Published in final edited form as:

J Biomech. 2018 August 22; 77: 16–25. doi:10.1016/j.jbiomech.2018.06.005.

Modification of a Three-Compartment Muscle Fatigue Model to Predict Peak Torque Decline During Intermittent Tasks

John M Looft, PHD^{1,2}, Nicole Herkert², and Laura Frey-Law, DPT, PHD²

¹Department of Physical Therapy, University of Minnesota, Minneapolis, MN, 55455, USA

²Department of Physical Therapy and Rehabilitation Science, University of Iowa, Iowa City, IA, 52242, USA

Abstract

This study aimed to test whether adding a rest recovery parameter, r , to the analytical three-compartment controller (3CC) fatigue model (Xia and Frey Law, 2008) will improve fatigue estimates during intermittent contractions. The 3CC muscle fatigue model uses differential equations to predict the flow of muscle between three muscle states: Resting (M_R), Active (M_A), and Fatigued (M_F). This model uses a feedback controller to match the active state to target loads and two joint-specific parameters: F , fatigue rate controlling flow from active to fatigued compartments) and R , the recovery rate controlling flow from the fatigued to the resting compartments. This model does well to predict intensity-endurance time curves for sustained isometric tasks. However, previous studies find when rest intervals are present that the model over predicts fatigue. Intermittent rest periods would allow for the occurrence of subsequent reactive vasodilation and post-contraction hyperemia. We hypothesize a modified 3CC- r fatigue model will improve predictions of force decay during intermittent contractions with the addition of a rest recovery parameter, r , to augment recovery during rest intervals, representing muscle re-perfusion. A meta-analysis compiling intermittent fatigue data from 63 publications reporting decline in peak torque (% torque decline) were used for comparison. The original model over-predicted fatigue development from 19 – 29% torque decline; the addition of a rest multiplier significantly improved fatigue estimates to 6 – 10% torque decline. We conclude the addition of a rest multiplier to the three-compartment controller fatigue model provides a physiologically consistent modification for tasks involving rest intervals, resulting in improved estimates of muscle fatigue.

Keywords

Muscle Fatigue; Isometric Contraction; Meta-analysis; Mathematical Modeling; Ergonomics

Address for correspondence, Laura Frey-Law, Department of Physical Therapy and Rehabilitation, 1-252 Medical Education Bldg., University of Iowa, Iowa City, Iowa 52242, USA, Phone: 319-335-9804, Fax: 319-335-9707, laura-freylaw@uiowa.edu.

Conflict of Interest Statement:

None of the authors have any financial or personal conflicts of interest to report. The authors were funded in part by the United States Council for Automotive Research (USCAR), the National Institutes for Health, K01AR056134, and the University of Iowa Heartland Center (graduate student stipend).

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Introduction

Musculoskeletal disorders (MSDs) account for 33% of all illnesses and injuries requiring days off work (Bureau of Labor Statistics, 2012). Accordingly MSDs continue to financially burden the U.S. with annual direct costs estimated at \$50 billion per year over a decade ago (Silverstein, et al., 2002, Yelin, et al., 1995). Realistically, the total economic burden of MSDs is on the order of 100's of billions of dollars per year (Buckle and Devereux, 2002, Yelin, et al., 1995) and MSDs contribute to reduced quality of life and well-being (Larsen, et al., 2017).

Muscle fatigue has been cited as a risk factor for injury in recreational activities (Small, et al., 2010) and in the workplace (Kinali, et al., 2016). However, whether muscle fatigue is a risk factor for MSDs remains unclear. Indirect survey methods (Rodgers, 1992) are often used to assess fatigue development during functional tasks. These subjective measures provide limited objective information, making it difficult to investigate associations between muscle fatigue and MSDs. The advancement of mathematical models may assist in quantifying muscle fatigue development.

Our analytical three-compartment controller (3CC) fatigue model (Figure 1A, Xia and Frey Law, 2008) can accurately predict endurance time for isometric tasks (Frey-Law, et al., 2012), and performs well when compared to other models (Rashedi and Nussbaum, 2015, Sonne and Potvin, 2016). However, under complex conditions (i.e., addition of rest intervals) the accuracy of the 3CC fatigue model declines, likely due to poorer representation of muscle recovery (Rashedi and Nussbaum, 2015, Sonne and Potvin 2015). This may be due to the recovery rate, R , being previously optimized using sustained isometric tasks to failure (Frey-Law, et al., 2012).

During muscle contraction, blood flow is reduced from increased intramuscular pressure on the vascular system (Degens, et al., 1998, Sejersted, et al., 1984). Muscle perfusion decreases with increasing muscle contraction (Humphreys and Lind, 1963, Robergs, et al., 1997), resulting in graded levels of ischemia. Intermittent rest periods allow for the occurrence of subsequent reactive vasodilation and post-contraction hyperemia (Humphreys and Lind, 1963, Nowak and Wennmalm, 1979, Robergs, et al., 1997, Wigmore, et al., 2004). This rebound perfusion can enhance force recovery following fatigue (Cerqueira, et al., 2017).

We propose a modification to the 3CC fatigue model to represent enhanced recovery resulting from reactive hyperemia. We hypothesized predictions of force decay during intermittent contractions would improve with the addition of a rest recovery multiplier, r , to augment recovery during rest intervals. Recognizing there may be additional factors contributing to model errors, the objective of the current study was to test this hypothesis and determine optimal r parameter values for this modified 3CC- r model relative to available data in the literature.

Methods

Modified Fatigue Model

The 3CC fatigue model (Frey-Law, et al., 2012, Xia and Frey Law, 2008) relies on three differential equations to dictate the “flow” between three muscle states: resting (M_R), active (M_A), and fatigued (M_F , Figure 1A). See Supplemental materials a brief summary with model equations. The proposed modified 3CC-r model (Figure 1B) only alters one equation, augmenting recovery from the fatigued state with a rest recovery multiplier, r :

When $TL > 0$	$dM_R/dt = -C(t) + (R)*M_F$	(original 3CC)
When $TL = 0$	$dM_R/dt = -C(t) + (R*r)*M_F$	(modified 3CC-r)

This enhanced recovery occurs during rest intervals only (i.e. $TL = 0$). For example, $r=1$ maintains the original 3CC model. An $r=10$ increases recovery 10-fold during rest intervals, leaving it unchanged during contractions.

Literature Review of Intermittent Task Fatigue

Because intermittent fatigue data has not been compiled previously, we performed a large-scale systematic review of available fatigue data for model prediction comparisons. As intermittent isometric fatiguing tasks are rarely maintained until endurance time, we extracted decline in peak torque (% torque decline) as the primary fatigue measure. That is, 0% torque decline represents no fatigue and 100% torque decline represents complete fatigue. Experimentally, participants perform maximal voluntary contractions (MVCs) occasionally throughout the fatigue protocol.

