Validation of Metabolic Models for Estimation of Energy Expenditure During Isolated Concentric and Eccentric Muscle Contractions

Lentz-Nielsen, Nicki; Boysen, Mads Daabeck; Munk-Hansen, Mathias; Laursen, Andreas D; Steffensen, Mike; Engelund, Bj Rn K; Iversen, Kristoffer; Larsen, Ryan G; de Zee, Mark

Published in:
Journal of Biomechanical Engineering

DOI (link to publication from Publisher):
10.1115/1.4063640

Publication date:
2023

Document Version
Accepted author manuscript, peer reviewed version

Citation for published version (APA):
Lentz-Nielsen, N., Boysen, M. D., Munk-Hansen, M., Laursen, A. D., Steffensen, M., Engelund, B. R. K., Iversen, K., Larsen, R. G., & de Zee, M. (2023). Validation of Metabolic Models for Estimation of Energy Expenditure During Isolated Concentric and Eccentric Muscle Contractions. *Journal of Biomechanical Engineering*, *145*(12), 1-15. Article BIO-23-1118. https://doi.org/10.1115/1.4063640

Journal of Biomechanical Engineering. Received April 07, 2023;
Accepted manuscript posted October 06, 2023. doi:10.1115/1.4063640

Title: Validation of metabolic models for estimation of energy expenditure during isolated concentric and eccentric muscle contractions

Journal

Journal of Biomechanical Engineering

Authors

Nicki Lentz-Nielsen*[1], E-mail: Nickilentz@hotmail.com, ORCID: 0000-0001-9847-2695

Mads Daabeck Boysen*[1], E-mail: Madsboysen20@hotmail.com, ORCID: 0000-0003-0990-6178

Mathias Munk-Hansen[1], E-mail: mathiasmh@hst.aau.dk, ORCID: 0000-0001-6402-3453

Andreas David Laursen[1], E-mail: andreasdavidlaursen@gmail.com, ORCID: 0000-0002-9622-8741
Mike Steffensen [1], E-mail: Mike.N.Steffensen@gmail.com, ORCID: 0000-0002-0488-6094

Bjørn Keller Engelund[2], Email: bke@anybodytech.com, ORCID: 0000-0003-2143-6658

Kristoffer Iversen[2], Email: ki@anybodytech.com, ORCID: 0000-0002-6466-9569

Ryan Godsk Larsen[1], E-mail: rl@hst.aau.dk, ORCID: 0000-0002-4622-1453

Mark de Zee[1], Email: mdz@hst.aau.dk, ORCID: 0000-0003-0584-271X

*The authors Nicki Lentz-Nielsen and Mads Daabeck Boysen have contributed equally to the manuscript

Affiliation:

[1] ExerciseTech, Department of Health Science and Technology, Faculty of Medicine, Aalborg University, Aalborg, Denmark

[2] Anybody Technology A/S, Aalborg, Denmark

Manuscript type: Full paper, original work

Address for correspondence: Associate professor Mark de Zee, ExerciseTech, Department of Health Science and Technology, Faculty of Medicine, Aalborg University, Selma Lagerløfs Vej 249, 9260 Gistrup, Denmark. Email: mdz@hst.aau.dk

Journal of Biomechanical Engineering. Received April 07, 2023;
Accepted manuscript posted October 06, 2023. doi:10.1115/1.4063640

Abstract

Musculoskeletal modeling uses metabolic models to estimate energy expenditure of human locomotion. However, accurate estimation of energy expenditure is challenging, which may be due to uncertainty about the true energy cost of eccentric and concentric muscle contractions. The purpose of this study was to validate three commonly used metabolic models, using isolated isokinetic concentric and eccentric knee extensions/flexions. Five resistance trained adult males (25.6 ± 2.4 yr, 90.6 ± 7.5 kg, 1.81 ± 0.09 m) performed 150 repetitions at four different torques in a dynamometer. Indirect calorimetry was used to measure energy expenditure during these muscle contractions. All three models underestimated the energy expenditure (compared with indirect calorimetry) for up to 55.8 % and 78.5 % for concentric and eccentric contractions, respectively. Further, the coefficient of determination was in general low for eccentric contractions ($R^2 < 0.46$) indicating increases in the absolute error with increases in load. These results show that the metabolic models perform better when predicting energy expenditure of concentric contractions compared with eccentric contractions. Thus, more knowledge about the relationship between energy expenditure and eccentric work is needed to optimize the metabolic models for musculoskeletal modeling of human locomotion.

Keywords:

musculoskeletal modeling; metabolism; validation; indirect calorimetry

Highlights

- All metabolic models underestimated compared to measured energy cost.
- All metabolic models showed a good correlation for concentric contractions.
- All metabolic models showed a poor correlation for eccentric contractions.

Journal of Biomechanical Engineering. Received April 07, 2023;
Accepted manuscript posted October 06, 2023. doi:10.1115/1.4063640

1. Introduction

Musculoskeletal modeling is a common tool for analyzing multibody dynamics to evaluate human performance. To estimate energy expenditure (EE) with musculoskeletal modeling, several metabolic models (MM) have been developed [1-6]. Three MMs were considered in this study: Margaria [1], Bhargava et al., [2] and Umberger [3]. Margaria [1] created a simple efficiency formula, depending on either concentric or eccentric muscle contractions. Bhargava et al., [2] and Umberger [3] integrated ATP utilization, using the first law of thermodynamics on different variations of the Hill-type model. Koelewijn et al., [7] found good correlations ($R^2 >$ 0.90) among the three MMs and EE based on indirect calorimetry (IC) during walking at different velocities and inclinations. Yet, Bhargava et al., [2] showed a 29 % overestimation, while Umberger et al., [4] reported a slight overestimation of 2-10 %. Umberger [3] modified the MM from Umberger et al., [4] to better account for eccentric contractions, however, the model still overestimated EE. Even though both Umberger models overestimated EE, the estimations were still within an acceptable margin to the experimental data. Miller [8] reported conflicting results, as the EE estimations were not in the measured range of EE during human walking at a velocity approximately 10 % higher than the velocity used by Bhargava et al., [2] and Umberger [3]. Hence, the velocity of human walking may impact the validity of the established MMs as increase in walking speed increases the eccentric work of the hamstrings [9].

