

## **Does human primary motor cortex represent sequences of finger movements?**

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### **Abbreviated title:**

Sequence representation in M1

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### **Open source programs:**

The MATLAB code used for the multivariate fMRI analysis (pattern component modelling) are available online ([https://github.com/jdiedrichsen/pcm\\_toolbox](https://github.com/jdiedrichsen/pcm_toolbox)).

1 **Abstract:**

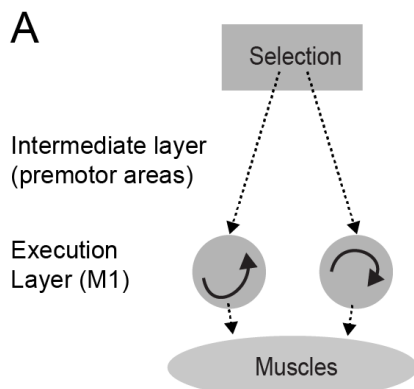
2 Human primary motor cortex (M1) is an essential structure for the production of  
3 dexterous hand movements. While distinct subpopulations of neurons are activated  
4 during single finger movements, it remains unknown whether M1 also represents  
5 sequences of multiple finger movements. Using novel multivariate fMRI analysis  
6 techniques, we show here that even after 5 days of intense practice there was little or  
7 no evidence for a true sequence representation in M1. Rather, the activity patterns for  
8 sequences in M1 could be explained by linear combination of patterns associated with  
9 the constituent individual finger movements, with the strongest weight on the finger  
10 making the first response of the sequence. These results suggest that M1 only  
11 represents single finger movements, but receives increased input at the start of a  
12 sequence. In contrast, the reliable differences between different sequences in premotor  
13 and parietal areas could not be explained by a strong weighting of the first finger,  
14 supporting the view that these regions exhibit a true representation of sequences.

## 15 Introduction

16 Primary motor cortex (M1) with its direct projection to spinal motoneurons is  
17 a critical structure for fine hand control (Lawrence and Kuypers, 1968; Muir and  
18 Lemon, 1983). Population of neurons in M1 involved in individuated finger  
19 movement show considerable overlap (Schieber and Hibbard, 1993). Yet, they form  
20 large enough clusters to be detected with functional magnetic resonance imaging  
21 (fMRI) as unique activation pattern associated with each individual finger (Indovina  
22 and Sanes, 2001; Ejaz et al., 2015). Each of these populations can be conceptualized  
23 as a dynamical system (Churchland et al., 2012) (illustrated by arrows inside the two  
24 circles in Fig. 1A), that produces the continuous sequence of muscle activities  
25 necessary for the movement of a single finger. Here we ask whether such sub-  
26 populations in M1 can also learn to represent longer sequences that span movements  
27 of multiple different fingers.

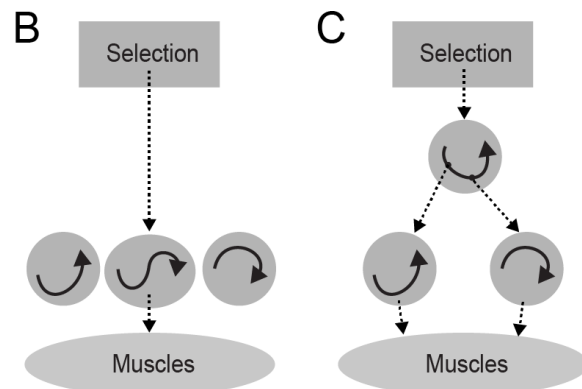
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Control of individual finger movement



29

Control of sequential finger movements



30 **Figure 1. Two ways of representing sequential movements.** (A) Before training  
31 sequences are produced through sequential selection of single finger movements. The  
32 execution layer (M1 and spinal cord) contains populations of neurons that, once  
33 activated, generate the muscle activity patterns necessary for a single finger  
34 movement through their intrinsic population dynamics. (B) After learning, the  
35 repeated sequential activation of two execution primitives leads to the formation of a  
36 new population of neurons that produces the two presses as a single unit. (C)  
37 Alternatively, a neural population in premotor areas could activate the execution  
38 primitives for the two fingers in the correct order.

39

40           Recent computational work has demonstrated that a randomly connected  
41 recurrent neural network can learn and store multiple dynamically evolving patterns  
42 (Laje and Buonomano, 2013). It is therefore conceivable that M1 develops dedicated  
43 populations of neurons that encode the sequences of two or more finger movements  
44 (Fig. 1B). In this scenario, the neural activity for pressing the 2<sup>nd</sup> digit would be  
45 different depending on whether it was executed in the sequence 1-2 or 3-2. Such a  
46 representation would be necessary if M1 was to autonomously generate the spatio-  
47 temporal activity pattern necessary for sequence production. Indeed, it has been  
48 suggested that M1 acquires such representations of finger movement sequences after  
49 multiple days of training (Karni et al., 1995).

50           Alternatively, the learned sequences could be represented in secondary motor  
51 areas (Hikosaka et al., 2002; Diedrichsen and Kornysheva, 2015), which then activate  
52 the corresponding execution-related populations in M1 (Fig. 1C). A number of  
53 recording studies have found evidence of neurons that are uniquely activated for  
54 different sequences in dorsal premotor cortex (PMd) and the supplementary motor  
55 area (SMA) (Mushiake et al., 1991; Shima and Tanji, 1998). In this scenario, M1  
56 would have no true sequence representation, as the neural activity would solely reflect  
57 the ongoing elementary movement independent of the sequential context (Mushiake et  
58 al., 1991; Ashe et al., 1993).

59           Here we sought to distinguish between these two possibilities, by analysing  
60 the fine-grained activity patterns in M1 using functional magnetic resonance imaging  
61 (fMRI) during the performance of well-learned finger sequences. Sequences consisted  
62 of different orderings of the same fingers presses. Because of the low temporal  
63 resolution of fMRI, we could not resolve the activity related to the individual presses,  
64 but could only measure the activity pattern averaged over the whole sequence.  
65 Nonetheless, if activity in M1 represented the movement sequence, we should find  
66 reliable differences between the sequences, as each sequence would activate a partly  
67 separate neuronal subpopulation (Fig. 1B).

68           Indeed, in previous studies (Wiestler and Diedrichsen, 2013; Kornysheva and  
69 Diedrichsen, 2014; Wiestler et al., 2014), we had found that sequences consisting of  
70 different permutations of the same five fingers can be reliably decoded from M1.  
71 However, the finding of decodeability alone does not provide unequivocal evidence  
72 for a true sequence representation. It is possible that activity in M1 only represents

73 individual movements (i.e. that the activity for the second press is the same whether it  
74 is executed in the sequence 1-2 or 3-2, Fig. 1C), but that the amount of activity for  
75 each individual finger press depends on the serial position in the sequence. For  
76 example, it is possible that the first finger press in the sequence always elicits more  
77 activity than subsequent presses. Because we can only observe a temporally integrated  
78 signal in fMRI, such unequal weighting would lead to differences in activity patterns  
79 between different sequences. Thus to show evidence for a true sequence  
80 representation, we not only need to show distinguishable activity patterns for different  
81 sequences, but also demonstrate that these differences cannot be explained by a  
82 weighted combination of the activity patterns for individual presses.

83 To test this idea, we compared the patterns for multi-finger sequence with  
84 those obtained for the execution of repeated presses of each single finger. We found  
85 that in M1 differences between the activity patterns for different sequences could be  
86 fully explained by the combination of activity patterns elicited by single finger presses.  
87 Specifically, sequence activation patterns in M1 reflected a stronger activation for the  
88 first finger in the sequence than subsequent fingers. In contrast, activation patterns in  
89 premotor and parietal cortices could not be explained by a combination of the activity  
90 patterns for the elementary movements. This suggests that premotor areas comprise  
91 representations of movement sequence, which then activate the representations of the  
92 individual component movements in M1 (Fig. 1C).

## 93 **Results**

### 94 **M1 “encodes” both single finger movements and sequences.**

95 We tested if sequences are represented within M1 by comparing the fine-grained  
96 fMRI brain activation pattern associated with fast finger sequences (6 finger presses  
97 within 2.5 sec) with those associated with single-finger movements. Participants  
98 practiced six sequences that comprised all orders of pressing the thumb, middle and  
99 little finger with their right hand (Fig. 2A,B). They also produced six repetitions of  
100 the same finger press with each of the fingers, as constituents of the sequences.  
101 Participants were trained for 3 days, approximately 6 hrs in total, until they could  
102 perform all sequences from memory without error and at the same speed. We  
103 localized areas that showed reliable differences between either single-finger or multi-  
104 finger sequences by using a surface-based search-light approach (Oosterhof et al.,

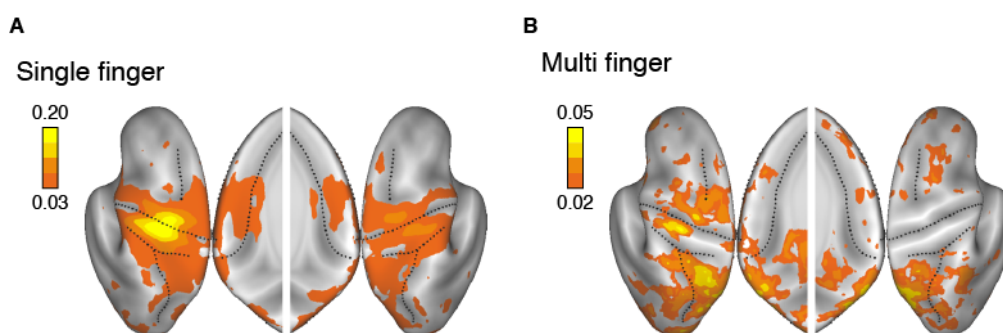
105 2011). Based on previous results (Wiestler and Diedrichsen, 2013), we expected that  
106 different single finger movements and different movement sequences would elicit  
107 differentiable activity patterns in M1.  
108



109  
110 **Figure 2. Methods for Experiment 1.** (A) Participants generated isometric finger  
111 presses on a custom-built keyboard with force transducers and pneumatic pistons  
112 embedded within each key. (B) Participants were trained on five single-finger and 6  
113 multi-finger sequences. (C) Schematic illustration for a trial during scanning. A  
114 roman numeral indicated the sequence to be executed. Participants then executed the  
115 sequence twice, receiving online visual feedback for each correct press. fMRI activity  
116 measurements were averaged across the two executions of the sequence, thereby  
117 removing temporal information from the activity profiles.

