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Functional muscle group- and sex-specific parameters for a three-compartment controller muscle fatigue model applied to isometric contractions

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ABSTRACT

The three-compartment controller with enhanced recovery (3CC-r) model of muscle fatigue has previously been validated separately for both sustained (SIC) and intermittent isometric contractions (IIC) using different objective functions, but its performance has not yet been tested against both contraction types simultaneously using a common objective function. Additionally, prior validation has been performed using common parameters at the joint level, whereas applications to many real-world tasks will require the model to be applied to agonistic and synergistic muscle groups. Lastly, parameters for the model have previously been derived for a mixed-sex cohort not considering the differece in fatigabilities between the sexes. In this work we validate the 3CC-r model using a comprehensive isometric contraction database drawn from 172 publications segregated by functional muscle group (FMG) and sex. We find that prediction errors are reduced by 19% on average when segregating the dataset by FMG alone, and by 34% when segregating by both sex and FMG. However, minimum prediction errors are found to be higher when validated against both SIC and IIC data together using torque decline as the outcome variable than when validated sequentially against hypothesized SIC intensity-endurance time curves with endurance time as the outcome variable and against raw IIC data with torque decline as the outcome variable.

1. Introduction

Muscle fatigue is an inevitable but reversible byproduct of physical exertion which manifests in a temporarily reduced force capacity for the muscles involved in the activity (Bigland-Ritchie et al., 1995). It is a complex biochemical process (Vøllestad, 1997) that affects all skeletal muscle for all activity types regardless of duration, but the extent to which each muscle is affected can depend on a multitude of physiological, task, and external factors (Chaffin, 1973). Since it is eminently desirable that tasks never demand more of the worker than their physical limits to prevent the incidence of injuries, it is immensely helpful to predict how a certain task affects muscle strength over time. Measuring strength declines over the course of a real-world task can be tedious, time-consuming, and invasive, and the results will likely be inapplicable to another person or situation. Mathematical models of fatigue overcome these difficulties with their predictive abilities. While each model may be suitable for a certain subset of tasks and may specify its own limitations, in general it can reasonably predict the course of strength decline for a particular joint in the human body (Rashedi and Nussbaum, 2015).

The three-compartment controller (3CC) family of models (Frey-Law et al., 2012; Looft et al., 2018; Xia and Frey-Law, 2008) divide the constituent motor units (MU) of a muscle into three states or compartments—resting, active, and fatigued—and calculate the relative size of each to estimate the extent of fatigue. They specify rules (Eqs. (1)–(6)) for determining the rate at which MUs transition from one state into another.

$$\frac{dM_R}{dt} = -C(t) + r(k, TL) \times R \times M_F \tag{1}$$

$$\frac{dM_A}{dt} = C(t) - F \times M_A \tag{2}$$

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Table 1
Studies included in the experimental dataset listed by author for ankle dorsiflexors, ankle plantarflexors, elbow extensors, elbow flexors, adductor pollicis, first dorsal interosseous, general grip muscles, and knee extensors derived from Frey Law and Avin (2010) and Looft et al. (2018).

