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4 **Title (120 characters):** The high energetic cost of rapid force development in cyclic muscle contraction

5 **Running title (40 characters):** High energetic cost of rapid force development

6 **Key words (3-6 words):** metabolic energy, muscle activation, isometric force, biomechanics, calcium  
7 transport.

8 **Summary statement (15-30 words):** The energetic cost of isometric muscle force production during  
9 cyclic muscle contraction increases sharply with cycle frequency and in proportion to the rate of force  
10 development

11

12 **Abstract (250 words):** Muscles consume metabolic energy for active movement, particularly when  
13 performing mechanical work or producing force. Less appreciated is the cost for activating and  
14 deactivating muscle quickly, which adds considerably to the overall cost of cyclic force production  
15 (Chasiotis et al., 1987). But the cost relative to mechanical work, which features in many movements,  
16 is unknown. We therefore tested whether fast activation-deactivation is costly compared to performing  
17 work or producing isometric force. We hypothesized that metabolic cost would increase with a proposed  
18 measure termed *force-rate* (rate of increase in muscle force) in cyclic tasks, separate from mechanical  
19 work or average force level. We tested humans (N = 9) producing cyclic knee extension torque against  
20 an isometric dynamometer (torque 22 N-m, cyclic waveform frequencies 0.5 – 2.5 Hz), while also  
21 quantifying the force and work of muscle fascicles against series elasticity (with ultrasonography), along  
22 with metabolic rate through respirometry. Net metabolic rate increased by more than fourfold (10.5 to  
23 46.7 W) with waveform frequency. At high frequencies, the hypothesized force-rate cost accounted for  
24 nearly half (41%) of energy expenditure. This exceeded the cost for average force (17%) and was  
25 comparable to the cost for shortening work (42%). The energetic cost is explained by a simple first-  
26 order model of rate-limiting steps in muscle contraction, primarily crossbridge dynamics. The force-rate  
27 cost could contribute substantially to the overall cost of movements that require cyclic muscle activation,  
28 such as locomotion.

29

## 30 **Introduction**

31 Humans often expend energy to perform movement tasks where muscles are only intermittently or  
32 cyclically active. Two notable contributions to the metabolic cost of such tasks are for the mechanical  
33 work performed by muscle fascicles (Abbott et al., 1952; Margaria, 1968), and for the force exerted  
34 when fascicles are isometric (Crow & Kushmerick, 1982). Less appreciated is the cost for muscle  
35 activation and deactivation during cyclic conditions. This cost increases with activation frequency (Hogan  
36 et al., 1998) or the rate of force production (Doke & Kuo, 2007), and can equal or even exceed the cost  
37 for producing continuous isometric force (Chasiotis et al., 1987). However, there is also substantial  
38 metabolic energy expended in tasks that also entail work, for example locomotion with the lower  
39 extremity (Margaria, 1976) or reaching with the upper extremity (H. J. Huang et al., 2012). But the  
40 relative cost for activating muscle vs. performing work remains unknown. It is therefore helpful to

41 determine whether the rate of muscle force production has a cost comparable to work and force  
42 production.

43 There is clearly an energetic cost for activating muscle under intermittent, isometric conditions. This has  
44 been demonstrated with square-wave, on-off activation patterns, which yield a considerably higher  
45 metabolic cost than continuous activation at similar overall contraction duration (Chasiotis et al., 1987;  
46 Spriet et al., 1988). Intermittent contraction also requires more metabolic energy when contraction  
47 frequency is higher (Bergström & Hultman, 1988; Hogan et al., 1998) or when duration of active force  
48 production is smaller (Beck et al., 2020), even when accounting for the cost of maintaining isometric  
49 force, which is roughly proportional to the force-time integral (Crow & Kushmerick, 1982). Instead, the  
50 metabolic cost may be related to the frequency of muscle activation-deactivation (Bergström & Hultman,  
51 1988), leading to a doubling of energetic cost per unit force compared to continuous isometric force  
52 (Chasiotis et al., 1987). The underlying mechanism may be different than for doing work, as the  
53 activation-deactivation cost has been attributed to active calcium transport rather than to crossbridge  
54 cycling (Hogan et al., 1998).

55 There is also a similar metabolic cost for cyclic, non-isometric movements. For example, cyclic leg  
56 swinging (Doke et al., 2005; Doke & Kuo, 2007) and ankle bouncing (Dean & Kuo, 2011) have costs  
57 increasing markedly with movement frequency (e.g., three- to four-fold for a 45% increase in frequency;  
58 Doke et al., 2005), and not explained by the amount of mechanical work (Doke & Kuo, 2007). This cost  
59 has instead been related to the rate of force production, or *force-rate*, which may be considered an  
60 analogue of the square-wave frequency, but for continuous, non-isometric movements. The cost of leg  
61 swinging, including a force-rate component, could account for one-third of the net metabolic cost of  
62 walking (Doke et al., 2005). The hypothesized force-rate cost may therefore be relevant to typical  
63 human activities.

64  
65 However, it remains unclear to what extent the force-rate cost contributes to overall metabolic cost of  
66 movement. Everyday movements can include some combination of muscle mechanical work, force  
67 production, and force-rate costs. But the previous studies have either eliminated mechanical work with  
68 isometric conditions (e.g., Chasiotis et al., 1987), or controlled for it without directly estimating the  
69 amount of work performed (e.g., Doke & Kuo, 2007). This makes it difficult to separate the force-rate  
70 cost and quantify its contribution relative to both work and force. Another confounding factor is series  
71 elasticity, which stores and returns elastic energy not observable from the work of the overall muscle-  
72 tendon unit. Even in apparently isometric conditions, muscle fascicles may perform shortening work  
73 against series elastic tissues, with a meaningful contribution to overall cost. After all, muscle fascicle  
74 work is biochemically and thermodynamically constrained to cost metabolic energy (Barclay, 2015). The  
75 hypothesized cost of force-rate therefore needs to be quantified alongside the actual shortening work  
76 performed by fascicles.

