

44 **Introduction**

45 The motor unit is the final common pathway by which an activation signal is transmitted to muscle and
46 transformed into contractile activity (1). As such, all voluntary actions are accomplished by varying the
47 amount of motor unit activity. Despite early claims to the contrary (2, 3), it is not possible to control
48 the activation of individual motor units (4). Instead, synaptic inputs are distributed broadly among the
49 neurons that comprise a motor nucleus and the motor units that are activated in response to these inputs
50 depends on their relative excitability (5–7). As a consequence of this scheme, the order in which motor
51 units are recruited during a voluntary action is relatively fixed (8–10).

52 It is the shared synaptic inputs received by the motor neurons that innervate a muscle and not the activity
53 of individual motor units that is responsible for the force it generates (11, 12). In general, the shared
54 inputs can arise from three sources (cortical, brain stem, spinal, and afferent pathways) with varying
55 distributions across different motor nuclei (5, 13–15). One advantage of this scheme is that the shared
56 inputs can engage the motor nuclei of the various muscles involved in an action and thereby facilitate
57 control of the net muscle torque.

58 It has been hypothesised that the control of multiple muscles is achieved by the activation of sets of
59 motor neurons, that have been referred to as “*neural modules*” or “*motor primitives*” (16–20). Neural
60 modules emerge from common synaptic inputs, or “neural manifolds” (21), that synergistically activate
61 a group of muscles to perform a specific action. For example, evidence from animal studies indicates
62 that the electrical stimulation of spinal interneurons produces coordinated movements that depend on
63 the location of stimulation (22–24). The modularity of neural control in humans has been estimated by
64 measuring the covariation in muscle activation patterns (EMG signals). The modules extracted by
65 factorization analysis have been termed muscle synergies (19, 25) and are assumed to emerge from
66 synaptic inputs that are common to the motor neurons involved in the action.

67 If the synaptic input is shared among the motor neurons that innervate synergistic muscles, it should
68 generate at least one latent neural module based on the covariance in the discharge times of the activated
69 motor units (21). Previous work has addressed this issue by factorizing EMG signals from different
70 muscles (19, 20, 26–29), which assumes that the motor neurons innervating the synergistic muscles
71 receive similar proportions of common synaptic input from one or more sources.

72 The neural modules determining coordinated control of multiple muscles can be investigated by
73 pairwise spike train correlations, an approach that gives access to the full statistical operating principles
74 of a neural network (30–32). The purpose of our study was to identify the low-dimensional latent
75 components, defined hereafter as *neural modules*, underlying the discharge rates of the motor units from
76 two knee extensors (vastus medialis and lateralis) and two hand muscles (index and thumb muscles)
77 during isometric contractions (19–21, 33). We hypothesized that the discharge rates of the motor
78 neurons innervating each muscle would be explained by more than one neural module.

79 We found that the discharge rates of motor units in individual quadriceps and hand muscles could be
80 characterized by two independent muscle-specific neural modules. The discharge rates of most motor
81 units were associated with the neural module for the muscle in which they resided, but others were
82 correlated with either the neural module for the synergistic muscle or both neural modules. We then
83 simulated the delivery of two independent common synaptic currents into integrate-and-fire motor
84 neurons and to validate our approach to identifying latent components. Our findings provide a greater
85 level of detail about the distribution of common synaptic input within and across the motor nuclei that
86 innervate synergistic muscles.

87 **Results**

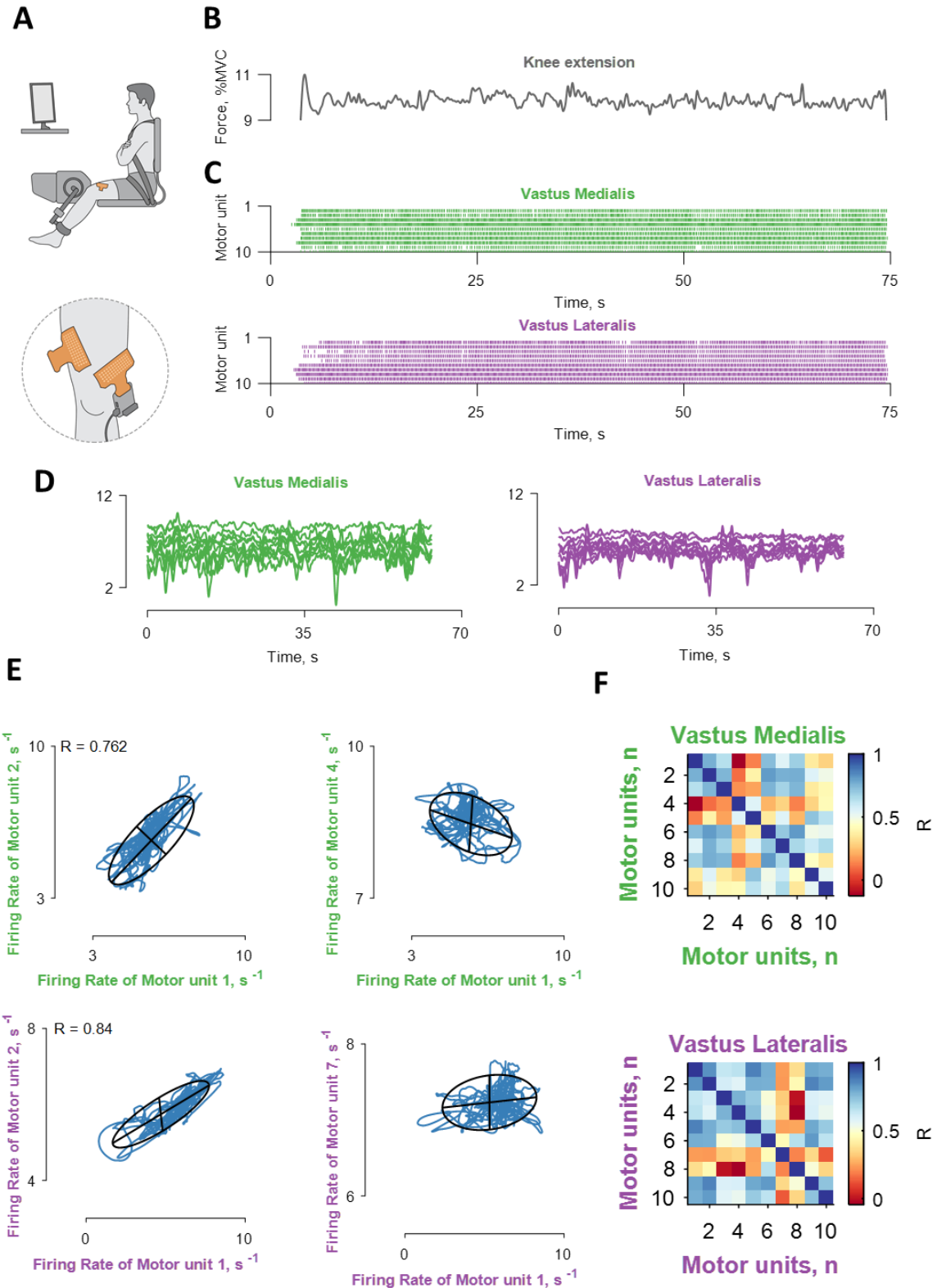
88 **Motor unit neural modules**

89 Our approach involved extending the classic method for muscle synergy analysis (17, 19, 20, 25, 28,
90 34) to motor unit recordings. Instead of treating muscles as individual elements, the discharge times of
91 motor units from different muscles were grouped together. We used a factor analysis that maximizes
92 the correlation between each motor unit and a set of unknown factors, referred to as neural modules.
93 We demonstrate that the factor analysis outperforms other factorization approaches (see Methods), such
94 as principal component analysis and non-negative matrix factorization (19, 35–37), in maximizing the
95 correlation between individual motor unit discharge rates and the latent low-dimensional modules.

96 Theoretical and indirect experimental observations suggest that a common motor command is
97 distributed to sets of motor nuclei (25, 26, 33, 38–41), which results in the discharge rates of motor
98 units across muscles being strongly correlated during voluntary contractions in humans (42–44) and
99 non-human primates (45). In our approach, we did not assume that there is only one latent signal for
100 each muscle (37, 46, 47). Instead, we decoded populations of motor units from surface EMG signals
101 into series of motor unit discharge times during two tasks that involved the synergistic activation of
102 pairs of muscles.

103 The experimental setup and correlation analysis for the two vastii muscles is shown in Figure 1. The
104 motor unit discharge times were decomposed with a blind source separation procedure, which identifies
105 each event with no a-priori knowledge on the physiological information conveyed by the individual
106 motor units (48–50). We identified on average across participants 6.9 ± 4.3 and 4.37 ± 2.34 motor units
107 for VL and VM, respectively during isometric contractions at 10% of maximum. As described in the
108 methods, we subsequently smoothed the motor unit discharge times with a Hann window, which
109 retained all the frequencies responsible for muscle force (<5 Hz (11)). As the applied force has a cut-
110 off frequency of ≤ 20 Hz, the low-pass filtered discharge times (the time series of zeros and ones, Fig.
111 1C) are strongly correlated with the variance in force during steady contractions (11, 51–53).
112 Consequently, we focused on finding the latent components (i.e., the neural modules) for the low-pass
113 filtered signals (Fig. 1D).

