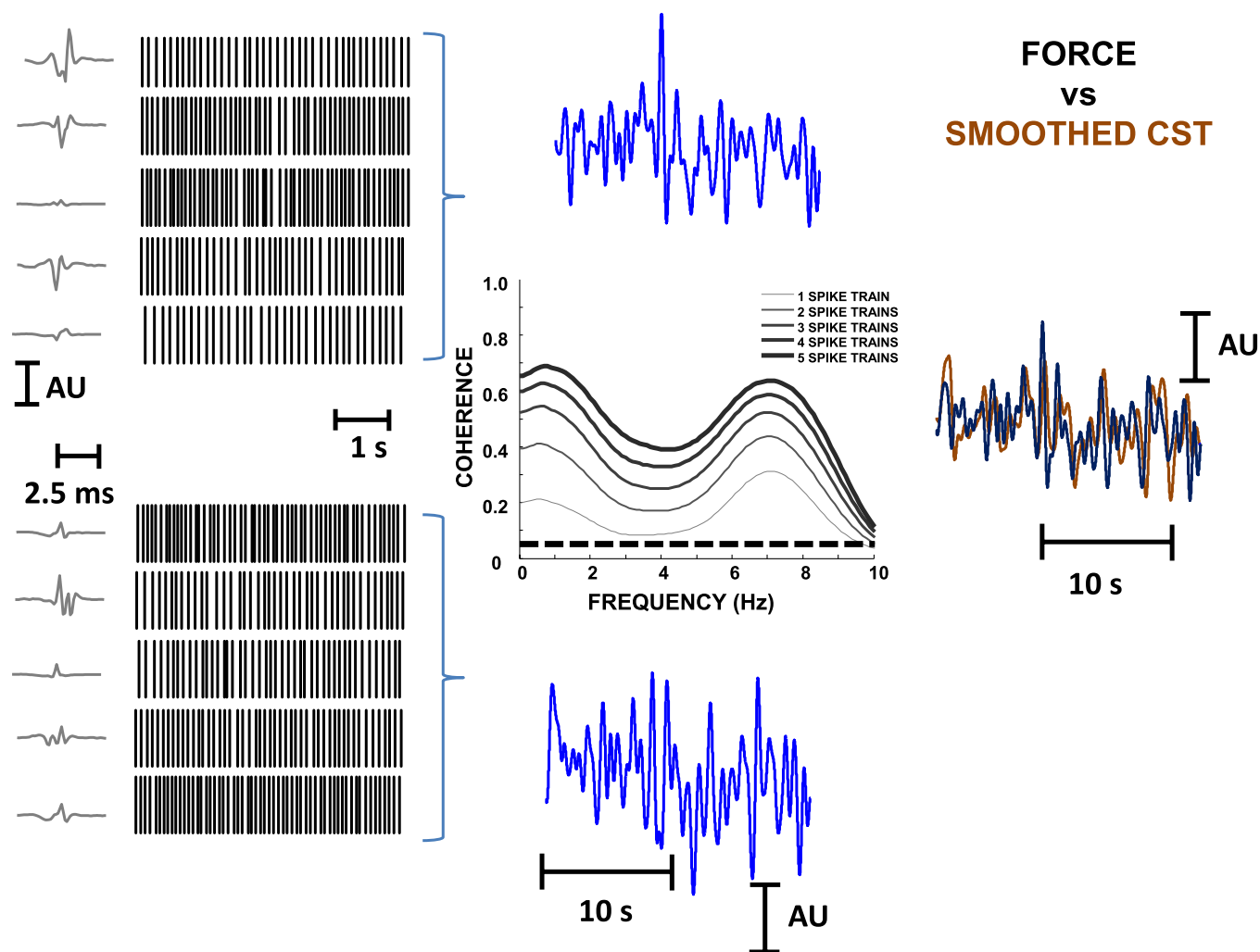
At the population level, it is possible to quantify the relative power of the common input to a pool of motor neurons, with respect to the independent input (23). The estimation is based on the observation that the rate of increase of the coherence function representatively shown in Figure 5 depends on the relative power of the common input (12,21,23). By fitting the coherence values versus number of motor units in Figure 5, it is possible to estimate the relative ratio between common and independent input power, which we propose as a more valid measure of synchronization and in general of correlated input to a population of motor neurons (23). Functionally, this ratio is related to the number of motor neurons that need to be recruited for the independent input to be canceled out completely in the neural drive to the muscle, that is, number of motor neurons needed to reach approximately the plateau value in the coherence values of Figure 5.