Functional muscle group	Author, Date	Male participants	Female participants	Target load (% MVC)	Duty cycle (%)	Cycle time (s)	Number of data points
Ankle dorsiflexors	(Birtles et al., 2002)	14	8	100	50	3	20
	(Birtles et al., 2003)	5	5	100	50	3	20
	(Chung et al., 2007)	12	0	100	50	10	35
	(Egaña and Green, 2007)	7	0	30, 40, 50, 60, 80	33	6	86
	(Russ and Kent-Braun, 2003)	8	0	100	50	10	4
	(Russ et al., 2008)	15	0	100	70	10	10
	(Fimland et al., 2010)	13	0	100	83	30	7
	(Christie and Kamen, 2009)	4	4	50	100	1	1
	(Ciubotariu et al., 2004)	6	4	50, 80	100	1	2
	(Farina et al., 2005)	11	0	40	100	1	1
	(Houtman et al., 2002)	6	2	30	100	1	1
	(Houtman et al., 2003)	3	2	30, 40	100	1	7
	(Hunter et al., 2008)	8	7	20	100	1	1
	(Kent-Braun, 1999)	5	4	100	100	1	1
	(Lévénez et al., 2005)	11	1	50	100	1	1
	(Molbech and Johansen, 1973)	2	3	50	100	1	5
	(Ng et al., 2000)	6	5	30	100	1	1
	(Shahidi and Mathieu, 1995)	4	5	15, 30, 45, 60, 75, 90	100	1	6
Ankle plantarflexors	(Alway et al., 1987)	8	0	100	50	10	1
	(Alway, 1991)	6	0	30	100	1	1
	(Ciubotariu et al., 2004)	6	4	50, 80	100	1	2
	(Mademli and Arampatzis, 2008)	12	0	40	100	1	1
	(Matthijsse et al., 1987)	7	1	60	100	1	16
	(Molbech and Johansen, 1973)	2	3	50	100	1	5
	(Nordez et al., 2009)	8	0	40	100	1	1
	(Ohashi, 1993)	6	0	30, 40, 50	100	1	3
	(Shahidi and Mathieu, 1995)	4	5	15, 30, 45, 60, 75, 90	100	1	6
Elbow extensors	(Bilodeau, 2006)	4	4	100	86	35	17
	(Thomas and Del Valle, 2001)	3	1	50	60	10	5
	(Bonde-Petersen et al., 1975)	2	1	10–75	100	1	22
	(Fallentin and Jørgensen, 1992)	7	0	10, 40	100	1	2
	(Griffin et al., 2001a)	4	3	20	100	1	1
	(Griffin et al., 2001b)	3	4	20	100	1	1
Elbow flexors	(Bazzucchi et al., 2005)	6	0	30, 50, 80	100	1	3
	(Bonde-Petersen et al., 1975)	2	1	20–70	100	1	22
	(Calder et al., 2008)	5	5	25	100	1	2
	(Carlson, 1969)	15	0	20, 30, 40, 50	100	1	4
	(Deeb et al., 1992)	10	0	40, 60, 80, 100	100	1	4
	(Dimitrova et al., 2009)	3	3	20, 40, 60, 80, 100	100	1	5
	(Esposito et al., 1998)	7	0	80	100	1	2
	(Fallentin and Jørgensen, 1992)	7	0	10, 40	100	1	2
	(Felici et al., 2001)	6	0	80	100	1	1
	(Gamet and Maton, 1989)	3	2	10–30	100	1	25
	(Greiwe et al., 1998)	7	0	50	100	1	1
	(Hagberg, 1981)	9	0	15–55	100	1	53
	(Hendrix et al., 2009b)	4	5	30–75	100	1	36
	(Hermiston and Bonde-Petersen, 1975)	2	1	25–70	100	1	14
	(Hoeger Bement et al., 2009)	0	20	25	100	1	1
	(Hunter and Enoka, 2001)	7	7	20	100	1	2
	(Hunter et al., 2002)	8	8	15	100	1	2
	(Hunter and Enoka, 2003)	7	7	20	100	1	2
	(Hunter et al., 2004a)	14	13	20	100	1	2
	(Hunter et al., 2004c)	10	10	20	100	1	2
	(Hunter et al., 2005)	8	0	20	100	1	1
	(Jubeau et al., 2012)	12	0	100	21	19	49
	(Kilbom et al., 1983)	18	0	25	100	1	2
	(Klass et al., 2008)	6	5	20	100	1	1
	(Krogh-Lund and Jørgensen, 1992)	11	0	15	100	1	1
	(Krogh-Lund, 1993)	11	0	40, 100	100	1	2
	(Krogh-Lund and Jørgensen, 1993)	10	0	30	100	1	1
	(Lloyd et al., 1991)	13	0	30	60	10	9
	(Lowery et al., 2002)	5	1	30, 50, 80	100	1	3
	(Lowery and O'Malley, 2003)	2	1	80	100	1	6
	(Mamaghani et al., 2001)	10	0	20, 40, 60	100	1	3
	(Mendez-Villanueva et al., 2009)	9	0	50	30, 60	20, 10	5
	(Mottram et al., 2006)	14	15	15	100	1	4
	(Muthalib et al., 2010)	10	0	100	21	19	49
	(Nicolas et al., 2008)	16	0	40	100	1	4

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Table 1 (*continued*)