The difficulties of estimating EE during locomotion might be caused by the presence of eccentric contractions, as it is challenging to estimate EE of eccentric compared with concentric and isometric contractions [7,8]. This can be due to lack of understanding about eccentric muscle contractions, as the cross-bridge theory and sliding filaments theory fail to explain certain phenomena, such as the increase in force following active muscle lengthening [10]. To gain a better understanding of the variation in EE between concentric and eccentric contractions and how the contraction type influences the accuracy of MMs, it is necessary to conduct a controlled study that examines muscle contractions during a monoarticular task. A similar approach was taken by Hawking & Molé [5] and Tsianos & MacFadden [11] who found good agreement between the metabolic model and EE estimated from IC during seated contraction of quadriceps. However, this validation only included their own metabolic models and not the three MMs investigated in the current study. A validation of these three MMs is required to assess their validity at different intensities of muscle contractions, as different locomotion velocities and torques affect EE.

The purpose of this study was to validate the metabolic models from Margaria [1], Bhargava et al., [2] and Umberger [3] compared to EE measured with IC, during isokinetic concentric and eccentric contractions of the quadriceps muscle at different torques.

Journal of Biomechanical Engineering. Received April 07, 2023;
Accepted manuscript posted October 06, 2023. doi:10.1115/1.4063640

2. Methods

Five resistance trained adult males (25.6 ± 2.4 yr, 90.6 ± 7.5 kg, 1.81 ± 0.09 m) participated in the study. Participants provided written consent prior to data collection. The experiment was carried out in accordance with the ethical guidelines of the North Denmark Region Committee on Health Research Ethics. Given the experimental protocol's design, it was deemed suitable to solely include a homogeneous group comprising resistance-trained adult males. This deliberate choice aimed to secure that all trials (peak torques at 20, 40, 60, and 80 Nm) could be completed and to minimize potential inter-subject variations arising from factors such as sex, age and resistance training experience.

2. 1 Pre-experimental procedures

Each subject participated in three sessions held on separate days; Session one familiarized the subject with the concentric and eccentric contractions during a seated isokinetic knee-extension/flexion in a dynamometer (HUMAC Model 770 by CSMi, Massachussets, U.S.) while wearing a mask to measure pulmonary gas exchange (PGE) (Vyntus CPX-system by Vyaire Medical inc., Illinois, U.S.). Afterwards, two sessions of experimental exercises (concentric- and eccentric contractions) were held, each lasting approximately three hours. The experimental sessions were separated by at least 48 hours, and the order of the two experimental sessions was randomized. The subjects were instructed to avoid intense bouts of physical activity within 48 hours of the experiments. The subjects were fasting for at least 12 hours prior to each experimental session and were instructed to prioritize using motorized transportation on the day of the experiments to avoid unnecessary physical activity. No alcohol or tobacco usage was allowed for 24 hours prior to the experimental sessions.

2.2 Experimental protocol

The dynamometer was adjusted to fit each subject such that the axis of rotation of the knee joint aligned with the axis of rotation of the crank arm on the dynamometer. The lower leg was fixed to the crank arm of the dynamometer with an ankle cuff. Dynamometer settings and the anthropometric data were saved to ensure identical conditions between sessions. From a seated position the subject's leg was put into extension until the lower leg was horizontal relative to the ground, and the resting flexion moment was measured as the sum of the gravitational moment of the lower leg, crank arm and passive tension of the knee flexors. The subjects were fitted with a mask to measure PGE-data and were then given 10 minutes of rest prior to measuring resting PGE for 10 minutes. The subjects then performed 150 isokinetic ($60° \cdot s^{-1}$) concentric knee extensions or eccentric knee flexions. The exercise duration was approximately 8 minutes per trial. Range of motion (ROM) for concentric knee extensions was aimed at ~80° (from 0° knee flexion (lower leg vertical) to ~80° knee flexion (almost full extension)), while the ROM for the eccentric knee flexions were mechanically bound to 60° (from 70° knee flexion (almost full extension) to 10° knee flexion). To aid the subjects in performing the contractions consistently, they were given live visual feedback of the legs position and measured torque, for the last 10 repetitions performed. Succeeding all repetitions, the subjects remained seated and relaxed while PGE measurement continued for 10 minutes. This procedure was repeated four times at peak torques of 20, 40, 60 and 80 Nm (not corrected for gravity). Between each set, the subjects were given an additional 10 minute break, which was not monitored. All PGE-data was measured under ambient temperature (22° ± 0.8° C), pressure (760 ± 7 mmHg) and saturation (53 ± 3 %).

2.3 Estimating energy expenditure

Energy expenditure was calculated by multiplying the oxygen consumption (breath-by-breath) with the corresponding thermal value relative to the respiratory exchange rate (RER), based on Péronnet and Massicotte's [12] non-protein respiratory quotient table. The first 30 seconds of the collected PGE-data were discarded and the EE during rest (resting EE) was determined by calculating the mean of the remaining 9.5 minutes of EE prior to the task performance. The EE during the task of isokinetic knee extension and flexion was summed with the subsequent 10 minutes of EE, representing working EE. This approach was used to account for the slow component of the VO_2 kinetics and the energy expenditure from anaerobic pathways during each exercise trial. Finally, the EE elicited by the muscle contractions was computed by extracting the resting EE from working EE.