## FORCE CONTROL

The synaptic input to motor neurons comprises independent input, a common input that determines the exact command for optimal force generation, and oscillations in the common input that determines common noise in the generation of the neural drive (Fig. 2). The independent component is filtered efficiently by the specific way in which the neural drive is generated, as previously discussed, whereas the

other two components of synaptic input both are transmitted to the output of the motor neurons and both influence the force output. We separate conceptually these two parts of common input to introduce the concept of common noise that is responsible for limitations in force tracking accuracy. These common input oscillations can be estimated experimentally from motor unit discharge trains and can be related to force variability (10,20).

Force is generated by the filtering the neural drive to the muscle with the average twitch force of the active motor units. This filter eliminates the contribution of oscillations above 10 to 12 Hz (3), so that, according to the previous discussion, the force signal corresponds to the low-frequency portion of the common synaptic input to motor neurons. The direct association between force and common synaptic input to motor neurons can be experimentally verified by the high similarity between the smoothed cumulative discharge rate of a group of active motor neurons and the generated force (20). Figure 6 shows experimental data from the abductor digiti minimi muscle. In this experiment, 10 motor units were identified by decomposition of intramuscular electromyogram (EMG) signals during a constant force contraction at 10% of the maximal voluntary contraction (MVC) force. The detected motor units are divided in two groups, each with the same number of units. The coherence between the cumulative trains of discharge times of the two groups of motor units in the force bandwidth (up to 10 Hz) tends to 1 when increasing the number of motor units in each group, indicating that each cumulative train of discharge times reflects the common input to each motor neuron. Moreover, the



**Figure 6.** The effective neural drive to the muscle and force in experimental data. A set of 10 motor units have been identified reliably during a 60-s isometric contraction of the abductor digiti minimi muscle at 5% of the maximal voluntary contraction (MVC) force from intramuscular electromyogram (EMG) signals. The intramuscular motor unit action potentials are shown on the left, next to the respective trains of discharges. The motor unit discharges are grouped arbitrarily into two sets of five motor units each. For each set, the cumulative train of discharges is filtered in the effective bandwidth (10 Hz). The coherence between the two resulting cumulative trains of discharge times has a peak of approximately 0.7, which is in agreement with the simulations in Figure 5, considering the number of detected motor units (five in each set). The coherence between sets of one to four motor units each also is shown, with the characteristic monotonic increase in coherence values for increasing number of motor units, also in agreement with the theoretical and simulation expectations (Fig. 5). Finally, the low-pass filtered cumulative train of discharge times from the 10 motor units (*blue trace*) is compared with the recorded muscle force (*red trace*), showing a high similarity between the two signals ( $R = 0.79$ , after compensating for the time lag caused by the electromechanical delay). AU indicates arbitrary units; CST, cumulative spike train.

cumulative train of discharge times of the full set of detected motor units resembles the force signal with a high degree of correlation ( $R = 0.79$  in this example) (20).

The control of force by the central nervous system is challenged by two sources of noise: independent noise and common input fluctuations to the motor neurons. Although the first noise component is filtered effectively, the second component is not attenuated by the pool of motor neurons and is transmitted with the same efficacy as the control command. Accuracy in force control is determined mainly by the variance of the common noise. Indeed, for forces above a small threshold, needed to cancel the independent noise in the averaging, the only factor influencing force accuracy is the variance of the common input, whereas, for lower forces, both the common and independent input have an influence but with a progressively vanishing effect of the independent input for

increasing force (Fig. 2). Therefore, the main determinant of the force characteristics is the total common input and the relation between the control part of this input and common noise (Fig. 2). For example, large common noise oscillations relative to the level of control input would determine a large force variability (10,20).