118  
119 To characterize the representation, we calculated the cross-validated  
120 Mahalanobis distance (Walther et al., 2016) between the activity patterns for different  
121 conditions. As expected, we found evidence for a representation of single fingers in  
122 the hand area of primary motor (M1) and somatosensory cortex (S1, Fig 3A).  
123 Consistent with previous studies (Wiestler et al., 2011; Diedrichsen et al., 2013; Ejaz  
124 et al., 2015), weaker differences between activity patterns of single finger movements  
125 were also found in secondary motor areas such as dorsal and ventral premotor (PMd  
126 and PMv), supplementary motor (SMA) areas, and in the anterior superior parietal  
127 lobules, (aSPL, for stats see Figure 3-Supplement A,B), and the ipsilateral hemisphere  
128 (Diedrichsen et al., 2013).

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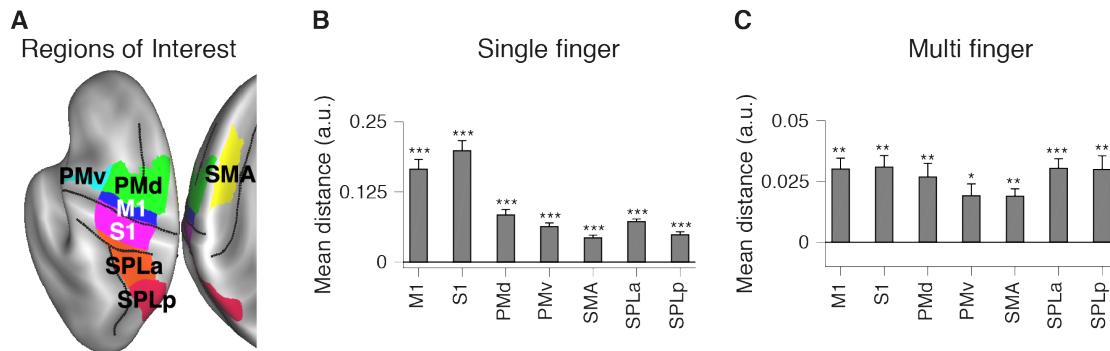
131 **Figure 3. Searchlight map for movement representation.** (A) Averaged distance for  
132 single finger sequences. (B) Averaged distance for multi finger sequences. Results are  
133 shown on an inflated view of the left and right hemisphere, with the inset showing  
134 distance on the medial wall.

135

136 The multi-finger sequences elicited differentiable activity patterns in premotor  
137 and parietal areas (Wiestler and Diedrichsen, 2013; Kornysheva and Diedrichsen,  
138 2014; Wiestler et al., 2014) (Fig 3B). Importantly, we also found significantly  
139 different activity patterns for different sequences in M1 and S1 (Figure 3-Supplement  
140 C). The pattern distances for sequences were only  $19\pm 9\%$  of those for single-finger  
141 movements, but they were reliable enough to decode which of the six sequences was  
142 performed with a cross-validated accuracy of  $25\pm 5\%$  (chance-level is 16.67%).

143 One may argue that, if M1 only represented the individual finger presses, the  
144 activity patterns for the different sequences should have been indistinguishable.  
145 However, this argument relies on the assumption that all component actions elicit the  
146 same amount of activation regardless of the order in which they were made. Before  
147 concluding that M1 exhibits a genuine sequence representation (i.e. is in a different  
148 neuronal state for each sequence), we therefore need to consider the possibility that  
149 the input from premotor areas (Fig. 1C) varied depending on whether the finger press  
150 was in the beginning or middle of the sequence. As different sequences start with  
151 different fingers, this effect could lead to distinguishable BOLD activity patterns for  
152 different sequences, without implying a true representation of the sequence in M1.

153



154

155 **Figure 3-Supplement. ROI analysis of movement representation.** (A) Seven ROIs  
156 were defined on the left hemisphere of reconstructed cortical surface. (B,C) Mean  
157 distances calculated for single finger sequences (B), and multi finger sequences (C).  
158 Asterisks indicate significance based on the group t-test. \*:  $p < 0.05$ , \*\*:  $p < 0.01$ , \*\*\*:  
159  $p < 0.001$ .

160

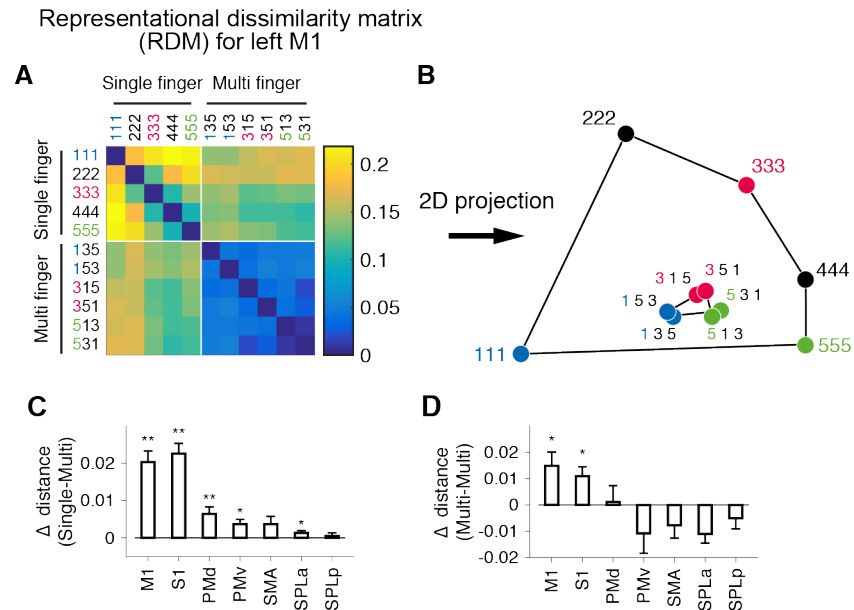
### 161 Differences in sequences depend on the first finger.

162 To test for this possibility, we systematically compare the activation patterns for the  
163 multi-finger sequences to those of the single-finger presses and in M1. We calculated  
164 the cross-validated distances between all pairs of conditions in an anatomically  
165 defined region-of-interest (ROI; Figure 3-Supplement A) for contralateral M1. The  
166 resultant matrix of pair-wise distances (55 pairs in total) – the representational  
167 dissimilarity matrix (RDM) - effectively summarizes the representational structure of  
168 the whole ROI (Fig. 4A).

169 To obtain insight into the representational structure, we applied a  
170 dimensionality reduction to the RDM by projecting it into a 2-dimensional space (Fig.  
171 4B, for detail, see Materials and Methods). For single-finger movements (111, 333,  
172 etc.) we replicated the characteristic representational structure with the thumb  
173 showing the most unique pattern and the other fingers arranged in a semi-circle (Ejaz  
174 et al., 2015).

175





176

177 **Figure 4. Representational structure in the left M1.** (A) Representational  
 178 dissimilarity matrix (RDM) calculated from the activation pattern within left M1  
 179 (contralateral to the performing hand). (B) Low-dimensional projection of the RDM  
 180 by multi-dimensional scaling (MDS). Each dot represents a movement condition (1-5:  
 181 single finger, 135-531: multi finger). (C, D) Test for first-finger effect (see Materials  
 182 and Methods). (C) Mean distance between the single-finger movement (1, 3, or 5) and  
 183 the multi-finger sequence that starts with the same finger MINUS the distance  
 184 between the same single finger movement and sequences that start with a different  
 185 finger. A positive difference indicates that the pattern for each multi-finger sequence  
 186 is weighted towards the pattern of the first finger. (D) Mean distance (calculated for  
 187 M1) between two multi-finger sequences that start with different fingers MINUS the  
 188 mean distance between fingers that start with the same finger. A positive difference  
 189 indicates that difference between sequences can partly be explained by the difference  
 190 between the first finger. Asterisks indicate statistical significance assessed by one-  
 191 sided paired t-test (\*:  $p < 0.05$ , \*\*:  $p < 0.01$ ).

192

193 The multi-finger sequences are arranged such that two sequences starting with  
 194 the same finger are clustered together (shown in the same colour in Fig. 4B).  
 195 Furthermore, among all multi-finger sequence patterns, each pattern was also the most  
 196 similar to the pattern associated with the first finger in the sequence. It should be  
 197 noted, however, that low-dimensional projections (here designed to maximize the  
 198 distances between single-finger movements, see Materials and Methods) do in general

199 not capture all the aspects of the representational structure. Therefore, to fairly  
200 quantify these two key observations, we compared the cross-validated distances  
201 between activity patterns of single- and multi-finger sequences in the (un-projected)  
202 high-dimensional space.