Journal of Biomechanical Engineering. Received April 07, 2023;
Accepted manuscript posted October 06, 2023. doi:10.1115/1.4063640

2.4 Processing of dynamometric data

At the start of the protocol, the mean measured torque (MT) of the leg at every angle was calculated by the dynamometer, and used to correct for gravity by adding a value corresponding to the Gravity Effected Torque (GET) as a function of the cosine of the angle of the shank relative to the horizontal plane and the maximal GET (MaxGET), to get the Gravity Corrected Torque (GCT) (Eq. 1):

$$GCT = MT \pm (MaxGET \cdot cos(\alpha)) \qquad \text{(Equation 1)}$$

Throughout both contraction tasks, the dynamometer repositioned the shank to its initial position between each repetition. Consequently, this movement necessitated no muscle activity, and participants were explicitly instructed to relax their muscles during this repositioning phase of the movement. The measured work caused by the gravitational forces upon the leg during the respective resting phases were discarded, to ensure that the measured torque would not be accounted for. The angular velocity of the knee joint was used to determine the phases. Each repetition in the dataset was normalized by applying zero-padding. This was done based on the maximum range of motion (ROM) performed by the subject. For example, if the highest ROM achieved among the 150 repetitions was 80° and one of the repetitions had a ROM of 78°, the remaining 2° (the difference between 80° and 78°) of the dataset were filled with zero values. This procedure allowed an average repetition (henceforth, the representative repetition) to represent all 150 repetitions, with a ROM from the largest measured degree of flexion to the largest degree of extension, resulting in eight average repetitions, one for each trial, for each subject. Each torque value was treated independently to the specific range of motion. For example, the torques performed at the 55° would only be compared to other torques produced at specifically that knee angle, which means that the mean repetition would be a mean of the torque for each specific knee angle. These data were used as input for the musculoskeletal modeling.

2.5 Musculoskeletal modeling

The musculoskeletal model used in this study was based on the human model included in the AnyBody Managed Model Repository v.2.3.0 [13] that is integrated in the AnyBody Modeling System v7.3.0 (Aalborg Denmark), which perform inverse dynamics. The lower extremity model was based on the TLEM 2.0, where it was scaled to the height and weight of the subject [14]. The musculoskeletal model was positioned to reflect the experimental setup. Adequate reaction forces and kinematic constraints were implemented to mimic the posture and restraints from the experimental setup and all the muscles in the lower body were modeled.

The measured angular orientations from the dynamometer were used to drive the rotation of the tibiofemoral joint in the model, while also including the specific torque at each degree of ROM. To calculate the reaction force of the dynamometer upon the leg during the experimental trials, the experimentally measured torque was divided by the moment arm, which was equal to the distance from the tibiofemoral joint to the attachment of the crank arm of the dynamometer onto the ankle. Attachment of the crank arm was individual, but always on the ankle within a few cm superior to the tibiotalar joint. In the model, this reaction force was applied to the tibia in a position identical to the proximal distance equal to the moment arm from the tibiofemoral joint. The applied force vector was interpolated and all interpolation was done with a 4th order Bspline function.

To minimize the relative load of each muscle force, f^M, a simple model was used where the muscle force was normalized to a fixed coefficient, N, based on the maximal strength potential of the muscle (Eq. 2).

$$G(f^{(M)}) = \sum_i [\frac{f_i^{(M)}}{N_i}]^p = [\frac{f_1^{(M)}}{N_1}]^p + [\frac{f_2^{(M)}}{N_2}]^p + ... + [\frac{f_{n^{(M)}}^{(M)}}{N_{n^{(M)}}}]^p \qquad \text{(Equation 2)}$$

Where $G(f^M)$ should be as low as possible. The synergists level of activity was controlled by the sum of the third power of the proportional activations (p = 3) [15].

To estimate EE, we utilized the three MMs provided by the AnyBody Modeling System. These models were employed to calculate the total metabolic power (Pmet) across all the simulated muscles. The metabolic power represents the computed EE obtained from the software. The average Pmet per degree was employed as a means to compare the metabolic models against the IC-data.

By using the MM from Margaria [1], Pmet was calculated by dividing the mechanical power of the muscle with the efficiency coefficients (0.25 and -1.20 for a concentric and an eccentric contraction, respectively). Using the MM from Bhargava et al., [2] and Umberger [3], Pmet was determined from the total external power and by calculating the rate of heat production which is the sum of the activation power (i.e., coefficient $\dot{A}$ in

Journal of Biomechanical Engineering. Received April 07, 2023;
Accepted manuscript posted October 06, 2023. doi:10.1115/1.4063640

Bhargava et al., [2] and coefficient $\dot{h}_A$ in Umberger [3]), the maintenance power (i.e., coefficient $\dot{M}$ in Bhargava et al., [2] and coefficient $\dot{h}_M$ in Umberger [3]), the shortening-lengthening power (i.e., coefficient $\dot{S}$ in Bhargava et al., [2] and coefficient $\dot{h}_{SL}$ in Umberger [3]) and the basal power (i.e., coefficient $\dot{B}$ in Bhargava et al., [2]). The MM from Umberger [3] combines $\dot{A}$ and $\dot{M}$ as one term ($\dot{h}_{AM}$) and therefore is coefficient $\dot{A}$ and coefficient $\dot{M}$ also combined in the AnyBody Modeling System. The MM from Bhargava et al., [2] and Umberger [3] separates the activation and the stimulation of the muscles in their equations. In current study, the activation value is found using equation 2. The AnyBody Modeling System does not model the excitation levels of the muscles. For that reason, the stimulation value is found by calculating the normalized muscle force for each muscle. The normalized muscle force is calculated as the muscle fiber force at time t divided by the maximal isometric force of the muscle at time t. The value of the coefficients published in the original work by the two MMs are included in the AnyBody Modeling System as default, which was employed in the current study. Information about the implementation of the three MMs is available in the AnyScript Reference Manual v.7.5.0 and in Appendix A.