114



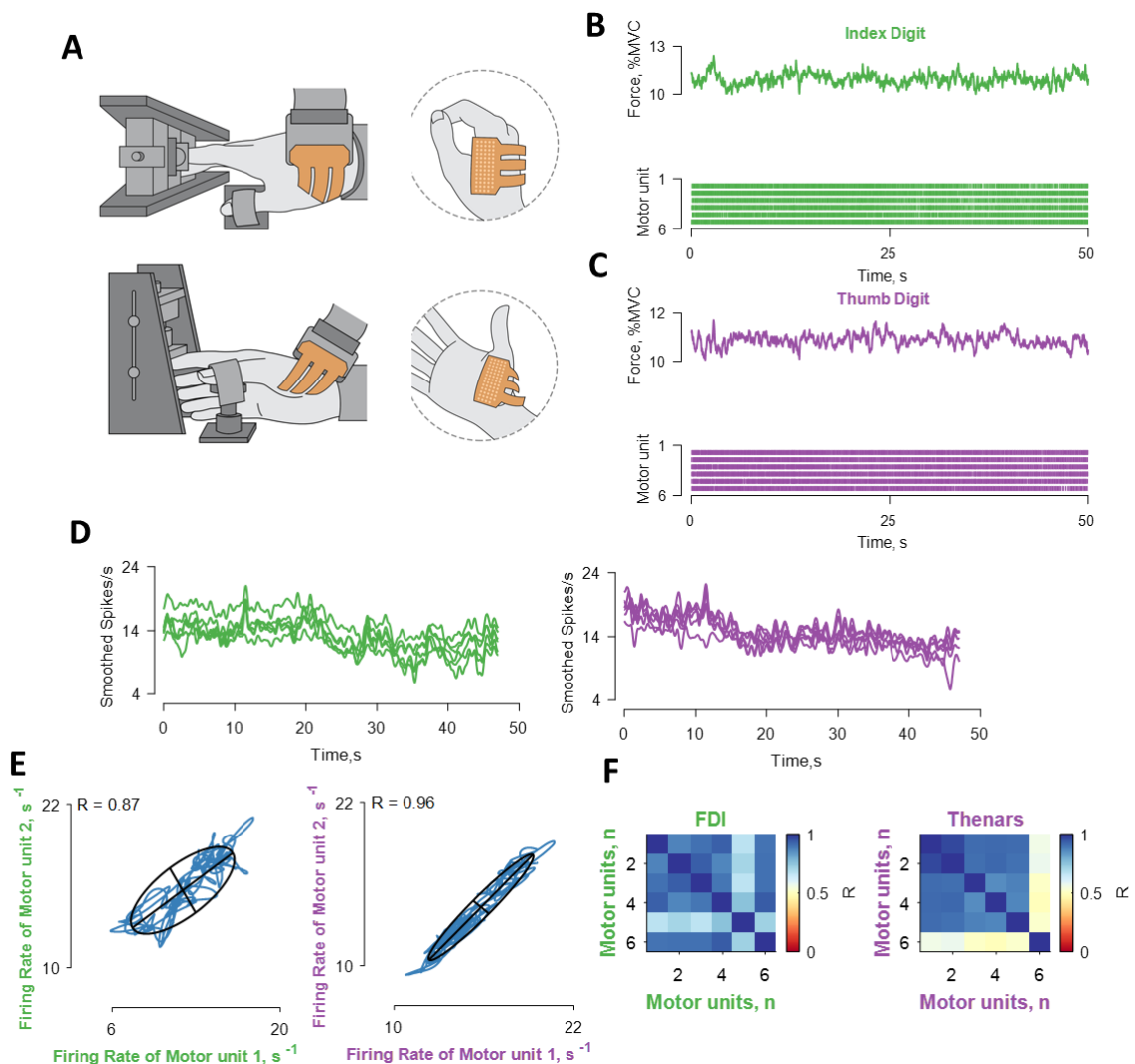
115

116 **Figure 1.** Recordings of muscle force and correlation analysis of motor unit discharge times. **A.** Experimental
 117 setup included high-density EMG grids over the vastus lateralis and medialis muscles during isometric
 118 contractions at 10% of maximal voluntary contraction (MVC). **B.** The applied force. **C.** The decomposed motor
 119 unit discharge times represented in a raster plot for the vastus lateralis (violet) and medialis (green) muscles. **D.**
 120 The motor unit discharge times (series of zeros and ones) were convolved with a 400 ms Hann window, which
 121 retains the motor unit oscillations responsible for the fluctuations in force during steady contractions. **E.** Four
 122 bivariate correlations between different motor units belonging to the same motor nuclei (the labels are color-coded

123 with respect to the muscle as indicated in panels C and D). The blue lines indicate the smoothed discharge rates
 124 during the steady-state contraction. **F.** Confusion matrix of the correlation strength between all the identified
 125 motor units for the two muscles. Note that the discharge rates within each homonymous motor nucleus exhibited
 126 a range of correlation values. R = correlation strength, for both correlations the Pearson's value was <0.0001 .

127 After converting the discharge times to rates and smoothing the signal, we computed pairwise
 128 correlations between each motor unit within the same muscle (Fig. 1E-F). We consistently found
 129 correlated and uncorrelated discharge rates of some motor units from the same vastus muscle, which
 130 indirectly indicates that not all motor neurons received the same common input (30, 31). Because most
 131 previous studies report high correlations among motor units within a motor nucleus (26, 42, 54), it was
 132 necessary to assess the level of cross-talk between muscles. Based on a recently developed method (55,
 133 56), we found that the identified motor units had action-potential amplitudes that were statistically
 134 similar to the other units in the homonymous muscle and, therefore, were not the result of cross-talk
 135 (see Methods).

136



137

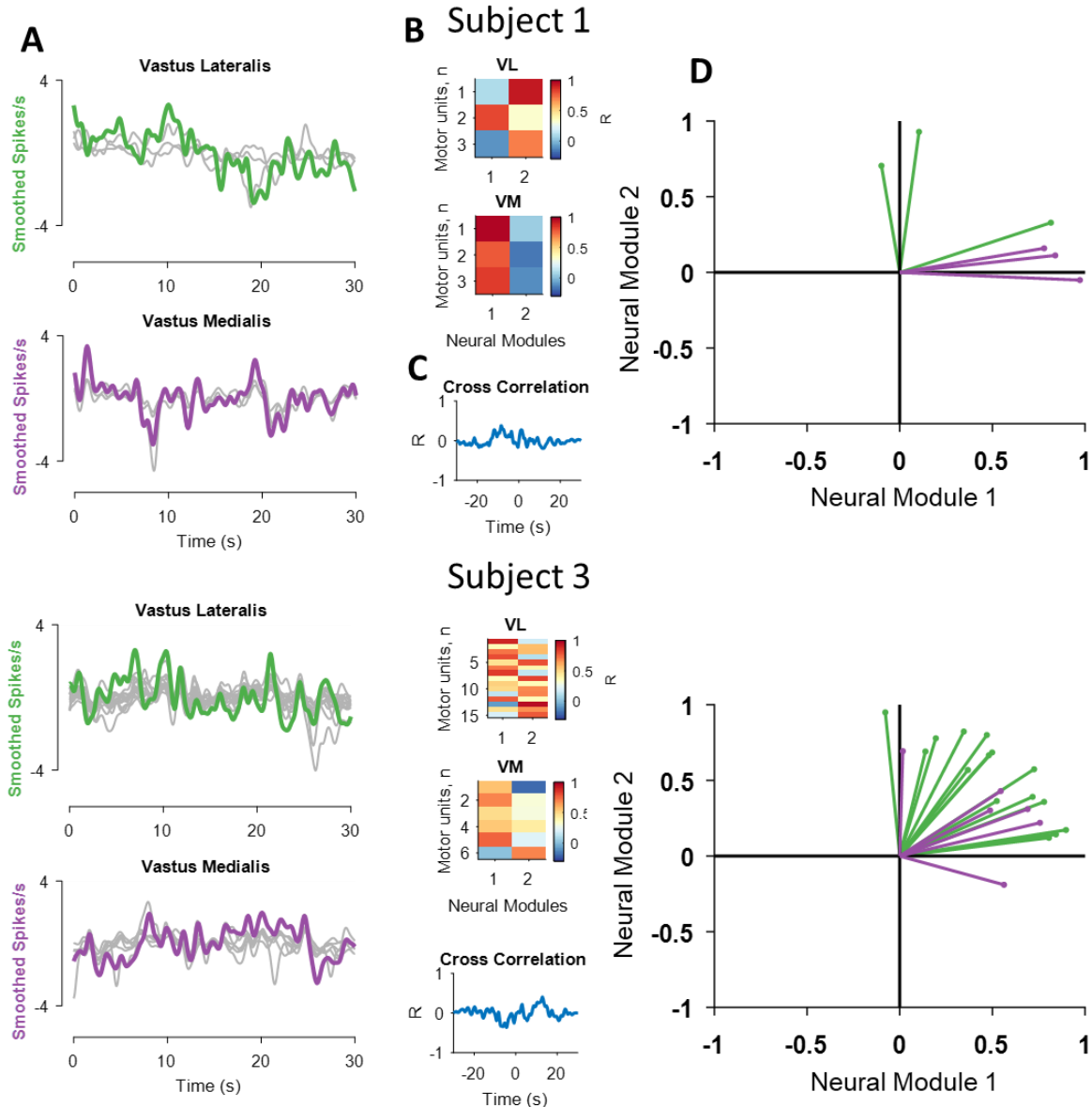
138 **Figure 2.** Recordings of muscle force and correlation analysis between the discharge times of motor units in hand
 139 muscles. **A.** Experimental setup involved high-density EMG grids placed over the first dorsal interosseus and
 140 thenar muscles. **B-C.** The applied force and the discharge times of motor units shown in a raster plot for the first
 141 dorsal interosseus (green) and thenar muscles (violet). **D** The motor unit discharge rates (series of zeros and
 142 ones) were convolved with a 2.5 s Hann window. **E.** Two bivariate correlations between different motor units
 143 belonging to the same motor nucleus (the labels are color-coded with respect to the muscle as indicated in panels

144 C and D). The blue lines indicate the smoothed discharge rates during the steady-state contraction. **F.** Confusion
145 matrix of the correlation strength between all the identified motor units the two muscles. Note that all motor units
146 are highly correlated within each motor nucleus. R = correlation strength, for both correlations the Pearson's value
147 was <0.0001.

148 The average number of identified motor units for the hand muscles was 12.2 ± 3.0 and 4.3 ± 1.2 for the
149 first dorsal interosseous and thenar muscles, respectively, across participants. In contrast to the vastii
150 muscles, Figure 2 shows that the discharge rates of all motor units in each hand muscle were strongly
151 correlated (>0.9), and there were few cases of low correlations (see cluster analysis below). Because of
152 differences in the strength of the correlations between motor units in the vastii and hand muscles, we
153 then examined the latent components between motor units across participants and muscles with a
154 factorization approach.