Functional muscle group	Author, Date	Male participants	Female participants	Target load (% MVC)	Duty cycle (%)	Cycle time (s)	Number of data points
	(Ohashi, 1993)	7	0	15–50	100	1	5
	(Ordway et al., 1977)	27	0	100	50	2	20
	(Orizio et al., 1992)	13	0	20, 40, 60, 80	100	1	4
	(Petrofsky and Phillips, 1980)	10	10	25–90	100	1	10
	(Riley et al., 2008)	7	8	20	100	1	1
	(Rudroff et al., 2005)	8	0	20	100	1	1
	(Rudroff et al., 2007a)	20	0	20	100	1	1
	(Rudroff et al., 2007b)	10	10	20	100	1	1
	(Rudroff et al., 2008)	10	0	20	100	1	1
	(Sacco et al., 1999)	4	6	20	100	1	1
	(Schulte et al., 2004)	13	2	40	100	1	1
	(Semmler et al., 1999)	6	6	15	100	1	1
	(Staudenmann et al., 2009)	10	0	20	100	1	1
	(Taylor et al., 2000)	5	4	50–86	50	10	65
	(Ulmer et al., 1989)	8	8	20, 25, 30, 50	100	1	4
	(Watanabe et al., 1995)	6	0	30	100	1	1
	(Yoon et al., 2007)	9	9	20, 80	100	1	4
	(Yoon et al., 2008)	6	9	20, 80	100	1	2
Adductor pollicis	(Ditor and Hicks, 2000)	12	12	100	71	7	18
	(Fulco et al., 2001)	12	21	50	50	10	6
	(Zattara-Hartmann et al., 1995)	6	0	80	100	1	1
First dorsal interosseous	(Fuglevand et al., 1995)	8	3	35	100	1	1
	(Fujimoto and Nishizono, 1993)	8	0	40	60	10	8
	(Huang et al., 2007)	4	10	75	100	1	1
	(Maluf et al., 2005)	20	0	20	100	1	1
	(Newham and Cady, 1990)	2	1	100	50	2	1
	(Tharion, 2006)	5	3	50	100	1	1
General grip	(Benwell et al., 2007)	6	6	30	60	5	4
	(Blackwell et al., 1999)	18	0	60	100	1	1
	(Bystrom and Sjøgaard, 1991)	4	4	10	100	1	1
	(Chatterjee and Chowdhuri, 1991)	74	0	40	100	1	3
	(Clark et al., 2008)	4	5	20	100	1	1
	(Ferguson and Brown, 1997)	10	0	40	100	1	1
	(Hunter et al., 2006)	16	18	20	100	1	2
	(Lind et al., 1978)	4	0	25, 40	100	1	2
	(Liu et al., 2005)	10	4	100	67	3	12
	(Longhurst et al., 1980)	24	0	40	100	1	1
	(Louhevaara et al., 2000)	21	0	46	100	1	1
	(Lydakis et al., 2008)	7	8	40	100	1	1
	(Momen et al., 2003)	7	6	40	100	1	1
	(Momen et al., 2004)	5	4	40	100	1	1
	(Momen et al., 2006)	10	10	40	100	1	2
	(Nagle et al., 1988)	10	0	30	100	1	1
	(Pepin et al., 1996)	9	16	30	100	1	1
	(Petrofsky et al., 1975)	0	51	40	100	1	1
	(Petrofsky and Lind, 1975)	62	3	40	100	1	2
	(Petrofsky et al., 1976)	0	3	40	100	1	1
	(Petrofsky and Laymon, 2002)	15	0	40	100	1	2
	(Saito et al., 2008)	8	8	100	50	10	12
	(Smolander et al., 1998)	10	0	20, 40, 60	100	1	3
	(Thompson et al., 2007)	18	20	20, 50	100	1	4
	(Urbanski et al., 1999)	10	0	67	100	1	1
	(Walamies and Turjanmaa, 1993)	13	27	50	100	1	1
	(West et al., 1995)	7	7	30, 50, 70	100	1	6
	(Williams, 1991)	6	0	70	100	1	1
Knee extensors	(Armatas et al., 2010)	13	0	100	50	10	10
	(Bigard et al., 2001)	11	0	25, 70	100	1	2
	(Burnley, 2009)	8	0	100	60	5	10
	(Callahan et al., 2009)	8	8	100	50	10	8
	(Callahan and Kent-Braun, 2011)	0	11	100	50	10	9
	(Christensen and Fuglsang-Frederiksen, 1988)	8	8	20	100	1	1
	(Clark et al., 2005)	11	11	25	100	1	2
	(Cox and Cafarelli, 1999)	5	5	30	100	1	1
	(Crenshaw et al., 1997)	9	2	25, 70	100	1	2
	(Deeb et al., 1992)	10	0	40, 60, 80, 100	100	1	4
	(Dias da Silva and Gonçalves, 2013)	0	9	20, 30, 40, 50	100	1	4
	(Easton et al., 2007)	5	5	30	100	1	10
	(Ebenbichler et al., 1998a)	9	9	30, 50, 70	100	1	3
	(Ebenbichler et al., 1998b)	9	9	30, 50, 70	100	1	3
	(Gerdle and Karlsson, 1994)	14	0	10, 25, 70	100	1	3
	(Grabiner et al., 1991)	9	0	30, 60	100	1	2
	(Greiwe et al., 1998)	7	0	100	100	1	1
	(Hamada et al., 2003)	4	0	100	63	8	30

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Table 1 (*continued*)

Functional muscle group	Author, Date	Male participants	Female participants	Target load (% MVC)	Duty cycle (%)	Cycle time (s)	Number of data points
	(Hendrix et al., 2009a)	4	5	30–81	100	1	35
	(Johnson, 1982)	15	0	100	100	1	1
	(Karlsson et al., 1975)	3	0	15–85	100	1	8
	(Kuroda et al., 1970)	6	0	25–100	100	1	4
	(Larsson and Karlsson, 1978)	28	0	50	100	1	1
	(Mademli et al., 2008)	12	0	25	100	1	1
	(Maïsetti et al., 2002a)	9	0	50	100	1	1
	(Maïsetti et al., 2002b)	14	0	50	100	1	1
	(Mathur et al., 2005)	11	11	20, 80	100	1	2
	(Maughan et al., 1986)	25	25	20, 50, 80	100	1	6
	(Maughan, 1988)	8	0	60	100	1	1
	(Mika et al., 2007)	10	0	50	100	1	1
	(Mulder et al., 2007)	5	0	45	60	2.5	5
	(Nagle et al., 1988)	10	0	30	100	1	1
	(Ng et al., 1994)	8	9	30, 50	100	1	2
	(Ordway et al., 1977)	27	0	100	50	2	20
	(Petrofsky and Laymon, 2002)	25	0	40	100	1	2
	(Place et al., 2005)	11	0	20	100	1	1
	(Place et al., 2006)	13	0	40	100	1	1
	(Place et al., 2007)	13	0	40	100	1	1
	(Ray and Mark, 1993)	7	1	30	100	1	1
	(Ray et al., 1998)	7	0	30	100	1	1
	(Rochette et al., 2003)	10	0	20	100	1	1
	(Rodriquez and Agre, 1991)	21	20	40	100	1	1
	(Rodriquez et al., 1993)	7	0	20, 40, 80	100	1	3
	(Saugen et al., 1997)	8	0	40	60	10	4
	(Smolander et al., 1998)	10	0	20, 40, 60	100	1	3
	(Urbanski et al., 1999)	10	0	67	100	1	1
	(Yamada et al., 2002)	14	0	20, 60	100	1	2
	(Zech et al., 2008)	12	0	50	100	1	1