77

78 The current study is intended to address that gap, by testing for a metabolic cost of cyclic muscle  
79 contraction, while accounting for and estimating the costs for mechanical work and force. We  
80 simultaneously quantified work (against series elasticity), force, and force-rate during a cyclic force  
81 production task, along with the overall metabolic energy expenditure. The task was to cyclically produce  
82 voluntary knee extension torque against an isometric dynamometer, at an amplitude and range of  
83 frequencies comparable to everyday human movements. We hypothesized that (1) work and force-time  
84 integral fall short in accounting for metabolic cost at higher frequencies, and (2) that the surplus cost is  
85 related to muscle force-rate. We tested this by parametrically relating each contribution as a function  
86 of waveform frequency and force-rate, and testing whether force-rate is separable from and comparable  
87 to the costs of work and force-time integral.

88

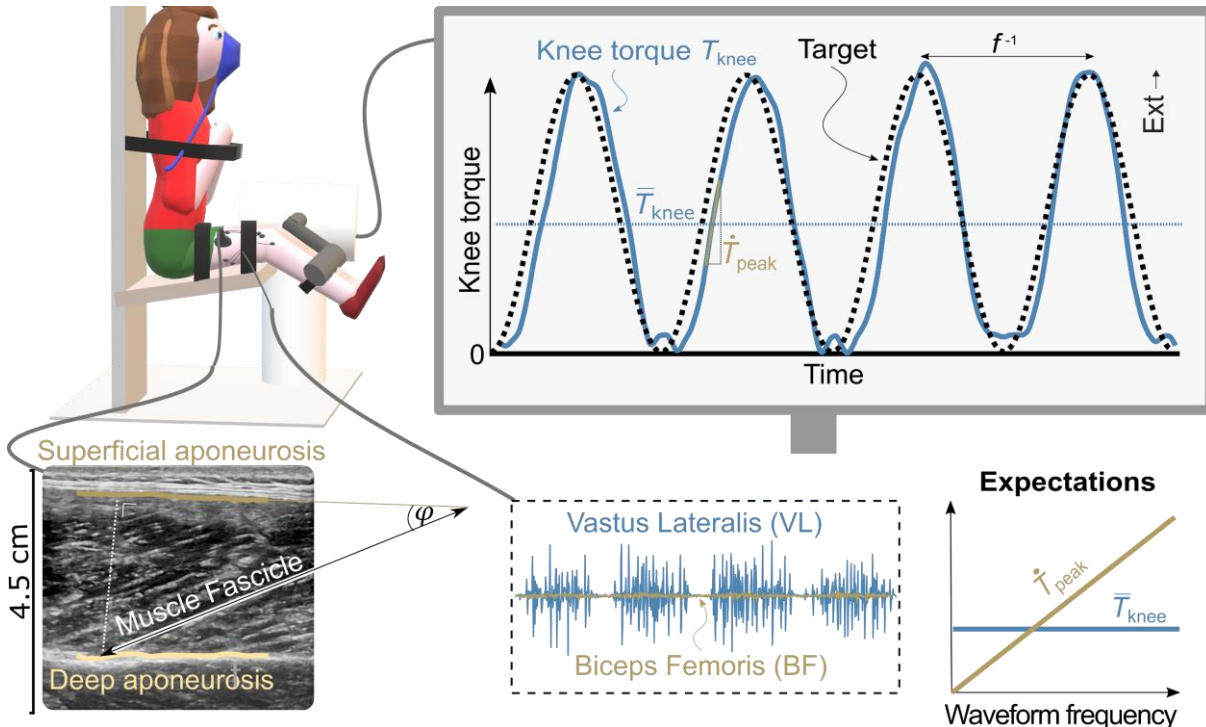
## 89 **Methods**

90 We estimated quadriceps muscle force and mechanical work, and net metabolic rate as healthy adults  
91 produced cyclic, isometric knee extension torque (Fig. 1). Increasing frequency of cyclic torque was  
92 expected to yield greater fluctuations in muscle force. We conducted a set of energetics trials to test for  
93 an associated metabolic cost, and a set of mechanics trials to quantify muscle fascicle mechanical work  
94 (against series elasticity) and force via ultrasound imaging.

95

96 Nine healthy participants (6 male, 3 female, leg length =  $87.4 \pm 4.9$  cm, body mass =  $70.6 \pm 13.1$  kg,  
97 mean  $\pm$  s.d.) produced cyclic bilateral knee extension torque against an isometric dynamometer. The  
98 task was intended to require about 10% of maximal quadriceps muscle force and to impose contraction  
99 frequencies  $f$  within ranges encountered in daily life (mean 11 N-m and 0.5-2.5 Hz, respectively). Real-  
100 time visual feedback was displayed to participants, showing measured and target waveforms (Fig. 1)  
101 for each frequency, all at a fixed torque range (0 - 22 N-m) from combined legs. Torques were exerted  
102 at 20 deg knee flexion (relative to straight leg) and measured with a dynamometer chair (Biodex, Biodex  
103 Medical Systems, NY, USA), which was also used to strap and constrain movement of the trunk and  
104 legs. As baseline, we evaluated knee extension torque during maximum voluntary contraction (MVC) at  
105 20 deg knee flexion ( $97 \pm 20$  N-m). As a reference, we also evaluated MVC extension torques at 70 deg  
106 knee flexion ( $221 \pm 70$  N-m), closer to the plateau of the knee extension torque-angle relationship (e.g.  
107 Kulig et al., 1984). For each condition, we quantified knee torque in terms of its time average  $\bar{T}_{knee}$ ,  
108 peak amplitude, and peak torque-rate  $\dot{T}_{peak}$  (Fig. 1). Peak torque-rate  $\dot{T}_{peak}$  was estimated from the  
109 change in torque from 50% to 150% of average, divided by the time duration of that change. Knee  
110 torque  $T_{knee}$  and its peak rate  $\dot{T}_{peak}$  were then divided by estimated muscle moment arm to estimate  
111 muscle fascicle force  $F_{fas}$  and its peak rate  $\dot{F}_{peak}$ . Prior to data collection, participants provided their  
112 written informed consent according to University of Calgary procedures.

113



**Fig. 1: Experimental set-up for estimating metabolic cost of cyclic, isometric torque production.**

Participants produced knee extension torque to match a displayed waveform target, while respirometry, electromyography (EMG) and ultrasound were recorded. Muscle fascicle length and pennation angle were estimated from ultrasound, and combined with dynamometer to estimate fascicle force and work (against series elasticity). Sinusoidal torques of increasing waveform frequency  $f$  (and fixed amplitude) were expected to result in increasing peak torque-rate  $\dot{T}_{\text{peak}}$  and fixed mean knee torque  $\bar{T}_{\text{knee}}$ , and therefore increasing fascicle force-rate and energetic cost.