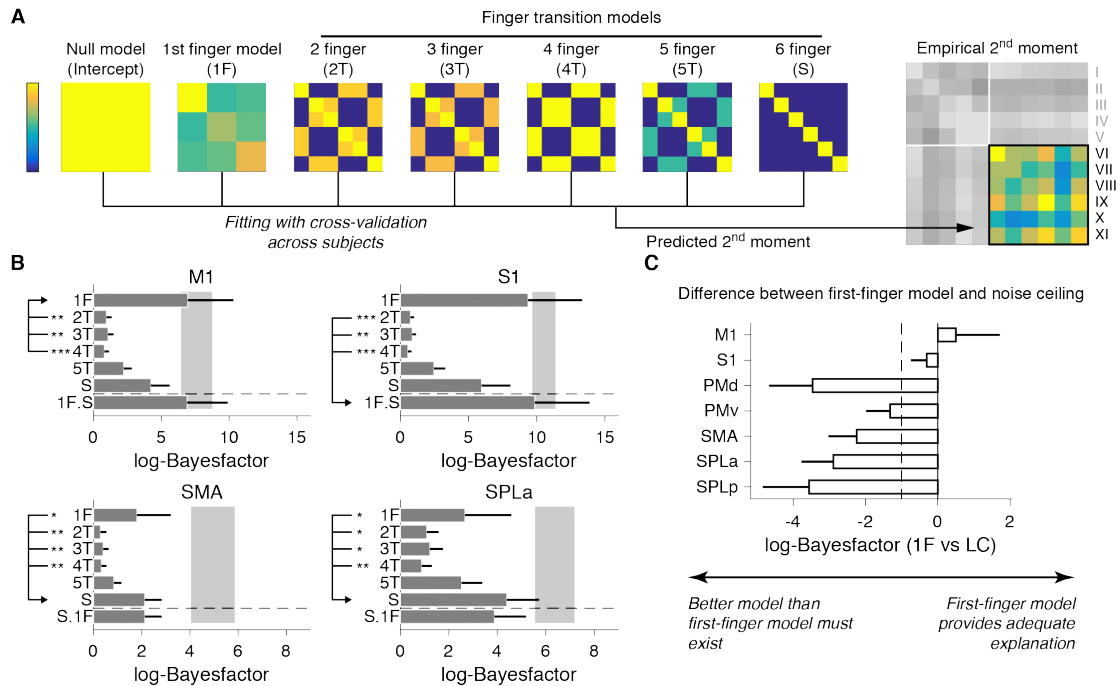
203 If the activity pattern of each sequence is the most similar to the starting finger,  
204 then the pattern for each individual finger should be closer to sequences starting with  
205 this finger than to other sequences. For instance, the pattern for the thumb (111, in Fig.  
206 4B) should be closer to sequence 135 and 153 than to other sequences (e.g., 351 or  
207 315). This was indeed the case in contralateral M1 ( $t_8=6.18$ ,  $p=1.3\times 10^{-4}$ ) and S1  
208 ( $t_8=4.09$ ,  $p=0.0018$ ) (Fig. 4C).

209 Furthermore, two sequences starting with the same finger should be more  
210 similar to each other than other pairs (e.g., the distance 135 vs. 153 should be smaller  
211 than 135 vs. 315). Again, this effect was significant in M1 (Fig. 4D,  $t_8=2.87$ ,  
212  $p=0.0104$ ) and S1 ( $t_8=3.08$ ,  $p=0.0075$ ). In contrast, no other tested ROI showed  
213 significance on both tests simultaneously (Fig. 4D).

214 One possible scenario which can explain both observations is that the activity  
215 patterns for sequences in M1 are a weighted sum of patterns elicited by the constituent  
216 single-finger presses, with the first finger having the highest weight. This would  
217 imply that there is no true sequence representation in M1. To evaluate whether this  
218 simple idea could fully explain the pattern differences between the multi-finger  
219 sequences in M1, we tested different candidate models for the activity patterns  
220 elicited by sequences using the framework of pattern component modeling (PCM)  
221 (Diedrichsen et al., 2011; Diedrichsen and Kriegeskorte, 2016; Diedrichsen et al.,  
222 2017). PCM allows us to directly compare different models for the representational  
223 structure inherent in the pattern of multi-voxel activities. Importantly, we can  
224 compare the model likelihood to a noise ceiling, to assess whether the model can fully  
225 account for the data given the level of measurement noise and inter-subject variability  
226 (see Materials & Method).

227 As a starting point, we assessed the “first-finger” model, in which the patterns  
228 for multi-finger sequences are the weighted sum of the single finger presses, with the  
229 first finger having the highest weight and all the subsequent fingers a lower, but equal,  
230 weights (see Materials & Method). This model predicts that sequences that start with  
231 the same finger do not have different patterns (Fig. 5A). We found that this model

232 could almost fully account for the representational structure found in M1: the  
 233 difference in log-likelihood to the Null-model (log-Bayes factor, see Materials &  
 234 Method) fell between the upper and lower bound of the noise ceiling (Fig. 5B: 6.95 vs  
 235 6.45).

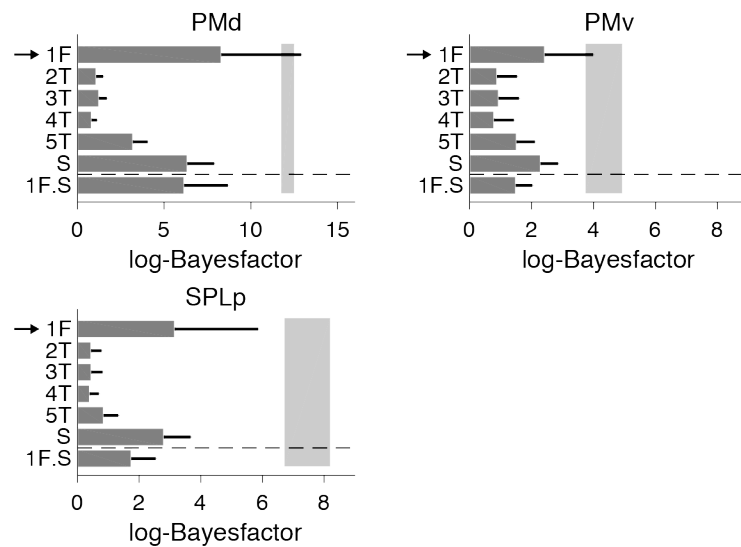


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237 **Figure 5. Evaluating representational models of multi-finger sequences.**

238 (A) The empirical second moment of the activity patterns is modelled using a  
 239 combination of the predicted second moment matrices for each of the models. (B)  
 240 Difference in log-likelihood as compared to the null-model (log-Bayes-factor) for  
 241 each component model. The grey area demarks the upper and lower noise ceiling.  
 242 The combination of the first-finger model and the 6-finger transition model (1F.S) is  
 243 shown below the horizontal dashed line. Winning model is marked by the arrow.  
 244 Significant differences (assessed by Wilcoxon's rank sum test on individual log-  
 245 Bayes-factors) in the fit between the winning and the other models are marked by  
 246 asterisks (\*:  $p < 0.05$ , \*\*:  $p < 0.01$ , \*\*\*:  $p < 0.001$ ). Error bars represent SE across  
 247 subjects. (C) Log-Bayes-factor of the first-finger model compared to the lower noise  
 248 ceiling for each ROI. Dashed line shows the typical threshold value for model  
 249 selection (e.g., Kaas and Raftery 1995).

250



251

252 **Figure 5-Supplement. Model fitting result for other ROIs.**

253

254 We then tested whether M1 might represent movement transitions between 2  
255 or more fingers (see Fig 5A). Note that a representation of a 6-finger transition would  
256 mean that each sequence would have a unique activity pattern. The log-Bayes factor  
257 for these models was clearly lower than that for the first-finger model (Fig. 5B),  
258 indicating a poorer fit of these models.

259 We then explored linear combinations of models. Because the relative weight  
260 of each component was an additional free parameter, we evaluated the model  
261 likelihood using cross-validation across participants (see Materials & Methods).  
262 When we combined the first-finger model with the sequence model, we achieved a  
263 slightly lower likelihood than the first-finger model alone for M1, the average log-  
264 Bayes factor reduced by 0.05. For S1, however, the addition of sequence model  
265 achieved a slightly higher likelihood (9.37 for first-finger model alone, vs 9.87 for  
266 combined model, Fig. 5B). However, on a common scale of Bayes factors (Kass and  
267 Raftery, 1995), such a small difference would be considered “*not worth more than a*  
268 *bare mention*”.

269 In premotor areas, on the other hand, the representational structure was not  
270 well explained by the first-finger model. For example, in SMA and SPLa, the fit of  
271 the sequence model was systematically better than the first-finger model (Fig. 5B, for  
272 other ROIs, see Figure 5-supplement), indicating that the activity patterns in these  
273 regions represented sequential information. Importantly, the likelihood of the first-  
274 finger model was systematically below the lower bound of the noise ceiling (Fig. 5C):

275 The mean difference in log  $BF$  to the lower noise ceiling was substantially larger than  
276 1, indicating strong evidence (Kaas and Raftery, 1995) that for these regions a better  
277 model exists.

278 In summary, on the group level our results provided very limited evidence for  
279 a true, unique sequence representation, or the representation of transitions between  
280 fingers in M1. Instead, the representational structure for sequences in this area could  
281 almost fully be explained by the first-finger model – i.e assuming that the patterns for  
282 multi-finger sequences are a linear combination of the patterns associated with the  
283 individual finger presses, with the first finger weighted more strongly than the others.  
284 The same observation held true for S1. In contrast, in premotor regions the first-finger  
285 model could not account for the differences between sequences, suggesting genuine  
286 encoding of sequential information in these regions.