There are minor differences between the original MM from Bhargava et al., [2] and the Bhargava model implemented in the AnyBody Modeling System. Calculating the activation power, the AnyBody Modeling System uses a constant decay function ϕ, while the decay function in the original paper models the heat production of a muscle contraction over time and assumes that most heat is produced early and decay with a time constant of 45 ms down to 6 % of the initial level [2]. Further, Bhargava et al., [2] included the possibility of negative metabolic power during eccentric contractions which later was corrected by Umberger [3]. The AnyBody Modeling System implementation of the Bhargava model can readily correct the external power produced by the muscle to the heat production for eccentric contractions. A full correction would require recalibrating the individual coefficients of the Bhargava model. However, this was deemed out of scope for the present study.

2.6 Analysis of the three metabolic models

All data were cleaned, preprocessed and analyzed with R statistical software package v4.1.3 and Python v.3.8.5. The validation of the three metabolic models were executed by analyzing both contraction types with the use of a least squared linear regression, mean absolute error (MAE), root mean square error (RMSE) and coefficient of determination, which are presented in Table 1. The agreement was analyzed with a plot showing the measured and calculated metabolic work, which also visualizes the variation for each model. Additionally, the mean and standard deviation of the subject's EE difference in joule per kilogram between measured metabolic power using IC and estimated metabolic power of the representative repetition at each mechanical load was plotted. Approximately 2 % of the PGE data was missing (NA values) due to technical issues. These missing values were imputed with a rolling average based on the nearest three points prior and after the missing value with an exponential weighting.

3. Results

The results are presented in Table 1 containing MAE, RMSE, linear regression and the coefficient of determination among the MMs and experimental data.

Journal of Biomechanical Engineering. Received April 07, 2023;
Accepted manuscript posted October 06, 2023. doi:10.1115/1.4063640

Table 1: *The MAE and RMSE values for each metabolic model in comparison to measurements using indirect calorimetry (IC), separated by concentric and eccentric contractions. The linear regressions and R^2 values are shown for each metabolic model, where y equals the metabolic work and x is the mechanical work performed in watt per kg bodyweight*

Model	MAE [watt/kg]	RMSE [watt/kg]	Linear regression	R^2
		Concentric		
IC			y = 7.60x - 0.36	0.82
Margaria	0.58	0.46	y = 4.08x - 0.07	0.92
Bhargava	1.17	1.59	y = 1.57x - 0.03	0.92
Umberger	0.93	1.07	y = 1.90x + 0.13	0.74
		Eccentric		
IC			y = 4.67x + 0.11	0.46
Margaria	1.07	1.35	y = 0.37x + 0.07	0.28
Bhargava	1.14	1.52	y = 0.20x + 0.04	0.25
Umberger	0.79	0.84	y = 0.05x + 0.43	0

Journal of Biomechanical Engineering. Received April 07, 2023;
Accepted manuscript posted October 06, 2023. doi:10.1115/1.4063640

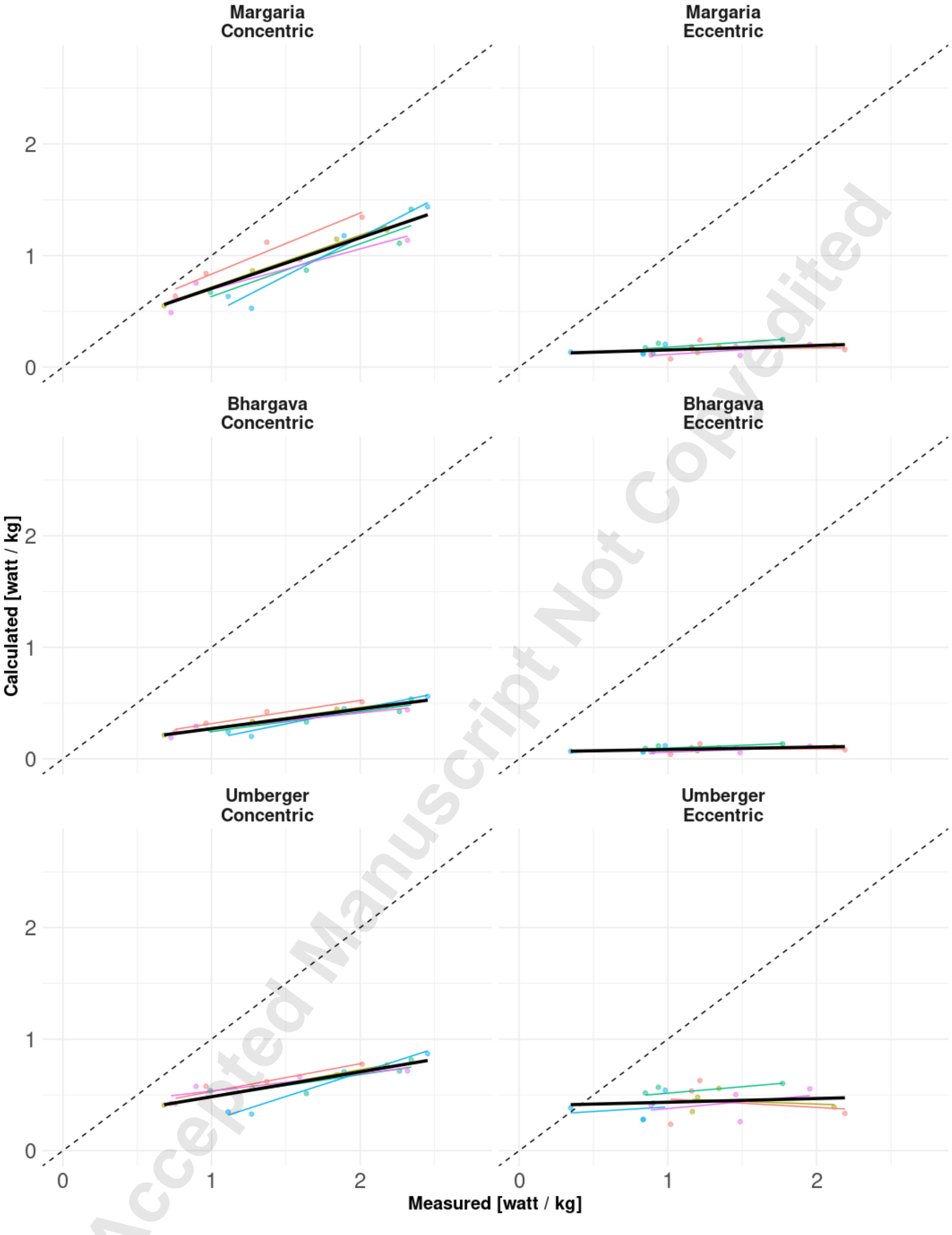

Figure 1: *Agreement between measured metabolic power using indirect calorimetry on the x-axis [watt/kg] and estimated metabolic power using a metabolic model on the y-axis [watt/kg]. The dashed line indicates a perfect agreement between measured and calculated output. Each color represents a subject, and the black line is the mean of all the subjects. Subplots are column wise arranged after contraction type, and row arranged after the metabolic models.*