114

115 The energetics trials entailed cyclic torque production while respirometry data were recorded.  
 116 Participants were first given practice with matching real-time torque targets for at least 5 min. They  
 117 then performed the five experimental task conditions for 6 min each, with torque and respirometry  
 118 (rates of oxygen consumption  $\dot{V}_{\text{O}_2}$  and carbon dioxide production  $\dot{V}_{\text{CO}_2}$ ; K5 system, Cosmed, Rome)  
 119 averaged only for the final 3 min, to allow time to reach steady-state activity. Metabolic rate was  
 120 determined from  $\dot{V}_{\text{O}_2}$  and the ratio between  $\dot{V}_{\text{CO}_2}$  and  $\dot{V}_{\text{O}_2}$  rates (Lusk, 1909). We also recorded  
 121 electromyography (EMG) to monitor muscle activity and co-contraction (vastus lateralis, rectus femoris,  
 122 biceps femoris, abbreviated as VL, RF and BF respectively). EMG amplitude was determined from the  
 123 band-pass filtered recordings (cut-off frequency  $f_c = 30\text{-}500$  Hz, Butterworth) and low-pass filtered to  
 124 obtain the envelop ( $f_c = 5$  Hz, Butterworth) (Hof, 1984). EMG amplitude was defined as the absolute of  
 125 the Hilbert transformed signal (N. E. Huang et al., 1998), expressed relative to its maximum value  
 126 during MVC and corrected for background noise using baseline-subtraction (La Delfa et al., 2014). The  
 127 order of task conditions was randomized, and with at least 1 min of rest between conditions.

128

129 The separate mechanics trials employed ultrasound imaging to estimate muscle fascicle shortening and  
 130 work against series elasticity. These trials consisted of single-legged isometric torque production at

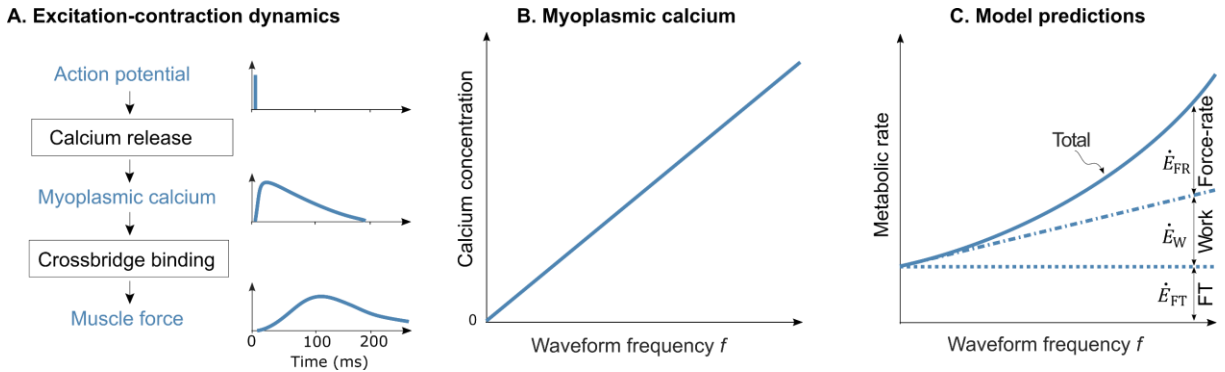
131 three knee angles ( $\theta_{\text{knee}} = 15, 20$  and  $25$  deg), guided by visual feedback of a low frequency triangle  
132 waveform torque target ( $f = 0.02$  Hz, range =  $0$ - $16$  N-m). Images were obtained for VL using ultrasound  
133 ( $5$  cm probe,  $11$  MHz basic-mode; Logiq E9, General Electric, Fairfield, USA), recorded at  $30$  Hz and  
134 approximately synchronized with torque recordings (via a sync pulse). Separate trials were performed  
135 for each of both legs and then averaged between legs.

136  
137 Muscle fascicle lengths  $L_{\text{fas}}$  and muscle pennation angles  $\varphi$  were estimated using a custom ultrasound  
138 algorithm (van der Zee & Kuo, 2020). The SEE length changes  $\Delta L_{\text{SEE}}$  were estimated from changes in  
139 fascicle lengths  $L_{\text{fas}}$  (sampled as a function of  $T_{\text{knee}}$  at  $450$  uniformly spaced points) and pennation angles  
140  $\varphi$  (Fukunaga et al., 2001) and were assumed to be solely dependent on SEE force  $F_{\text{SEE}}$ . Consequently,  
141 at fixed knee torque  $T_{\text{knee}}$  (and thus fixed  $F_{\text{SEE}}$ ), quadriceps muscle-tendon complex (MTC) length change  
142 could be estimated from the component of fascicle length change along the SEE. The moment arm  $r_{\text{MTC}}$   
143 of the quadriceps MTC about the knee (at  $\theta_{\text{knee}} = 20$  deg) was estimated from the average difference in  
144 MTC length between the  $15$  deg and the  $25$  deg trials, divided by the corresponding knee angle difference  
145 (i.e.  $\Delta\theta_{\text{knee}} = 10$  deg). The corresponding force  $F_{\text{SEE}}$  was estimated as knee torque  $T_{\text{knee}}$  divided by  $r_{\text{MTC}}$ .

146  
147 The effects of knee torque  $T_{\text{knee}}$  on muscle fascicle length change  $\Delta L_{\text{fas}}$  and pennation angle change  $\Delta\varphi$ ,  
148 as well as the effect of SEE force  $F_{\text{SEE}}$  on SEE length change  $\Delta L_{\text{SEE}}$  were averaged across knee angles  
149 and fitted using exponentials. An exponential toe region was used for the SEE force-length curve,  
150 appropriate for the relatively low torque levels, less than  $10\%$  of maximal torque (Kulig et al., 1984;  
151 Lichtwark & Wilson, 2008). The mechanical work done on SEE by the fascicle ( $W_{\text{fas}}$ ) was quantified by  
152 the integral of the (fitted) SEE force  $F_{\text{SEE}}$  with respect to the (fitted) SEE length  $L_{\text{SEE}}$ , for the torques  
153 applied during the energetics trials. Fits were done for each subject individually; fascicle work estimates  
154 were averaged across subjects.