The systematic literature review consisted of two stages. The first stage involved database searches, including: PubMed, CINAHL, Web of Science, and Google Scholar thru December, 2012. A total of 17 search terms/keywords, alone and in multiple combinations, were used, such as: “intermittent”, “static fatigue”, “fatigue”, “isometric”, “endurance”, “muscle torque decline”. In addition, early searches found several studies evaluating fatigue with creatine supplementation compared to controls. Thus, “creatine supplementation” was added as a secondary search term (control group data only). The second stage involved searching the bibliographies of included studies.

Inclusion criteria included: healthy adults, 18–55 years old, voluntary contractions, intermittent isometric tasks at a known intensity and duty cycle, force/torque data reported at discrete time points, and published in English. Exclusion criteria included: dynamic contractions, simultaneous multi-joint functional testing (e.g. squat lifts), body/limb weight as primary resistance, interventional arms of cohort studies (i.e. creatine supplementation) and electrical stimulation. The primary outcome variable, % torque decline, was extracted at 30 second intervals as available. We also extracted sample size, joint region, intensity (%MVC), duty cycle, assessment time (min), author, date, and subject gender(s). A minimum of two authors reviewed potential studies to minimize recording errors.

The literature search produced 2392 potential publications. Applying the inclusion criteria and removing duplicates reduced the number of appropriate articles to 59. Four additional articles were found from bibliographies, for a total of 63 publications. Fatigue data was found for four joint regions (ankle, knee, elbow and hand/grip) but no shoulder or trunk studies met all inclusion/exclusion criteria. Data from each joint region were considered separately because a previous study found endurance times differed between joints for sustained isometric tasks (Frey Law and Avin, 2010). The hand/grip region included studies of grip, first dorsal interosseus, abductor pollicis brevis, and adductor pollicis, similar to previous fatigue meta-analyses (Frey Law and Avin, 2010). A total of 351 data points were extracted (Table 1), ranging from 58 (knee) to 144 (ankle). Multiple intensity-duty cycle combinations were found for each joint region: ankle (14), knee (9), elbow (9), and hand/grip (17), with as few as 1 or as many as 20 time points reported for each combination. The majority of studies used task conditions at 100% MVC with 50% or higher duty cycle (52.1% of datapoints). Average sample size per datum was 11.9 participants (range 4 – 74). Most studies included males (M, 59.8%) or were a mixed cohort (MX, 26.5%), thus separate analyses by sex were not performed.

Original Model Predictions

We assessed the accuracy of the original 3CC fatigue model (e.g., $r=1$) to predict torque decline for intermittent tasks. This was accomplished by running the model for each joint and set of task conditions extracted from the literature. Because F and R parameter values previously were found to differ between joint regions, we used joint-specific F and R values when assessing the model (Frey-Law, et al., 2012). That is, the F and R values previously optimized for sustained isometric tasks were used to simulate muscle fatigue for intermittent tasks. Model errors between predicted and observed fatigue were assessed in two ways. Directional errors, where positive errors indicated over-estimated fatigue, as well as absolute errors (absolute values) were assessed. Due to varying assessment times reported in the literature, model errors were also adjusted to account for the additive nature of fatigue error over time by dividing each error value by the square root of the assessment time (minutes). That is, at one minute there was no change (divided by one), but as time increased there was a nonlinear reduction in total error, resulting in relatively constant error levels across time (Supplemental Materials, Figure S1).

Modified Model Predictions

A large sensitivity analysis of the new rest recovery parameter, r , was performed. Values from 2–100 were used to predict fatigue (% torque decline) using the 3CC- r fatigue model. That is, for each joint, % torque decline was estimated for all intensity-duty cycle permutations found in the literature at time points from 30 seconds to 40 minutes at 30 second intervals for each r value. Errors between predicted and observed % torque decline were calculated as described above for each value of r . A range of potential optimal r values for each joint region were identified as those producing the smallest marginal mean errors. Ranges for r_{opt} , producing errors within ± 1 % torque decline of these minima, were assessed in lieu of confidence intervals as a measure of the sensitivity of r . Four error determinations were considered: directional and absolute errors, with and without time adjustment, to ensure robust results.

Statistical Analyses

To test our hypothesis, mixed repeated measures analysis of covariance (RM ANCOVA) assessments were performed (SPSS V. 24.0; Chicago, IL) to determine if directional or absolute model errors differed across values of r , for each anatomical joint region. Both unadjusted and time-adjusted errors (see above) were considered. For each analysis, the dependent variable was observed error and r was the repeated independent variable. Intensity (%MVC) and duty cycle were included as covariates in all models, with time only included as a covariate in the unadjusted error models. Sample size was used as a weighting factor. Each joint region was assessed separately as observed fatigue behavior (Frey Law and Avin, 2010) and F and R model parameters differ by joint (Frey-Law, et al., 2012). When r produced significant differences in error, simple contrasts (i.e., using general linear model matrices) were performed to compare the resulting mean errors for each $r = 2$ to the original 3CC model ($r=1$). We then considered whether these improved errors met an operationally defined minimally important difference (MID) of at least 50% improvement. Finally, Akaike's Information Criterion (AIC) was calculated for the original 3CC and modified 3CC- r models, using potential optimal r values, to determine which model produced the best fit for each joint region. Secondary analyses were performed to explore whether task condition (100% MVC vs. < 100% MVC) and/or duty cycle (> 50% vs. < 50%) influenced optimal r values. Significance was set at $p = 0.05$ for all analyses.

Results

Model Comparisons

The original 3CC fatigue model consistently over-predicted fatigue by 23.3% torque decline on average across all joints, task conditions, and times assessed. When predicted versus observed fatigue was plotted (Figure 2), the errors (i.e., deviations from the identity line) tended to increase with greater fatigue (and time Supplemental Figure S1).

The addition of a rest recovery multiplier improved fatigue predictions for intermittent tasks across all joints ($p < 0.001$; see Supplemental Materials Table S1 for RM ANCOVA results). Contrasts revealed all r values from 2 to 100 resulted in significant improvements in model predictions ($p < 0.05$) compared to the original model ($r = 1$) for ankle and elbow data, but only $r = 2$ to 37 and $r = 2$ to 66 for the knee and hand/grip data, respectively (Table S1). Similar results were found for directional errors and after adjusting for assessment time (Supplemental Materials Figure S2).

Optimal Rest Recovery Multiplier

The regions of minimal absolute error ($\pm 1\%$ torque decline) overlapped for each of the joint regions (Figure 3). The knee, ankle, and elbow regions had their lowest prediction errors for r values ranging from 5 to 26, while the hand/grip region had lowest error with r values ranging from 14 to 69 (Table 2). Fatigue predictions were more centered on the identity line (Figure 4) using the modified compared to the original fatigue model. The AIC analysis confirmed the best fits were with the modified 3CC- r model, even accounting for an additional parameter. The potential r_{opt} values producing the lowest AICs for the knee, elbow, and ankle were not different from each other ($r_{opt} = 15$). While the absolute minimum

error for the elbow occurred at $r = 8$ to 10 , the AICs for r of 8 versus 15 were not different. Conversely, the lowest AIC for hand/grip occurred for $r_{\text{opt}} = 30$, which was an improvement over $r = 15$. Thus, 15 was chosen as the optimal value for all regions except for hand/grip muscles.