287

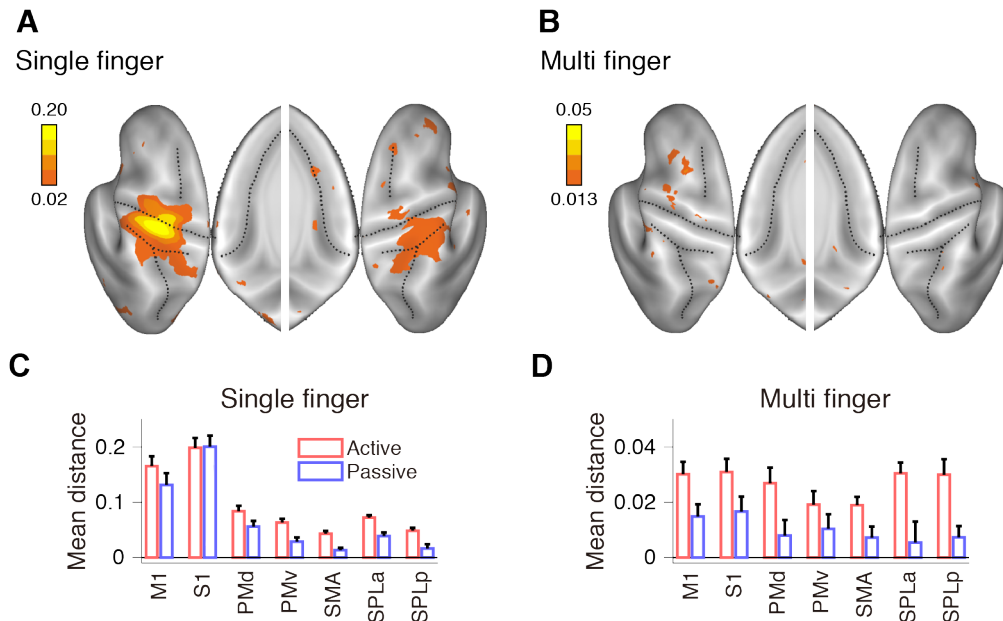
### 288 **First-finger effect in M1 is related to neural planning and execution processes**

289 We hypothesize that that the prominent activity for the first finger press in M1 is  
290 related to active planning and execution processes. Given that the BOLD signal more  
291 closely reflects synaptic input than spiking activity of output neurons (Logothetis et  
292 al., 2001), one possible explanation is that M1 receives strong input from premotor  
293 regions at the beginning of the sequence to push the neural state from resting to active  
294 state at movement initiation. While M1 would still rely on premotor input to produce  
295 the subsequent finger presses, the amount of this input would be smaller as M1 is  
296 already in an active state.

297 Alternatively, the prominence of the first finger pattern could be due to the passive  
298 properties of M1. Specifically, the effect could have hemodynamic rather than  
299 neuronal causes. That is, the neural activity for each finger in the sequence could be  
300 exactly the same, but because of the non-linear integration of the BOLD signal for  
301 inter-stimulus intervals of  $<6s$  (Dale and Buckner, 1997), it may be that the first  
302 finger press achieved the majority of the vasodilatory response and hence dominates  
303 the overall activity pattern.

304 To rule out this possibility, we exploited the fact that the single-finger patterns  
305 in M1 and S1 can also be elicited by passive stimulation (Wiestler et al., 2011). In the  
306 scanner, we therefore “replayed” the recorded force traces during the active trials  
307 through pneumatic pistons mounted under each finger. If we can elicit comparable

308 single-finger activity patterns in M1 through both active and passive movements, and  
309 if the timing of the presses is identical across conditions, then any hemodynamic, or  
310 passive neural effect, should apply equally in both situations. Thus, if the first-finger  
311 effect is due to the non-linear translation from neural to BOLD signals, we should  
312 find a similar representational structure for active and passive multi-finger movements.



313

314 **Figure 6. Passive stimulation elicited comparable single finger representation, but**  
315 **reduced multi-finger sequence representation.** (A) Averaged distance for single  
316 finger sequences, and (B) multi finger sequences shown on an inflated view of the left  
317 and right hemisphere, with the inset showing distance on the medial wall. Scaling for  
318 the multi finger sequences were determined based on the reduction of distance from  
319 active movement condition for single finger sequences.

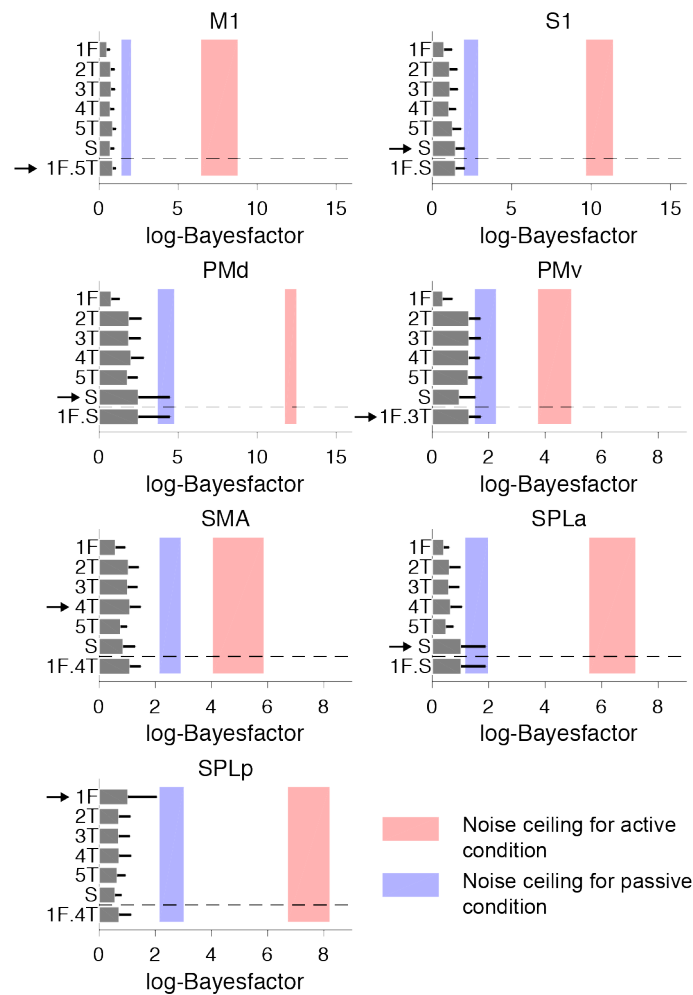
320 (C) Average distance in the cortical ROIs (see Fig. 3 supplement) for single finger  
321 sequences for active (red) and passive (blue) conditions. (D) Average distance across  
322 all pairs for multi-finger sequences. Error bars represent SE across subjects.

323 As can be seen from Figure 6A, the spatial distribution of single finger  
324 representations was comparable to that obtained in the active condition (Fig. 3A). For  
325 a direct comparison, we calculated the average distances in each of the cortical ROIS  
326 (Fig. 6C). The distance in M1 was  $82 \pm 11\%$  of what was elicited in active condition,  
327 and  $101 \pm 10\%$  in S1. Additionally, the elicited patterns matched the active patterns on  
328 a finger-by-finger basis. The average correlation between active and passive patterns  
329 (after subtracting out the mean activity pattern) of the same finger were  $r=0.76 \pm 0.37$ ,  
330  $p=8.86 \times 10^{-5}$ , and  $r=0.89 \pm 0.05$ ,  $p=6.8 \times 10^{-11}$ , respectively for M1 and S1. Therefore,

331 we confirmed that almost comparable single-finger activity patterns are elicited in M1  
332 through the passive stimulation.

333 In contrast to single-finger representations, encoding of multi-finger sequences  
334 reduced dramatically over the whole cortical surface (Fig. 6B). The distances between  
335 sequences reduced to  $47\pm 29\%$  in M1 and  $42\pm 42\%$  in S1 compared to the active  
336 condition (Fig. 6D). Critically, the reduction was larger than what would be expected  
337 from the reduction in the single-finger representations (Fig. 6B, M1:  $t_{16}=1.7601$ ,  
338  $p=0.049$ , and S1:  $t_{16}=2.587$ ,  $p=0.001$ ). If the first-finger effect had been solely due to a  
339 hemodynamic non-linearity, or to a passive adaptation of neural activity, then the  
340 effect should have equally applied to both active and passive conditions. Instead, the  
341 differences between active and passive conditions indicate that the high weighting of  
342 the first-finger press in M1 is caused by active preparation or initiation of the  
343 sequence.

344 The results also show that the sequence representations found in premotor  
345 regions are due to the active planning and execution of a sequence, and not to  
346 processing of the sensory inflow. The distances for multi-finger movements were  
347 substantially lower (24% on average) in premotor regions (Fig 6B) and not  
348 significantly different from zero in 4 of the 5 premotor ROIs. Furthermore, the  
349 remaining representational structure was relatively inconsistent between subjects, as  
350 can be seen in the low noise ceiling of the model fits (Supplemental Fig 6). These  
351 findings clearly indicate that the sequence representation observed in premotor  
352 regions requires the active execution of a sequence.