155  
156 We hypothesized that overall metabolic cost should include contributions from muscle force-rate  $\dot{F}$ , as  
157 well as from mechanical work and steady force production. The force-rate cost was hypothesized to be  
158 a consequence of rate-limiting dynamics between muscle excitation and force production (excitation-  
159 contraction dynamics, Fig. 2A), particularly due to the rate of cross-bridge binding (Brenner & Eisenberg,  
160 1986). It should be noted that Hill-type muscle models (Zajac, 1989) do not generally include cross-  
161 bridge binding dynamics between calcium release (Ebashi and Endo, 1968) and force production. Here  
162 we illustrate the consequence of rate-limited force production with simple first-order dynamics, which  
163 show how an increasing amount of calcium would need to be released (for example via motor unit  
164 recruitment) to produce cyclic force waveforms of constant amplitude but increasing frequency (Fig.  
165 2B). Calcium release requires active calcium pumping to deactivate muscle, with an associated metabolic  
166 cost  $E_{\text{FR}}$  increasing with rate of force production (FR for force-rate). This general concept is illustrated  
167 with an example time constant of  $30$  ms (Fig. 2B).

168



**Fig. 2: Hypothesized mechanism for force-rate cost.**

(A) Excitation-contraction dynamics start with an action potential that triggers calcium release into the myoplasm, which enables cross-bridge binding and muscle force production. The rate-limiting effect of cross-bridge binding is illustrated by hypothetical transients of action potential, myoplasmic calcium, and muscle force vs. time. (B) The excitation-contraction dynamics require increasingly large input (myoplasmic calcium) amplitudes, for cyclic forces of increasing waveform frequency and constant amplitude. As demonstration, this is modeled as a first-order dynamical system ( $\tau = 30$  ms), with greater calcium (e.g. via recruitment of additional motor units) costing energy for active transport following force production. (C) This results in greater metabolic cost per muscle contraction, as well as per time. Associated metabolic rate  $\dot{E}_{FR}$  for force-rate (FR) is expected to increase quadratically with waveform frequency. In contrast, metabolic rate for force maintenance  $\dot{E}_{FT}$  and mechanical work  $\dot{E}_W$  (FT for force-time integral, W for work) are expected to remain fixed and increase linearly, respectively.

169

170 The force-rate cost hypothesis may be expressed as a metabolic cost per contraction, and experimentally  
 171 tested in terms of a metabolic rate (or cost per time). The cost per muscle contraction  $E_{FR}$  should increase  
 172 in proportion to how quickly the force  $F$  increases,

$$173 \quad E_{FR} \propto \dot{F},$$

174

175 and particularly the peak force-rate  $\dot{F}_{peak}$ . For a sinusoidal force waveform of fixed amplitude, peak force-  
 176 rate is expected to increase with waveform frequency  $f$ ,

$$177 \quad \dot{F}_{peak} \propto f$$

178

179 Under steady-state conditions, the corresponding metabolic rate  $\dot{E}_{FR}$  (Fig. 2C) depends on the cost per  
 180 contraction  $E_{FR}$  and on the frequency of contractions, yielding

$$181 \quad \dot{E}_{FR} \propto E_{FR} \cdot f \propto \dot{F}_{peak} \cdot f \propto f^2$$

182

183 The work and force-time contributions should have separable dependencies on frequency  $f$ . Despite an  
 184 isometric joint, muscle fascicles perform work, against series elastic tendon and aponeurosis, and  
 185 imperfectly rigid leg and dynamometer. For a fixed torque amplitude, work should be performed in fixed  
 186 amount per contraction, and the rate of mechanical work  $\dot{W}$  should therefore increase with the rate of  
 187 contractions, or waveform frequency  $f$ . Assuming fixed biochemical costs for fascicle work, the  
 188 corresponding metabolic rate  $\dot{E}_W$  for work production should increase as

$$189 \quad \dot{E}_W \propto f^1.$$

190

191 The force maintenance contribution is for energy expended even when muscle fascicles are isometric.  
192 Metabolic cost should be proportional to the force amplitude and duration of force (or *force-time integral*,  
193 Crow & Kushmerick, 1982). Due to constant amplitude of the waveform, average knee torque  $\bar{T}_{\text{knee}}$  and  
194 therefore average muscle force was expected to be independent of waveform frequency. The  
195 corresponding force-time metabolic rate  $\dot{E}_{\text{FT}}$  should be independent of waveform frequency,

$$\dot{E}_{\text{FT}} \propto f^0.$$

197  
198 In experiment, we tested for an overall metabolic cost with all three of these contributions. We  
199 hypothesized that net metabolic rate  $\dot{E}_{\text{net}}$  would be the sum of force-rate, work, and force-time integral  
200 terms:

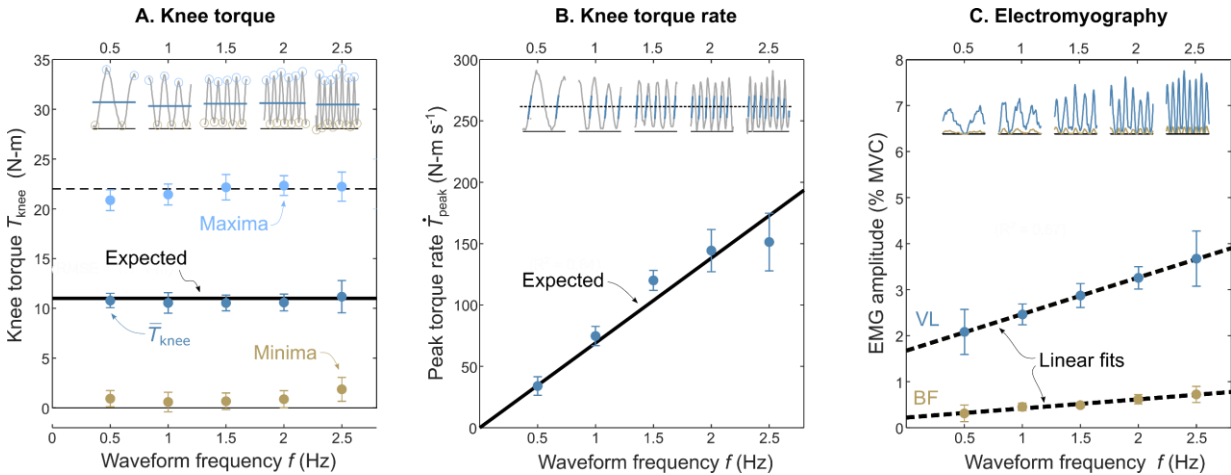
$$\dot{E}_{\text{net}} = \dot{E}_{\text{FR}} + \dot{E}_{\text{W}} + \dot{E}_{\text{FT}} = c_2 f^2 + c_1 f^1 + c_0 f^0$$