$$\frac{dM_F}{dt} = F \times M_A - r(k, TL) \times R \times M_F \tag{3}$$

$$\text{If } M_A < TL \text{ and } M_R > TL - M_A,\ C(t) = L_D \times (TL - M_A) \tag{4}$$

$$\text{If } M_A < TL \text{ and } M_R < TL - M_A, C(t) = L_D \times M_R \tag{5}$$

$$\text{If } M_A \geq TL, C(t) = L_R \times (TL - M_A) \tag{6}$$

Here, M_R, M_A, and M_F are the fraction of motor units in the muscle that are currently resting, active, and fatigued, respectively. $C(t)$ is a bidirectional activation-deactivation drive. F and R are the fatigue and recovery rate constants, respectively, and r is a recovery multiplier that is a discontinuous function of target load (TL) and a unitless optimization parameter k. r is defined by Eq. (7). The model is relatively insensitive to the muscle force development (L_D) and relaxation (L_R) factors (Xia and Frey-Law, 2008), so a constant value of 10 is chosen for both.

$$r = \begin{cases} k \text{ if } TL = 0 \\ 1 \text{ if } TL > 0 \end{cases} \tag{7}$$

The 3CC model, in its present form, was developed by first determining the values of F and R by running a 2-parameter sweep against sustained isometric contraction (SIC) data. Endurance time (ET) was chosen as the output variable for differing input task intensities (Frey-Law et al., 2012). This approach ensured the best possible F and R values for predicting ET for a given sustained task intensity, but not necessarily for predicting the precise course of fatigue during that period. k was then determined by running a 1-parameter sensitivity analysis using the predetermined F and R values against intermittent isometric contraction (IIC) data, but at this stage the input and output variables were reversed—torque declines were estimated for given input times (Looft et al., 2018). k—subsequently calculated—produced the best fit to IIC data for the given F and R values. Ideally, all three parameters would have been chosen independently for IIC data, but it is likely that the F and R values obtained thereby would have conflicted with those obtained from the SIC data since the two optimization steps had different variables as their objective functions. It is therefore of interest to analyze the performance of the model when SIC data is held to the same standard as IIC data, and to obtain parameter sets that represent all isometric tasks equally well.

Additionally, most real-world tasks asymmetrically and alternately load agonistic and antagonistic muscle groups around the active joints. Furthermore, since synergists assist the agonistic muscles, it is desirable to obtain parameters that represent both agonists and synergists together—hereon referred to as functional muscle groups (FMG)—for a given directional contraction. Also of interest are the differences in fatigability between men and women, which, if present, will manifest in different model parameters for the sexes and reduced prediction errors. In this study, we analyze the effects of segregating a large isometric contraction (IC) database variously on the basis of sex and FMG to refine the applicability of the 3CC-r model to specific individuals and situations. We treat both SIC and IIC data as belonging to a continuum of isometric contraction (IC) data bearing three common attributes—TL, duty cycle (DC) and cycle time (CT). The distinction between SICs and IICs are made by assigning DC = 100% for SICs while IICs inherently have DC < 100%. We segregate the data by active joint, by FMG, and then by both FMG and sex and run this data through the model to estimate the parameters that best represent each segregated dataset.

2. Methods

2.1. Data aggregation and extraction

The data drawn on here has previously been used to derive, in parts, the F and R parameters for the original 3CC model, and the enhanced recovery parameter (r) for modified 3CC-r model. The publications considered for inclusion in the dataset were those cited in the prior exhaustive meta-analyses of SICs (Frey-Law and Avin, 2010) and of IICs (Looft et al., 2018), but with additional exclusion criteria. As with the original meta-analyses, data from adults 18–55 years of age with no musculoskeletal impairments or morbidities performing single-joint isometric contractions were included. Since one of the primary goals was to estimate separate model parameters for the sexes, studies that did not specify the composition of their subject pool by sex were excluded. Also excluded were studies that specifically tested trained athletes or professionals requiring special physical training such as astronauts or long-distance runners. The training required for these activities has been shown to change muscle fiber composition over time (Aagaard et al., 2011; Ellefsen et al., 2014) resulting in significantly different fatigabilities and endurance times for these subjects. Studies included in this analysis are listed in Table 1.

IIC data is readily available in standardized form for input to the model—each study specifies the DC, CT and *TL*. The resulting torque decline over time is mostly presented in the form of a graph, in which case data was extracted using a MATLAB routine (Jiro, 2021; MATLAB, 2019), or table. SIC data, on the other hand, is generally listed in the form of ET for a specific *TL*. They are converted to the more general IIC format by assigning DC = 100% and (arbitrarily) CT = 1 s. *TL* remains at the specified value. The torque decline (*TD*) is then calculated as:

$$TD = 100 - TL \tag{8}$$

and the specified ET is marked as the corresponding time. Certain studies record endurance times at the moment when the subject fails to maintain a specified load slightly lower than the experimental *TL*, such as 45% MVC for an experimental *TL* of 50% MVC. In those cases, *TL* in Eq. (8) is substituted by the lower value of TL (45% instead of 50% in the above example) at which ET is marked.