155 **Factor analysis reveals a distinct organization of common synaptic inputs**

156 Factorization analysis identifies the latent components that covary among sets of variables. This method
157 enables the identification of the potential 'neural modules'. Figure 3 shows the results obtained from
158 the factor analysis for the vastii muscles of two participants. The factor analysis was applied to all motor
159 units from both muscles; therefore, the extracted neural modules did not have any a-priori muscle-
160 specific constraint. The latent neural modules are superimposed on each muscle (grey lines indicate
161 individual motor unit discharge rates from that muscle). The first two modules explained most of the
162 signal (>80%); therefore, we only used these two factors in the subsequent analysis.



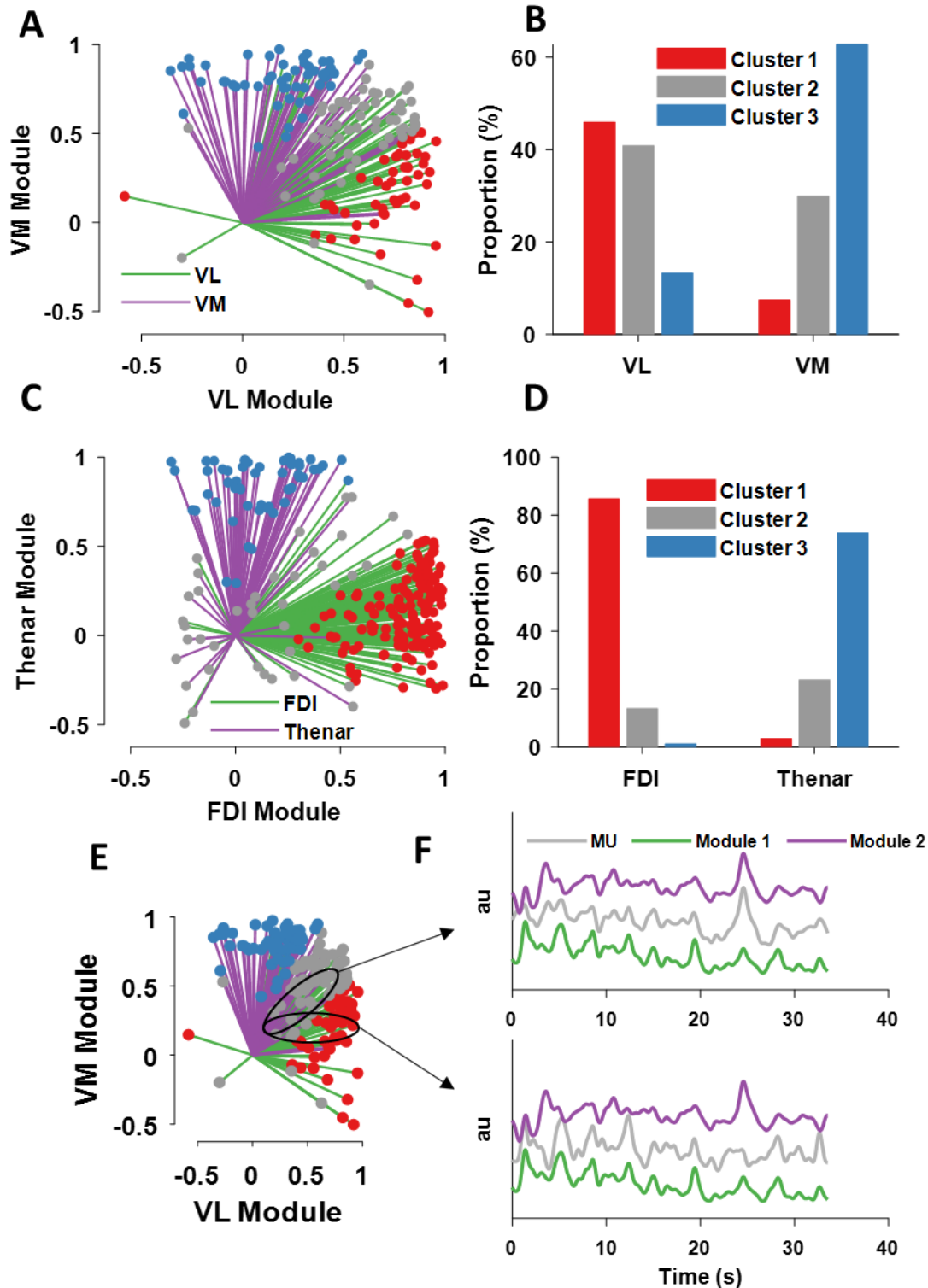
163

164 **Figure 3** Results of the factorization analysis for the vastii muscles of two subjects. **A.** The smoothed
 165 motor unit discharge rates (grey lines, with the mean = 0 spikes/s) and two neural modules derived from
 166 the factor analysis (green for the vastus lateralis and violet for vastus medialis). Note the high correlation
 167 between the two factors and the discharge rates of some, but not all, motor units for the two subjects.
 168 **B.** The two factors were then correlated with the smoothed discharge rates of all motor units. **C.** The
 169 cross-correlation values between the two modules. **D.** Projections of the bivariate correlation values for
 170 each motor unit with respect to the neural modules. Values close to 1 indicate that a motor unit carries
 171 ~100% of the respective module. Note that some vastus lateralis and medialis motor units invade the
 172 territory of the other neural module; for example, intermingling of the green and violet lines for Subject
 173 3. Also note that some motor units are only correlated with one module.

174 We then determined the level of correlation between the discharge rate of each motor unit and the two
 175 neural modules (Fig. 3B). This analysis shows, for example, that motor unit number 2 in vastus lateralis
 176 for Subject 1 had a stronger correlation with the first neural module, whereas the two other motor units
 177 were more correlated with the second factor (Fig. 3D). However, the two modules were not correlated
 178 (Fig. 3C). Projections of the two modules (Fig. 3D) indicated that one motor unit in vastus lateralis was
 179 located in the module of the vastus medialis motor units. Subject 3 exhibited more intermingling of the
 180 motor unit data in the space of the two neural modules (Fig. 3 lower right graph).

181 We then looked at the overall distribution of the identified motor units within each neural module across
182 participants for the vastii (n=8) and hand muscles (n=8) (Fig. 4). We found that although many motor
183 units from each muscle shared the same module (Fig. 4A-D), the discharge rates of some motor units
184 were correlated with both neural modules. There were also some motor units that showed negative
185 correlations with one of the modules. These negative correlations were more common for the hand
186 muscles.

187 We clustered the correlation values of the motor units with the respective modules based on specific
188 centroids (x and y coordinates: [0.66 1.00], [0.40 0.40], [1.00 0.65]), (Fig. 4 B-D). The largest cluster
189 for all muscles was the group belonging to the homonymous muscle; that is, a motor nucleus-specific
190 cluster. Interestingly, the proportion of motor units belonging to the shared cluster was greater for vastus
191 lateralis than vastus medialis (Fig. 4B). The motor nucleus-specific cluster was stronger for the hand
192 muscles, with few motor units present in the shared cluster (<20% for both first dorsal interosseous and
193 thenar muscles). Moreover, there were some motor units for both sets of muscles that diverged from
194 the homonymous control and were more correlated with the other synergistic muscle. This was more
195 evident for the vastii (>10% of motor units) than hand muscles (<3% of motor units).



196

197 **Figure 4.** The output of the factor and cluster analysis across all subjects and motor units. **A.** The motor
 198 units from vastus lateralis (green) and vastus medialis (violet). Each line indicates the strength (line
 199 length) and sign of the correlation between the discharge rate of one motor unit and the neural module.
 200 Note that some motor units shared the same module space (indicated in grey dots), whereas others
 201 diverged from synergistic control (blue and red) and a few invaded the territory of the other muscle. **B.**
 202 A cluster analysis identified three main clusters. Note the grey cluster that indicates the percentage of
 203 motor units that shared both neural modules. **C-D.** The same analysis as in A-B but for the hand muscles.
 204 Note the smaller proportion of motor units belonging to the shared (grey) cluster in comparison with

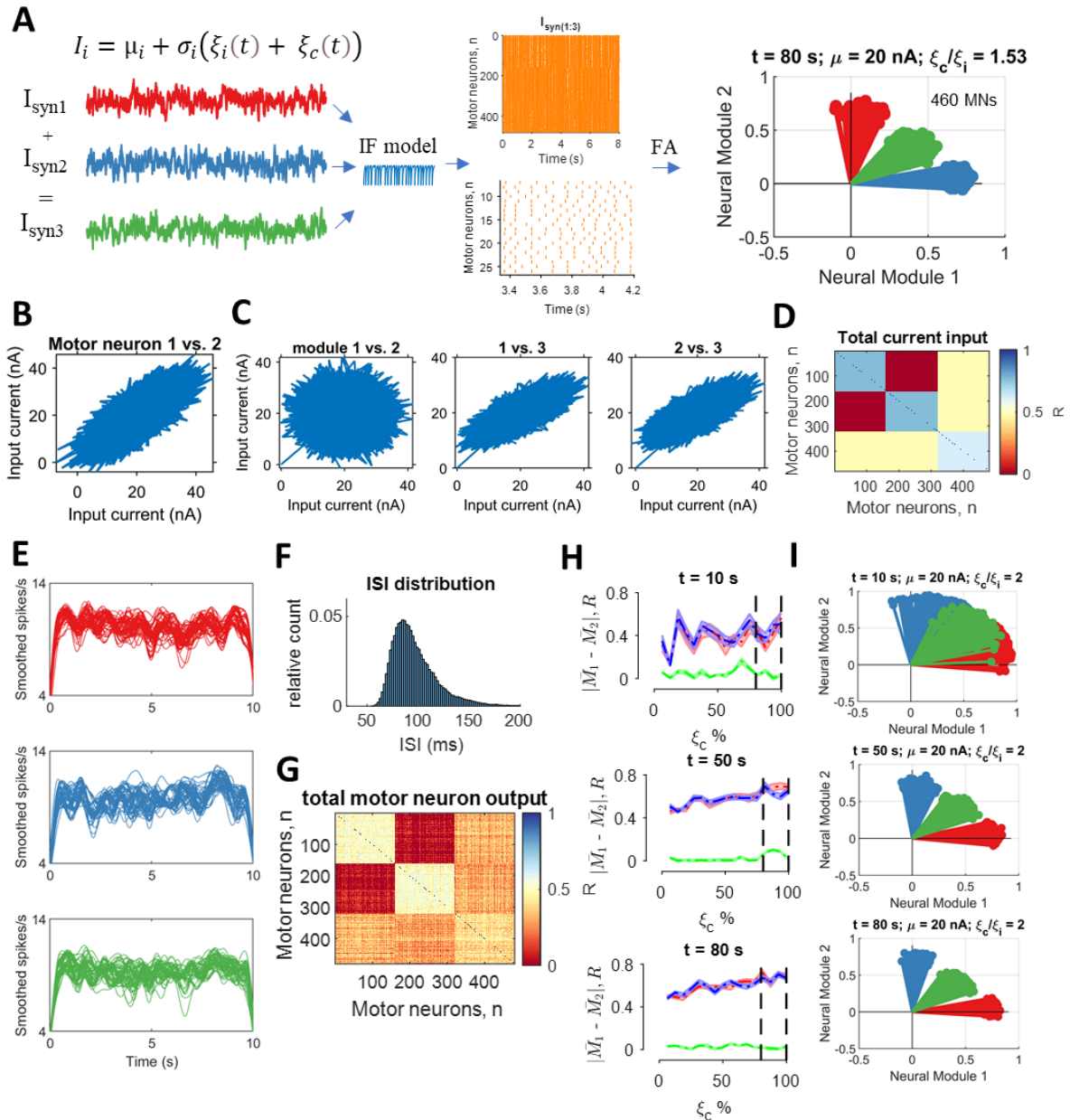
205 the vastii muscles. **E-F** An example of two motor units that occupy different module space. The black
206 ellipse is a visual guidance of the territory occupied by the motor unit 1 (top panel in F), which shows
207 the firing rate of that unit correlated to both module 1 and module 2. In contrast, the lower panel in F
208 shows a motor unit that is only correlated with module 1.