201 where “net” is defined as gross minus the cost of quiet sitting. The expected cost of performing fascicle  
202 work is derived from the inverse product of the efficiencies of (1) obtaining ATP from food stuff (about  
203 60%, van Ingen Schenau et al., 1997) and (2) cross-bridge formation (about 50%, Barclay, 2015),  
204 yielding the linear coefficient  $c_1$  of 3.33. The other coefficients ( $c_0$  and  $c_2$ ) were determined using  
205 regression with  $f$  as independent variable. Unless stated otherwise, standard deviations (s.d.) refer to  
206 between-subjects variability.  
207

208  
209

## 210 **Results**

211 Prior to examining the metabolic rate of cyclic force production, we first examine the experimental  
212 conditions, which showed that participants matched target torques well. As expected, participants knee  
213 torque  $T_{\text{knee}}(t)$  had approximately sinusoidal waveform, with constant average  $\bar{T}_{\text{knee}}$  and variable peak  
214 rate  $\dot{T}_{\text{peak}}$ . There was no significant dependency of waveform frequency  $f$  on average torque  $\bar{T}_{\text{knee}}$  (slope  
215  $0.2 \pm 0.4 \text{ N}\cdot\text{m}\cdot\text{Hz}^{-1}$ , mean  $\pm$  95% confidence interval CI,  $P = 0.5$ , linear regression). Average knee torque  
216  $\bar{T}_{\text{knee}}$  and torque minima and maxima were  $10.7 \pm 1.0 \text{ N}\cdot\text{m}$ ,  $1.0 \pm 1.0 \text{ N}\cdot\text{m}$  and  $21.8 \pm 1.2 \text{ N}\cdot\text{m}$  respectively  
217 (mean  $\pm$  s.d. across subjects and conditions; Fig. 3A). Despite constant average torque  $\bar{T}_{\text{knee}}$ , quadriceps  
218 EMG amplitude increased with waveform frequency by about 76% (VL:  $2.1 \pm 0.5 \text{ \%MVC}$  at 0.5 Hz to  
219  $3.7 \pm 0.6 \text{ \%MVC}$  at 2.5 Hz, mean  $\pm$  s.d.). The increase was approximately linear in frequency  $f$ , at rates  
220 of  $0.8 \pm 0.2 \text{ \%MVC}\cdot\text{Hz}^{-1}$ ,  $1.0 \pm 0.3 \text{ \%MVC}\cdot\text{Hz}^{-1}$  and  $0.2 \pm 0.1 \text{ \%MVC}\cdot\text{Hz}^{-1}$  for VL, RF and BF respectively  
221 (mean  $\pm$  95% CI, repeated measures linear regression). There was some co-contraction, with BF EMG  
222 amplitude less than 1% MVC in all conditions (Fig. 3C), on average about one-eighth of VL EMG  
223 amplitudes. Peak knee torque-rate  $\dot{T}_{\text{peak}}$  increased with waveform frequency  $f$  (slope  $68.3 \pm 3.4 \text{ N}\cdot\text{m}$ ,  
224 mean  $\pm$  95% confidence interval CI, linear regression without offset), and closely resembled the increase  
225 expected from the torque targets (slope  $69.1 \text{ N}\cdot\text{m}$ ,  $R^2 = 0.84$ , RMSE =  $1.1 \text{ N}\cdot\text{m}$ , root-mean-square-error;  
226 Fig. 3B).  
227



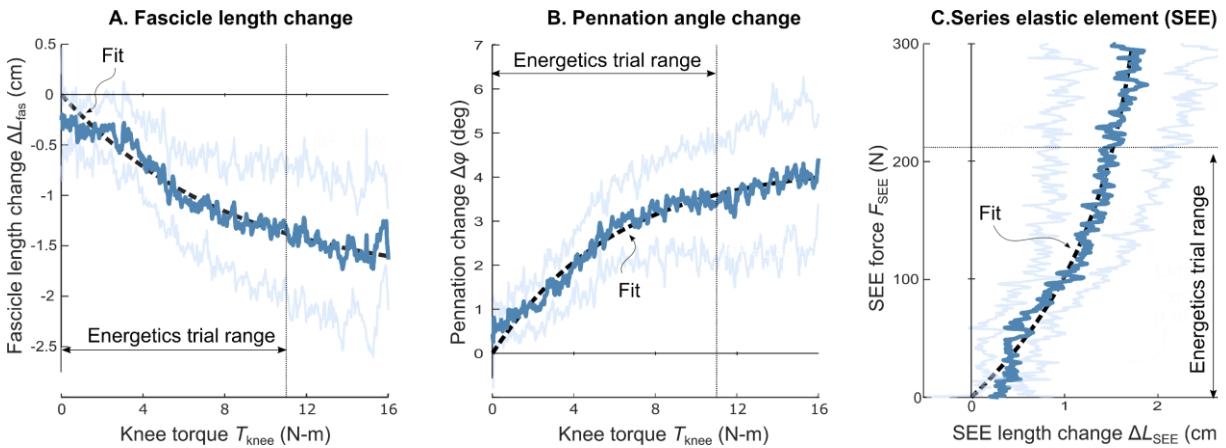
**Fig. 3: Experimentally measured torque, torque-rate, and electromyography vs. waveform frequency.** (A) Knee torque vs. waveform frequency  $f$ , in terms of time-average, minima, and maxima of waveforms (shown in insets). Time-average torque  $\bar{T}_{knee}$  was relatively constant across conditions, comparable to the expected 11 N-m. (B) Peak torque-rate vs. waveform frequency  $f$ . Torque-rate  $\dot{T}_{peak}$  (shown in inset) increased with frequency  $f$ , comparable to expected (solid line). (C) Electromyography (EMG) amplitudes vs. frequency  $f$ , for Vastus Lateralis (VL) and Biceps Femoris (BF). EMG amplitude increased approximately linearly with waveform frequency. Filled symbols denote means across subjects ( $N = 9$ ); error bars denote s.d.