2.2. Error calculation

The root mean square (RMS) error for a specific study j using a specific set of model parameters is calculated as shown in Eq. (9).

$$RMSE_j(F,R,k) = \sqrt{\frac{1}{nd_j}\sum_i (exp_i - sim_i(F,R,k))^2} \tag{9}$$

where j indexes across studies, i indexes across the available data points in a study, exp_i is the i-th experimentally determined data point (torque decline), $sim_i(F,R,k)$ is the i-th predicted data point using the model parameters F, R, k and using the same time coordinate as exp_i, and nd_j is the number of data points in the j-th study.

The widely differing sample sizes for the contributing studies (varying from 3 to 74) are accounted for by a linear mapping, with smaller studies contributing proportionally less to the overall error than larger studies. The normalized RMS error for sex s across all studies for a given joint using a specific set of model parameters F, R, k is then given by:

$$nRMSE_s(F,R,k) = \frac{\sum_j np_{gj} RMSE_j(F,R,k)}{\sum_j np_{sj}} \tag{10}$$

where np_{sj} is the number of participants of sex s in the j-th study. This allows the data contributed by each participant to influence the overall error equally, preventing overrepresentation by participants from smaller studies.

The method in Eq. (10) is contrasted with one in which no distinction is made between the sex and each study contributes equally to the prediction error. This raw RMS error is calculated as:

$$rRMSE(F,R,k) = \frac{\sum_j RMSE_j(F,R,k)}{\sum_j 1} \tag{11}$$

2.3. Parameter sweep

With the error calculation algorithm in place, the parameter sweep is set up as follows. A coarse grid of candidate F, R and k values is created. F and R both initially vary from 0 to 0.1 in increments of 0.002. k varies from 0 to 100 in steps of 5, giving 51 × 51 × 21 = 54,621 unique combinations of F, R, k. The sex-normalized RMS error from Eq. (10) and

Table 2
Optimal parameters for the different segregated datasets. ADF: ankle dorsiflexors; APF: ankle plantarflexors; EE: elbow extensors; EF: elbow flexors; AP: adductor pollicis; FDI: first dorsal interosseous; G/GEN: general handgrip; KE: knee extensors. '-' indicates that insufficient IIC data was available to estimate that parameter.

Joint	Functional muscle group	Female				Male				Combined sexes				Combined sexes, combined FMGs			
		F	R	k	Min. error	F	R	k	Min. error	F	R	k	Min. error	F	R	k	Min. error
Ankle	ADF	0.00746	0.00081	4.97	7.07	0.00725	0.00096	10.36	10.32	0.00828	0.00204	7.07	10.44	0.01485	0.00333	9.31	15.66
	APF	0.00702	0.00098	–	10.00	0.00683	0.00093	–	9.84	0.00695	0.00096	–	11.06				
Elbow	EE	0.01874	0.00206	21.22	10.75	0.01269	0.00085	30.21	10.20	0.01559	0.00125	25.52	12.83	0.01086	0.00225	4.93	15.13
	EF	0.00965	0.00197	6.22	15.93	0.01302	0.00188	8.99	14.40	0.01703	0.00494	4.68	16.97				
Hand/grip	AP	0.00476	0.00093	6.62	1.92	0.00586	0.00202	1.00	5.23	0.00558	0.00283	1.00	4.22	0.01227	0.00134	9.10	12.18
	FDI	0.03999	0.03983	–	10.66	0.01637	0.00360	3.66	8.56	0.02686	0.00656	3.41	16.89				
	G/GEN	0.01159	0.00217	7.39	9.73	0.01238	0.00178	8.00	6.81	0.01235	0.00135	12.51	8.47				
Knee	KE	0.01407	0.00185	6.32	11.41	0.01420	0.00153	10.96	12.27	0.00825	0.00076	14.85	13.66	0.00825	0.00076	14.85	13.66

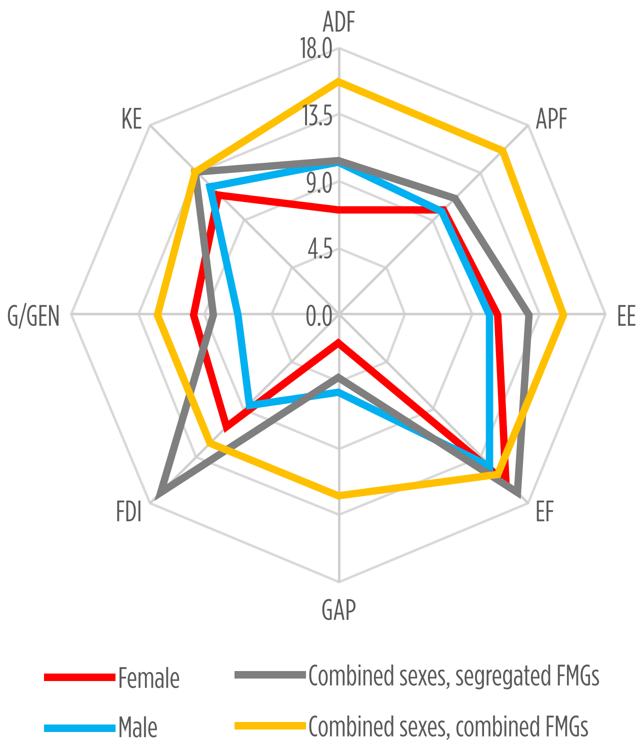

Fig. 1. Radar plot of model prediction errors by resulting from different levels of segregation (male, female, combined sexes and segregated FMGs, combined sexes and combined FMGs) for the ankle dorsiflexors (ADF), ankle plantarflexors (APF), elbow extensors (EE), elbow flexors (EF), grip/adductor pollicis (G/AP), grip/first dorsal interosseous (G/FDI), general handgrip (G/GEN) and knee extensors (KE).

