Statistically sound calculations do not support Common Input and Long-Term synchronization of motor unit firings

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Motivation

- Methods to measure synchronization of motor unit (MU) firings are used to infer that common inputs to motoneurons cause synchronization.
- All synchronization methods are based on work by Perkel et al. (1967); but all disregard relevant statistics necessary to detect synchronization, and their results provide misleading physiological interpretations such as the existence of universal common inputs to all motoneurons and the presence of long-term synchronization.
- We developed a statistically based synchronization detection method based on the approach by De Luca et al. (1993), which we will refer to as the SigMax method, to overcome the shortcomings of other approaches.

Experimental Protocol

Subjects: All healthy, 4 males and 2 females, ages ranging from 21 – 23 years

Muscles: First Dorsal Interosseous (FDI) and Vastus Lateralis (VL)

Contractions: voluntary isometric trapezoidal, 35 s constant force region

FDI: 5, 10, 15…30 %MVC; VL: 20, 25, 30…50 %MVC

Data Analysis

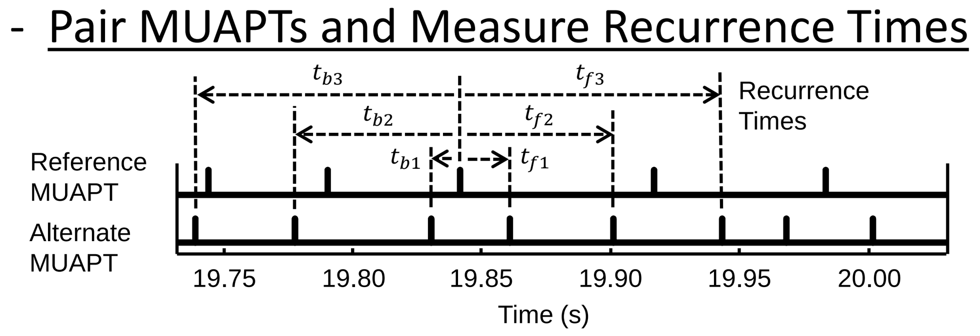
- Surface EMG (sEMG) signals were recorded with a Delsys dEMG™ Sensor and decomposed using dEMG algorithms developed by De Luca et al (2006).
- Error reduction algorithm (Kline and De Luca 2014) mitigated decomposition errors amongst motor unit action potential trains (MUAPTs).
- Synchronization was studied between MUAPTs obtained with >95% accuracy.

SigMax Synchronization Detection Method – 3 Step Test

No assumptions that synchronization exists or firings are normally distributed.

1) Test for Stationary MUAPTs - Pair MUAPTs and Measure Recurrence Times

- Use Kwiatkowski, Philips, Schmidt and Shin (KPSS) test
- Find stationary MUAPTs (KPSS stat < 0.463)



2) Test for Dependence

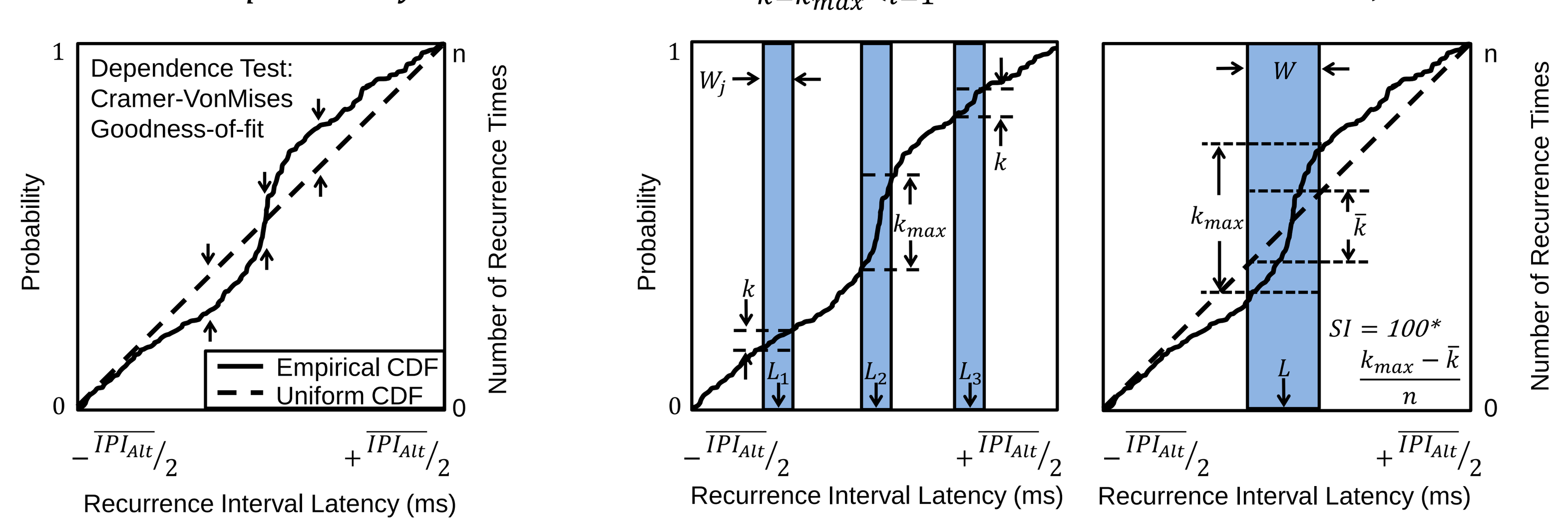
if the recurrence times are not uniformly distributed (correlated)