The resulting 3CC- r models over-predicted fatigue by 1.2% torque decline (directional error), with an absolute error of 8.2% torque decline overall (Table 3). The modified recovery to fatigue ratios (R^*r/F) during rests using the r_{opt} values (Table 4) varied from 1.41 – 1.96 (i.e. increase in recovery to fatigue ratio during rest intervals).

Intensity, duty cycle and time all had significant influences on the original model ($r=1$) error estimates (Supplemental Materials, Table S1, Figure 5). Overall, higher errors ($\sim 27\%$ torque decline) occurred for lower intensity tasks ($\text{MVC} < 100\%$) with longer intermittent rest intervals (duty cycle $< 50\%$) compared to 20% error for high intensity tasks ($\text{MVC} = 100\%$) with shorter rest intervals (duty cycle $\sim 50\%$). This trend was observed for all but the ankle regions (see $r=1$ values, Figure 5). However, the ranges of optimal r -values for the 3CC- r model were not consistently different between task conditions when stratifying by high versus low intensity and duty cycle (Figure 5).

Discussion

The primary finding of this study was that our initial hypothesis was supported. That is, the addition of a rest recovery parameter to augment recovery during rest intervals improved fatigue model predictions of force decay during intermittent contractions. For all but the hand/grip muscles, a 15 -fold increase in recovery rate was optimal. In addition, a large meta-analysis was performed assimilating intermittent fatigue data from the literature. Fatigue behavior had not previously been compiled in this manner for intermittent tasks. This systematic review compiled a large number of available data, while also identifying gaps in the literature.

Muscle fatigue development is a complex, nonlinear phenomenon. For sustained static contractions, simple statistical models have been applied, often referred to as Rohmert's curves (Rohmert, 1960). Unfortunately, there is no simple counterpart to describe normative fatigue behavior for tasks involving rests. This is the first study to compile such a large set of fatigue data for intermittent tasks. However, despite including 351 data points from 63 studies, the distribution of task conditions remained unequal. While many functional tasks occur at low intensities or duty cycles, only 14% of the data involved $< 50\%$ MVC or duty cycle: none for elbow or knee, 9% for hand/grip and 29% for ankle. Thus, these results do not fully represent all possible task conditions. Further, comparisons with raw data points result in inherently greater measurement noise than summary models of fatigue. Indeed, heterogeneous estimates of $\%$ torque decline occurred even for similar task conditions across publications. Despite this obstacle, the fatigue model errors were reduced from approximately 20% (3CC) to only 5 – 10% (3CC- r). Variance between studies reaffirms the importance of using larger datasets when possible for fitting parameters or evaluating model behavior.

Rashedi & Nussbaum (2015) previously suggested improvements in representing muscle recovery were strategic areas for fatigue model advancement. Our current study targeted one aspect of recovery, namely augmenting recovery during rest intervals to represent reactive hyperemia. Decreases in blood flow are well documented during sustained contraction due to increased intramuscular pressure on the vascular system (Degens, et al., 1998, Humphreys and Lind, 1963, Sejersted, et al., 1984, Wigmore, et al., 2004). However, increases in blood flow during low level contractions have also been observed (Bystrom and Sjogaard, 1991, Larsson, et al., 1995), possibly due to metabolite accumulation triggering vasodilation. Immediately following contraction, however, reactive vasodilation and resultant hyperemia occurs (Humphreys and Lind, 1963, Robergs, et al., 1997, Sejersted, et al., 1984, Wigmore, et al., 2004). This subsequently increases oxidative adenosine triphosphate (ATP) synthesis, thereby increasing muscle recovery (Layec, et al., 2013).

Similar results have been seen following cuff occlusion (Birtles, et al., 2003, Chung, et al., 2007) to manipulate ischemia, where blood flow rebounds once occlusion is released (Larsson, et al., 1995). Muscle recovery, as measured by phosphocreatine levels, also rebounds after blood flow is restored (Blei, et al., 1993, Greiner, et al., 2007). Similarly, greater force recovery occurs following release of cuff occlusion compared to recovery in the non-occluded state (Cerqueira, et al., 2017). Lastly, psychophysical studies show disproportionately longer endurance times for intermittent versus sustained isometric contractions of the same intensity (Iridiastadi and Nussbaum, 2006, Iridiastadi and Nussbaum, 2006b, Wood, et al., 1997). Collectively, these physiologic studies are consistent with our modeled augmented muscle recovery rates during postcontraction rests. Yet, this physiologically driven modification does not alter the original 3CC model's fatigue predictions of sustained isometric contractions as it is only applied at rest. Additionally, this modification does not preclude the influence of other mechanisms on fatigue recovery that may result in future advancements.

While F and R parameters of the 3CC model are joint-specific (Frey-Law, et al., 2012), consistent with observed fatigue behavior (Frey Law and Avin, 2010), a common optimal r value for all but hand/grip muscles was observed. This different response for hand/grip may be due to methodology, i.e., heterogeneity of muscles or task conditions tested. For example, unlike the other regions, hand/grip data included isolated small finger muscles (67% cases) and larger muscle grip contractions (33%). Further the response surface for r was flatter for the hand/grip than the other regions. This suggests hand/grip data appears less sensitive to change in r . Another possible explanation is that a single optimal r is an oversimplification. Rashedi and Nussbaum (2016) found more frequent, shorter rests induced less fatigue than equivalent workloads with less frequent, longer rest periods, suggesting recovery augmentation may be cycle time dependent. Thus, these preliminary results support a common r value for all but hand/grip muscles, recognizing additional insights may be uncovered in the future.

There are several limitations worth noting. The first is our model does not take into account muscle fibertype composition. This may contribute to observed recovery errors. It is possible varying muscle fiber distributions may contribute to differences in fatigue errors and reperfusion responses between anatomical regions. Yet, differences in fatigue to recovery

ratios between joint regions were less for the modified than the original model. Future studies may be useful to determine whether accounting for different muscle fiber concentrations would provide yet another improvement to fatigue estimates. A second limitation is the lack of data available for shoulder or trunk regions. To mitigate this, we fit a general 3CC-r fatigue model to all data combined. The common r_{opt} value for all but the hand/grip region suggests a rest recovery value of 15 is a reasonable initial estimate until more data become available. A third limitation is the improvements noted here may not translate to dynamic tasks, where muscle reperfusion and hyperemia can also occur. Thus, future studies are needed to assess whether this model modification also improves fatigue estimates for more complex, dynamic tasks. The improvements noted with the addition of a rest recovery parameter to represent muscle reperfusion does not address all potential sources of model error. For example, cycle time may be an important consideration in fatigue development and recovery (Rashedi and Nussbaum, 2016), which our model cannot account for explicitly. Thus, the remaining 5–10% error may be a result of multiple additional sources of nonlinear muscle behavior. Finally, the use of ANOVA for the comparison of multiple r values may increase the potential for Type I errors. The lack of robust between-joint statistical analyses limits our ability to clearly discern whether the rest recovery parameter varies between joint regions. Future studies evaluating the Jacobian of the equations may be useful to assess for potential parameter interactions.