353

354 **Figure 6-Supplement. Model-fitting of multi-finger sequences for passive**  
355 **stimulation evaluated at each ROI. We applied the same model-fitting procedure as**  
356 **shown in Figure 5 to the data of passive stimulation condition. In contrast to the**  
357 **active movement case, the models performed almost equally poor for all ROI tested.**  
358 **Furthermore, group-wise consistency of representational structure (blue shaded**  
359 **areas, lower and upper noise-ceilings) was much lower compared with active**  
360 **movements (red shaded areas).**



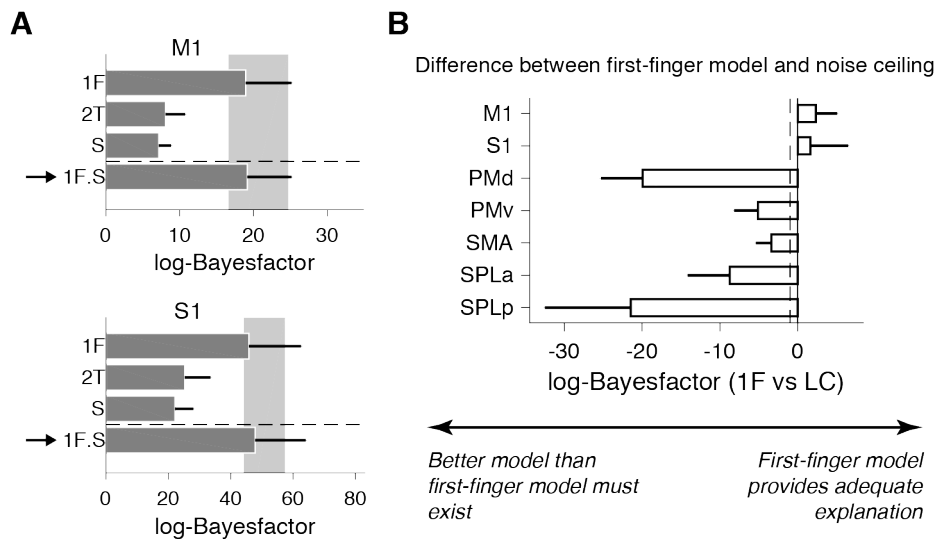
361 **A sequence representation with longer training?**

362 So far, we have found little or no evidence for a real sequence representation in M1.

363 We considered two reasons for this failure. First, it may be that the training period  
364 was too short. Secondly, the simple structure of our sequences (i.e. permutations of  
365 digit 1, 3, and 5) may have reduced the chances of forming representations of finger  
366 transitions.

367 We therefore conducted a second experiment, this time with 5-6 days of  
368 training of 2 hrs each, during which participants learned 8 arbitrary sequences, each  
369 11 presses long consisting of all five fingers. The trained sequences were executed at  
370 preferred speed (average 4.3 presses / s) in the scanner (see Material & Methods).

371



372

373 **Figure 7. More intensive training with complex sequences (Experiment 2) revealed**

374 **highly similar results.** Participants in the second experiment practiced 8 different

375 sequences of 11 presses-long for 5 days and 2 hrs per a day before the imaging

376 session. (A) log-Bayes-factor (Fig. 5) for the data of M1 and S1 for the first finger

377 model (1F), the 2-finger transition model (2T), sequence model (S) and the

378 combination between first finger and sequence model (1F+S). The arrow again

379 indicates the winning model. Error bars represent SE across subjects. (B) Log-Bayes

380 factor between first-finger and noise ceiling model. As in Experiment 1, the first-

381 finger model provides an adequate explanation for M1 and S1, but not for secondary

382 motor areas. Dashed line shows the typical threshold value for model selection (e.g.,

383 Kaas and Raftery 1995).

384

385 First, due to the fact that experiment 2 had more data, the evidence for  
386 movement representation was substantially stronger. The scale of log-Bayes factor  
387 was approximately 3~4 times larger in Figure 7 compared with Figure 5. However,  
388 despite increased signal and despite ample opportunity to form representations of at  
389 least two or three finger transitions, the representational structure in M1 was again  
390 fully explained by the first finger model. The log-Bayes factor of the first-finger  
391 model was above the noise ceiling. Addition of the sequence representation or a 2-  
392 finger transition model did not substantially improve the fit (Fig. 7A, 18.95 vs 19.16  
393 for single model and combined model, respectively). Similar result was obtained for  
394 S1. However, in this region the addition of the sequence model slightly improved the  
395 likelihood of the model (Fig. 7A, 45.84 vs 47.84 for single model and combined  
396 model, respectively). In contrast, the representational structure in premotor and  
397 parietal regions could not be explained by the first-finger model, suggesting the  
398 presence of a more complex and higher-level sequence representation (Fig. 7B). The  
399 content of these representations, and their dependence on cognitive mechanisms of  
400 movement chunking, will be reported in a subsequent paper. For M1, however, these  
401 results confirm that even after week-long training, the activity pattern reflect  
402 processes related to the individual finger presses, but not to their sequential context.

## 403 **Discussion**

404 We demonstrated that even after 5-6 days of intensive practice, there was very little  
405 evidence for a genuine sequence representation in M1. We also did not find evidence  
406 for a representation of partial sequences, such as the transition between 2 or more  
407 finger presses. Instead, we found that the activity patterns for sequences could be  
408 explained by a linear combination of the activity patterns for single finger presses, in  
409 which the weight of the first finger was higher than for the other presses. This resulted  
410 in an above-chance classification accuracy for sequences beginning with different  
411 fingers. We also provided evidence that this first-finger effect was much larger during  
412 active compared to passive sequence production, arguing that it is related to active  
413 movement preparation and initiation. These results also indicate that the first-finger  
414 effect had a neural origin, rather than being based on a hemodynamic non-linearity. In  
415 contrast to the absence of any sequential information in M1, sequences were robustly  
416 represented in secondary motor areas, such as PMd, SMA, and the anterior SPL.  
417 These areas have been shown to represent sequences such that the neural activity  
418 pattern reflects the sequential order of movement elements (Mushiaki et al., 1991;  
419 Tanji and Shima, 1994; Wiestler and Diedrichsen, 2013; Wiestler et al., 2014).

420

### 421 **Advances from the earlier studies.**

422 Although there have been numerous imaging studies on sequence production and  
423 acquisition (Karni et al., 1995; Honda et al., 1998; Karni et al., 1998; Doyon et al.,  
424 2002), our approach makes several advances over these earlier studies. First, we  
425 designed our experiment specifically for multi-voxel pattern analysis, which allowed  
426 us to test directly for sequence representations in M1. This is not possible when  
427 looking only at the average BOLD activity within a region. Indeed, the increases and  
428 decreases reported in previous studies (Grafton et al., 1995; Karni et al., 1995; Honda  
429 et al., 1998; Karni et al., 1998; Kawashima et al., 1998; Sakai et al., 1998) may not  
430 necessarily reflect plastic changes in M1. Rather, they could equally well reflect  
431 changes in the input to M1, caused by sequences being learned and represented in  
432 secondary motor regions. Multi-voxel pattern analysis is also sensitive to inputs from  
433 other regions, but reveals the local organization of how these inputs arrive in M1.  
434 Specifically, our results suggest that the activity patterns for the first finger press are

435 especially high, but that the underlying activity patterns still only reflect the  
436 individual finger movements.

437         Second, we not only measured the activation pattern for the sequences, but  
438 also compared them to the patterns of their constituent single finger movements. This  
439 allowed us to determine whether the activity patterns for multi-finger sequences could  
440 be explained by a combination of single-finger movements, or whether there was  
441 evidence for a new representation that encoded the sequential context (Fig 1B). Our  
442 results clearly argue for the former, implying that the significant differences between  
443 sequence patterns in M1 in our earlier work (Wiestler and Diedrichsen, 2013;  
444 Kornysheva and Diedrichsen, 2014; Wiestler et al., 2014) did not reflect an encoding  
445 of the order of finger presses (i.e. a genuine sequence representation), but of the  
446 sequential position of finger presses. In these studies, the different sequences started  
447 with a different finger, such that we could not distinguish a real sequence  
448 representation from one caused by the first-finger effect. Importantly, our current  
449 result confirmed that the pattern differences reported in secondary motor areas reflect  
450 genuine sequence encoding.

451         Finally, we demonstrated that in secondary motor areas no robust sequence  
452 representation could be elicited using passive sensory stimulation. This suggests that  
453 the sequence representations observed in these areas actually reflects active  
454 movement planning/execution process, rather than sensory re-afferent signals. Of  
455 course, the sensory feedback during the passive stimulation condition was not exactly  
456 the same as during active sequence production. However, nearly identical activity  
457 patterns in the single-finger conditions elicited in primary sensory cortex by the  
458 passive stimuli demonstrated that the sensory feedback closely mimicked that during  
459 active presses.

460

#### 461 **The origin of the first-finger effect**

462 The results from the passive stimulation also argue that the first-finger effect is related  
463 to the active preparation and initiation of the sequence, rather than just to the sensory  
464 inflow. More generally, the results show that the effect has a neural origin, and is not  
465 purely caused by a non-linear integration of neural events in the production of the  
466 hemodynamic response (Dale and Buckner, 1997). Recent electrophysiological  
467 findings seem to support this conclusion (Hermes et al., 2012; Siero et al., 2013).

468 These studies recorded the electrophysiological potentials using intracranial ECoG  
469 electrodes above M1 while human participants performed rhythmic open and close  
470 movements of hand at  $\sim 2$ Hz. Power in the high-gamma frequency band was much  
471 more pronounced for the first movement of a sequence as compared to subsequent  
472 movements (Hermes et al., 2012). Siero et al. (2013) also showed that the high-  
473 gamma activity tightly related to the observed BOLD activity recorded when subjects  
474 performed the same task in the scanner. While the “sequence” in these experiments  
475 consisted of the repetition of the same movement elements, our results lead to the  
476 prediction that similar effect should occur for more complex, multi-finger sequences.

477       What is the neural origin of this first-finger effect? First note that both BOLD  
478 and high-frequency gamma power relate mainly to synaptic input to a region. Thus, it  
479 is not unlikely that this effect arises only on the input side and that the firing of output  
480 neurons would be matched for the different finger presses (Picard et al., 2013). The  
481 most likely explanation therefore is that the neural circuits in M1 require a large input  
482 drive to initiate a series of movements. Recent results have shown that the largest  
483 change in neural activity occurs when transitioning between a “resting” sub-space to  
484 the active sub-space (Elsayed et al., 2016). In our case the driving input for this  
485 movement would arrive in form of the intention to move the first finger. Subsequent  
486 finger presses would still require input from higher-order areas, as M1 would not be  
487 able to generate the sequence autonomously, but the input drive would be much  
488 smaller as the state of the neurons would already be in the vicinity of the active  
489 subspace. This idea also predicts that if the sequence is executed slowly enough, the  
490 state in M1 should relax back to the resting sub-space and the first-finger effect  
491 should disappear.