228

229 Muscle fascicles performed work during isometric torque production, as evidenced by fascicle shortening  
 230 (Fig. 4A) and pennation angle changes (Fig. 4B) observed during ultrasound trials. As a baseline, vastus  
 231 lateralis fascicle length was estimated at  $9.5 \pm 0.8$  cm (mean  $\pm$  s.d.) during rest (20 deg knee flexion).  
 232 Fascicle lengths decreased with greater torque, as described by a fitted exponential ( $R^2 = 0.38$ ; see Fig.  
 233 4A). At 11 N-m, muscle fascicles had shortened  $1.3 \pm 0.6$  cm. Pennation angle was  $15.9 \pm 1.2$  deg (mean  
 234  $\pm$  s.d.) during rest. Pennation angle increased with greater torque, also described by a fitted exponential  
 235 ( $R^2 = 0.46$ ; Fig. 4B). Pennation angle was  $15.9 \pm 1.2$  deg (mean  $\pm$  s.d.) at rest, and increased by  $3.5 \pm 1.3$   
 236 deg at 11 N-m. Combining fascicle length and pennation angle changes with knee angle, quadriceps  
 237 muscle-tendon complex moment arm was estimated at  $5.2 \pm 2.3$  cm (mean  $\pm$  s.d.). These data also  
 238 yielded an estimate of length change of series elastic elements, fit by an exponential toe region ( $R^2 =$   
 239  $0.42$ ; Fig. 4C). From that fit, muscle fascicle mechanical work  $W_{fas}$  was estimated at  $1.2 \pm 0.6$  J (mean  $\pm$   
 240 s.d.) for an 11 N-m contraction. The increase in mechanical work rate  $\dot{W}_{fas}$  with waveform frequency  
 241 was therefore about  $2.4 \pm 1.2$  J.

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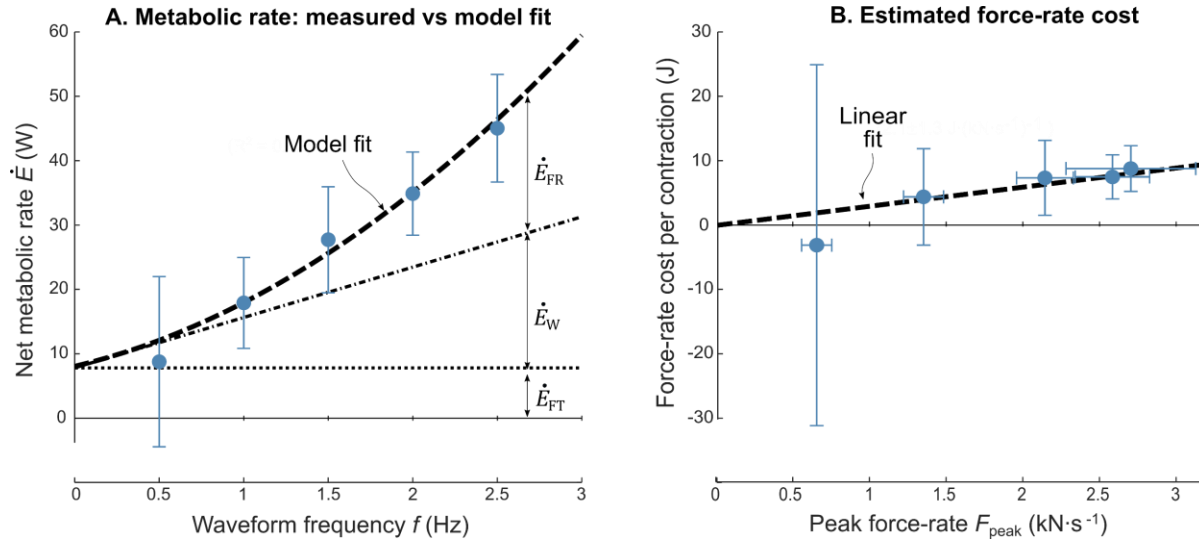




**Fig. 4: Muscle fascicle and series elastic element elongation as a function of knee torque.** (A) Muscle fascicle length change (relative to relaxed)  $\Delta L_{FAS}$  vs. knee torque  $T_{knee}$ . Fascicle length decreased with greater knee torque, with exponential fit. (B) Muscle pennation angle change  $\Delta\phi$  vs. knee torque  $T_{knee}$ . Pennation angle increased with greater knee torque, with exponential fit. (C) Series elastic element (SEE) force  $F_{SEE}$  vs. length change  $\Delta L_{SEE}$ . SEE length increased with greater SEE force, with fit to exponential toe region. Data here were obtained during isometric mechanics trials. Resulting fit was used to estimate mechanical work done by fascicles on SEEs during the energetics trials. Dark lines indicate means across subjects ( $N = 9$ ); light lines denote s.d.

243

244 Net metabolic rate  $\dot{E}_{net}$  increased with waveform frequency  $f$  (Fig. 5A), in agreement with predictions  
 245 ( $P = 4 \cdot 10^{-6}$ , repeated measures regression). Net metabolic rate  $\dot{E}$  increased from a value of  $10.5 \pm 13.2$   
 246 (mean  $\pm$  s.d.) at the lowest frequency ( $f = 0.5$  Hz), to  $46.8 \pm 8.4$  W (mean  $\pm$  s.d.) at the highest  
 247 frequency ( $f = 2.5$  Hz). The overall cost appeared to agree with hypothesized contributions from force-  
 248 rate  $\dot{E}_{FR}$ , work  $\dot{E}_W$ , and force-time  $\dot{E}_{FT}$ . At the highest frequency, these three costs were estimated at  
 249 19.1 W, 19.7 W and 7.9 W respectively, or about 41%, 42% and 17% of net metabolic rate  $\dot{E}$ . Costs of  
 250 force-rate  $\dot{E}_{FR}$  and force-time  $\dot{E}_{FT}$  had coefficients of  $3.2 \pm 1.4$  J·s and  $7.9 \pm 10.2$  W respectively (mean  $\pm$   
 251 CI,  $P = 0.007$ , repeated measures regression). Examining the force-rate cost as a cost per contraction  
 252  $E_{FR}$ , it increased approximately linearly with measured peak force-rate  $\dot{F}_{peak}$  ( $2.6 \pm 1.9 \cdot 10^{-3}$  m·s, mean  
 253  $\pm$  CI, linear regression without offset; Fig. 5B).