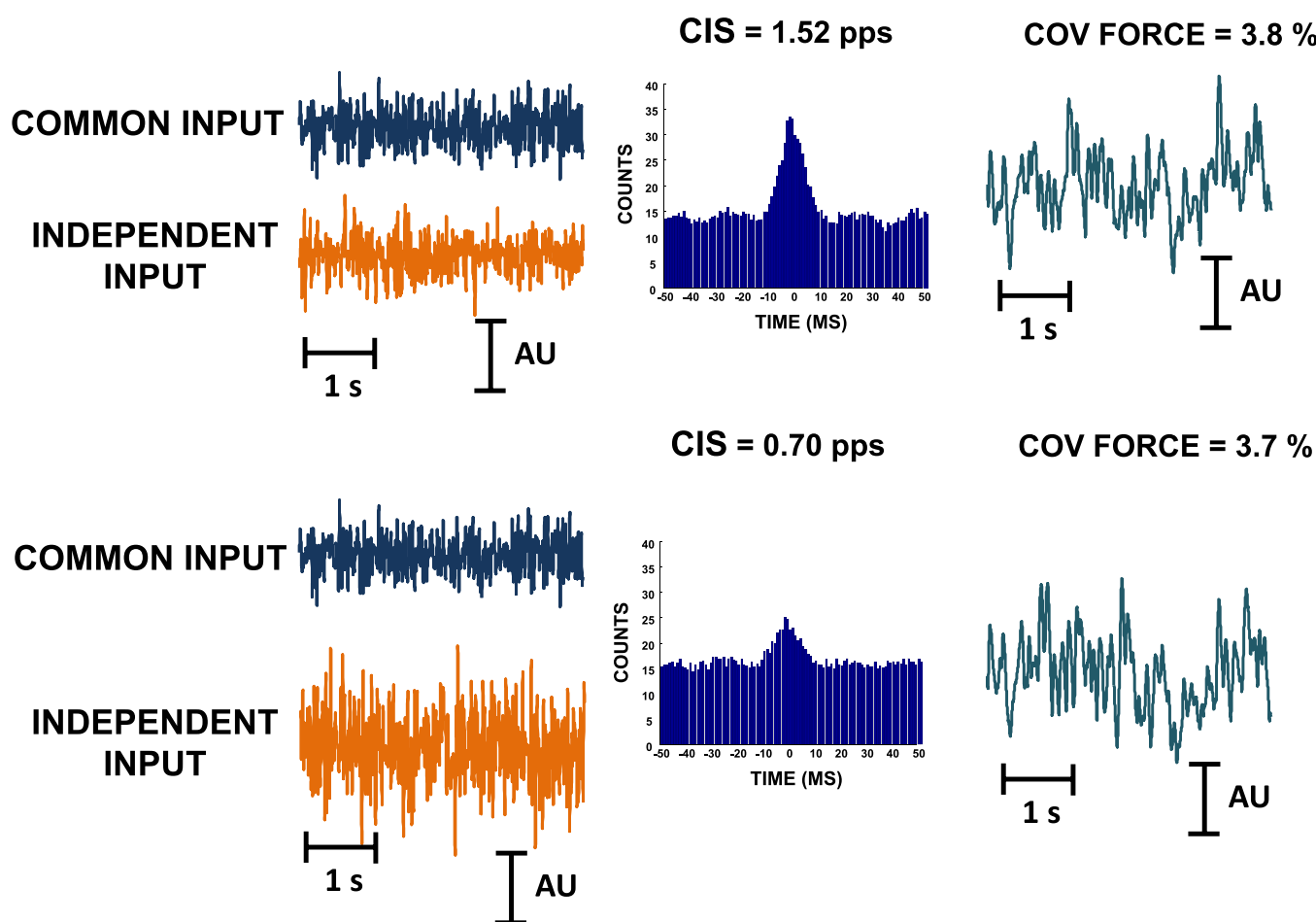
Given the main role of oscillations in the common synaptic input to determine force variability, synchronization by itself, in the classic or in the new population-based definition previously provided, is not a strong determinant of force accuracy. For example, the force produced by a certain muscle may be highly variable because of high common input oscillations and this may correspond to either high synchronization (in case the independent input has low variance) or low synchronization (if there is a strong independent input). This possibility is shown in Figure 7 where the forces generated



by the same common input but different independent inputs are compared. In the first case (upper traces), the independent input is relatively small and, therefore, *motor unit synchronization*, defined at the motor neuron population level as the ratio between the powers of the common and independent inputs to the pool, is relatively high (50% in the bandwidth 0–50 Hz). This also is identified by the classic measure of synchronization as a cross histogram of trains of action potentials of pairs of motor units that, in this case, shows a large peak, corresponding to an estimated CIS of 1.52 pps. In the second case, the common input oscillations are the same, but the independent noise is greater than in the first case (power ratio 25% in the bandwidth 0–50 Hz; CIS, 0.70 pps). The increase in independent input influences the estimated level of synchronization both in the proposed definition (ratio between powers of common and independent input) and in the classic quantification methods but does not substantially influence the neural drive to the muscle and muscle force variability, which indeed is comparable to that of the first case. The observation done by Yao *et al.* (31) in simulation that synchronization would increase force variability is strongly related to the way in which synchronization was induced in that study. The authors changed the timings of some

discharges to introduce correlation between discharge times. This operation necessarily introduced common oscillations in the motor neurons superimposed to their average rates and was thus equivalent to increasing the variance of the common noise to motor neurons, which would increase force fluctuations. However, increased force variability would not be associated exclusively with an increased synchronization, as demonstrated in Figure 7. Similarly, the relation between force variability and absolute force depends mainly on the rate of change of the variance of the common noise with respect to the level of excitation. The latter is the concept of signal-dependent noise, here rephrased in the view of common input.