492

#### 493 **Limitations: length of training and sequence representation in M1.**

494 Our data provides very little or no evidence for a sequence representation in M1 after  
495 1 week of intensive training (1.5-2 hours per a day). However, this does not exclude  
496 the possibility that longer period of training might result in the unique neural circuits  
497 for sequences acquired within M1. After 2 years of training, a single-cell recording  
498 study in the monkey revealed some evidence for sequential representations in M1  
499 (Matsuzaka et al., 2007). Note however, that in this study, sequence representations  
500 were assessed as the difference between neuronal responses to trained and untrained

501 sequences, not as in our study between different trained sequences. On a much shorter  
502 time scale, Karni et al. (1995) reported an expansion of activated area in M1 over 4  
503 weeks of daily practice. The total amount of practice was similar for the experiments  
504 reported here (approx. 3.5~7 hrs vs. 6~10 hrs in our study). Again, the results only  
505 indicated that trained sequences elicited more activity than untrained sequences (a  
506 result that we failed to replicate, Wiestler and Diedrichsen, 2013), but does not show  
507 the presence of neural processes that would relate to the sequential order of movement  
508 elements.

509         Using our methods, we did not find evidence for the representation of short  
510 sequence components, such as the transition between 2 or 3 fingers. There was some  
511 indication that there was a weak component of the activity pattern in M1 which may  
512 reflect the sequence itself. We are now investigating whether these patterns constitute  
513 the beginning of a “true” sequence representations that will increase in strength with  
514 extended training.

515

## 516 **Conclusion.**

517 Using representational fMRI analysis, we demonstrated that up to about 1 week of  
518 intensive practice, activity in M1 relates to individual finger presses, but not to  
519 transitions between multiple fingers or even full sequences. At the same time, we  
520 found robust and genuine sequence representation in other higher motor areas, such as  
521 PMd, SMA, or aSPL, which is consistent with previous studies (Mushiaké et al.,  
522 1991; Shima and Tanji, 1998). The next challenge is to dissect the content of these  
523 representations in detail (Lashley, 1951).

524

## 525 **Materials & Methods**

### 526 **Participants**

527 Nine healthy, right-handed volunteers (3 females, age: 23±4) participated in  
528 Experiment 1, and 14 healthy, right-handed volunteers (8 females, age: 23±3)  
529 participated in Experiment 2, after providing written informed consent. The  
530 experimental procedures were approved by local ethics committees at the University  
531 of Western Ontario (London, Canada) and University College London (London, UK).  
532 None of the participants was professional musician nor has any known neurological  
533 history.

534

### 535 **Apparatus**

536 We used custom-build five-finger keyboards (Fig. 2A) with a force transducer  
537 (Honeywell FS series) mounted underneath each key (Wiestler and Diedrichsen;  
538 Wiestler et al.). The keys were immobile and measured isometric finger force  
539 production. Dynamic range of the force transducers was 0-16N and the resolution  
540 <0.02 (N). A finger press/release was detected when the force value crossed a  
541 threshold of approximately 3 N. This threshold was slightly adjusted for each finger to  
542 ensure that each key could be pressed easily. The signal from the keyboard were low-  
543 pass filtered, amplified and sent to PC for online task control and data recording. The  
544 forces were recorded at 200 Hz. For passive stimulation of the fingers, a pneumatic air  
545 piston was mounted underneath each key. The pistons were driven by compressed air  
546 (100 psi) from outside the MRI scanning room through poly-vinyl tubes. The force  
547 exerted by each piston was controlled by a pressure-regulating valves. The  
548 movements of the fingers was restricted by a device mounted above the fingers.

549

### 550 **Sequence production task for Experiment 1**

551 During the training sessions, participants were seated in front of the LCD monitor and  
552 placed their fingers on the keyboard. They learned to produce five single finger  
553 sequences and six multi-finger sequences. For the single-finger sequences, one of five  
554 fingers had to be pressed 6 times (e.g., 3 3 3 3 3 3); for the multi-finger sequences one  
555 of the six possible permutations of fingers 1, 3, and 5 was pressed twice (e.g., 5 3 1 5  
556 3 1) (Fig. 2B). All fingers remained on the keyboard at all times, such that the overt  
557 movement of the fingers was minimized.

558           The participants practiced the sequences for 3 days so they were able to  
559 produce the sequences in the scanner within 2.5 seconds from memory given only  
560 visual cue, which was presented for 1.5 seconds at the start of each trial (Fig. 2C).  
561 Each sequence was indicated by a different Roman numeral (I, II, ..., XI). In the  
562 beginning of training we provided both the sequence cue (roman numeral) and all six  
563 to-be-pressed digits on the screen. Subsequently, we replaced the digits with asterisks  
564 (\*), to encourage the participants to memorise the sequences (Fig. 2C).

565           A total 1716 sequence executions were made (156 executions per one  
566 sequence type). The order of 11 sequences was pseudo-randomised throughout the  
567 sessions. The colour of a asterisks turned to green immediately after a press was  
568 correctly registered, while it turned to red if the press was incorrect. To guide  
569 participants' speed, the sequence cue blinked at a reference frequency that gradually  
570 increased during the training sessions at constant rate until it reached to 4 Hz. On the  
571 last day of training sessions, participants practiced actual task for the scanning session,  
572 lying on the mock MRI scanner bed for familiarisation.

573

#### 574 **Sequence production task for Experiment 2**

575           The general methods were similar to the first experiment. Participants learned to  
576 produce 8 different sequences with 11 presses from the memory. Initially we trained  
577 participants for 5 days, but for the other half added a 6<sup>th</sup> day, such that all could  
578 correctly produce the sequences within 2.5 seconds. On average, the training lasted  
579 cumulatively 10-12 hrs. As in Experiment 1, the sequences were cued with Roman  
580 numerals I–VIII. All the sequences were matched with the number of finger presses  
581 used; 2 presses with thumb, middle, ring, and little fingers, and 3 presses with index  
582 finger, respectively. Four of the sequences started with the thumb, two sequences  
583 started with middle finger, and the rest of two sequences started with little finger. The  
584 detailed training protocol and the behavioural results of training and transfer test  
585 (conducted after the imaging) will be reported in a separate paper.

586

#### 587 **Imaging session**

588           During the imaging session, the participants lay supine on the scanner bed with knees  
589 slightly bent supported by a wedge-shaped cushion. The pneumatic keyboard was



590 comfortably placed on their lap, and visual stimuli were presented on a back-  
591 projection screen which was viewed through a mirror attached to the head coil.

592 For Experiment 1, we conducted both active and passive conditions. In each  
593 trial of the active condition, the participants were first provided with the sequence cue  
594 for 1.5 seconds and then they were required to execute the specified sequence twice  
595 within the time limit of 2.5 seconds for each execution (Fig. 2C). Each execution was  
596 triggered by the fixation cross turning green. During the execution period, the fixation  
597 cross blinked at the reference frequency (4 Hz) to provide the participants with a  
598 pacing signal. The order of the 11 sequences was pseudo-randomised and included 1  
599 rest trial of 8 seconds, during which the participants only passively viewed the  
600 fixation cross. This set of sequences was repeated three times within each imaging run,  
601 resulting in a total of 66 sequence executions per run. We conducted seven runs in the  
602 active condition. For these runs, there was also no significant difference in the  
603 pressing frequency (Hz) between single and multi-finger sequences ( $4.58 \pm 0.36$ ,  
604  $4.59 \pm 0.39$ ,  $t_8 = -0.176$ ,  $p = 0.865$ ). The average number of incorrect presses per each  
605 execution was close to zero, but slightly larger for multi finger sequences ( $0.02 \pm 0.02$ ,  
606  $0.22 \pm 0.13$ ,  $t_8 = -4.884$ ,  $p = 0.001$ ).

607 Alternating with the active runs, we conducted seven imaging runs in the  
608 passive condition. During the active run, we recorded the force data to replay these  
609 forces through the pistons in the passive run. The visual stimuli and timing were  
610 exactly the same as in the active runs, except that the participants were told not to  
611 produce any active finger movement, but to only passively receive stimulations to  
612 their fingers. Each passive run used the exact timings of the preceding active run, only  
613 that the sequence of trials was randomly shuffled on each run. Due to the nonlinear  
614 response property of pneumatic pistons, the resultant passive forces were lower than  
615 the forces in the active condition. We confirmed, however, that we could elicit  
616 robust single finger representation almost comparable to the active condition,  
617 especially in S1 (see Results).

618 The structure of Experiment 2 was similar. In the beginning of each trial, the  
619 sequence cue (I-VIII) was presented for 2.5 seconds. This was followed by two  
620 execution phases of 4 seconds each, with 0.5-second ITI. During the execution phase,  
621 only fixation cross and asterisks were presented. The order of sequences was  
622 randomised, and each of the 8 sequences was repeated three times during each run.

623 During scanning the average pressing frequency was  $4.47 \pm 1.05$  Hz, which was not  
624 significantly different from that in the Exp 1 ( $t_{19} = 0.298$ ,  $p = 0.769$ ). Four resting  
625 trials of 10.5 seconds were randomly interspersed. We conducted a total of 9 runs,  
626 each of which lasted a total of about 7 min. Short breaks (up to a few minutes) were  
627 interleaved when subjects required. There was no passive condition for this  
628 experiment. The average number of incorrect presses per each execution was again  
629 close to zero, but significantly larger than that in the Exp 1 ( $0.40 \pm 0.16$ ,  $t_{19} = 4.84$ ,  
630  $p = 1.13 \times 10^{-4}$ ).