then the stationary firing from two MUs do not occur independently

3) Test For Statistically Significant Synchronization

- Find occurrences (k) at all latencies (L) and widths (W)
- Find W and L that gives most significant k_{max}.

$$P_j(Any\ bin \geq k_{max}) = \sum_{k=k_{max}}^{n}\left\{\sum_{i=1}^{m}(-1)^{i+1}\binom{m}{i}P(i\ bins = k)\right\}$$



SigMax Results

FDI Data: 794 stationary MUAPTs, 6,453 pairs, 333,633 firing instances

VL Data: 1,206 stationary MUAPTs, 11,283 pairs, 701,592 firing instances

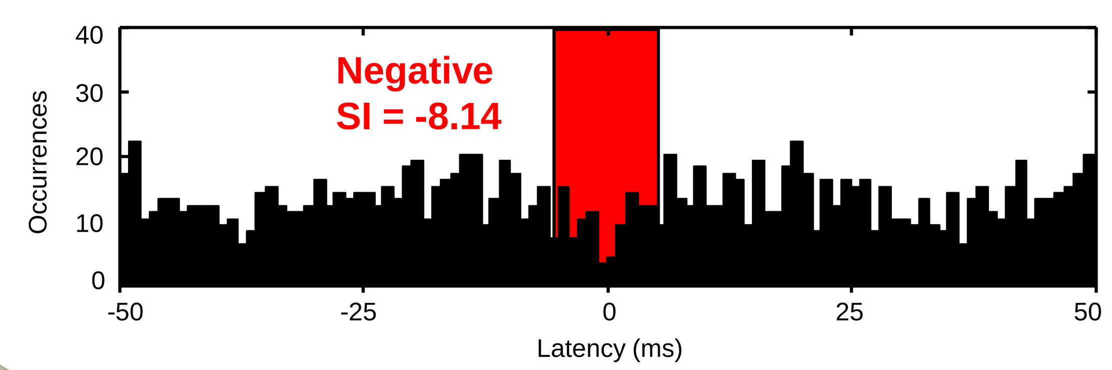
Muscle	MU Pairs with Synch. (n)	Synch. Index	Peak Width	Latency
FDI	42.0% (6,453)	19.8 [7.1, 32.4]	25.8 [6.9, 44.7] ms	-0.1 [-7.4, 7.2] ms
VL	54.8% (11,283)	16.9 [3.4, 30.6]	18.5 [9.5, 27.5] ms	-0.3 [-6.0, 5.5] ms

Other Synchronization Methods Compared to SigMax:

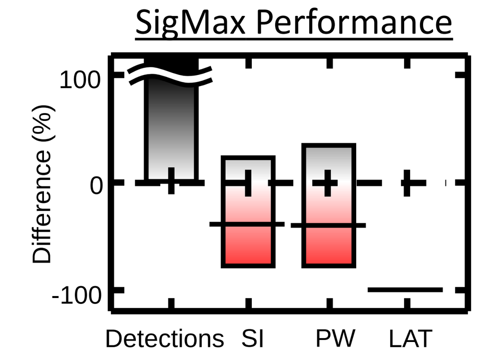
A) Common Input – Assumes Synchronization in 100% MUs

- Synchronization in 11 ms region at 0 ms latency.
- Assumes common inputs cause synchronization in 100% of MUs.
- Results in negative values of synchronization from 13.2% of MUs.