209 We then removed the motor units that shared both neural modules and performed coherence analysis
210 between the motor pools. We found approximately a two-fold decrease in the coherence value without
211 the common motor units. For some subjects, the coherence in any of the physiological bandwidths (0-
212 50 Hz), did not differ than for frequencies >50 Hz, which means that there was no coherence between
213 motor units that did not share the same neural module. Conversely, the coherence for the motor units
214 that shared both modules was similar to what previously reported (26, 44). This finding strongly
215 indicates that previous coherence found between muscles from thigh and from the hand is due to the
216 shared inputs that generate the significant coherence value (26, 56).

217 **Integrate and fire model: factor analysis accurately reflects the interplay of two common inputs**

218 We performed computer simulations to generate a dataset of motor neuron discharge times to determine
219 the optimal convergence and accuracy of factorization analysis on the extraction of neural modules
220 from motor unit data. The aim was to assess the influence of known distributions of two synaptic inputs
221 ($I_{syn1,2}$) and their average $I_{syn3} = (I_{syn1} + I_{syn2})/2$ + independent inputs on the number of identifiable neural
222 modules. The common and independent inputs, as well as the spike times, were approximated by tuning
223 the parameters of an integrate-and-fire model (32, 57).

224 Because we have no information on the dimensions of the latent components, which reflect common
225 inhibitory and excitatory synaptic inputs, we can model these inputs realistically with an integrate-and-
226 fire model (32, 57) and study the outputs with pairwise correlations and factor analysis. Moreover, the
227 model allowed us to test the influence of time (total duration of spike times), net synaptic currents, and
228 the strengths of the common and independent inputs.



229

230 **Figure 5.** Integrate-and-fire model. We injected correlated and uncorrelated fluctuating currents (I_i)
 231 into 480 motor neurons. Two-thirds of the population received two distinct common inputs (ξ_c), and
 232 the one-third received the average of the two common inputs plus its own independent noise. The
 233 proportion of common and independent inputs ranged in values to reflect the cross-correlation values
 234 observed in the experimental data. Similarly, the injected current (20 nA) generated interspike intervals
 235 that matched *in-vivo* motor unit data. Each neuron received gaussian synaptic noise reflecting its unique
 236 connections (independent input, ξ_i). **A.** μ_i is the temporal average of the current (20 nA) and σ_i sets the
 237 global network state. Raster plot (orange lines) showing some of the data from an 80-s simulation with
 238 the proportion of common-to-independent inputs set at 1.53. Note the output of the factorization
 239 analysis clearly depicting the space of three injected currents (top right graph), as observed in the
 240 experimental recordings. **B.** Pairwise correlation for the first neural module between motor neurons 1
 241 and 2 from a pool of 160 neurons that each received I_{syn1} . **C.** The averaged total current across all cells
 242 plotted between the neural modules. Note that module 1 and module 2 are uncorrelated, whereas there
 243 was a high correlation with module 3 due to the shared averaged synaptic current. **D.** Confusion matrix
 244 of the correlation strength across all 480 neurons. **E.** The output of the integrate-and-fire model was
 245 low-pass filtered at 25 Hz for a 10-s trial. The first and last second was excluded when calculating the

246 correlations to avoid the influence of spike frequency adaptation. Each line corresponds to one motor
247 neuron. **F.** Distribution of interspike intervals across all 480 neurons for an 80-s trial. **H.** Accuracy of
248 factor analysis computed as the average difference of all neurons belonging to each module ($|M_1 - M_2|$)
249 at three time points during the simulation. The absolute difference between the modules corresponds to
250 the accuracy of factor analysis in converging in that specific module. The values for the shared module
251 (green) were close to 0, which indicates perfect separation from the two modules. We injected low
252 percentages of common input (0% indicates that the common and independent input are the same). The
253 dashed vertical lines indicate the range of values that reflect in-vivo motor unit correlation values. There
254 was a strong influence of time, so that 10 s of data were insufficient to obtain reliable estimates of the
255 proportion of common input, whereas there were no differences for the data at 50 s and 80 s. **I.** Three
256 representative neural modules extracted by factor analysis at three time points (10, 50, and 80 s) when
257 the common input was twice as much as the independent input.

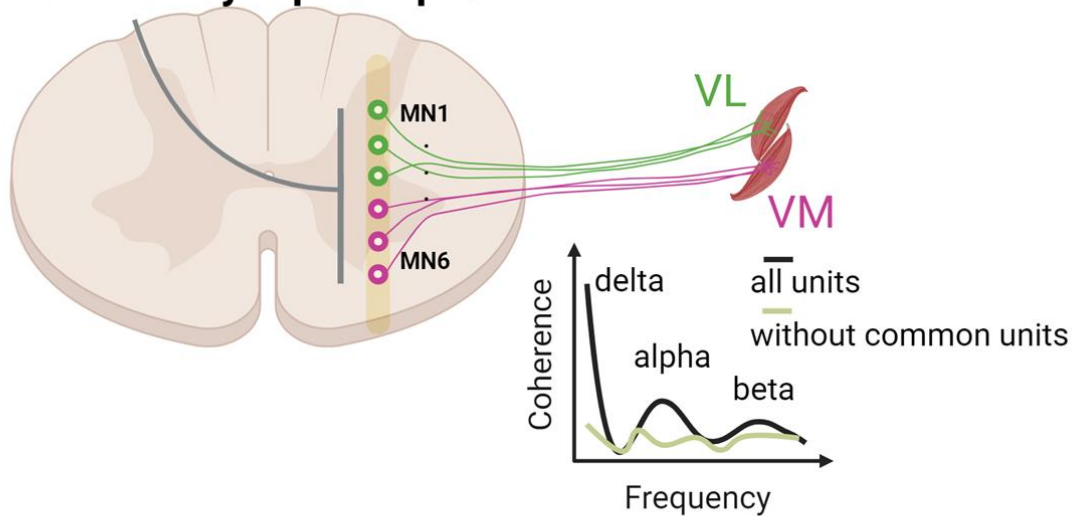
258 We simulated 480 integrate-and-fire neurons that were activated by applying an independent input and
259 a common input. Two-thirds of the population of neurons received the uncorrelated inputs, I_{syn1} and
260 I_{syn2} , and a one-third received I_{syn3} , which represented the average of the two other inputs (Fig. 5A). We
261 then looked at the correlations between the inputs and outputs (smoothed motor unit discharge rates) as
262 well as the average and standard deviation of the neural modules extracted by the factorization method
263 (Fig. 5). Due to the influence of low-pass filtering of the discharge rates, there was a strong influence
264 of trial duration with the 10-s data being unable to distinguish between the unique and shared inputs.
265 With longer time signals, we were able to retrieve the full dimensions of the three common synaptic
266 input signals by increasing the simulation to 50 s or 80 s (Fig 5. H-I), independently of common and
267 independent input strength.

268 **Discussion**

269 We analysed the correlation between the discharge times of motor units from different synergistic
270 muscles during isometric contractions with the knee extensors and index finger and thumb muscles. We
271 found two neural modules for the motor units of the vastii muscles, which contrasts with previous
272 findings of only one dominant common input to individual (42) or synergistic muscles (26). As shown
273 in Figure 6, large groups of motor units innervating the VL and VM muscles were associated with
274 specific neural module for each of these muscles, but some motor units were associated with both neural
275 modules. In contrast, fewer motor units innervating the hand muscles (<20%) were associated with both
276 neural modules. Moreover, the discharge rates of some motor units were not correlated with the neural
277 module for the muscle in which they reside, but instead were correlated with the neural module for the
278 synergistic muscle.