the raw RMS error from Eq. (11) are calculated for each muscle using each of the 54,621 permutations. The volume of *F*, *R*, *k* yielding the lowest errors (exceeding the minimum error by 10% of difference between the minimum and maximum errors) in the first iteration for each muscle group was chosen as the region of interest for the second iteration, and the mesh size was adjusted to yield results in a reasonable amount of time. The possibility of infinitely long endurance times for any muscle group was precluded by limiting *R*-values at each iteration to be less than the corresponding *F*-values. The data was passed through this finer mesh, and the parameter volume corresponding to the lowest errors chosen again. The process was repeated until the volume of interest did not shrink between successive iterations. The parameter values resulting in the minimum error in the last iteration were chosen as the representative values for that group.

3. Results

While quantifying the effects of segregating joint level data by FMG, averages are calculated only for the ankle, elbow, and hand/grip joints and their respective constituent muscle groups. The knee joint is excluded from these analyses since data was only available for knee extensors, so no further division of data on the basis of FMG was possible for that joint. The simplest error calculation method, with no distinction being made regarding sex (S) or FMG but with separate model parameters for each of the ankle, elbow, and hand/grip joints, predicts torque declines with an average error of 14.32% across the 3 joints as seen in Table 2. Dividing the data based on FMG yields an average error of 11.55% for those three joints representing a marginal decrease. The average error for all FMGs studied including the knee extensors is 11.17%.

Further dividing the dataset by sex in addition to FMG brings the average prediction error down to 9.69%, with similar errors for females (9.69%) and males (9.70%). However, significant disparity exists between the minimum errors for each S/FMG dataset, ranging from a minimum of 1.92% for the adductor pollicis to a maximum of 15.93% for the elbow flexors, both in females. Fig. 1 shows that the minimum and maximum errors for males also occur in the same muscle groups (5.23% for the adductor pollicis, and 14.40% for the elbow flexors). It is worth noting that of the 1,068 unique data points considered in the analysis, 449 (42%) represent elbow flexor data, possibly posing a greater challenge to the optimization algorithm in finding a common parameter set that accurately represents the performance of a diverse group of participants.

Table 3
F/R ratios for the different segregated datasets, calculated from parameters in Table 2.

Joint	Functional muscle group	Female	Male	Combined sexes	Combined sexes, combined FMGs
Ankle	ADF	9.22	7.53	4.05	4.46
	APF	7.17	7.32	7.22	
Elbow	EE	9.10	14.99	12.48	4.82
	EF	4.90	6.94	3.45	
Hand/ grip	AP	5.12	2.91	1.98	9.13
	FDI	1.00	4.54	4.09	
	G/GEN	5.35	6.97	9.13	
Knee	KE	7.62	9.28	10.87	10.87

In a departure from previous work that found common values for the augmented recovery parameter for multiple joints (Looft et al., 2018), no such attempt has been made here. Notably, (Looft et al., 2018) found that hand/grip joint data could not be reconciled with the common r-value chosen for the other joints, but significant reduction in prediction error was still observed for that joint using $r = 30$. The fact that at least one joint was found to have a different augmented recovery parameter indicates that a common value for all joints (and especially for individual muscle groups) may not be possible, and we therefore instead report only the values that result in minimum error. *k*-values for some groups have been omitted due to insufficient IIC sample sizes available for making those predictions, but that data has nevertheless been used in aggregation with SIC samples to predict *F* and *R* for those same groups.

4. Discussion

It is generally accepted that agonistic and antagonistic muscle groups around a joint have different force production capabilities, but less attention has been paid to any potential difference in their fatiguabilities. Markedly different fatigue rates have been observed in a handful of experimental studies involving the hip and the knee (Brasileiro et al., 2018; Kawabata et al., 2000; Krantz et al., 2020), but it remains to be seen whether this result holds true for joints in the upper body. Judging by F/R ratios estimated for combined sexes in Table 3, it can be surmised that ankle dorsiflexors (4.05) are more fatigue resistant than plantarflexors (7.22), and elbow flexors (3.45) are more fatigue resistant than the elbow extensors (12.48).

The difference in fatiguability between the sexes has been the subject of considerable scrutiny. Several studies indicate that men may fatigue faster than women when performing submaximal SICs (Yoon et al., 2007), IICs (Hunter et al., 2004b, Hunter et al., 2009), and maximal isokinetic contractions (Pincivero et al., 2003). However, similar fatiguabilities were observed for strength-matched men and women when performing submaximal IICs of the elbow flexors (Hunter et al., 2004c), and it is suggested that the difference in fatiguability is related to the absolute intensity of contractions and is affected by mechanisms distal to the neuromuscular joint (Hunter and Enoka, 2001). On the other hand, it has also been reported that while women are significantly more fatigue-resistant than men at the elbow joint, there is no significant difference at the ankle (Avin et al., 2010). Our results seem to confirm these general observations, with average F/R ratios being similar at the ankle for

Table 4
A comparison of the sample sizes and minimum prediction errors in Looft et al. (2018) and in the current study, broken down by contraction type (SIC/IIC). For both studies only IIC data contributed to estimation of the augmented recovery parameter k. F, R were not estimated in Looft et al. (2018), but are estimated in the current study using both SIC and IIC data. For the current study, minimum errors reported are averaged across both sexes and the constituent FMGs about each joint.