Detections of Negative Synchronization in Single MU Pair



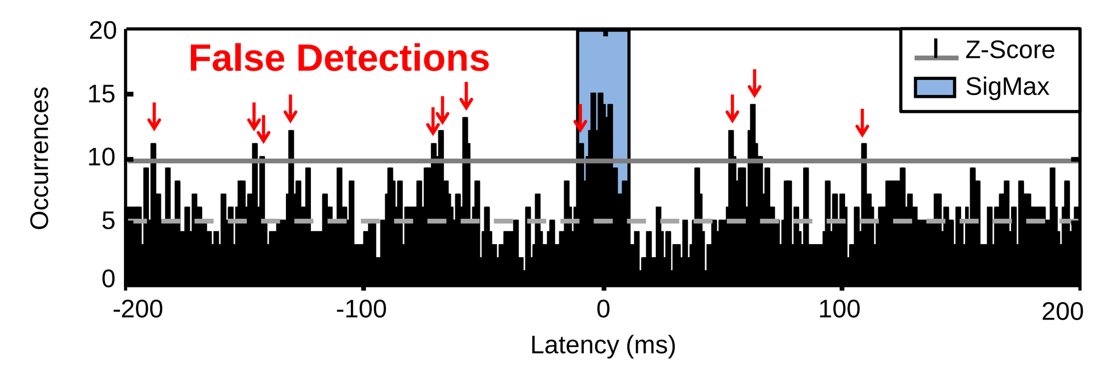
Compared to SigMax Performance



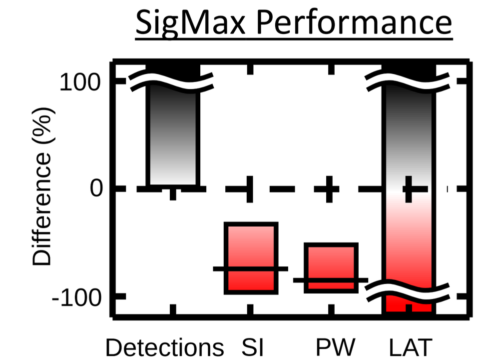
B) Z-Score – Falsely Detects Synchronization

- Peaks beyond the 0.05 z-score significance threshold based on the standard deviation and mean bin amplitude of the histogram.
- Results in synchronization peaks at 16 different latencies from each MU.

False Detections in Single MU Pair



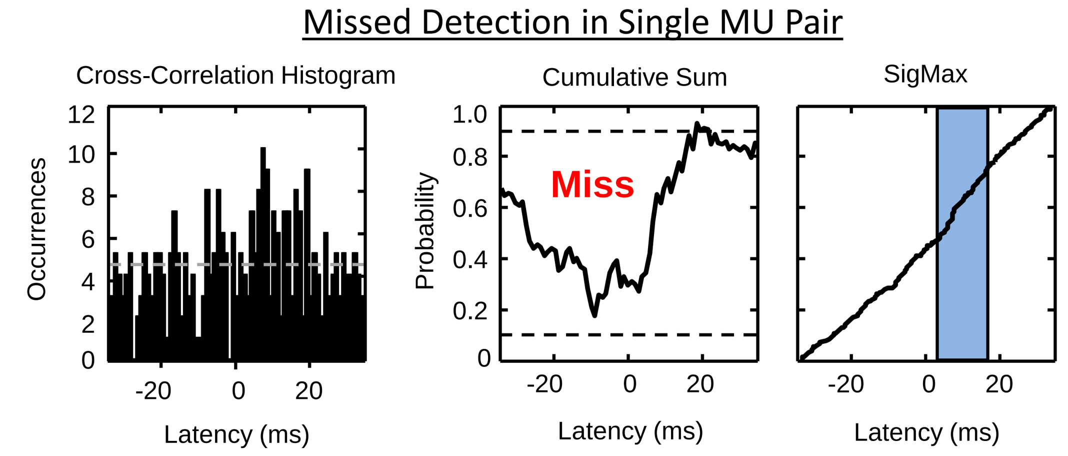
Compared to SigMax Performance



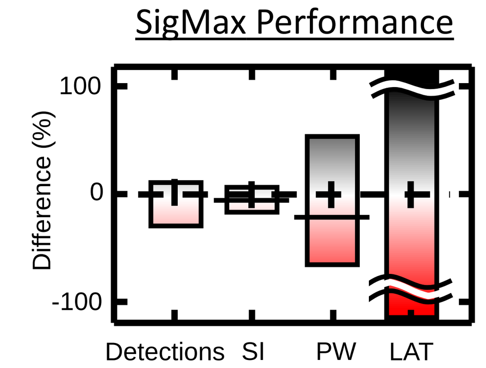
C) Cumulative Sum – Misses Synchronization Detections

- The running sum of the difference between the baseline mean and the amplitude of each bin in the cross-correlation histogram.
- Results in missed synchronization for 1 out of every 4 detections by SigMax.