In summary, this study found the addition of a physiologically based rest recovery multiplier reduced fatigue model errors for intermittent contractions by over 50%. Because the additional parameter only alters model recovery during rest intervals, this modification maintains the heuristic nature of the original model.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

The authors were funded in part by the United States Council for Automotive research (USCAR), the National Institutes for Health, K01AR056134, and the University of Iowa Heartland Center (graduate student stipend). However these sponsors had no involvement in the study design, implementation, data analysis or writing of this publication.

References

- Abdel-Malek K , Arora J , Yang JZ , Marler T , Beck S , Swan C , Frey-Law L , Kim J , Bhatt R , Mathai A , Murphy C , Rahmatalla S , Patrick A Obusek J , 2009 A physics-based digital human model. *International Journal of Vehicle Design* 51, 324–340.
- Allman BL Rice CL , 2003 Perceived exertion is elevated in old age during an isometric fatigue task. *European Journal of Applied Physiology* 89, 191–197. [PubMed: 12665984]
- Alway SE , Hughson RL , Green HJ , Patla AE Frank JS , 1987 Twitch Potentiation after Fatiguing Exercise in Man. *European Journal of Applied Physiology and Occupational Physiology* 56, 461–466. [PubMed: 3622489]
- Armatas V , Bassa E , Patikas D , Kitsas I , Zangelidis G Kotzamanidis C , 2010 Neuromuscular Differences Between Men and Prepubescent Boys During a Peak Isometric Knee Extension Intermittent Fatigue Test. *Pediatric Exercise Science* 22, 205–217. [PubMed: 20567042]

- Baker-Fulco CJ , Fulco CS , Kellogg MD , Glickman E Young AJ , 2006 Voluntary muscle function after creatine supplementation in acute hypobaric hypoxia. *Medicine and Science in Sports and Exercise* 38, 1418–1424. [PubMed: 16888454]
- Bemben MG , Massey BH , Bemben DA , Misner JE Boileau RA , 1996 Isometric intermittent endurance of four muscle groups in men aged 20–74 yr. *Medicine and Science in Sports and Exercise* 28, 145–154. [PubMed: 8775367]
- Bemben MG , Tuttle TD , Bemben DA Knehans AW , 2001 Effects of creatine supplementation on isometric force-time curve characteristics. *Medicine and Science in Sports and Exercise* 33, 1876–1881. [PubMed: 11689738]
- Benwell NM , Mastaglia FL Thickbroom GW , 2007b Changes in the functional MR signal in motor and non-motor areas during intermittent fatiguing hand exercise. *Experimental Brain Research* 182, 93–97. [PubMed: 17549462]
- Bilodeau M , 2006 Central fatigue in continuous and intermittent contractions of triceps brachii. *Muscle & Nerve* 34, 205–213. [PubMed: 16691603]
- Birtles DB , Minden D , Wickes SJ , Puxley MKP , Llewellyn AMG , Casey A , Rayson MP , Jones DA Newham DJ , 2002 Chronic exertional compartment syndrome: muscle changes with isometric exercise. *Medicine and Science in Sports and Exercise* 34, 1900–1906. [PubMed: 12471294]
- Birtles DB , Rayson MP , Casey A , Jones DA and Newham DJ , 2003 Venous obstruction in healthy limbs: a model for chronic compartment syndrome? *Medicine and Science in Sports and Exercise* 35, 1638–1644. [PubMed: 14523298]
- Blei ML , Conley KE and Kushmerick MJ , 1993 Separate measures of ATP utilization and recovery in human skeletal muscle. *Journal of Physiology* 465, 203–222. [PubMed: 8024651]
- Buckle PW and Devereux JJ , 2002 The nature of work-related neck and upper limb musculoskeletal disorders. *Applied Ergonomics* 33, 207–217. [PubMed: 12164505]
- Bureau of Labor Statistics, 2012 Nonfatal occupational injuries and illnesses requiring days away from work. U.S. Department of Labor Washington, D. C. Report USDL-12–2204.
- Burnley M , 2009 Estimation of critical torque using intermittent isometric maximal voluntary contractions of the quadriceps in humans. *Journal of Applied Physiology* 106, 975–983. [PubMed: 19150854]
- Bystrom S Sjogaard G , 1991 Potassium homeostasis during and following exhaustive submaximal static handgrip contractions. *Acta Physiologica Scandanavica* 142, 59–66.
- Callahan DM , Foulis SA Kent-Braun JA , 2009 Age-Related Fatigue Resistance in the Knee Extensor Muscles Is Specific to Contraction Mode. *Muscle & Nerve* 39, 692–702. [PubMed: 19347926]
- Callahan DM Kent-Braun JA , 2011 Effect of old age on human skeletal muscle force-velocity and fatigue properties. *Journal of Applied Physiology* 111, 1345–1352. [PubMed: 21868683]
- Cerqueira MS , Pereira R , Rocha T , Mesquita G , de Paiva Lima CRO , Falcao Raposo MC , De Moura Filho AG , 2017 Time to failure and neuromuscular response to intermittent isometric exercise at two different levels of vascular occlusion: a randomized crossover study. *International Journal of Applied Exercise Physiology* 6, 55–70.
- Chung LH , Callahan DM and Kent-Braun JA , 2007 Age-related resistance to skeletal muscle fatigue is preserved during ischemia. *Journal of Applied Physiology* 103, 1628–1635. [PubMed: 17690199]
- Degens H , Salmons S and Jarvis JC , 1998 Intramuscular pressure, force and blood flow in rabbit tibialis anterior muscles during single and repetitive contractions. *European Journal of Applied Physiology and Occupational Physiology* 78, 13–19. [PubMed: 9660151]
- Delp SL , Anderson FC , Arnold AS , Loan P , Habib A , John CT , Guendelman E and Thelen DG , 2007 OpenSim: open-source software to create and analyze dynamic Simulations of movement. *Ieee Transactions on Biomedical Engineering* 54, 1940–1950. [PubMed: 18018689]
- Ditor DS and Hicks AL , 2000 The effects of age and gender on the relative on the relative fatigability of the human adductor pollicis muscle. *Canadian Journal of Physiology and Pharmacology* 78, 781–790. [PubMed: 11077978]
- Duchateau J , Balestra C , Carpentier A and Hainaut K , 2002 Reflex regulation during sustained and intermittent submaximal contractions in humans. *Journal of Physiology-London* 541, 959–967.