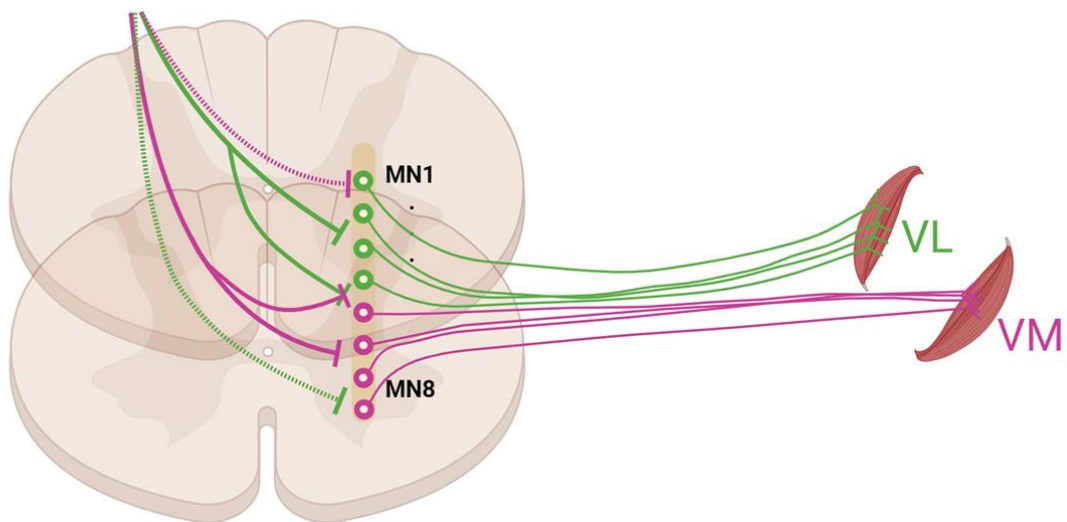
A

one common synaptic input



B

two common synaptic inputs



279

280 **Figure 6.** Schematic representation of the results and suggested neural connectivity of voluntary motor
281 commands to motor neuron pools. **A.** Previous studies that have grouped the vastii or hand muscles
282 based on global EMG signals have found strong coherence between the two muscles, indicating a
283 unique common input to the synergistic muscles. After we removed those motor units that shared both
284 neural modules, the correlation between the two pools of motor units was significantly reduced, as
285 indicated in the coherence graph. This indicates that the coherence found in previous studies is mainly
286 attributable to those motor units that shared two distinct sources of common synaptic. **B.** Visual
287 representation of our current findings. With factorization dimensionality techniques, we found that there
288 are at least two sources of common synaptic input to motor neurons that innervate the vastii and hand
289 muscles. Most motor neurons, but not all of them, innervating each vastus muscle receive common
290 input from a unique source (green and violet lines), but some motor neurons receive inputs from the
291 source directed to the other muscle (dashed green and violet lines; upper graph) and some receive inputs
292 from both sources (lower graph).

293 The correlation between each motor unit and its neural module reveals the potential nature of shared
294 synaptic inputs by the motor neuron pools that is inevitably obscured in the global EMG signal. With
295 this analysis we show that the motor neurons from two hand muscles during an independent task can
296 be fully retrieved by the module they carry, but the motor units for each knee extensor muscle receives
297 common input from two unique sources.

298 Previous experiments reported a single dominant common input governing coordination of the vastus
299 medialis and lateralis muscles (26). Similarly, previous studies on one motor unit pool have identified
300 a single common synaptic input (42, 44). The identification of a single dominant common input in
301 previous studies is based on a pooled-coherence approach to estimate neural connectivity. This analysis
302 averages the correlation between motor unit spike trains with several permutations, therefore, the
303 averaging process inevitably generates significant correlations because ~50% of the homonymous
304 motor unit pool receives a similar input. Because we found that the motor units innervating an individual
305 muscle can receive more than one common input, our results demonstrate that pooled coherence is not
306 an appropriate approach to assess neural connectivity.

307 It is important to note that our experimental task involved isometric contractions in contrast to the
308 dynamic actions typically used to identify ‘muscle synergies’. Perhaps, the sources of common input,
309 such as the type and intensity of feedback from sensory receptors (58, 59), differ during isometric and
310 dynamic contractions and the common input received by the motor neurons innervating the synergistic
311 muscles is more homogeneous. For example, we found that in macaque monkeys during rapid high
312 force contractions most motor units share the same neural module (60).

313 Even for isometric contractions, however, the sources of common input may differ with the details of
314 the task being performed. Based on the interpretation that the fluctuations in force during steady
315 isometric contractions are attributable to the variance in the common synaptic input (11, 12, 53),
316 differences in the coefficient of variation for force during a specific action suggest adjustments in the
317 common input across tasks. For example, the coefficient of variation for force during index finger
318 abduction, which is mainly due to the activity of the first dorsal interosseus muscle, was 2x greater
319 when participants performed index finger abduction and wrist extension at the same time even though
320 the abduction force was the same in both tasks (61). Based on the finding of an increase in the coefficient
321 of variation for force during the double-action task (index finger abduction + wrist extension) in the
322 study by Almuklass et al. (2016), it seems reasonable to predict that the neural modules for the two
323 hand muscles in the current study would differ from those observed during the independent actions.
324 Consistent with this possibility, Desmedt and Godaux suggested that the synaptic inputs delivered to
325 the motor neurons that innervate the first dorsal interossei muscle differed when the direction of the
326 force applied by the index finger changed from abduction to flexion (62). The basis for this conclusion
327 was the finding that the recruitment order for some pairs of motor units (~8%) consistently reversed
328 recruitment order when the task was changed from abduction to flexion. They hypothesized that this
329 effect, although relatively modest, was attributable to differences in the distribution of the motor
330 command for each task.

331 Despite the limited scope of the tasks examined in our current study, the findings indicate that the
332 derivation of muscle synergies is based on the common synaptic input that is shared by the motor
333 neurons involved in the action but that this common input is not shared among most of the motor
334 neurons within a given motor nucleus. Moreover, we found that the modulation of discharge rate for all
335 motor units could be classified into three clusters distributed across two neural modules. These results
336 indicate that synergistic motor neuron pools receive common synaptic inputs from at least two different
337 sources during submaximal isometric contractions.

338 **Methods**

339 **Participants**

340 Eight subjects were recruited for each experiment (hand and knee extensor). All procedures were
341 approved by the local ethical committees at the University of Rome Foro Italico (approval number
342 44680, knee extension experiments) and Imperial College London (approval number 18IC4685, hand
343 experiments) and conformed to the standards set by the *Declaration of Helsinki*. The subjects signed an
344 informed consent before participating in the study. Some results from these datasets have been
345 published previously (56, 63).

346 As described subsequently, high-density EMG recordings (Quattrocento, OTBioelettronica, Turin,
347 Italy) and decomposition of the acquired signals (64) were performed in both experiments.

348 **Experiment 1 (knee extensors)**

349 Participants visited the laboratory on two occasions. In the first visit, they were familiarized with the
350 experimental procedures by performing a series of maximal and submaximal isometric contractions
351 with the knee extensors. In the second visit, which occurred 24 hours after the familiarization session,
352 simultaneous recordings of the force generated by the knee extensors during maximal and submaximal
353 voluntary contractions and HDsEMG signals were recorded from vastus lateralis and vastus medialis.
354 After standardized warm-up contractions, participants were verbally encouraged to push 'as hard as
355 possible' for ~3-5 s to achieve peak maximal voluntary force (MVC). They performed ≤ 4 trials with
356 ~60 s of rest between trials. Approximately 5 min later, they performed steady contractions (2 x 10 %
357 MVC for 70 s) and submaximal trapezoidal contractions at three target forces (2 x 35, 50, 70% MVC
358 force). The trapezoidal contractions required participants to match a prescribed trajectory that
359 comprised a ramp-up phase (5% MVIF s⁻¹), a plateau (10 s of constant force at target), and a ramp-
360 down phase (-5% MVIF s⁻¹). Three minutes of rest was provided between all submaximal contractions.
361 In this study we only used the submaximal steady state contractions at 10% of maximum.

362 All measurements were performed with both legs with the order determined randomly. Participants
363 were asked to avoid exercise and caffeine intake for 48 hours before testing. Participants were
364 comfortably seated and secured in a Kin-Com dynamometer (KinCom, Denver, CO, USA) by means
365 of three Velcro straps (thigh, chest, pelvis), with the knee joint fixed at 45° of flexion (full knee
366 extension at 0°). HDsEMG signals were acquired from the vastii muscles with two grids of 64 electrodes
367 each (5 columns x 13 rows; gold-coated; 1 mm diameter; 8 mm inter-electrode distance; OT
368 Bioelettronica, Turin, Italy) (Fig. 1A). Placement of the electrode grids was based on existing guidelines
369 (Barbero et al. 2012) and adjusted as necessary. After shaving and cleaning the skin (70% ethanol),
370 both electrode grids were attached to muscle surfaces using two layers of disposable double-sided foam
371 (SpesMedica, Battapaglia, Italy). Skin-electrode contact was ensured by filling the holes of the foam
372 layer with conductive paste (SpesMedica). A ground electrode was placed on the contralateral wrist,
373 whereas the reference electrodes for both vastus lateralis and vastus medialis grids were attached to the
374 skin over the ipsilateral patella and medial malleolus, respectively. Monopolar HDsEMG signals were
375 recorded using a multichannel amplifier (EMG-Quattrocento, A/D converted to 16 bits; bandwidth 10-
376 500 Hz; OT Bioelettronica).

377 **Experiment 2 (hand muscles)**

378 The experimental setup involved a chair, table, and computer monitor. Participants were comfortably
379 seated with both arms resting on the table. A custom-made apparatus that was secured to the table
380 supported the dominant hand (self-reported) in a position midway between pronation and supination
381 and the forearm and wrist were immobilized. The index finger was aligned with the longitudinal axis
382 of the forearm, and the thumb was held in a resting position at the same height as the index finger. The
383 applied force was displayed on a monitor that was positioned 60 cm in front of the subject. The visual
384 gain was fixed at 66 pixels per percentages of MVC force for each muscle (axis). The forces exerted by
385 the index finger and thumb were measured with a three-axis force transducer (Nano25, ATI Industrial
386 Automation, Apex, NC, USA), digitized at 2048 Hz (USB-6225, National Instruments, Austin, TX,

387 USA), and low-pass filtered with a cut-off frequency of 15 Hz. HDsEMG signals were recorded with a
388 multichannel amplifier (OT Bioelettronica Quattrocento, Turin, Italy; bandwidth: 10-500 Hz;
389 resolution: 16 bits) at a sampling rate of 2048 Hz. Two flexible grids of high-density EMG electrodes
390 (13×5 pins, 4 mm interelectrode spacing) were placed on the skin over the FDI and thenar muscles
391 (flexor pollicis brevis and abductor pollicis brevis).