Journal of Biomechanical Engineering. Received April 07, 2023;
Accepted manuscript posted October 06, 2023. doi:10.1115/1.4063640

For the linear regression of the experimental data, the R^2-value for concentric and eccentric contractions was 0.82 and 0.46, respectively. The slope coefficient was found to differ between the EE measurements and the MMs with up to 132 % for concentric contractions and 196 % for eccentric contractions, indicating a larger discrepancy in metabolic power during eccentric work and an increasing underestimation as a product of increased workload for both contraction types. The three MMs underestimated the metabolic output for both contraction types, compared to EE measurements (Figure 1). Margaria [1] showed the best agreement with EE measurements for concentric contractions, with a MAE of 0.58 watt/kg and RMSE of 0.46 watt/kg. Additionally, Margaria [1] had the most similar slope to the IC data, and revealed the strongest correlation between mechanical and metabolic work (R^2 = 0.92). Bhargava et al., [2] resulted in the highest error for both contraction types. Both Bhargava et al., [2] and Umberger [3] demonstrated an almost level slope coefficient compared to the EE measurements, especially for the eccentric contractions. Umberger [3] also showed a poor coefficient of determination, for eccentric contractions, which is visualized in Figure 1, where the individual data points (colored lines in Figure 1) show a heteroskedastic pattern.

Figure 2 illustrates the measured EE and calculated MM for one executed repetition, revealing a mean relative underestimation of the MMs of up to 55.8 ± 19.5 % and 78.5 ± 19.4 % for concentric and eccentric contractions, respectively.

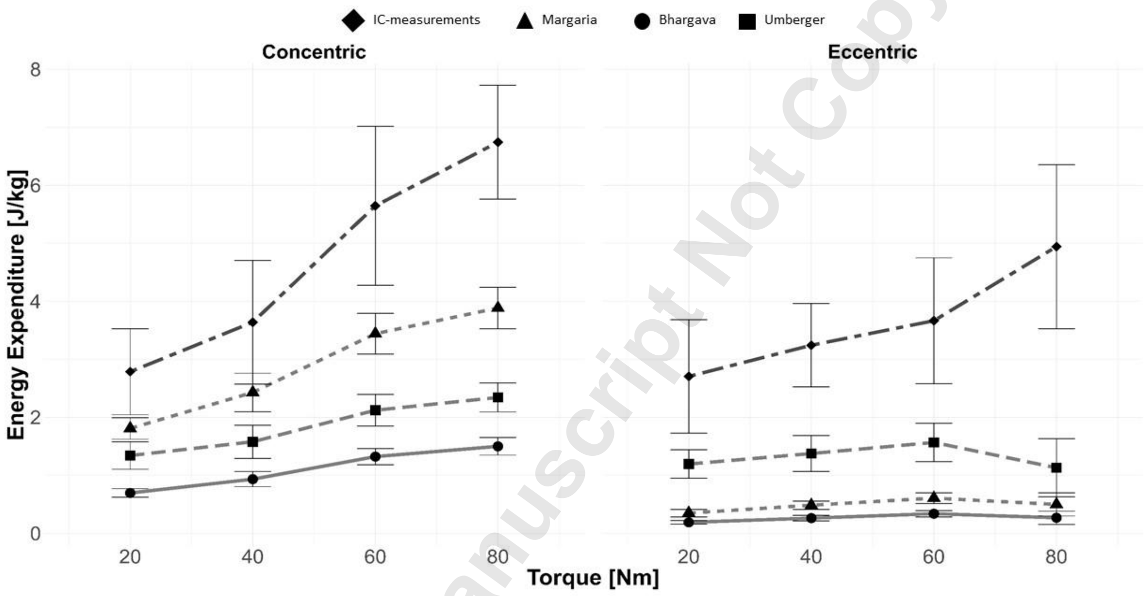

Figure 2: The y axis represents a mean and one standard deviation of the subject's energy difference in joule per kilogram between EE from IC-measurements and MMs of the representative repetition at each mechanical load [Nm] on the x-axis.

Journal of Biomechanical Engineering. Received April 07, 2023;
Accepted manuscript posted October 06, 2023. doi:10.1115/1.4063640

4. Discussion

The purpose of the study was to validate MM from Margaria [1], Bhargava et al., [2] and Umberger [3] by comparing metabolic output of simulated knee extension and flexion tasks at different torques with EE measured using IC. The results from the MMs for the concentric and eccentric contractions showed an overall underestimation of the metabolic output ranging from an RMSE of 0.46 to 1.59 watt/kg compared to EE and showed a mean relative underestimation of up to 55.8 % and 78.5 % for concentric and eccentric contractions, respectively. Further, the slope coefficient for the EE measurements for both the concentric and eccentric contractions was higher than for the corresponding estimations by the three MMs, indicating greater underestimations by the models at increasing mechanical load. In general, concentric contractions showed a superior trend and validity across the MMs, as seen in the coefficient of determination, slope coefficient and error margins, compared to eccentric contractions. Taken together, these results demonstrate that the MMs perform better when predicting EE from concentric contractions compared to eccentric contractions.