- Egana M Green S , 2007 Intensity-dependent effect of body tilt angle on calf muscle fatigue in humans. *European Journal of Applied Physiology* 99, 1–9. [PubMed: 17013590]
- Fimland MS , Helgerud J , Knutsen A , Ruth H , Leivseth G and Hoff J , 2010 No effect of prior caffeine ingestion on neuromuscular recovery after maximal fatiguing contractions. *European Journal of Applied Physiology* 108, 123–130. [PubMed: 19760253]
- Finlayson MHM , Majerus AL , Temes AL , Wright AM and Gajdosik RL , 2008 Influence of an isometric fatiguing exercise on the length and passive-elastic properties of the calf muscle-tendon unit of minimally active young women. *Isokinetics and Exercise Science* 16, 1–9.
- Frey-Law LA , Looft JM and Heitsman J , 2012 A three-compartment muscle fatigue model accurately predicts joint-specific maximum endurance times for sustained isometric tasks. *Journal of Biomechanics* 45, 1803–1808. [PubMed: 22579269]
- Frey Law LA and Avin KG , 2010 Endurance time is joint specific: A modelling and meta-analysis investigation. *Ergonomics* 53, 109–129. [PubMed: 20069487]
- Fujimoto T and Nishizono H , 1993 Involvement of Membrane Excitation Failure in Fatigue-Induced by Intermittent Submaximal Voluntary Contraction of the 1st Dorsal Interosseous Muscle. *Journal of Sports Medicine and Physical Fitness* 33, 107–117. [PubMed: 8412046]
- Fulco CS , Cymerman A , Muza SR , Rock PB , Pandolf KB and Lewis SF , 1994 Adductor Pollicis Muscle Fatigue during Acute and Chronic Altitude Exposure and Return to Sea-Level. *Journal of Applied Physiology* 77, 179–183. [PubMed: 7961231]
- Fulco CS , Rock PB , Muza SR , Lammi E , Braun B , Cymerman A , Moore LG and Lewis SF , 2001 Gender alters impact of hypobaric hypoxia on adductor pollicis muscle performance. *Journal of Applied Physiology* 91, 100–108. [PubMed: 11408419]
- Gonzales JU and Scheuermann BW , 2007 Absence of gender differences in the fatigability of the forearm muscles during intermittent isometric handgrip exercise. *Journal of Sports Science and Medicine* 6, 98–105. [PubMed: 24149231]
- Greiner A , Esterhammer R , Bammer D , Messner H , Kremser C , Jaschke WR , Fraedrich G and Schocke MF , 2007 High-energy phosphate metabolism in the calf muscle of healthy humans during incremental calf exercise with and without moderate cuff stenosis. *European Journal of Applied Physiology* 99, 519–531. [PubMed: 17206438]
- Hamada T , Sale DG , MacDougall JD and Tarnopolsky MA , 2003 Interaction of fibre type, potentiation and fatigue in human knee extensor muscles. *Acta Physiologica Scandinavica* 178, 165–173. [PubMed: 12780391]
- Hornby TG , Lewek MD , Thompson CK and Heitz R , 2009 Repeated Maximal Volitional Effort Contractions in Human Spinal Cord Injury: Initial Torque Increases and Reduced Fatigue. *Neurorehabilitation and Neural Repair* 23, 928–938. [PubMed: 19478056]
- Humphreys PW and Lind AR , 1963 The blood flow through active and inactive muscles of the forearm during sustained hand-grip contractions. *Journal of Physiology* 166, 120–135. [PubMed: 13955706]
- Hunter SK , Critchlow A , Shin IS and Enoka RM , 2004 Men are more fatigable than strength matched women when performing intermittent submaximal contractions. *Journal of Applied Physiology* 96, 2125–2132. [PubMed: 14966025]
- Hunter SK , Griffith EE , Schlachter KM and Kufahl TD , 2009 Sex differences in time to task failure and blood flow for an intermittent isometric fatiguing contraction. *Muscle Nerve* 39, 42–53. [PubMed: 19086076]
- Iridiastadi H and Nussbaum MA , 2006 Muscle fatigue and endurance during repetitive intermittent static efforts: development of prediction models. *Ergonomics* 49, 344–360. [PubMed: 16690564]
- Iridiastadi H and Nussbaum MA , 2006b Muscular Fatigue and Endurance During Intermittent Static Efforts: Effects of Contraction Level, Duty Cycle, and Cycle Time. *Human Factors* 48, 710–720. [PubMed: 17240719]
- Jakobi JM , Rice CL , Curtin SV and Marsh CD , 2000 Contractile properties, fatigue and recovery are not influenced by short-term creatine supplementation in human muscle. *Experimental Physiology* 85, 451–460. [PubMed: 10918084]

- Jaskolska A and Jaskolski A , 1997 The influence of intermittent fatigue exercise on early and late phases of relaxation from maximal voluntary contraction. *Canadian Journal of Applied Physiology-Revue Canadienne De Physiologie Appliquee* 22, 573–584. [PubMed: 9415830]
- Jubeau M , Muthalib M , Millet GY , Maffiuletti NA and Nosaka K , 2012 Comparison in muscle damage between maximal voluntary and electrically evoked isometric contractions of the elbow flexors. *European Journal of Applied Physiology* 112, 429–438. [PubMed: 21573775]
- Kalmar JM and Cafarelli E , 2006 Central excitability does not limit postfatigue voluntary activation of quadriceps femoris. *Journal of Applied Physiology* 100, 1757–1764. [PubMed: 16424071]
- Katayama K , Amann M , Pegelow DF , Jacques AJ and Dempsey JA , 2006 Effects of arterial oxygenation on quadriceps fatigability during isolated muscle exercise. *American Journal of Physiology Regulatory, Integrative and Comparative Physiology* 292, 1279–1286.
- Kent-Braun JA , Ng AV , Doyle JW and Towse TF , 2002 Human skeletal muscle responses vary with age and gender during fatigue due to incremental isometric exercise. *Journal of Applied Physiology* 93, 1813–1823. [PubMed: 12381770]
- Kent-Braun JA , Sharma KR , Weiner MW and Miller RG , 1994 Effects of exercise on muscle activation and metabolism in multiple sclerosis. *Muscle & Nerve* 17, 1162–1169. [PubMed: 7935523]
- Kinali G , Kara S and Yildirim MS , 2016 Electromyographic analysis of an ergonomic risk factor: overhead work. *Journal of Physical Therapy Science* 28, 1924–1927. [PubMed: 27390448]
- Lanza IR , Russ DW and Kent-Braun JA , 2004 Age-related enhancement of fatigue resistance is evident in men during both isometric and dynamic tasks. *Journal of Applied Physiology* 97, 967–975. [PubMed: 15145914]
- Lanza IR , Wigmore DM , Befroy DE and Kent-Braun JA , 2006 In vivo ATP production during free-flow and ischaemic muscle contractions in humans. *Journal of Physiology-London* 577, 353–367.
- Larsen FB , Pedersen MH , Friis K , Glumer C and Lasgaard M , 2017 A Latent Class Analysis of Multimorbidity and the Relationship to Socio-Demographic Factors and Health-Related Quality of Life. A National Population-Based Study of 162,283 Danish Adults. *PLoS One* 12, e0169426. [PubMed: 28056050]
- Larsson SE , Cai H , Zhang Q , Larsson R and Oberg PA , 1995 Measurement by laser-Doppler flowmetry of microcirculation in lower leg muscle at different blood fluxes in relation to electromyographically determined contraction and accumulated fatigue. *European Journal of Applied Physiology and Occupational Physiology* 70, 288–293. [PubMed: 7649138]
- Layec G , Haseler LJ , Trinity JD , Hart CR , Liu X , Le Fur Y , Jeong EK and Richardson RS , 2013 Mitochondrial function and increased convective O₂ transport: implications for the assessment of mitochondrial respiration in vivo. *Journal of Applied Physiology* 115, 803–811. [PubMed: 23813526]
- Liu JZ , Zhang L , Yao B , Sahgal V and Yue GH , 2005 Fatigue induced by intermittent maximal voluntary contractions is associated with significant losses in muscle output but limited reductions in functional MRI-measured brain activation level. *Brain Research* 1040, 44–54. [PubMed: 15804425]
- Lloyd AR , Gandevia SC and Hales JP , 1991 Muscle Performance, Voluntary Activation, Twitch Properties and Perceived Effort in Normal Subjects and Patients with the Chronic Fatigue Syndrome. *Brain* 114, 85–98. [PubMed: 1998892]
- Ma L , Chablat D , Bennis F and Zhang W , 2009 A new simple dynamic muscle fatigue model and its validation. *International Journal of Industrial Ergonomics* 211–220.
- Mademli L and Arampatzis A , 2008 Effect of voluntary activation on age-related muscle fatigue resistance. *Journal of Biomechanics* 41, 1229–1235. [PubMed: 18342865]
- McNeil CJ , Murray BJ and Rice CL , 2006 Differential changes in muscle oxygenation between voluntary and stimulated isometric fatigue of human dorsiflexors. *Journal of Applied Physiology* 100, 890–895. [PubMed: 16282429]
- Mendez-Villanueva A , Baudry S , Riley ZA and Rudroff T , 2009 Influence of rest duration on muscle activation during submaximal intermittent contractions with the elbow flexor muscles. *Journal of Sports Medicine and Physical Fitness* 49, 255–264. [PubMed: 19884876]