392 Participants performed force-matching tasks (10% MVC force) involving concurrent abduction of the
393 index finger and flexion of the thumb (Fig. 2A). Subjects performed two sustained index finger
394 abduction and thumb flexion contractions for 60 s. Visual feedback was provided as a moving dot cursor
395 in which the x-axis and y-axis corresponded to the thumb and index finger forces, respectively. Subjects
396 had to maintain the force signal within 10% of the target.

397 The experiments began with MVCs (as described in Experiment 1). After the MVCs were determined,
398 the required target forces were displayed on a monitor. Participants performed two 60-s trials with a 30
399 s of rest between trials. As noted in the introduction, we designed our tasks to determine the extent to
400 which distinct motor neuron pools would receive common inputs. To achieve this goal, subjects were
401 instructed to exert forces in the same sagittal plane, which required ~10 minutes of practice.

402 Data analysis

403 The 64 monopolar HDsEMG signals were filtered offline with a zero-lag, high-pass (10 Hz) and low-
404 pass filter (500 Hz). The force signals were corrected for the influence of gravity and normalized to
405 MVC force. HDsEMG channels with poor signal-to-noise ratios were inspected with a semi-automated
406 function that identified spurious EMG signals based on the power spectrum. Those channels with a poor
407 signal-to-noise ratio (defined as 3 standard deviations from the mean, power spectrum averaged across
408 all signals in the band 10 - 500 Hz) were visually inspected and removed from the analysis. The number
409 of EMG channels containing noise was low; > 95% of the channels had good signal-to-noise ratios.

410 Subsequently, the HDsEMG signals were decomposed with a gradient convolution kernel compensation
411 algorithm (48). The general decomposition procedures have been described previously (49). Briefly,
412 the EMG signals can be described as time-series of Dirac delta functions that contain the sources (s)
413 representing the discharge times of motor units. The time series of the motor unit discharge times can
414 be described as delta (δ) functions:

415

$$416 \quad s_j(k) = \sum_r \delta(k - \varphi_{jr}) \quad (1)$$

417

418 where φ_{jr} corresponds to the spike times of the j th motor unit. Each channel of the EMG signal can be
419 then described as convolution of the motor unit discharge times (s) into the muscle fiber action
420 potentials. Because each motor unit innervates multiple muscle fibres, it is possible to observe a
421 compound action potential from the muscle fibers innervated by that motor axon. Therefore, the
422 HDsEMG recordings can be described mathematically in a matrix \underline{x} form as:

423

$$424 \quad \underline{x}(k) = \sum_{l=0}^{L-1} \underline{H}(l) \underline{s}(k-l) + \underline{n}(k) \quad (2)$$

425

426 where $\underline{s}(k) = [s_1(k), s_2(k), \dots, s_n(k)]^T$ represents the n motor unit discharge times derived from the
427 EMG signal (\underline{x}) and \underline{n} is the noise to for each electrode. The matrix \underline{H} contains the two-dimensional
428 information of the motor unit action potential and has size $m \times l$ with l th sample of motor unit action
429 potentials for the n motor units and m channels.

430 Before the beginning the blind source separation procedure, the spatial sparsity of the matrix x was
431 enhanced by extending the observation numbers. This procedure improves the decomposition as the
432 gradient descent update rule maximises the diversity of the motor unit waveform to converge the
433 discharge times of each motor unit (the sources, s). Because this process is blind, it is possible to inspect
434 the shapes of the motor unit action potentials obtained by spike triggered averaging and to perform
435 visual inspections of the 2D and 3D waveforms (see 50, 60).

436 **Factorization analysis**

437 The neural control of muscles by motor neurons can be described and predicted analytically. If the
438 discharge times of the motor units are known, it is possible to predict modulation of muscle force with
439 near perfect correlations (52, 65). By recording of large samples of motor units, it is possible to
440 reconstruct modulation of muscle force (11) due the low-pass filtering properties of the muscle to a
441 given neural drive (51, 52). When motor unit discharge rates are filtered in the low-frequency range
442 (muscle bandwidth <20 Hz), it is possible to predict oscillations in the applied force close to $\sim 1\%$ MVC
443 (51). Consequently, the factorization analysis used in the current study focussed on the low-pass filtered
444 motor unit discharge rates. The discharge rates were filtered by convolving with a Hann window of 400
445 ms (2.5 Hz). The motor unit discharge times were factorized with three methods: factorization analysis
446 (66, 67), principal component analysis, and non-negative matrix factorization (see Figure 1 in
447 supplementary materials).

448 These factorization methods were applied on the matrix containing the smoothed discharge rates with
449 rows equal to the number of motor units identified for both muscles and columns equal to the smoothed
450 discharge times. Figures 1 and 2 shows examples of this procedure for the vastii and hand muscles.

451 Factorization analysis is based on the rationale that muscle force is the consequence of the activation of
452 many motor units, which can be represented as time sequences of M dimensional vectors (see equation
453 1) due to the activation of the motor neurons $\mathbf{m}(t)$ in response to various common and independent
454 synaptic inputs. Thus, the response of the motor neuron population can be described as combinations
455 of N varying synaptic inputs that are constrained by the non-linear properties of the motor neuron, which
456 construct a specific motor unit characteristic, or *neural module*, expressed as $\{w_i(t)\}_{i=1,\dots,N}$

$$457 \quad m(t) = \sum_{i=1}^N c_i w_i \quad (3)$$

458 where c_i is a non-negative scaling coefficient of the i -th neural module. We were interested in finding
459 the matrix w_i without making any assumptions about the relations between muscles or motor neurons.
460 We found that factor analysis was the best method in terms of correlations of the neural modules to the
461 discharge times of individual motor units. Moreover, we demonstrate with an integrate-and-fire model
462 (see below) that factor analysis can separate the neural modules with high levels of accuracy. We also
463 examined the performance of non-negative matrix factorization and principal component analysis by
464 using previous approaches to identify muscle synergies (i.e., >100 iterations and reconstruction of the
465 original signal, (19, 20, 25)).

466 The factor analysis models the associations between variables into fewer latent variables (factors). It
467 assumes that for a collection of observed variables (x) there are a set factors (f) that explain most of the
468 total variance, which is the common variance. The function *factoran* (in Matlab) computes the
469 maximum likelihood estimate of the factor loadings matrix (Λ)

$$470 \quad x = \mu + \Lambda f + e$$

471 where e is the vector of independent specific factors. Alternatively, the model can be specified as

$$472 \quad cov(x) = \Lambda \Lambda^T + \Psi$$

473 Where $\Lambda \Lambda^T$ is the common variance matrix and $\Psi = cov(e)$ is the diagonal matrix of specific variances.

474 The unique variance in the model with no a priori assumption of orthogonality between factors (when
475 allowing for factor rotations such as *promax*) makes the factor analysis an appropriate choice to extract
476 the latent discharge rate of the synergistic motor nucleus. It is supposed that the model mimics the
477 common and independent inputs impinging into the two motor nuclei.

478 **Crosstalk and realigning**

479 Motor unit action potentials from the first dorsal interosseous into the thenar muscles (and vice versa)
480 and from the vastus medialis into vastus lateralis can experience cross-talk up to 95%; that is, 95% of
481 motor units from one muscle being conducted with minimal shape distortion to the neighbouring muscle
482 (55). Consequently, we examined the level of cross-talk with a validated method (55, 56). Briefly, this
483 procedure takes advantage of the distance from the activated muscle fibers (muscle unit) to the
484 electrode, which is less for motor units in a targeted muscle. Motor units from a targeted muscle are
485 expected to show greater action potential amplitudes with minimal shape distortion (action potential
486 conduction velocity in the grid, see Germer et al. 2021 for the detailed assessment of statistically
487 significant crosstalk of individual motor units).

488 Another step was to realign motor unit action potentials with respect to the averaged motor unit action
489 potential that was obtained after spike-triggered averaging. Because the action potential at individual
490 time instants shows some variability due to surface EMG stochasticity, we convoluted the average
491 action potential to retrieve the time instants of activation of the motor units. Although this procedure
492 was critical for assessing accurate brain-spinal transmission latencies (68), it did not influence our
493 results because corticospinal latencies are so small (<50 ms). In our study, the firing rate was smoothed
494 in the frequency of force production (2.5 Hz, 400 ms). The effects of action potential onset timing,
495 therefore, are removed when low-pass filtering the motor unit discharge timings at <2.5 Hz.

496 **Computer simulations**

497 We simulated 480 integrate-and-fire motor neurons, each of which received a computer-generated
498 current input (set at 20 nA). The synaptic currents that were shared among all neurons to represent the
499 common synaptic input, but the neurons also received some independent synaptic inputs. Because motor
500 neurons can exhibit synchronous discharge times, the common input currents were close to maximal
501 values in the low frequency range <2.5 Hz (see below). The resting membrane potential and reset
502 voltage was set at -70 mV, the spike threshold was set at -50 mV, and a membrane time constant was
503 20 ms. The timestep duration was set at 0.1 ms.