4.1 Accuracy of the metabolic models

The correlation between the Margaria [1] model and IC-data was superior for concentric contractions compared to eccentric contractions, with a coefficient of determination value of 0.92 which coincides with Koelewijn et al., [7]. Regardless of the strong correlation for concentric contractions, the Margaria [1] model still showed an overall underestimation for both contraction types, with the greatest underestimation during eccentric contractions (Figure 2). Our study used isolated isokinetic concentric and eccentric contractions and only found a slope difference of ~50 % between concentric and eccentric contractions. In contrast, Margaria [1] uses efficiency values of 0.25 and -1.2 for concentric and eccentric contractions respectively, which is a ~140 % difference between concentric and eccentric contractions. This discrepancy indicates that the assumptions made by Margaria [1] regarding the efficiency coefficients do not correspond to the efficiency differences for the thigh muscles during isolated isokinetic knee flexions and extensions. The underestimation of energy efficiency can perhaps be attributed to the utilization of a fixed coefficient in the model, which is determined solely by the type of muscle contraction. In the study conducted by Margaria [1], it was assumed that downhill and uphill walking exclusively involved eccentric and concentric work, respectively, while level walking included equal contributions from both eccentric and concentric work. The dissimilarities in outcomes between Koelewijn's study and our own were expected due to the distinctive experimental protocols employed. Koelewijn primarily focused on walking trials, which serve as the foundation for the Margarias model, whereas our investigation involved leg extensions. Given these variations, we speculate that the static coefficients within the Margarias model might necessitate revision depending on the specific task being examined. It is plausible that coefficients customized for activities such as cycling, running, or other exercises could differ from one another. This notion highlights the importance of adjusting the coefficients to suit the task at hand, thus enhancing the accuracy of the Margarias model.

The MM from Bhargava et al., [2] and Umberger [3] also showed good correlations with EE measurements during concentric contraction, with coefficient of determination values of 0.92 and 0.74, which also coincides with Koelewijn et al., [7]. The eccentric contractions showed low coefficient of determination values of 0.25 and 0.00, indicating that there was no association between the mechanical work during eccentric contractions and the EE calculated by MMs. These MMs also showed an overall underestimation for both contraction types, where the MM underestimation was less pronounced for concentric contractions. The underestimation may be explained by the data used to develop the MMs. The Bhargava et al., [2] model is based on amphibian muscle fibers and the Umberger [3] model is based on primary mammalian muscle fibers. The EE is considerably greater in amphibian muscles compared with mammals due to a higher body temperature and a greater proportion of fast-twitch fibers [4]. Specifically, studies have reported four to six times greater EE in human fast-twitch fibers compared with human slow-twitch fibers [4,16,17]. As Bhargava et al., [2] was developed with data from amphibian muscles, an overestimation would be expected as humans have a lower body temperature and a smaller proportion of fast-twitch muscle fibers compared to amphibians. Consistent with this notion, Bhargava et al., [2] reported a 29 % overestimation of EE during walking. Notably, the current study found an underestimation of up to ~125 % and ~180 % for concentric and eccentric contractions, respectively (Figure 2). As Umberger [3] was developed with data from mammalian muscles, a more accurate estimation of EE was expected. However, this model underestimated EE by up to ~97 % and ~125 % for concentric and eccentric contractions, respectively (Figure 2). These discrepancies may result from fundamental differences between walking and isolated isokinetic knee flexions and extensions. Therefore, the thermodynamic coefficients in the Bhargava et al., [2] and Umberger [3] models may require revaluation depending on the task, particularly during activities involving a large component of eccentric work.

4.2 Influence of contraction type

Energy expenditure measured from IC showed large differences in both slope and coefficient of determination between concentric and eccentric contractions. According to Bigland-Ritchie and Woods [18], concentric contractions require four times more energy than eccentric contractions, when performing the same

Journal of Biomechanical Engineering. Received April 07, 2023;
Accepted manuscript posted October 06, 2023. doi:10.1115/1.4063640

task during steady-state ergometer cycling. The current study did not find a four-fold difference in EE between contraction types at the same load, but only up to ~48 % higher EE for concentric than eccentric contractions (based on the relative difference of the slope coefficients). Ryschon et al., [19] estimated the efficiency of ATP utilization for concentric and eccentric contractions in the tibialis anterior and found the mechanochemical efficiency (i.e., ATP production rate / work) to be ~15 % and ~35 % for concentric and eccentric contractions, respectively. This equals a relative difference in ATP cost of 80 % between contraction types, which coincides closer with our results of a 48 % difference in EE between contraction types.

The efficiency advantage of eccentric contractions may be explained by factors such as; recruitment of more efficient muscle fibers and lower discharge rate of action potentials [20], lower neural activity [18], and lower ATP requirement during mechanical work [19]. More knowledge of the relationship between EE and eccentric work is, therefore, needed to optimize the energy estimations by MMs in musculoskeletal software.

4.3 Limitations

A fixed coefficient was used to normalize the muscle force and minimize the relative load of each muscle force instead of using a Hill-type muscle model during musculoskeletal modeling. However, changing to a Hill-type model does not systematically increase or decrease EE, as it is dependent on the contribution of e.g., force-length relationship, elasticity of the muscle and tendon, and pennation angle of the fibers [21]. Therefore, it was not anticipated to make a substantial contribution to the present findings of the current study. It is worth emphasizing that the outcomes of the metabolic models relied not only on the quality of the MMs but also on the selected processing approach, such as inverse dynamics and forward dynamics [15].

The energy expenditure of muscle contractions was measured with IC and pulmonary gas exchange. While this approach did not allow for assessment of EE within the exercising muscles, Poole et al., [22] showed a strong correlation between EE measured via IC and muscle oxygen uptake (measured by thermodilution and arterial-venous O_2 difference) within the exercising leg during cycle ergometry, suggesting that this approach is suitable.