- Mitsukawa N , Sugisaki N , Kanehisa H , Fukunaga T and Kawakami Y , 2009 Fatigue-Related Changes in Fascicle-Tendon Geometry over Repeated Contractions: Difference between Synergist Muscles. *Muscle & Nerve* 40, 395–401. [PubMed: 19705427]
- Morse CI , Pritchard LJ , Wust RCI , Jones DA and Degens H , 2008 Carbon monoxide inhalation reduces skeletal muscle fatigue resistance. *Acta Physiologica* 192, 397–401. [PubMed: 17970829]
- Mulder ER , Kuebler WM , Gerrits KHL , Rittweger J , Felsenberg D , Stegeman DF and de Haan A , 2007 Knee extensor fatigability after bedrest for 8 weeks with and without countermeasure. *Muscle & Nerve* 36, 798–806. [PubMed: 17661376]
- Muthalib M , Jubeau M , Millet GY , Maffiuletti NA , Ferrari M and Nosaka K , 2010 Biceps brachii muscle oxygenation in electrical muscle stimulation. *Clinical Physiology and Functional Imaging* 30, 360–368. [PubMed: 20618357]
- Newham DJ and Cady EB , 1990 A 31P Study of Fatigue and Metabolism in Human Skeletal Muscle with Voluntary, Intermittent Contractions at Different Forces. *NMR in Biomedicine* 3, 211–219. [PubMed: 2288860]
- Nowak J and Wennmalm A , 1979 A study on the role of endogenous prostaglandins in the development of exercise-induced and post-occlusive hyperemia in human limbs. *Acta Physiologica Scandinavica* 106, 365–369. [PubMed: 506771]
- Ordway GA , Kearney JT and Stull GA , 1977 Rhythmic Isometric Fatigue Patterns of Elbow Flexors and Knee Extensors. *Research Quarterly* 48, 734–740. [PubMed: 271319]
- Pitcher JB and Miles TS , 1997 Influence of muscle blood flow on fatigue during intermittent human hand-grip exercise and recovery. *Clinical and Experimental Pharmacology and Physiology* 24, 471–476. [PubMed: 9248662]
- Quaine F , Vigouroux L and Martin L , 2003 Finger flexors fatigue in trained rock climbers and untrained sedentary subjects. *International Journal of Sports Medicine* 24, 424–427. [PubMed: 12905090]
- Rashedi E and Nussbaum MA , 2015 Mathematical Models of Localized Muscle Fatigue: Sensitivity Analysis and Assessment of Two Occupationally-Relevant Models. *PLoS One* 10, e0143872. [PubMed: 26656741]
- Rashedi E and Nussbaum MA , 2016 Cycle time influences the development of muscle fatigue at low to moderate levels of intermittent muscle contraction. *Journal of Electromyography and Kinesiology* 28, 37–45. [PubMed: 26995711]
- Roberts RA , Icenogle MV , Hudson TL and Greene ER , 1997 Temporal inhomogeneity in brachial artery blood flow during forearm exercise. *Medicine and Science in Sports and Exercise* 29, 1021–1027. [PubMed: 9268958]
- Rodgers SH , 1992 A Functional Job Analysis Technique. *Occupational Medicine-State of the Art Reviews* 7, 679–711.
- Rohmert W , 1960 Determination of the recovery pause for static work of man. *Internationale Zeitschrift Fur Angewandte Physiologie, Einschliesslich Arbeitsphysiologie* 18, 123–164.
- Russ DW and Kent-Braun JA , 2003 Sex differences in human skeletal muscle fatigue are eliminated under ischemic conditions. *Journal of Applied Physiology* 94, 2414–2422. [PubMed: 12562681]
- Russ DW , Towse TF , Wigmore DM , Lanza IR and Kent-Braun JA , 2008 Contrasting influences of age and sex on muscle fatigue. *Medicine and Science in Sports and Exercise* 40, 234–241. [PubMed: 18202580]
- Saito Y , Iemitsu M , Otsuki T , Maeda S and Ajisaka R , 2008 Gender differences in brachial blood flow during fatiguing intermittent handgrip. *Medicine and Science in Sports and Exercise* 40, 684–690. [PubMed: 18317376]
- Saugen E , Vollestad NK , Gibson H , Martin PA and Edwards RHT , 1997 Dissociation between metabolic and contractile responses during intermittent isometric exercise in man. *Experimental Physiology* 82, 213–226. [PubMed: 9023519]
- Seghers J and Spaepen A , 2004 Muscle fatigue of the elbow flexor muscles during two intermittent exercise protocols with equal mean muscle loading. *Clinical Biomechanics* 19, 24–30. [PubMed: 14659926]