504 Our model comprised randomly distributed gaussian noises at each time step to represent the common
505 and independent synaptic inputs. Figure 6 shows the overall architecture of the model. Two random
506 uncorrelated gaussian input currents were created at each time step to represent the *neural modules* that
507 were identified experimentally. One-third of the neurons (160 neurons) received I_{syn1} as a unique
508 common input. I_{syn2} received the same common input strength but orthogonal to I_{syn1} . I_{syn3} was the
509 average of I_{syn1} and I_{syn2} plus its unique independent noise (see eq. 5). The input current for each neuron
510 i and population j ($j = 1,2,3$) can be summarized by the following equation:

$$511 \quad I_{i,j} = \mu_i + \sigma_i(\xi_i(t) + \xi_c(t)) \quad (4)$$

512 where μ_i is the temporal average of the current that was set at 20 nA and σ_i sets the global network state
513 by taking into account the unique independent inputs for each cell (ξ_i) and the gaussian-distributed
514 random common inputs (ξ_c). The tuning of these parameters was matched to those observed in vivo.
515 The values of μ , ξ_i , and ξ_c were adjusted to reflect physiological values for the variability in motor unit
516 interspike intervals and common input. Interspike interval variability was examined with histogram
517 distributions, as found in the current study and by others (69). The common and independent inputs
518 were tuned based on the cross-correlogram function derived from previously reported motor unit data
519 (44). Therefore, each combination of three randomly assigned groups of 160 neurons from the total

520 pool (n=480) received two independent synaptic currents ($I_{i,2}$ equal to equation 4) and a third
521 randomized subpopulation ($j = 3$) of motor neuron received the average of the two inputs:

$$522 \quad I_{i,j} = \frac{I_{i1}+I_{i2}}{2} + \xi_i(t) \quad \text{eq. 5}$$

523 The bivariate correlations between the synaptic currents are shown in Figure 5. The total duration of
524 the simulation was set at 10, 50, and 80 s. We removed the first and last 2 s of spiking activity for all
525 simulations to minimize the influence of spike-frequency adaptation. The spike trains emitted by the
526 i th neuron after generating the spike times were stored as a binary time series, which was equal to 1
527 when the neuron reached voltage threshold. The successive analysis followed the same steps as the
528 experimental data. Briefly, the binary spike trains were low-pass filtered with a 2.5 Hann window and
529 the factorization analysis was then performed on the low-pass filtered signals. Because the distribution
530 of inputs to each neuron were known (i.e., I_{i1-3}), it was possible to retrieve the performance accuracy
531 of the factorization analysis. Moreover, it was possible to investigate the relation between motor neuron
532 responses to increased synaptic currents with changes in common and independent inputs. As reported
533 in the results, we found that when a large number of spikes was included in the analysis (simulation of
534 80 s), the factorization analysis provided a perfect prediction of the three sources of common synaptic
535 inputs. Our model confirmed that the three clusters observed experimentally in the neural modules arise
536 due from two distinct oscillatory common synaptic inputs and that the third component (the shared
537 neural modules) is an average of the two other modules.

538 **Statistical analysis**

539 We performed linear regression analysis between the smoothed motor unit discharge rates within and
540 between muscles. The significant level was extracted from bivariate Pearson's correlations and
541 Bonferroni method was applied with multiple comparisons. The same procedure was used to find the
542 modules carried by each neuron (decoding function). Each neural module extracted by the factorization
543 algorithm (66, 67) was compared to the firing rate of the individual motor units. Significance was
544 accepted for P values < 0.05.

545 **References**

- 546 1. J. Duchateau, R. M. Enoka, Human motor unit recordings: Origins and insight into the
547 integrated motor system. *Brain Res.* **1409**, 42–61 (2011).
- 548 2. J. V. Basmajian, Control and Training of Individual Motor Units. *Science (80-.)*. **141**, 440–
549 441 (1963).
- 550 3. V. F. Harrison, O. A. Mortensen, Identification and voluntary control of single motor unit
551 activity in the tibialis anterior muscle. *Anat. Rec.* **144**, 109–116 (1962).
- 552 4. E. Henneman, B. Shahani, R. Young, R., “Voluntary control of human motor units” in *The*
553 *Motor System: Neurophysiology and Muscle Mechanisms*, M. Shahani, Ed. (Elsevier, 1976),
554 pp. 73–78.
- 555 5. C. J. Heckman, R. M. Enoka, Motor Unit. *Compr. Physiol.* **2**, 2629–2682 (2012).
- 556 6. E. Henneman, C. Olson, Relations between structure and function in the design of skeletal
557 muscles. *J Neurophysiol* **28**, 581–598 (1965).
- 558 7. E. Henneman, G. Somjen, D. O. Carpenter, Functional Significance of Cell Size in Spinal
559 Motoneurons. *J. Neurophysiol.* **28**, 560–580 (1965).
- 560 8. J. E. Desmedt, E. Godaux, Fast motor units are not preferentially activated in rapid voluntary
561 contractions in man. *Nature* **267**, 717–9 (1977).
- 562 9. J. E. Desmedt, E. Godaux, Ballistic contractions in fast or slow human muscles; discharge

- 563 patterns of single motor units. *J. Physiol.* **285**, 185–196 (1978).
- 564 10. H. S. Milner-Brown, R. B. Stein, R. Yemm, The contractile properties of human motor units
565 during voluntary isometric contractions. *J. Physiol.* **228**, 285–306 (1973).
- 566 11. F. Negro, A. Holobar, D. Farina, Fluctuations in isometric muscle force can be described by
567 one linear projection of low-frequency components of motor unit discharge rates. *J. Physiol.*
568 **587**, 5925–5938 (2009).
- 569 12. C. K. Thompson, *et al.*, Robust and accurate decoding of motoneuron behaviour and prediction
570 of the resulting force output. *J. Physiol.* **0**, 1–5 (2018).
- 571 13. M. J. Ferreira-Pinto, L. Ruder, P. Capelli, S. Arber, Connecting Circuits for Supraspinal
572 Control of Locomotion. *Neuron* **100**, 361–374 (2018).
- 573 14. E. Henneman, L. M. Mendell, Functional Organization of Motoneuron Pool and its Inputs.
574 *Compr. Physiol.* (2011) <https://doi.org/10.1002/cphy.cp010211>.
- 575 15. C. G. Phillips, R. Porter, The Pyramidal Projection to Motoneurons of Some Muscle Groups
576 of the Baboon's Forelimb. *Prog. Brain Res.* **12**, 222–245 (1964).
- 577 16. S. Grillner, Biological Pattern Generation: The Cellular and Computational Logic of Networks
578 in Motion. *Neuron* **52**, 751–766 (2006).
- 579 17. F. Sylos-Labini, *et al.*, Distinct locomotor precursors in newborn babies. *Proc. Natl. Acad. Sci.*
580 **117**, 9604–9612 (2020).
- 581 18. E. Bizzi, V. C. K. Cheung, The neural origin of muscle synergies. *Front. Comput. Neurosci.* **7**,
582 1–6 (2013).
- 583 19. M. C. Tresch, C. C. K. V., A. d'Avella, Matrix Factorization Algorithms for the Identification
584 of Muscle Synergies: Evaluation on Simulated and Experimental Data Sets. *J. Neurophysiol.*
585 **95**, 2199–2212 (2005).
- 586 20. Y. P. Ivanenko, R. E. Poppele, F. Lacquaniti, Five basic muscle activation patterns account for
587 muscle activity during human locomotion. *J. Physiol.* **556**, 267–282 (2004).
- 588 21. J. A. Gallego, M. G. Perich, L. E. Miller, S. A. Solla, Neural Manifolds for the Control of
589 Movement. *Neuron* **94**, 978–984 (2017).
- 590 22. M. C. Tresch, P. Saltiel, E. Bizzi, The construction of movement by the spinal cord. *Nat.*
591 *Neurosci.* **2**, 162–167 (1999).
- 592 23. E. Bizzi, F. Mussa-Ivaldi, S. Giszter, Computations underlying the execution of movement: a
593 biological perspective. *Science (80-)*. **253**, 287–291 (1991).
- 594 24. M. A. Lemay, Modularity of Motor Output Evoked By Intraspinial Microstimulation in Cats. *J.*
595 *Neurophysiol.* **91**, 502–514 (2003).
- 596 25. A. D'Avella, P. Saltiel, E. Bizzi, Combinations of muscle synergies in the construction of a
597 natural motor behavior. *Nat. Neurosci.* **6**, 300–308 (2003).
- 598 26. C. M. Laine, E. Martinez-Valdes, D. Falla, F. Mayer, D. Farina, Motor Neuron Pools of
599 Synergistic Thigh Muscles Share Most of Their Synaptic Input. *J. Neurosci.* **35**, 12207–12216
600 (2015).
- 601 27. A. d'Avella, A. Portone, L. Fernandez, F. Lacquaniti, Control of Fast-Reaching Movements by
602 Muscle Synergy Combinations. *J. Neurosci.* **26**, 7791–7810 (2006).
- 603 28. C. Alessandro, *et al.*, Coordination amongst quadriceps muscles suggests neural regulation of
604 internal joint stresses, not simplification of task performance. *Proc. Natl. Acad. Sci.* **117**,
605 201916578 (2020).