631

### 632 **Imaging data acquisition.**

633 Experiment 1 was conducted on a Siemens Magnetom Syngo 7T MRI scanner system  
634 with a 32-channel head coil at the Centre for Functional and Metabolic Mapping,  
635 Robarts Research Institute (London, Ontario, Canada). Inhomogeneity of main  
636 magnetic field was adjusted by B0 and B1 shimming at the beginning of the whole  
637 session. Functional images were acquired for 14 imaging runs of 300 volumes per  
638 each using multi-band 2-D echo-planer imaging sequence (TR = 1.00 sec, multi-band  
639 acceleration factor = 2, in-plane acceleration factor = 3, resolution: 2.0 mm isotropic  
640 with 0.2 mm gap between slices, and 44 slices interleaved). The first 4 volumes were  
641 discarded to ensure stable magnetization. The slices were acquired close to axial to  
642 cover the dorsal aspects of the brain, including most of the frontal, parietal, occipital  
643 lobes, and basal ganglia. The ventral aspects of the frontal and temporal lobes,  
644 brainstem, and the cerebellum were not covered. Each functional imaging run lasted  
645 for 5 minutes. T1 weighted anatomical image was obtained on a separate session  
646 using MP2RAGE sequence (TR = 6.0 sec, resolution: 0.75 mm isotropic).

647 Experiment 2 was conducted on a Siemens Trio 3T scanner system with a 32-  
648 channel head coil at the Wellcome Trust Centre for Neuroimaging (London, United  
649 Kingdom). B0-field maps were acquired at the beginning of the whole session to  
650 correct for inhomogeneity of main magnetic field (Hutton et al., 2002). Functional  
651 images were acquired for 9 runs of 135 volumes each using 2-D echo-planer imaging  
652 sequence (TR=2.72 sec, in-plane acceleration factor = 2, resolution = 2.3mm isotropic  
653 with 0.3 mm gap between each slice, and 32 slice interleaved). The first 5 volumes  
654 were discarded to ensure stable magnetization. The coverage was similar to

655 Experiment 1. A T1 weighted anatomical image was obtained using MPRAGE  
656 sequence (1mm isotropic resolution).

657

### 658 **Behavioural data analysis**

659 Recorded force data were analyzed offline. The data for both the training and  
660 scanning sessions was first smoothed with second-order Butterworth filter with cutoff  
661 frequency of 10 Hz to remove remaining RF noise and then submitted to the  
662 subsequent analysis. Press and release timings were defined as the time point where  
663 the press force first crossed the threshold (3 N) and then returned to the below-  
664 threshold level. Reaction time (RT) from the go cue, movement time (MT) starting  
665 from first press time to the last release time, inter-press intervals (IPIs), and the  
666 number of incorrect presses at each execution were calculated.

667

### 668 **Imaging data analysis**

#### 669 *Preprocessing and first-level model*

670 Experiment 1: Functional imaging data were pre-processed using SPM12  
671 (<http://www.fil.ion.ucl.ac.uk/spm/>). Functional images were first motion corrected,  
672 and the mean images were co-registered to the individual anatomical image. As we  
673 had relatively fast TR (1.0 sec), we did not correct for slice acquisition timing. The  
674 data were then submitted to the 1st-level GLM to estimate the size of the evoked  
675 activity for each sequence type and run. We modelled the temporal autocorrelation  
676 using the “fast” option, which provides a flexible basis function to model  
677 dependencies on longer time scales. High-pass filtering was achieved by temporally  
678 pre-whitening the matrix using the temporal autocorrelation estimate.

679 *Experiment 2:* Pre-processing and GLM was conducted as in Experiment 1 – with the  
680 exception that we corrected for slice timing (given the slower TR). We also corrected  
681 for B0 inhomogeneity by using field map images. Given the slower TR, for the 1st-  
682 level GLM we used the standard high-pass filtering with a cut-off frequency of 128s  
683 and robust-weighted least square (RWLS, Diedrichsen and Shadmehr, 2005). The  
684 data from two participants in Experiment 2 was excluded from further analyses due to  
685 poor behavioural performance during scanning. These participants lacked a single  
686 correct trial in one of sequence types at more than one session. Hence, only the data  
687 from the remaining 12 participants were submitted to subsequent analyses.

688

689

### 690 *Searchlight and ROI definition*

691 Individual cortical surfaces (i.e., the pial and white-grey matter surfaces) were  
692 reconstructed from the anatomical image by using Freesurfer software (Fischl et al.,  
693 1999). We defined a continuous surface-based searchlight (Oosterhof et al.) as small  
694 circular cortical patches (approximately 11 mm radius) centred on each node defined  
695 on the reconstructed cortical surface that contains 160 voxels. Anatomical regions of  
696 interest (ROIs) were defined on this reconstructed surface (Fig. 3-SA) exactly as  
697 reported in previous studies (Wiestler and Diedrichsen; Kornysheva and Diedrichsen,  
698 2014; Wiestler et al.).

699

### 700 *Multivariate fMRI analysis*

701 Within each of these groups of voxels (surface-based searchlight or anatomically-  
702 defined ROIs) we extracted the beta-weights for each sequence type and imaging run.  
703 We then spatially pre-whitened this the activity estimates across voxels in each area  
704 using multivariate noise-normalization with a regularized estimate of the overall  
705 noise-covariance matrix (Walther et al., 2016). This procedure renders the resultant  
706 voxels approximately uncorrelated in the noise (Diedrichsen and Kriegeskorte, 2016).

707 For these voxels, we then analyzed how the different multivariate activity  
708 patterns represented the sequences, using the representation model framework  
709 (Diedrichsen and Kriegeskorte, 2016). In this framework, the representational  
710 structure is described either by asking how the measured activity profiles of individual  
711 voxels are distributed in the space of experimental conditions, or – equivalently - how  
712 distinguishable each pair of activity patterns associated with these conditions are from  
713 each other. Both viewpoints rely on a single central sufficient statistic, namely the  
714 second moment matrix of the activity patterns.

715 If  $\mathbf{U}$  represents the true pattern of interest for the  $K$  experimental conditions  
716 times  $P$  voxels, then the second moment between the activity patterns is defined as

717

$$\mathbf{G} = \mathbf{U}\mathbf{U}^T/P$$

718 We analyzed this quantity using two complementary approaches: representational  
719 similarity analysis (RSA) to establish basic features of the representation and for

720 visualization and Pattern component modelling (PCM) to compare more complex  
721 representational models.

722

723 *Representational Similarity Analysis (RSA)*

724 In RSA, we quantify the representational structure by measuring how distinct each  
725 pair of activity patterns are from each other. The squared Euclidean distance between  
726 the activity pattern  $\mathbf{u}_1$  and  $\mathbf{u}_2$  for example is:

727 
$$\mathbf{d}_{1,2} = (\mathbf{u}_1 - \mathbf{u}_2)(\mathbf{u}_1 - \mathbf{u}_2)^T = \mathbf{G}_{1,1} - 2\mathbf{G}_{1,2} + \mathbf{G}_{2,2}.$$

728 Calculated on spatially pre-whitened data, this distance is equal to the squared  
729 Mahalanobis distance. One problem is that estimates of this distance based on noisy  
730 data are positively biased. We therefore used here a cross-validated estimate of the  
731 second moment matrix  $\mathbf{G}$ ,

732 
$$\hat{\mathbf{G}} = \frac{1}{M} \sum_{m=1}^M \hat{\mathbf{U}}_m \hat{\mathbf{U}}_{\sim m}^T / P.$$

733 where  $M$  is the total number of partitions (e.g. imaging runs),  $\hat{\mathbf{U}}_m$  is estimated pre-  
734 whitened activity pattern for partition  $m$ , and  $\hat{\mathbf{U}}_{\sim m}$  is the estimate of the pattern  
735 independent of the partition  $m$ . The “crossnobis estimator” (Diedrichsen and  
736 Kriegeskorte, 2016; Walther et al., 2016) is a distance calculated using this second  
737 moment matrix. This distance estimator is unbiased – meaning it can be used to  
738 directly test whether a distances is larger than zero. Finding consistently positive  
739 distance estimates therefor implies that the two condition activity patterns differ from  
740 each other more than expected by chance.

741 To visualize the representational structure, we used classical multi-  
742 dimensional scaling. We first projected the activity patterns into a lower dimensional  
743 sub-space by finding the Eigenvectors of group-averaged  $\hat{\mathbf{G}}$  matrix, which were then  
744 weighted by the square root of corresponding Eigenvalues. The projection displayed  
745 in Fig. 4B was then rotated to maximize the differences between the single-finger  
746 movements.

747

748 *Pattern component modelling (PCM)*

749 To compare full models of the representational structure, we used PCM (Diedrichsen  
750 et al., 2011; Diedrichsen et al., 2017), which directly evaluates the likelihood of the  
751 data under the linear model

752 
$$\mathbf{Y} = \mathbf{ZU} + \mathbf{XB} + \mathbf{E}.$$

753 Here,  $\mathbf{Y}$  is a  $N$ -by- $P$  matrix representing noise-normalized activity pattern after the  
754 1st-level GLM (Walther et al., 2016), where  $N$  is the number of estimates (number of  
755 conditions x number of runs) and  $P$  is the number of voxels.  $\mathbf{Z}$  ( $N$ -by- $K$  matrix) is the  
756 design matrix that associates  $\mathbf{U}$  and  $\mathbf{Y}$ .  $\mathbf{B}$  represents the patterns of no interest, in our  
757 case the mean activity pattern in each run. Finally,  $\mathbf{E}$  represents trial-by-trial  
758 measurement errors.