Joint	This study			Looft et al. (2018)	
	SIC	IIC	Average min. error: SIC + IIC (% MVC)	IIC	Min. error: IIC (% MVC)
Ankle	167	95	9.3	247	5.7
Elbow	586	92	12.8	143	9.9
Hand/grip	605	110	7.2	362	8.7
Knee	559	92	11.8	168	8.6

males (7.42) and females (8.20), but much greater at the elbow for males (10.97) than for females (7.00). The F/R ratio for women averaged across all joints is 6.19 compared to 7.56 for men, indicating a somewhat greater propensity for fatigue-resistance in women. It may be noted that since there is only a single parameter set representing each group of participants, it is difficult to obtain a statistical measure of the significance of these differences based on those parameters alone.

It must be noted that the difference between the minimum errors of 3CC-r as dealt with previously (Looft et al., 2018) and in the present work are not necessarily representative of flaws in either methodology but rather of differences in the way the data is handled. The experimental datasets underlying both studies are different—this work excludes studies that do not specify the composition of the participants by sex but includes those reporting SIC data. The previous 3CC-r analysis calculates errors only for IIC data which forms a relatively minor part of the dataset in this study, whereas this analysis reports prediction errors for both SIC and IIC data simultaneously, leading to a large disparity in the sample sizes for the two studies as seen in Table 4 and Fig. 2 (a). Data from only 41% of the participants listed in (Looft et al., 2018) were able to be used in this work due to the unavailability of information about the sex of the remaining participants, and this was the only data that contributed to estimation of the *k*-parameters here. However, this IIC data was also used along with the entirety of the SIC data to estimate *F* and *R* parameters for each group, unlike previous efforts where *F* and *R* were determined solely by optimizing predicted endurance times against curve fits of SIC data (Frey-Law et al., 2012; Frey-Law and Avin, 2010).

When averaged across sex and FMGs, we find prediction errors for all isometric contractions to be in the range of 7–13% MVC. (Looft et al., 2018) found errors in the range of 6–10% MVC for IICs alone. A visual comparison of the model errors may be seen in Fig. 2 (b).

A number of important limitations remain in the techniques employed in this analysis. With each data point being associated with a different but not necessarily unique set of task parameters, the point-by-point method of evaluation of torque decline for this data lends itself poorly to the weeding out of outliers, and their inclusion in the dataset may skew the estimated model parameters especially in cases where the total number of studies in the evaluation group is small. An inevitable amount of transcription error also arises during the conversion of torque decline data from a graphical to the tabular form, in addition to those generated during the recording of the original data. The inclusion of studies where data is reported as an aggregate for its male and female participants can lead to a misrepresentation of the torque decline values for both sexes since the average value is assumed to be true for each of the reported number of participants of each sex. The exclusion of studies not specifying participant sexes also reduces the overall sample size, but this was a necessary compromise to ensure the data was more representative of each sex. While data from every participant has been given equal weightage regardless of the associated task parameters, there exists a preponderance of data from SICs with only 17% of the participants performing IICs as evident from Table 4. The combined analyses are also more representative of the male population who comprised 72% of the contributing 2,306 participants. Males comprised 71% of the participants contributing to SIC data and 76% of those performing IICs. The fraction of participants performing IICs that were female was rather low in the case of the ankle and elbow (10–14%), but better for the remaining joints (23–47%) as seen in Fig. 3 (a) and Table 5. For SICs, this