The absence of external validation, such as surface electromyography, for the specific contraction types employed in our study is worth noting. As a result, we were unable to dismiss the possibility of co-contraction during the contraction types. Co-contraction would elevate the overall energy demand, leading to an increased underestimation by the model, which assumes the absence of co-contraction. Nonetheless, our experimental protocol facilitated muscle relaxation during the repositioning phase.

Only five young and resistance-trained adult men participated in the study. Future studies are therefore warranted to verify the relationship between modeled and experimental EE data in other populations such as women, older adults, obese and non-resistance trained participants. Studies have shown gender differences in muscle metabolism, such that men oxidize more carbohydrate and less lipids than women during exercise [23]. Further, age-related changes such as sarcopenia and increased adiposity have shown to affect the metabolic health negatively [24-26]. Lastly, strength training mainly results in increased muscle mass, increased ability to generate force and an enhanced capacity of the non-oxidative processes [27]. Despite small differences in muscle metabolism across populations, it is not expected that the relationship between modeled and experimental EE data will be different in the general population.

5. Conclusion

The metabolic models from Margaria [1], Bhargava et al., [2] and Umberger [3] showed an underestimation of EE compared to EE measured by IC during isokinetic concentric and eccentric contractions of the quadriceps muscles. Notably, the underestimation was greatest for eccentric contractions. For both the concentric and eccentric contractions, the slope coefficients of EE based on IC were higher than for the corresponding estimations by the three metabolic models, indicating greater underestimations as mechanical load increases. Therefore, concentric contractions showed higher correlation with mechanical load compared to eccentric contractions.

Supplementary Information Not applicable.

Acknowledgements Not applicable

Funding No funding was received.

Journal of Biomechanical Engineering. Received April 07, 2023;
Accepted manuscript posted October 06, 2023. doi:10.1115/1.4063640

Nomenclature

EE	Energy expendityre, J
GCT	Gravity Corrected Torque, N*m
GET	Gravity Effected Torque, N*m
IC	Indirect Calorimetry
MaxGET	Maximum Gravity Effected Torque, N*m
MM	Metabolic Models
MT	Mean measured torque, N*m
PGE	Pulmonary gas exchange
ROM	Range of motion

Author contributions NLN, MDB, MDZ and RGL drafted the manuscript. All authors provided critical feedback on the intellectual content, and approved the final manuscript.

Data availability: Available upon reasonable request.

Code availability: https://github.com/Lentz92/MetabolicModelValidation

Declaration of competing interest

Mark de Zee is co-founder, and Bjørn Keller Engelund and Kristoffer Iversen are employees of the company AnyBody Technology A/S that owns and sells the AnyBody Modeling System, which was used for the simulations. Mark de Zee is also a minority shareholder in the company.

References

[1] Margaria , R., 1968, “Positive and negative work performances and their efficiencies in human locomotion,” Int Z Angew. Physiol., 25 pp. 339-351. https://doi.org/10.1007/BF00699624.

[2] Bhargava, L. J., Pandy, M. G., and Anderson, F. C., 2004, “A phenomenological model for estimating metabolic energy consumption in muscle contraction,” J Biomech., 37 pp. 81-88. https://doi.org/10.1016/S0021-9290(03)00239-2.

[3] Umberger, B. R., 2010, “Stance and swing phase costs in human walking,” J R Soc Interface., 7 pp. 1329-1340. https://doi.org/10.1098/rsif.2010.0084.

[4] Umberger, B. R., Gerritsen, K. G. M., and Martin, P. E., 2003, “A Model of Human Muscle Energy Expenditure,” Comput Methods Biomech Biomed Engin, 6 pp. 99-111.

[5] Hawkins, D., and Molé, P., 1997, “Modeling energy expenditure associated with isometric, concentric, and eccentric muscle action at the knee,” Ann Biomed Eng., 25 pp. 822-830. https://doi.org/10.1007/bf02684166.

[6] Anderson, F. C., and Pandy, M. G., 2001, “Dynamic Optimization of Human Walkingk,” J Biomech Eng, 123 pp. 381-390. https://doi.org/10.1115/1.1392310.

[7] Koelewijn, A. D., Heinrich, D., and van den Bogert, A. J., 2019, ”Metabolic cost calculations of gait using musculoskeletal energy models, a comparison study,” PLOS ONE, 14:e0222037. https://doi.org/10.1371/journal.pone.0222037.

[8] Miller., R. H., 2014, “A comparison of muscle energy models for simulating human walking in three dimensions,” J Biomech, 47 pp. 1373-1381. https://doi.org/10.1016/j.jbiomech.2014.01.049.

[9] Neptune, R. R., Sasaki, K., and Kautz, S. A., 2008, “The effect of walking speed on muscle function and mechanical energetics,” Gait Ampmathsemicolon Posture, 28 pp. 135-143. https://doi.org/10.1016/j.gaitpost.2007.11.004.

[10] Herzog, W., 2014, “Mechanisms of enhanced force production in lengthening (eccentric) muscle contractions,” J Appl Physiol 116 pp. 1407-1417. https://doi.org/10.1152/japplphysiol.00069.2013.

[11] Tsianos, G. A., and MacFadden, L. N., 2016, “Validated Predictions of Metabolic Energy Consumption for Submaximal Effort Movement,” PLoS Comput Biol, 12. https://doi.org/10.1371/journal.pcbi.1004911.

[12] Peronnet, F., Massicotte, D., 1991, “Table of nonprotein respiratory quotient: an update,” Can J Sport Sci., 16 pp. 23-29.

Journal of Biomechanical Engineering. Received April 07, 2023;
Accepted manuscript posted October 06, 2023. doi:10.1115/1.4063640

[13] Lund, M. E., Tørholm. S., Pieri, D. E., Simonsen, S. T., Iversen, K., and Engelund, B. K., 2021, "The AnyBody Managed Model Repository (AMMR)". Zenodo 2021. https://doi.org/10.5281/zenodo.4305559.