759 Importantly, PCM considers the true activity patterns  $\mathbf{U}$  to be a random  
760 variable that follows multivariate normal distribution as,  $\mathbf{U} \sim \mathbf{N}(\mathbf{0}, \mathbf{G})$ , where  $\mathbf{G}$  is the  
761 second moment matrix of activity pattern  $\mathbf{U}$ , which determines the similarity structure  
762 across movement conditions. In evaluating models, PCM integrates the actual activity  
763 patterns out, i.e. it evaluates the marginal likelihood (simply termed likelihood in this  
764 paper);

765 
$$p(\mathbf{Y}|\boldsymbol{\theta}) = \int p(\mathbf{Y}|\mathbf{U}, \boldsymbol{\theta})p(\mathbf{U}|\boldsymbol{\theta})d\mathbf{U}$$

766 , where  $\boldsymbol{\theta}$  represents model parameters that determine the shape of  $\mathbf{G}$  and the signal  
767 and noise variances (see Diedrichsen et al., 2017). We fitted a number of models to  
768 explain the representational structure of the patterns associated with the multi-finger  
769 sequences.

770

771 *1st-finger model:* In this model, we assumed that the activity patterns for the  
772 multi-finger sequences are a weighted linear combination of the patterns for the  
773 constituent single finger presses. If all fingers were weighted equivalently, the overall  
774 patterns would be identical, as each sequence contains exactly the same fingers. The 1st-  
775 finger model assumes that the first finger press is more strongly weighted than  
776 subsequent presses. Thus, the activity pattern for the multi-finger sequences are  
777 modelled as weighted sum of the activity pattern for the single-finger sequences,

778 
$$\mathbf{U}_{sq} = \mathbf{M}_{1f}\mathbf{U}_{sf},$$

779 where  $\mathbf{U}_{sq}$  is the pattern for multi-finger sequences ( $6 \times P$  matrix),  $\mathbf{U}_{sf}$  is the activation  
780 patterns for the single finger presses of thumb, middle, and little fingers ( $3 \times P$  matrix),  
781 and  $\mathbf{M}_{1f}$  is the weight matrix. Because each finger is present in each sequence equally  
782 often, we can simply model the difference in weight between the first and the  
783 subsequent fingers, such that  $\mathbf{M}_{1f}$  is set to 1 for the first finger, and 0 otherwise ( $6 \times 3$   
784 matrix). Therefore, the predicted similarity structure across multi-finger sequences

785 (i.e., the second moment of the pattern  $\mathbf{G}_{1f}$ ) is fully determined from the similarity  
786 across the single finger presses (i.e.,  $\mathbf{G}_{sf}$ )

$$787 \quad \mathbf{G}_{1f} = \frac{1}{P} \mathbf{U}_{sq} \mathbf{U}_{sq}^T = \frac{1}{P} \mathbf{M}_{1f} \mathbf{U}_{sf} \mathbf{U}_{sf}^T \mathbf{M}_{1f}^T = \mathbf{M}_{1f} \mathbf{G}_{sf} \mathbf{M}_{1f}^T.$$

788 This results in the specific similarity structure depicted in Figure 5A. For modelling  
789 the activity at different ROIs, the empirical estimate of  $\mathbf{G}_{sf}$  was derived for each ROI  
790 from the data – therefore no free parameter was required for this model.

791 *N-finger transition model:* This model family predicts the similarity structure  
792 based on neural circuits that encode the transitions between finger presses. Unique  
793 transitions can be defined between pairs of presses, or based on 3 or more presses. For  
794 instance, each sequence has five specific two-finger transitions, four three-finger  
795 transitions, etc. Thus, the predicted activity patterns of the multi-finger sequences are

$$796 \quad \mathbf{U}_{sq} = \mathbf{M}_{trans} \mathbf{U}_{trans}.$$

797 In this case the weighting matrix  $\mathbf{M}_{trans}$  indicates, for each sequence, how many of  
798 the possible 2-digit transitions (9 total), 3-digit transitions (27 total), etc. the  
799 sequences contained, and  $\mathbf{U}_{trans}$  represents specific activation patterns for each  
800 possible transition. Because we did not measure patterns for individual transitions, we  
801 assumed that each transition would be equally-strongly and independently represented,  
802 i.e.,  $\mathbf{U}_{trans} \mathbf{U}_{trans}^T = \alpha \mathbf{I}$ , where  $\alpha$  is constant and  $\mathbf{I}$  is identity matrix. Thus, the  
803 predicted second moment matrix is

$$804 \quad \mathbf{G}_{trans} = \frac{1}{P} \mathbf{M}_{trans} \mathbf{U}_{trans} \mathbf{U}_{trans}^T \mathbf{M}_{trans}^T = \frac{\alpha}{P} \mathbf{M}_{trans} \mathbf{M}_{trans}^T.$$

805 The resultant predicted similarity structure for each  $N$ -finger transition model  
806 can be seen in (Fig. 5A). Note that the six-finger transition model predicts that all  
807 sequences are equally distinct from each other, as each sequence has only one unique  
808 six-finger transition (the sequence).

809

810 *Model comparison:* We first fitted the six individual models (see previous section)  
811 separately. To account for individual differences in the signal-to-noise ratio, we  
812 maximized the likelihood in respect to a noise and signal strength parameter  
813 (Diedrichsen et al., 2017) – thus each model had the same two free parameters,  
814 allowing us to compare their likelihoods directly. We also fitted combinations of  
815 models, where the overall representation was a mixture of the hypothesized  
816 representations (i.e., the second moment matrix the weighted sum of those models). In

817 this case, each component weight added an additional free parameter. Therefore, each  
818 single model has 2 free parameters (i.e., signal and noise parameters), and each  
819 mixture of two models has 3 free parameters (i.e., signal, noise, and the mixing ratio  
820 of one model over the other). Note that the  $\alpha$  in the finger transition models is  
821 absorbed into the signal parameter.

822 To compare models with different number of parameters, we used group  
823 cross-validation: We fitted the parameters using the data from  $n-1$  subjects, and then  
824 use the estimated  $\mathbf{G}$  to fit the data from the left-out subject, fixing the parameters for  
825  $\mathbf{G}$  (for more details, see Diedrichsen et al., 2017). Note that in this process an overall  
826 signal and noise parameter was always fitted individually to each subject. Through  
827 this process, we obtained a cross-validated likelihood for each candidate models and  
828 subject, which serves as an estimate of the model evidence for each model.

829 We then compared models by calculating the log-Bayes factor which tells us  
830 to what degree one model can better describe the observed data over the other  
831 calculated (Hackett and Kaas, 2004) as the difference between the log-likelihoods:

832

$$833 \quad \log BF(\text{model A vs model B}) = \log L(\text{model A}) - \log L(\text{model B}).$$

834

835  $\log BF$  were computed separately for each subject. We then used standard  
836 criteria for the average  $\log BF$  proposed by Kaas and Raftery (1995) to judge if a  
837 model is meaningfully “better” than the other. Instead of using the group log-Bayes  
838 factor (Stephan et al., 2009), i.e. the sum of the individual log-Bayes factor, we report  
839 here the average  $\log BF$ , which is invariant to the number of participants. This  
840 provides a much more stringent criterion for model selection.

841

842 *Noise ceiling:* We also estimated the likelihood that the best achievable model should  
843 reach, called noise ceiling. The noise ceiling is an important measure to assess  
844 whether the selected model is a sufficient model, or whether the model misses a  
845 substantial aspect of the representational structure that is consistently observed across  
846 individuals. For this we used a free (fully flexible) model, which has as many  
847 parameters as the number of the elements in the second-moment matrix. For an  
848 estimate of the free model, we simply used the mean of cross-validated second



849 moment matrix  $\hat{\mathbf{G}}$  across subject, which gives nearly identical results as using the  
850 maximum-likelihood estimate (for details see Diedrichsen et al., 2017).

851 To determine the free model, we first used the data of all subjects combined.  
852 This results in the best achievable likelihood for a group model and therefore  
853 constitutes an upper bound for the likelihood. Because this estimate is over-fitted, we  
854 also determined the cross-validated likelihood of the free model, which constitutes a  
855 lower bound estimate of noise ceiling. Therefore, even if a model performs better than  
856 the lower noise ceiling, it remains be possible that a better model still exists. However,  
857 based on the absolute performance we can conclude that the model captures all clearly  
858 consistent effects in the data.

### 859 **Statistics**

860 We used one-sided, one-sample t-test for the evaluation of positive mean distance  
861 across subjects. To assess the first-finger effect, we performed two kinds of separate  
862 paired-t tests; a) if distances between two multi-finger sequences sharing the same  
863 first finger are smaller than distances between any other pair of multi-finger  
864 sequences not sharing the same first finger, b) if distances between a single-finger  
865 sequence and a multi-finger sequence sharing the same first finger are smaller than  
866 distances between any other pairs between single-finger and multi-finger sequences  
867 not sharing the same first finger. Significant difference for both of above comparisons  
868 (a and b) was deemed as the evidence of the first-finger effect. The ratio between  
869 active and passive distances (i.e., the reduction of passive distance) was estimated  
870 using linear-regression without intercept. Estimated slopes between single- and multi-  
871 finger sequences were then compared using simple t-contrast.

872 For the model comparison using PCM, we employed the standard  
873 interpretation of the size of the BF (Kaas and Raftery, 1995, see above. Additionally,  
874 we also report a Wilcoxon's rank sum test on the log-Bayes factors between the  
875 winning and other models. Significance level was set to  $p=0.05$ . All the statistical  
876 analyses were performed on MATLAB (Mathworks, Inc.).

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