- Sejersted OM , Hargens AR , Kardel KR , Blom P , Jensen O and Hermansen L , 1984 Intramuscular fluid pressure during isometric contraction of human skeletal muscle. *Journal of Applied Physiology: Respiratory, Environmental and Exercise Physiology* 56, 287–295.
- Silverstein B , Viikari-Juntura E and Kalat J , 2002 Use of a prevention index to identify industries at high risk for work-related musculoskeletal disorders of the neck, back, and upper extremity in Washington State, 1990–1998. *American Journal of Industrial Medicine* 41, 149–169. [PubMed: 11920960]
- Small K , McNaughton L , Greig M and Lovell R , 2010 The effects of multidirectional soccer specific fatigue on markers of hamstring injury risk. *Journal of Science in Medicine and Sport* 13, 120–125.
- Sonne MW and Potvin JR , 2016 A modified version of the three-compartment model to predict fatigue during submaximal tasks with complex force-time histories. *Ergonomics* 59, 85–98. [PubMed: 26018327]
- Stackhouse SK , Stevens JE , Lee SC , Pearce KM , Snyder-Mackler L and Binder-Macleod SA , 2001 Maximum voluntary activation in nonfatigued and fatigued muscle of young and elderly individuals. *Physical Therapy* 81, 1102–1109. [PubMed: 11319935]
- Taylor JL , Allen GM , Butler JE and Gandevia SC , 2000 Supraspinal fatigue during intermittent maximal voluntary contractions of the human elbow flexors. *Journal of Applied Physiology* 89, 305–313. [PubMed: 10904066]
- Thickbroom GW , Sacco P , Kermode AG , Archer SA , Byrnes ML , Guilfoyle A and Mastaglia FL , 2006 Central motor drive and perception of effort during fatigue in multiple sclerosis. *Journal of Neurology* 253, 1048–1053. [PubMed: 16607472]
- Thomas CK and del Valle A , 2001 The role of motor unit rate modulation versus recruitment in repeated submaximal voluntary contractions performed by control and spinal cord injured subjects. *Journal of Electromyography and Kinesiology* 11, 217–229. [PubMed: 11335152]
- Vigouroux L and Quaine F , 2006 Fingertip force and electromyography of finger flexor muscles during a prolonged intermittent exercise in elite climbers and sedentary individuals. *Journal of Sports Sciences* 24, 181–186. [PubMed: 16368628]
- Wigmore DM , Damon BM , Pober DM and Kent-Braun JA , 2004 MRI measures of perfusion-related changes in human skeletal muscle during progressive contractions. *Journal of Applied Physiology* 97, 2385–2394. [PubMed: 15298991]
- Wood DD , Fisher DL and Andres RO , 1997 Minimizing fatigue during repetitive jobs: Optimal work-rest schedules. *Human Factors* 39, 83–101. [PubMed: 9302881]
- Xia T and Frey Law LA , 2008 A theoretical approach for modeling peripheral muscle fatigue and recovery. *Journal of Biomechanics* 41, 3046–3052. [PubMed: 18789445]
- Yelin E , Callahan LF , Arnett F , Dennis D , Deyo R , Felson D , Felts W , Giannini E , Helmick C , Heyse S , Hirsch R , Hochberg M , Hunder G , Lawrence R , Liang M , Pillemer S , Shulman L , Steen V and Wolfe F , 1995 The Economic Cost and Social and Psychological Impact of Musculoskeletal Conditions. *Arthritis and Rheumatism* 38, 1351–1362. [PubMed: 7575685]

Figure 1.

A) Visual representation of the three-compartment controller (3CC) fatigue model proposed by Xia and Frey Law (2008) and **B)** the modified (3CCr) fatigue model with the addition of a rest multiplier, r , to augment recovery during rest intervals, when the target load, TL , equals 0 in the simulated task.

Figure 2.

Scatterplot of observed versus predicted fatigue (relative decline in peak torque, % torque decline) by joint region for the original 3CC fatigue model ($r = 1$): A) ankle (blue circles); B) knee (red squares); C) elbow (green diamonds); and D) hand/grip (cyan triangles). The identity line is shown to indicate 100% agreement. Data above the identity line reflect over-predictions of muscle fatigue whereas data below the line reflect under-predictions (i.e., directional errors).

Figure 3.

Absolute errors, unadjusted for time, between modeled and observed percent torque decline (%TD) across values of r for muscles about each joint region: A) ankle, B) knee, C) elbow, D) hand/grip, and E) all muscles. The original three-compartment controller (3CC) fatigue model error is shown as the red square ($r = 1$) and the modified 3CC- r fatigue model errors are shown as solid lines across varying r values ($r \geq 2$). Optimal r values (r_{opt}) are displayed as solid vertical lines, representing the best estimates for r_{opt} . Errors resulting in ± 1 %TD error from the lowest possible error represent the range of potential optimal r values (vertical

dashed lines). Minimally important differences (MID) of 50% reduction in original model errors ($r = 1$) are shown as the horizontal dashed line.

Figure 4.

Scatterplot of observed versus predicted fatigue (relative decline in peak torque, % torque decline) by joint region for the modified 3CCr fatigue model using the optimal r value: A) ankle (blue circles); B) knee (red squares); C) elbow (green diamonds); and D) hand/grip (cyan triangles). The identity line is shown to indicate where 100% agreement is located. Note that data are distributed more evenly above and below the identity lines than when $r = 1$ (see Figure 2).

Figure 5.

Absolute errors for each joint region: **A)** ankle; **B)** knee; **C)** elbow; and **D)** hand/grip, as a function of r (x-axis). The errors are stratified by 2 task conditions: 100% MVC and duty cycle (duty cycle) $\geq 50\%$ (dark red solid line) or MVC < 100% and duty cycle < 50%. Note the largest differences in error (% torque decline) between task conditions are seen at $r=1$ (original 3CC model), but are less for the modified model in the region of r_{opt} values (vertical gray lines).

Table 1:

Studies included in the meta-analysis by author for the ankle, knee, elbow, and hand/grip regions.