**Fig. 5: Metabolic cost of cyclic force production.** (A) Net metabolic rate  $\dot{E}_{net}$  versus waveform frequency  $f$ , along with three separate hypothesized contributing terms: (1) a force-time term  $\dot{E}_{FT}$  independent of  $f$ , (2) a work term  $\dot{E}_W$  increasing linearly with  $f$ , and (3) the hypothesized force-rate term  $\dot{E}_{FR}$ , increasing with  $f^2$ . Net metabolic rate  $\dot{E}_{net}$  was largely explained by a quadratic fit ( $R^2 = 0.66$ ) where the linear coefficient was fixed to the cost of work  $c_1$ . (B) Force-rate cost per contraction  $E_{FR}$  versus measured peak force-rate  $\dot{F}_{peak}$ . Force-rate cost  $E_{FR}$  (isolated from force-time and work terms) increased approximately linearly with measured peak force-rate  $\dot{F}_{peak}$ . Filled symbols denote means across subjects ( $N = 9$ ); error bars denote s.d.

254

## 255 Discussion

256 The current study aimed at investigating the metabolic cost related to muscle force-rate, separately  
 257 from both force and mechanical work costs. Net metabolic rate increased with the frequency of isometric  
 258 torque production, faster than would be expected for force production alone. We also estimated muscle  
 259 fascicle shortening, and observed non-negligible work performed by fascicles, but also insufficient to  
 260 explain metabolic cost. A considerable portion of this cost can be ascribed to the proposed force-rate  
 261 cost. We next examine the hypothesis in relation to the data, the potential mechanisms for metabolic  
 262 cost, and implications for movement.

263 We first consider why force and work production do not explain the observed metabolic cost. The cyclic,  
 264 isometric task resulted in nearly the same average force across conditions. The fascicle force-time  
 265 integral was therefore unchanged as a function of frequency. Fascicles did, however, shorten and  
 266 perform work that increased with frequency. But the expected metabolic cost for work  $\dot{E}_W$ , based on  
 267 physiological (Margaria, 1968) and biochemical (Barclay, 2015) grounds, was far below the observed  
 268 metabolic cost. Our estimate does not include the dependency of work coefficient  $c_1$  on contraction  
 269 velocity, as described by a parabolic efficiency-velocity curve (Barclay, 2015). Mechanical efficiency is  
 270 highest at about 33% of maximal contraction velocity (37 cm·s<sup>-1</sup> for VL) (Barclay et al., 1993; Ruiters  
 271 et al., 2000; van Soest & Bobbert, 1993), which is substantially higher than contraction velocity in the  
 272 highest frequency condition here (6.5 cm·s<sup>-1</sup>). Therefore, higher waveform frequencies could allow for  
 273 a higher mechanical efficiency and thereby a lower work cost, potentially making ours an overestimate  
 274 of the work cost at higher frequencies. We have also treated force-time and work costs as separate and

275 additive, when both result from the same mechanism, namely actomyosin ATPase activity (Barclay et  
276 al., 2007). Crossbridges have a fixed amount of energy per cycle, with much of it dissipated as heat in  
277 isometric conditions, as described by force-time coefficient  $c_0$ . But that coefficient might be expected to  
278 decrease with contraction velocity, so that actomyosin ATPase activity might produce relatively more  
279 shortening work at higher contraction velocities. This would make the force-time cost an overestimate  
280 at higher frequencies. Yet another concern is muscle co-contraction, which could lead to greater cost  
281 not explained by shortening work. We did observe antagonist EMG of relatively small and linearly  
282 increasing amplitude, but consider it unlikely to explain the quadratically increasing energetic cost with  
283 waveform frequency. Most of the assumptions we have applied would lead to overestimation of work  
284 and force-time costs, so that their sum might in reality explain less than the 59% of net metabolic cost  
285 we have estimated.

286 This leaves a substantial cost explained by the hypothesized force-rate cost. The sharp increase in  
287 metabolic cost with muscle contraction frequency (Fig. 5) was consistent with the expected force-rate  
288 cost increasing with the square of contraction frequency. The hypothesis is based on the rate-limited  
289 dynamics between muscle excitation and force production, which acts as a low-pass filter of excitation  
290 and associated calcium release into the myoplasm. In the present experiment, increasing contraction  
291 frequencies called for higher force-rates ( $\dot{F}$ , Fig. 3), which are expected to require more calcium release  
292 per muscle contraction. Active calcium pumping returns the calcium to the sarcoplasmic reticulum, with  
293 an associated metabolic cost (SERCA ATPase; (Inoue et al., 2019)). This contrasts with the energetic  
294 costs for force maintenance or work production, both associated with cycling of actomyosin crossbridges  
295 (actomyosin ATPase). Our hypothesis is that the combination of rate-limiting dynamics and calcium  
296 pumping imply a separate force-rate cost. This cost is in addition to the traditional force- and work-  
297 related costs, and could explain 41% (or more, if work and force-time costs are overestimated) of  
298 metabolic cost observed at the higher movement frequencies of the present experiment. In movement  
299 conditions that require cyclic muscle contraction, the force-rate cost could be quite substantial.