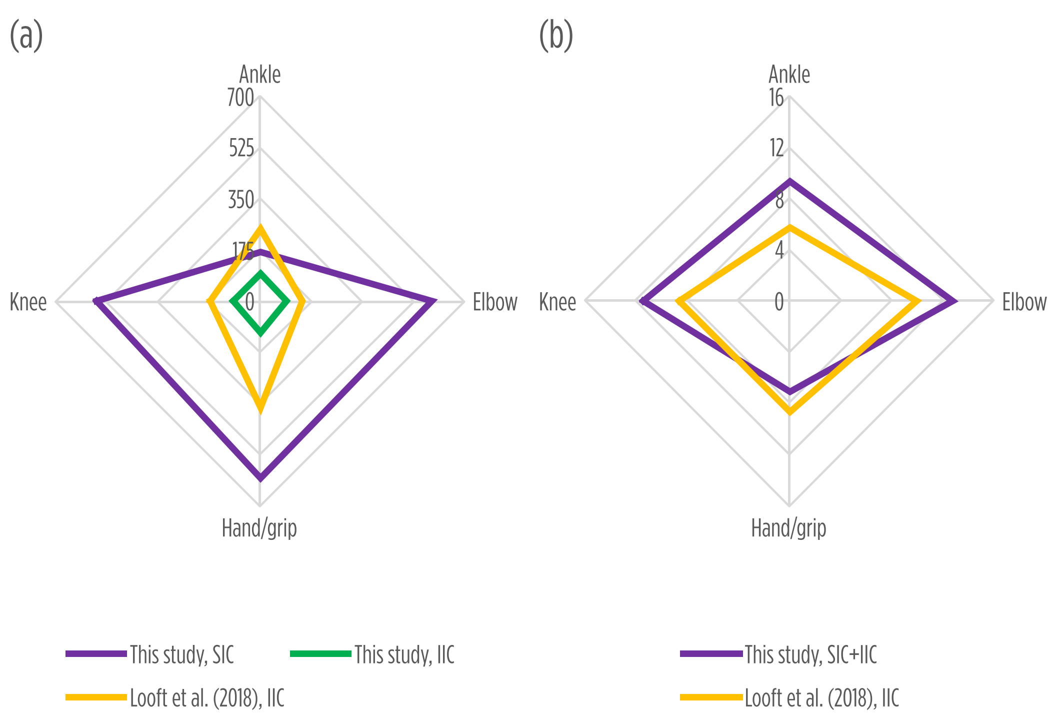

Fig. 2. Radar plots of (a) the sample sizes used in this work and in Looft et al. (2018), broken down by contraction type, and (b) the minimum prediction errors (in % MVC) of the two studies.

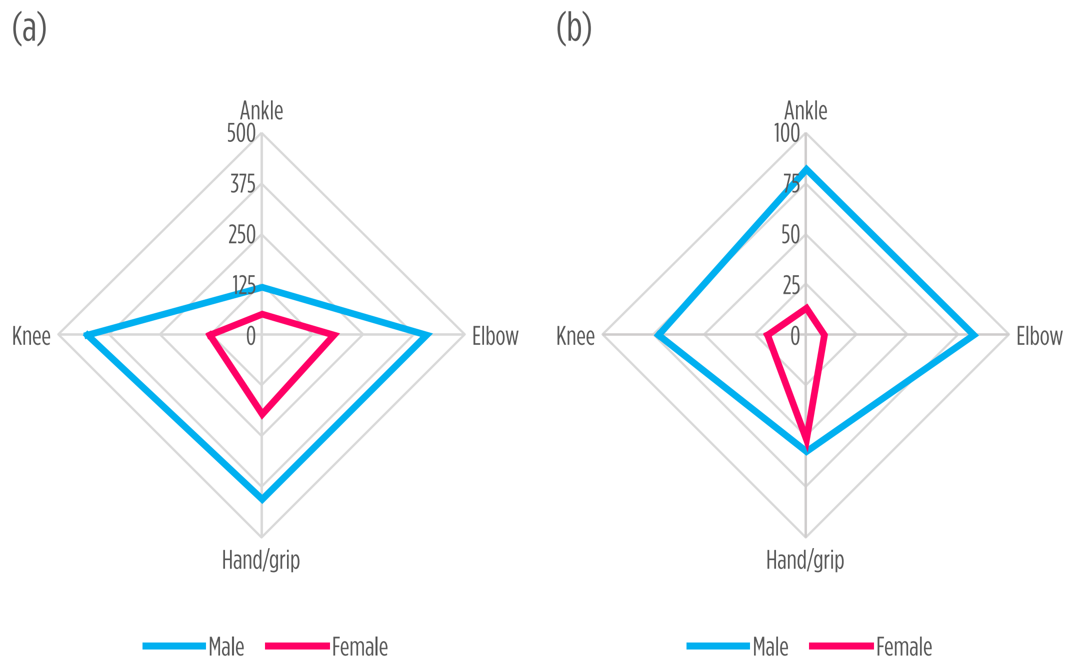

Fig. 3. Distribution of male and female participants contributing to (a) SIC data and (b) IIC data for each of the joints in this study.

Table 5
Sample sizes broken down by sex for each of the contraction types studied.

Joint	SIC		IIC	
	Male	Female	Male	Female
Ankle	117	50	82	13
Elbow	406	180	83	9
Hand/grip	407	198	58	52
Knee	430	129	73	19

figure ranged from 23 to 30% for all joints (Fig. 3 (b) and Table 5). It is hoped that future experimental work focused on fatigue will have more equitable distributions of male and female participants to so that the findings of this and other similar studies can be refined, and so that the models developed thereby are equally representative of both sexes.

The primary impetus for this analysis was to develop a clearer understanding of the 3CC-r model's predictions as applied uniformly to predicting torque declines for both SICs and IICs in a method targeted to tease out differences between the sexes and between different FMGs. We split the aggregated data into subgroups first by FMG and then additionally by participant sex, and found that each split reduced average prediction errors by approximately 19% compared to the previous segregation level and resulted in a net reduction of 34% average error when compared to segregation only on the basis of active joint. The currently employed dataset, though vast, underrepresents IICs, and it is expected that as more detailed experimental IIC data is available the model parameters can be similarly recalculated to reduce prediction errors further. Further work to extend this model to more realistic tasks may focus on the velocity dependence of the force development and relaxation factors for dynamic tasks.

In summary, we find that male and female populations are best represented by different model parameters calculated individually for different FMGs, and that this approach significantly reduces the average prediction error for each joint. Sustained and intermittent isometric contractions are treated equally as belonging to a continuum of isometric contractions to allow the estimation of model parameters that best fit the entire dataset.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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