In addition to force accuracy, other proposed effects of motor unit synchronization on force generation also are questionable, according to current evidence. For example, it has been suggested that synchronization may help increase the rate of force development (28), but it can be demonstrated, both in simulation and experimentally, that this is mainly determined by the maximal discharge rate of the motor neurons (7). In addition, the synchronization levels observed across human muscles, do not reveal a clear association between the function of the muscle and strength of synchronization but rather a gradient between proximal and distal muscles (16). Finally, it



**Figure 7.** Motor unit synchronization and force variability. A pool of 120 simulated motor neurons receive a common and an independent input of power ratio 50% (*upper traces*) and 25 % (*lower traces*). As expected, the synchronization estimated by cross histogram of pairs of motor units is greater (common input strength (CIS) = 1.52) in the first than in the second case (CIS = 0.70), as also shown by representative cross histograms. Despite the different ratio between common and independent input and different CIS values in the two cases, the variability in the generated force by the motor neuron pool is very similar between the two conditions (CoV for force, 3.8% vs 3.7%). AU indicates arbitrary units.

has to be noticed that any functional effect of synchronization should be related to synchronized oscillations at low frequency — frequencies corresponding to the effective bandwidth of the neural drive — because higher-frequency components are filtered when the neural signal is transformed into force. With the aim of finding a potential functional effect of synchronization, it would, thus, be appropriate to limit the analysis to this bandwidth — mainly representing the phenomenon often referred to as *common drive* (5) — rather than to the entire frequency bandwidth (see, e.g., (10)) that is represented in classic synchronization indexes.

Overall, a small degree of correlation between discharge times for pairs of motor units as well as the tendency for high similarities between cumulative discharge times of groups of units within a muscle are necessary and nonexclusive observations in human muscle control. Nonetheless, these observations do not necessarily imply a functional role of synchronization in force generation (rather the opposite). Results associating synchronization levels with specific characteristics of muscle performance (28) may be caused partly by the large variability and many factors of influence of classic synchronization indexes (Fig. 4B).

## HIGH-FREQUENCY COMPONENTS IN THE NEURAL DRIVE

We have introduced the concept of effective neural drive to the muscle to indicate the low-frequency portion of the neural drive that is transformed into force, on which this review has focused. However, the neural drive has a larger bandwidth with respect to force; therefore, in this last part of the review, we briefly comment on higher frequencies.

When analyzing coherence between motor units, it often is possible to identify peaks in the alpha (8–15 Hz) and beta (15–30 Hz) bands (21). Moreover, beta components are coherent to concurrently recorded electroencephalogram (EEG) activity, thus, they have a cortical origin. These components are difficult to explain from a functional view because most of their power is reduced substantially by the low-pass filtering effect of the muscle dynamics. For example, it was shown that the frequency content below 2 Hz in the neural drive to the muscle accounts for 60% to 70% of the total variance of the generated joint force in a static contraction (20) (see also Fig. 6), whereas higher frequencies in the trains of discharge times had negligible influence on force. Neural components in the beta band have a negligible influence on the generated force.

The presence of oscillations at frequencies above the effective bandwidth of the neural drive is unclear because functionally they are not needed. Several explanations for their presence could be discussed (8); however, the simplest one is that these oscillations may be used to transfer information from different parts of the neuromuscular system without necessarily containing the control information. For example, information could be transmitted by a high-frequency oscillatory signal whose amplitude is modulated at a slower rate (this would be a so-called *amplitude modulation* (14)). The information would be contained in the slow amplitude modulation. This hypothesis is partly in agreement with the observation that the neural drive to muscle is coherent with EEG in the beta, but not in the alpha, band.

The cutoff frequency of the muscle contraction is not far from the alpha band; thus, the presence of a strong alpha contribution in the neural drive could be transmitted to the force output and be detrimental (fast oscillations). Alpha oscillations in the neural drive seem to be filtered by specific neural pathways at the spinal level (30). These oscillations correspond to pathological tremor that appears when the alpha components in the neural drive are not reduced enough. Conversely, the beta band is attenuated completely by the muscle dynamics and, thus, it is not necessary for the system to attenuate it with neural mechanisms. This may explain the reason why large beta oscillations, contrary to alpha components, remain in the neural drive to the muscle and are observable in the EEG-EMG coherence analysis.

## CONCLUSIONS/SUMMARY

The specific characteristics of motor neurons implies that the effective neural drive to the muscle replicates the common synaptic input to motor neurons. Therefore, motor unit synchronization is a necessary observation because of force control by common input. The roles of common and independent inputs for force generation explained in this review do not point to an obvious functional role of synchronization in force production.

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