300 A source of uncertainty was our estimate of muscle shortening work. We estimated Vastus Lateralis (VL)  
301 muscle fascicle work (about 1.2 J, see Fig. 4) done while shortening against SEEs during isometric torque  
302 production. Whereas such shortening is similar as reported elsewhere (Ichinose et al., 1997), others  
303 have estimated considerably less shortening (e.g. 0.64 cm for VL) (van Soest & Bobbert, 1993). Some  
304 of the fascicle shortening we observed could be due to dynamometer deformation and tendon slackness.  
305 Biodex dynamometer deformation has been estimated to account for up to 0.2 cm VL aponeurosis length  
306 change during maximal "isometric" torque production (Bojsen-Møller et al., 2003). Slack tendon refers  
307 to the idea that tendons become slack at short muscle-tendon complex length (Fukutani et al., 2017).  
308 During isometric torque production at 10% maximal force, VL fascicles shorten about six times more  
309 when the knee is extended than when flexed (about 3 cm versus 0.5 cm, Fukunaga et al., 1997). Since  
310 any non-zero muscle force may remove the slack in the tendon, considerable SEE length change may  
311 occur at small forces, requiring little work. In our experiment, a considerable portion of total fascicle  
312 shortening occurred at the smallest torque values (see Fig. 4). We found it challenging to estimate

313 shortening work at very low torque levels, and dynamometer deformation and tendon slackness may  
314 have caused ours to be an overestimate of the work done on SEEs. However, such errors would tend  
315 toward a conservative, underestimate of the hypothesized force-rate cost.

316  
317 Evidence for the proposed force-rate cost has previously been demonstrated in both muscle and whole-  
318 body experiments. For cyclic isometric contraction of mouse muscle *in situ* (1:3 on/off duty factor), rate  
319 of oxygen consumption is higher when cycle frequency is higher (Hogan et al., 1998). For prolonged  
320 isometric contraction of human VL muscle *in vivo*, rate of ATP utilization is higher when stimulation is  
321 cyclic (1:1 on/off duty factor) compared to constant (Chasiotis et al., 1987; Spriet et al., 1988). For  
322 cyclic isometric contraction of human calf muscle at constant frequency, metabolic cost decreases with  
323 increasing duty factor (Beck et al., 2020). While these studies have indicated a metabolic cost for cyclic  
324 muscle contraction, this cost was not parametrically related to muscle force-rate. We believe that force-  
325 rate, rather than work or force-time, could explain many such findings on metabolic cost of cyclic  
326 isometric contraction. In contrast to previous studies on isometric contraction varying on-off durations,  
327 we parametrically related such metabolic cost to muscle force-rate, which we find more suitable for the  
328 continuously varying forces of most daily movements. Furthermore, metabolic cost of cyclic movement  
329 has been observed to increase with movement frequency in leg swinging (Doke et al., 2005; Doke &  
330 Kuo, 2007), ankle bouncing (Dean & Kuo, 2011) and arm reaching (Wong et al., 2018). Altogether, the  
331 force-rate cost seems to be observable during a variety of movements and contraction conditions. We  
332 here provide evidence that the force-rate cost exists during voluntary isometric contraction,  
333 independently of work and force-time costs.

334  
335 We have separated total metabolic cost into three terms: work-, force-time and force-rate. Such  
336 phenomenological division is potentially explained mechanistically as costs due to individual ATPases,  
337 particularly actomyosin (for work and force-time) and SERCA ATPases (for force-rate). Whether SERCA  
338 is primarily responsible for the force-rate cost could be tested in future experimental studies on isolated  
339 muscle, for example using cross-bridge (and therefore actomyosin ATPase) blocking agents (Barclay et  
340 al., 2007). We expect SERCA ATP consumption rate to increase with contraction frequency because of  
341 the increase in calcium release amplitudes, due to rate-limiting force production dynamics. Higher  
342 calcium amplitudes would require higher muscle activation levels, which agrees with the observed  
343 increase in quadriceps EMG amplitude with waveform frequency. Such properties are not included in  
344 Hill-type muscle models (Zajac, 1989), which do have activation dynamics attributed to calcium release  
345 (sometimes called 'active state') and muscle force-length and -velocity dependency, but not rate-limiting  
346 dynamics between calcium release and muscle force. As demonstration, we simulated the present  
347 experiment with a commonly used metabolic muscle model (OpenSim software, Uchida et al., 2016). It  
348 predicted a 2.4 W increase in metabolic rate with waveform frequency, only about 7% of the amount  
349 experimentally measured. Current models therefore appear to underestimate the energetic cost of cyclic  
350 force production. Improved estimates might be obtained by including rate-limiting dynamics, crudely  
351 modeled as a low-pass filter here, such as calcium release and binding (Baylor & Hollingworth, 2012)

352 and Huxley-type crossbridge binding (van Soest et al., 2019). Future modelling studies could develop  
353 such mechanistic models that explain the force-rate cost.

354

355 Fast contraction of muscle may require high calcium release and pumping rates, at the cost of metabolic  
356 energy spend by SERCA. Such energetic penalty for rapid increase in muscle force may explain why  
357 (ground reaction) forces during human walking are smoother than expected based on work  
358 considerations (Rebula & Kuo, 2015). Nevertheless, there may be a considerable force-rate cost during  
359 human locomotion, as vastus lateralis fascicles produce relatively short bursts of high force (0 - 30% of  
360 stride; Bohm et al., 2018). The force-rate cost may also apply to a variety of other animals. In locust  
361 flight muscle, oxygen consumption during cyclic isometric contraction is 87% of the consumption during  
362 maximal power output, indicating high cost for cyclic muscle activation (Josephson & Stevenson, 1991).  
363 Locusts use synchronous muscle with one contraction per wing beat, whereas other insects such as  
364 beetles use asynchronous muscle with fewer contractions per beat (Josephson et al., 2001), which could  
365 reduce the activation cost as a potentially advantageous adaptation (Syme & Josephson, 2002). A force-  
366 rate cost could be an important factor in energy expenditure in a wide range of movements and species.

367

### 368 **Conclusion**

369 We observed an increase in average net metabolic rate with frequency of cyclic torque production, which  
370 could not be explained by force-time nor by muscle fibre mechanical work. Average net metabolic rate  
371 was related to force-rate, suggesting that increasing muscle force abruptly requires more metabolic  
372 energy than when done slowly. We propose that this force-rate metabolic cost may be explained by an  
373 increase in the amount of required active calcium transport in the muscle fibre, and may be relevant for  
374 human and animal movement.

375

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378

### 379 **Competing interests**

380 The authors declare no competing or financial interests

381

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385

### 386 **Data availability**

387 Ultrasound algorithm and typical example of ultrasound data is available on:

388 <https://github.com/timvanderzee/ultrasound-automated-algorithm>

389

390

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