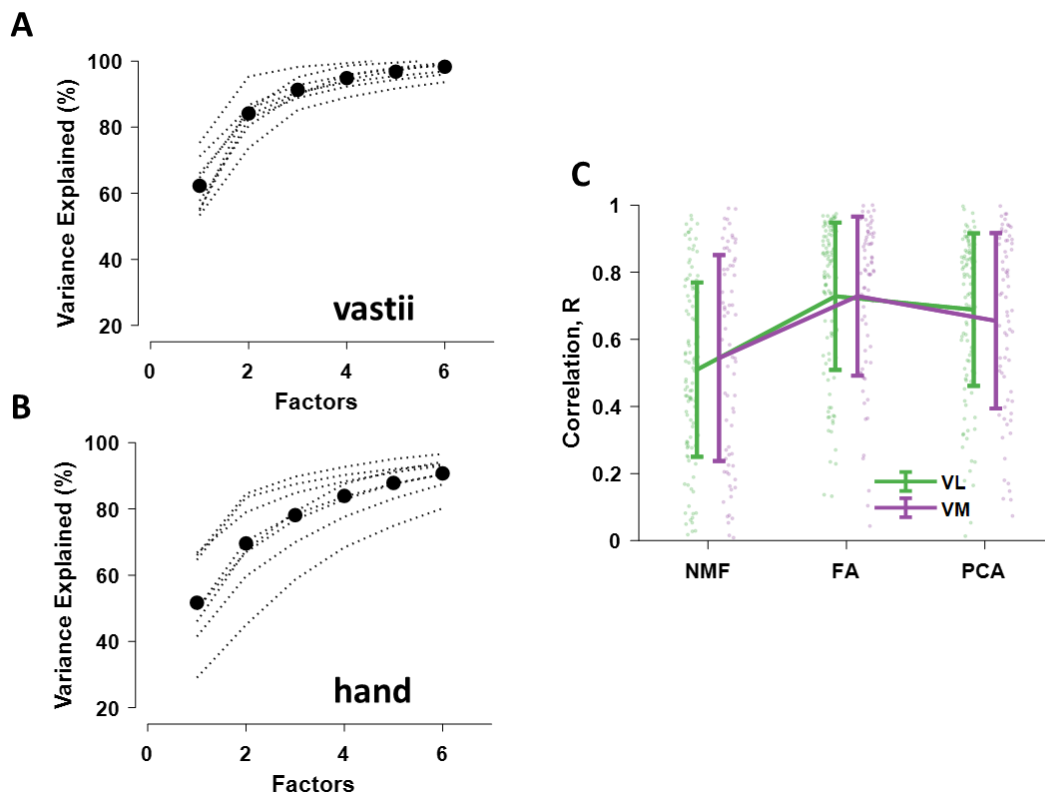
- 606 29. S. Muceli, A. T. Boye, A. D'Avella, D. Farina, Identifying representative synergy matrices for
607 describing muscular activation patterns during multidirectional reaching in the horizontal
608 plane. *J. Neurophysiol.* **103**, 1532–1542 (2010).
- 609 30. J. Shlens, *et al.*, The structure of multi-neuron firing patterns in primate retina. *J. Neurosci.* **26**,
610 8254–8266 (2006).
- 611 31. E. Schneidman, M. J. Berry, R. Segev, W. Bialek, Weak pairwise correlations imply strongly
612 correlated network states in a neural population. *Nature* **440**, 1007–1012 (2006).
- 613 32. J. de la Rocha, B. Doiron, E. Shea-Brown, K. Josić, A. D. Reyes, Correlation between neural
614 spike trains increases with firing rate. *Nature* **448**, 802–6 (2007).
- 615 33. A. d'Avella, E. Bizzi, Shared and specific muscle synergies in natural motor behaviors. *Proc.*
616 *Natl. Acad. Sci.* **102**, 3076–3081 (2005).
- 617 34. D. D. Lee, H. S. Seung, Learning the parts of objects by non-negative matrix factorization.
618 *Nature* **401**, 788–791 (1999).
- 619 35. J. E. Ting, *et al.*, Sensing and decoding the neural drive to paralyzed muscles during attempted
620 movements of a person with tetraplegia using a sleeve array. *J. Neurophysiol.* (2021)
621 <https://doi.org/10.1152/jn.00220.2021>.
- 622 36. S. Tanzarella, S. Muceli, A. Del Vecchio, A. Casolo, D. Farina, Non-invasive analysis of
623 motor neurons controlling the intrinsic and extrinsic muscles of the hand. *J. Neural Eng.* **17**,
624 046033 (2020).
- 625 37. S. Tanzarella, S. Muceli, M. Santello, D. Farina, Synergistic Organization of Neural Inputs
626 from Spinal Motor Neurons to Extrinsic and Intrinsic Hand Muscles. *J. Neurosci.* **In press**
627 (2021).
- 628 38. G. B. Hockensmith, S. Y. Lowell, A. J. Fuglevand, Common input across motor nuclei
629 mediating precision grip in humans. *J. Neurosci.* **25**, 4560–4 (2005).
- 630 39. T. L. McIsaac, A. J. Fuglevand, Motor-Unit Synchrony Within and Across Compartments of
631 the Human Flexor Digitorum Superficialis. *J. Neurophysiol.* **97**, 550–556 (2006).
- 632 40. S. A. Winges, M. Santello, Common input to motor units of digit flexors during multi-digit
633 grasping. *J. Neurophysiol.* **92**, 3210–20 (2004).
- 634 41. G. S. Sawicki, O. N. Beck, I. Kang, A. J. Young, The exoskeleton expansion : improving
635 walking and running economy (2020) <https://doi.org/10.1186/s12984-020-00663-9>.
- 636 42. C. J. De Luca, Z. Erim, Common drive of motor units in regulation of muscle force. *Trends*
637 *Neurosci.* **17**, 299–305 (1994).
- 638 43. B. Y. A. J. Fuglevand, *et al.*, Impairment of neuromuscular propagation during human
639 fatiguing contractions at submaximal forces. *J. Physiol.* **460**, 549–572 (1993).
- 640 44. F. Negro, U. Ş. Yavuz, D. Farina, The human motor neuron pools receive a dominant slow-
641 varying common synaptic input. *J. Physiol.* **594**, 5491–5505 (2016).
- 642 45. A. Del Vecchio, *et al.*, Interfacing Spinal Motor Units in Non-Human Primates Identifies a
643 Principal Neural Component for Force Control Constrained by the Size Principle (2021)
644 <https://doi.org/https://doi.org/10.1101/2021.12.07.471592>.
- 645 46. F. Hug, S. Avrillon, A. Sarcher, Networks of common inputs to motor neurons of the lower
646 limb reveal neural synergies that only partly overlap with muscle innervation. 1–34 (2021).
- 647 47. S. Avrillon, *et al.*, Individual differences in the neural strategies to control the lateral and
648 medial head of the quadriceps during a mechanically constrained task. *J. Appl. Physiol.* **130**

- 649 (2021).
- 650 48. A. Holobar, D. Zazula, Multichannel blind source separation using convolution Kernel
651 compensation. *IEEE Trans. Signal Process.* **55**, 4487–4496 (2007).
- 652 49. D. Farina, A. Holobar, Characterization of Human Motor Units from Surface EMG
653 Decomposition. *Proc. IEEE* **104**, 353–373 (2016).
- 654 50. A. Del Vecchio, *et al.*, Spinal motoneurons of the human newborn are highly synchronized
655 during leg movements. *Sci. Adv.* **6**, eabc3916 (2020).
- 656 51. A. Del Vecchio, *et al.*, Central nervous system modulates the neuromechanical delay in a
657 broad range for the control of muscle force. *J. Appl. Physiol.* **125**, 1404–1410 (2018).
- 658 52. F. Baldissera, P. Cavallari, G. Cerri, Motoneuronal pre-compensation for the low-pass filter
659 characteristics of muscle. A quantitative appraisal in cat muscle units. *J. Physiol.* **511**, 611–627
660 (1998).
- 661 53. D. F. Feeney, D. Mani, R. M. Enoka, Variability in common synaptic input to motor neurons
662 modulates both force steadiness and pegboard time in young and older adults. *J. Physiol.* **596**,
663 3793–3806 (2018).
- 664 54. D. Farina, F. Negro, J. L. Dideriksen, The effective neural drive to muscles is the common
665 synaptic input to motor neurons. *J. Physiol.* **49**, 1–37 (2014).
- 666 55. C. M. Germer, *et al.*, Surface EMG cross talk quantified at the motor unit population level for
667 muscles of the hand, thigh, and calf. *J. Appl. Physiol.* **131**, 808–820 (2021).
- 668 56. A. Del Vecchio, *et al.*, The human central nervous system transmits common synaptic inputs
669 to distinct motor neuron pools during non-synergistic digit actions. *J. Physiol.* **597**, 5935–5948
670 (2019).
- 671 57. L. . Abbott, Lapicque’s introduction of the integrate-and-fire model neuron (1907). *Brain Res.*
672 *Bull.* **50**, 303–304 (1999).
- 673 58. J. B. Nielsen, Human Spinal Motor Control. *Annu. Rev. Neurosci.* **39**, 81–101 (2016).
- 674 59. A. R. Sobinov, S. J. Bensmaia, The neural mechanisms of manual dexterity. *Nat. Rev.*
675 *Neurosci.* **22**, 741–757 (2021).
- 676 60. A. Del Vecchio, *et al.*, Interfacing Spinal Motor Units in Non-Human Primates Identifies a
677 Principal Neural Component for Force Control Constrained by the Size Principle (2021)
678 <https://doi.org/https://doi.org/10.1101/2021.12.07.471592>.
- 679 61. A. Almklass, R. Price, J. Gould, R. Enoka, Force steadiness as a predictor of time to complete
680 a pegboard test of dexterity in young men and women. *J. Appl. Physiol.* **in press** (2016).
- 681 62. J. E. Desmedt, E. Godaux, Spinal Motoneuron Recruitment in Man: Rank Deordering with
682 Direction But Not with Speed of Voluntary Movement. *Science (80-.)*. **214**, 933–936 (1981).
- 683 63. S. Nuccio, *et al.*, Deficit in knee extension strength following anterior cruciate ligament
684 reconstruction is explained by a reduced neural drive to the vasti muscles. *J. Physiol.* **599**,
685 5103–5120 (2021).
- 686 64. A. Del Vecchio, *et al.*, Tutorial: Analysis of motor unit discharge characteristics from high-
687 density surface EMG signals. *J. Electromyogr. Kinesiol.* **53**, 102426 (2020).
- 688 65. L. D. Partridge, Modifications of neural output signals by muscles: a frequency response
689 study. *J. Appl. Physiol.* **20**, 150–156 (1965).
- 690 66. K. G. Jöreskog, Some contributions to maximum likelihood factor analysis. *Psychometrika* **32**,
691 443–482 (1967).

- 692 67. A. E. Maxwell, H. H. Harman, Modern Factor Analysis. *J. R. Stat. Soc. Ser. A* **131** (1968).
693 68. J. Ibáñez, A. Del Vecchio, J. C. Rothwell, S. N. Baker, D. Farina, Only the fastest
694 corticospinal fibers contribute to B corticomuscular coherence. *J. Neurosci.* **41**, 4867–4879
695 (2021).
696 69. C. T. Moritz, B. K. Barry, M. A. Pascoe, R. M. Enoka, Discharge Rate Variability Influences
697 the Variation in Force Fluctuations Across the Working Range of a Hand Muscle. *J.*
698 *Neurophysiol.* **93**, 2449–2459 (2005).

699 **Supplementary materials**

700



701

702 **Figure 1S.** Reconstruction accuracy (% variance explained) for each subject (dotted black lines). The
703 black dots in **A** and **B** represent the average neural modules across subjects. **C.** The correlation values
704 (mean \pm SD) between the modules and the motor units discharge rates.

705