Missed Detection in Single MU Pair



Compared to SigMax Performance



Statistics Disprove the Common Input Assumption

SigMax Results: synchronization exists between 50% of MUs in the muscles.

Common Input Assumption: Common inputs cause synch in 100% of MUs.

Consider: requirements to prove MUs are dependent on common inputs:

- Dependence can be proven only between stationary MUs using synchronization methods robust to false detections from MU refractoriness.

  According to basic statistics

  If two MUs are independent
  Then their firings are uncorrelated.

  Note the inverse indicates that:

  If their firings are uncorrelated
  Then the two MUs may or may not be independent

  While the contrapositive specifies:

  If their firings are correlated
  Then the two MUs are not independent

  Thus dependence between MUs can only be proven from correlated firings.
- Yet even if MU firings are correlated, ***correlation does not prove causality***: correlated firings indicative of synchronization between MUs do not prove that synchronized firings are caused by common inputs to the motoneurons.

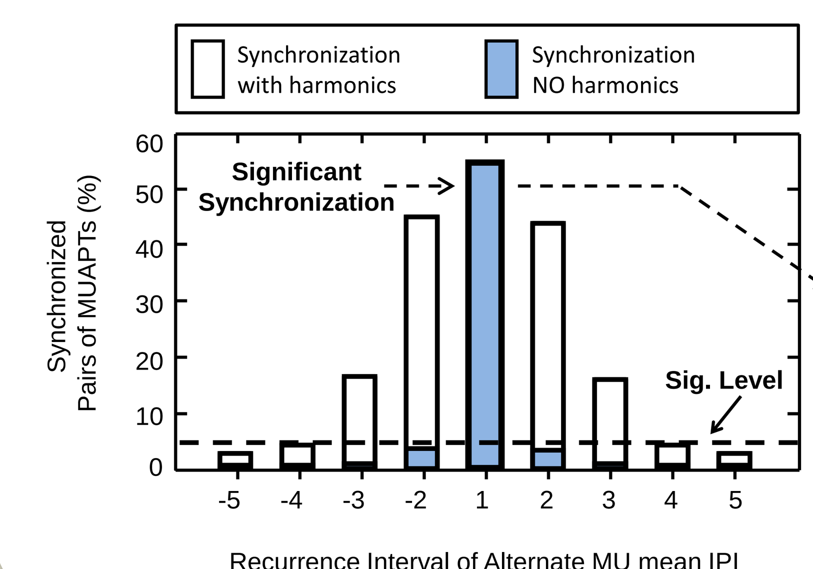
Therefore: Common inputs are NOT a proven cause of synchronization.

Long-term Synchronization is NOT a Physiological Event

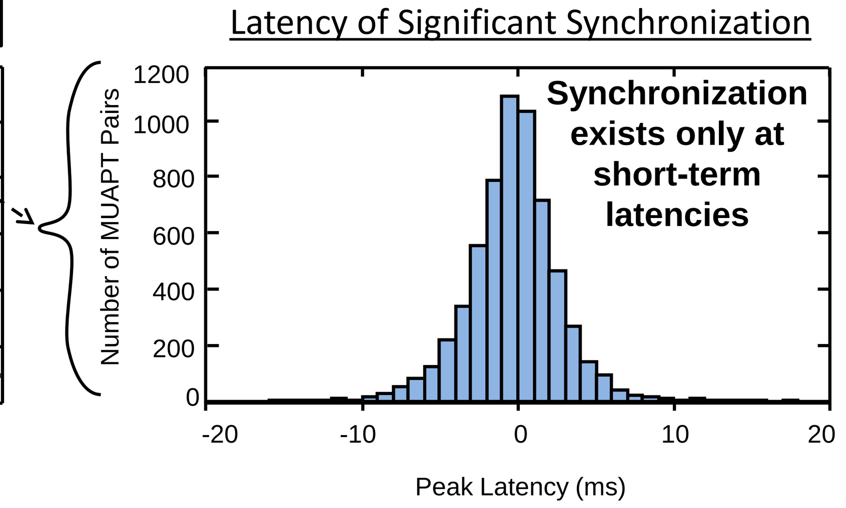
Long-term synchronization is an artifact from two main factors:

1. False positive detections of synchronization from an insufficient and low synchronization detection threshold (See z-score in Panel B).
2. Harmonics in the cross-correlation data (depicted below).

To avoid error of falsely detecting long-term synchronization we calculate synchronization exclusively from first-order recurrence times using the objectively derived and statistically reasoned SigMax method.



Latency of Significant Synchronization



References

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