Joint	Author, Date	Subjects	Intensity (%MVC)	Duty Cycle (%)	Data Points	Time (min)
Ankle	(Alway, et al, 1987)	8M	100	50	1	5
	(Bemben, et al., 1996)	74M	100	40	2	1
	(Birtles, et al., 2002)	22MX	100	50	20	1 – 20
	(Birtles, et al., 2003)	10MX	100	50	17	1 – 20
	(Chung, et al., 2007)	12M	100	50	11	0.5–5.5
	(Egana and Green, 2007)	7M	30, 40, 50, 60, 80, 90	33	57	1 – 20
	(Fimland, et al., 2010)	13M	100	83	6	1–3.5
	(Finlayson, et al., 2008)	8F	80	80	1	5
	(Kent-Braun, et al., 1994)	8MX	10	40	1	0.5
	(Kent-Braun, et al., 2002)	20MX	10	40	1	0.5
	(Lanza, et al., 2004)	9M	100	50	3	1–3
	(Lanza, et al., 2006)	12MX	100	50	1	2
	(Mademli and Arampatzis, 2008)	11M	65	40	2	3,6
	(McNeil, et al., 2006)	10M	50	67	1	2
	(Mitsukawa, et al., 2009)	7M	100	50	2	3,4
	(Russ and Kent-Braun,2003)	8M,8F	100	50	8	1–4
	(Russ, et al., 2008)	16MX	100	70	10	1–5
Knee	(Armatas, et al., 2010)	13M	100	50	7	0.5–6
	(Baker-Fulco, et al., 2006)	7M	32	50	1	35
	(Bemben, et al., 2001)	8M	100	50	2	1
	(Burnley, 2009)	8M	100	60	9	0.5 – 4.5
	(Callahan, et al., 2009)	16MX	100	50	7	0.5 – 4
	(Callahan and Kent-Braun, 2011)	11F	100	50	7	0.5 – 3.5
	(Hamada, et al., 2003)	4M	100	63	3	0.5 – 2
	(Homby, et al., 2009)	10MX	100	50	3	0.5 – 2.5
	(Kalmar and Cafarelli, 2006)	8M	50	67	1	1
	(Katayama, et al., 2006)	6M	62	50	1	1.5
	(Morse, et al., 2008)	12M	100	50	1	1
	(Mulder, et al., 2007)	10M	45	60	5	1–5
	(Ordway, et al., 1977)	27M	100	50	5	1–5
	(Saugen, et al., 1997)	8M	40	60	4	5–40
	(Stackhouse, et al., 2001)	20MX	100	71	2	1.5,2
Elbow	(Allman and Rice, 2003)	6M	60	60	1	1
	(Bemben, et al., 2001)	8M	100	50	2	1
	(Bilodeau, 2006)	8MX	100	86	6	0.5–3
	(Hunter, et al., 2004)	10M, 10F	50	60	2	9, 23
	(Jakobi, et al., 2000)	7M	50	60	1	5

Joint	Author, Date	Subjects	Intensity (%MVC)	Duty Cycle (%)	Data Points	Time (min)
	(Jubeau, et al., 2012)	12M	100	21	10	1 – 15.5
	(Lloyd, et al., 1991)	13M	30	60	8	5–40
	(Mendez-Villanueva, et al., 2009)	9M	50	30, 60	5	4–33
	(Muthalib, et al., 2010)	10M	100	21	10	1 – 15.5
	(Ordway, et al., 1977)	27M	100	50	5	1–5
	(Seghers and Spaepen, 2004)	10MX	25, 50	50, 25	2	20
	(Taylor, et al., 2000)	9MX	100	50	4	2–8
	(Thomas and del Valle, 2001)	4MX	50	60	5	3–12
Hand/Grip	(Bemben, et al., 1996)	74M	100	40	2	1
	(Benwell, et al., 2007b)	12MX	30	60	5	2–5
	(Ditor and Hicks, 2000)	12M, 12F	100	71	12	0.5–3
	(Duchateau, et al., 2002)	13MX	25	60	1	8
	(Fujimoto and Nishizono, 1993)	8M, 6M	40	60	7	2–8
	(Fulco, et al., 1994)	8M	50	50	3	1–3
	(Fulco, et al., 2001)	12M, 21F	50	50	6	1–3
	(Gonzales and Scheuermann, 2007)	11M, 11F	50	50	4	2–13
	(Hunter, et al., 2009)	20M, 20F	50	60	2	5,7
	(Jaskolska and Jaskolski, 1997)	22M	100	50	1	6
	(Liu, et al., 2005)	14MX	100	67	4	0.5 – 2
	(Newham and Cady, 1990)	6MX	25, 50, 100	50	12	1 – 10
	(Pitcher and Miles, 1997)	9M	80	60	1	15
	(Quaine, et al., 2003)	10M	80	50	1	2
	(Saito, et al., 2008)	8M, 8F	100	50	12	0.5 – 4
	(Thickbroom, et al., 2006)	15MX	40	70	1	20
	(Vigouroux and Quaine, 2006)	10M	80	50	1	3
	(Wood, et al., 1997)	20F	16, 32, 48	63, 31, 21	12	9 – 36

Table 2:

Range of optimal rest recovery multiplier (r_{opt}) values [range ± 1 % torque decline] resulting in minimum fatigue prediction errors relative to observed fatigue, for the modified three-compartment controller (3CC) model based on absolute and directional model errors, with and without adjustment for time. All net error estimates were adjusted for MVC and duty cycle.

Joint region	r_{opt} Candidate Values				Final r_{opt}
	Absolute Error (unadj)	Absolute Error (time adj *)	Directional Error (unadj)	Directional Error (time adj *)	
Ankle	15 [12 – 19]	15 [9 – 26]	16 [14 – 18]	17 [13 – 22]	15
Knee	12 [8 – 17]	13 [7 – 21]	13 [12 – 14]	15 [13 – 17]	15
Elbow	8 [7 – 15]	8 [5 – 17]	10 [9 – 11]	10 [8 – 12]	15
Hand/Grip	27 [18 – 42]	28 [14 – 69]	30 [27 – 34]	37 [31 – 45]	30
General (All)	15 [11 – 22]	15 [8 – 29]	17 [15 – 18]	19 [15 – 23]	15

* errors divided by $\sqrt{\text{time}}$ in minutes to adjust for variations in time of assessment between studies and conditions, as prediction errors increase over time.

Table 3:

Mean absolute and directional model errors for the original three-compartment controller (3CC) model ($r = 1$) and the modified 3CC-r model at the optimal rest multiplier (r_{opt}) for each joint region.

Joint region	r_{opt}^*	Absolute Error (% torque decline)		Directional Error (% torque decline) [†]		Change in AIC ^{**}
		$r = 1$	r_{opt}	$r = 1$	r_{opt}	$AIC_{opt} - AIC_1$
Ankle	15	20.7	5.7	19.3	0.5	-68.2
Knee	15	21.0	8.6	21.0	-2.1	-54.8
Elbow	15	25.6	9.9	25.5	5.8	-43.8
Hand/Grip	30	29.2	8.7	28.9	0.1	-38.3
General (All)	15	23.9	8.2	23.3	1.2	-442.3

[†] A positive error indicates over-prediction of fatigue, across all task conditions adjusting for intensity, duty cycle, and time.

^{*} r_{opt} values are based on the four error methods and the Akaike's Information Criterion (AIC).

^{**} Negative values indicate superior fit of modified 3CC-r model despite addition of r parameter over original 3CC model.

Table 4:

Optimal fatigue (F), recovery (R), and rest multiplier (r) parameters by joint region.

Joint Region	3CC and 3CCr model parameters				During contraction		During rest intervals	
	F*	R*	r	R*r	F:R Ratio*	R:F Ratio*	F:(R*r) Ratio	(R*r):F Ratio
Ankle	0.00589	0.00058	15	0.0087	10.2	0.098	0.68	1.47
Knee	0.01500	0.00149	15	0.02235	10.1	0.099	0.67	1.49
Elbow	0.00912	0.00094	15	0.0141	9.70	0.103	0.65	1.55
Grip	0.00980	0.00064	30	0.0192	15.3	0.065	0.51	1.96
General	0.00970	0.00091	15	0.01365	10.1	0.094	0.67	1.41

* Optimal parameters reported by (Frey-Law et al., 2012); controller parameters set at L_D and $L_R = 10$