[14] Carbone, V. et al., 2015, "TLEM 2.0 – A comprehensive musculoskeletal geometry dataset for subject-specific modeling of lower extremity," J Biomech, 48 pp. 734-741. https://doi.org/10.1016/j.jbiomech.2014.12.034.

[15] Damsgaard, M., Rasmussen, J., Christensen, S. T., Surma, E., and de Zee, M., 2006, "Analysis of musculoskeletal systems in the AnyBody Modeling System," Simul Model Pract Theory 14 pp. 1100-1111. https://doi.org/10.1016/j.simpat.2006.09.001.

[16] Bolstad, G., and Ersland, A., 1978, "Energy metabolism in different human skeletal muscles during voluntary isometric contractions," Eur J Appl Physiol, 38 pp. 171-179. https://doi.org/10.1007/bf00430075.

[17] Stienen, G. J., Kiers, J. L., Bottinelli, R., and Reggiani, C., 1996, "Myofibrillar ATPase activity in skinned human skeletal muscle fibres: fibre type and temperature dependence," J Physiol., 493 pp. 299-307. https://doi.org/10.1113/jphysiol.1996.sp021384.

[18] Bigland-Ritchie, B., and Woods, J. J., 1976, "Integrated electromyogram and oxygen uptake during positive and negative work," J Physiol, 260 pp. 267-277. https://doi.org/10.1113/jphysiol.1976.sp011515.

[19] Ryschon, T. W., Fowler, M. D., Wysong, R. E., Anthony, A. R., and Balaban, R. S., 1997, "Efficiency of human skeletal muscle in vivo: comparison of isometric, concentric, and eccentric muscle action," J Appl Physiol., 83 pp. 867-874. https://doi.org/10.1152/jappl.1997.83.3.867.

[20] Enoka, R. M., 1996, "Eccentric contractions require unique activation strategies by the nervous system," J Appl Physiol., 81 pp. 2339-2346. https://doi.org/10.1152/jappl.1996.81.6.2339.

[21] Hill, A., 1938, "The heat of shortening and the dynamic constants of muscle," Proc R Soc Lond Ser B Biol Sci., 126 pp. 136-195. https://doi.org/10.1098/rspb.1938.0050.

[22] Poole, D. C., Gaesser, G. A., Hogan, M. C., Knight, D. R., and Wagner, P. D., 1992, "Pulmonary and leg VO2 during submaximal exercise: implications for muscular efficiency," J Appl Physiol., 72 pp. 805-810. https://doi.org/10.1152/jappl.1992.72.2.805.

[23] Tarnopolsky, M. A., 2000, "Gender Differences in Metabolism; Nutrition and Supplements," *Journal of Science and Medicine in Sport* 3 (3): 287–98. https://doi.org/10.1016/s1440-2440(00)80038-9.

[24] Hunter, Gary R., Harshvardhan Singh, Stephen J. Carter, David R. Bryan, og Gordon Fisher., 2019, "Sarcopenia and Its Implications for Metabolic Health," *Journal of Obesity* 2019: 8031705. https://doi.org/10.1155/2019/8031705.

[25] Palmer, Allyson K., og Michael D. Jensen., 2022, "Metabolic Changes in Aging Humans: Current Evidence and Therapeutic Strategies," *The Journal of Clinical Investigation* 132 (16): e158451. https://doi.org/10.1172/JCI158451.

[26] Singla, Parul, Animesh Bardoloi, og Anuj A Parkash., 2010, "Metabolic effects of obesity: A review," *World Journal of Diabetes* 1 (3): 76–88. https://doi.org/10.4239/wjd.v1.i3.76.

[27] MacInnis, Martin J., Brendan Egan, og Martin J. Gibala., 2022, "The Effect of Training on Skeletal Muscle and Exercise Metabolism," *Exercise Metabolism*: 215–42. Physiology in Health and Disease. Cham: Springer International Publishing. https://doi.org/10.1007/978-3-030-94305-9_10.

Journal of Biomechanical Engineering. Received April 07, 2023;
Accepted manuscript posted October 06, 2023. doi:10.1115/1.4063640

Appendix A

Table 2: *Descriptions of various variables along with their default values for the metabolic models by Bhargava and Umberger, as integrated within AnyBody Modeling System according to the specifications outlined in the AnyScript Reference Manual v.7.5.0.*

Variable	Purpose	Default value	Metabolic Model
CoefBasalPower	Basal heat rate per muscle mass [W/kg]. This is the Ḃ per weight.	0.0225	Bhargava
CoefSLPowerConIso	Shortening-Lenghtening heat rate coefficient per isometric force in concentric case.	0.16	Bhargava
CoefSLPowerCon	Shortening-Lengthening heat rate coefficient per actual force in concentric case. Contributes to S.	0.18	Bhargava
CoefSLPowerEcc	Shortening-Lenghtening heat rate coefficient per actual force in eccentrric case. Contributes to S.	0.157	Bhargava
CoefActPowerPhi0	Activation heat rate ratio (constant). Used in A.	0.06	Bhargava
CoefActPowerSlow	Activation heat rate coefficient (per mass) for slow twitch fibers used in A.	40.0	Bhargava
CoefActPowerFast	Activation heat rate coeffcient (per mass) for fast twitch fibers. Used in A.	133.0	Bhargava
CoefMaintPowerSlow	Maintenance heat rate coefficient for slow twitch fibers. Used in M	74.0	Bhargava
CoefMaintPowerFast	Maintenance heat rate coefficient for fast twitch fibers. Used in M	111.0	Bhargava
MuscleDensity	Muscle density [kg/m^3]	1059.7	Bhargava
AddMusclePowerForEcc	Switch for whether to add the muscle power to the heat production in the eccentric case	On	Bhargava
AddMusclePowerForEccCoef	Fraction to the muscle power to add when 'AddmusclePowerForEcc' is 'on'. Default is '1.0' like in the paper. A Values of '-1.0' will subtract the negative eccentric muscle power, i.e. add a positive value	1.0	Bhargava
CoefActMaintPowerSlow	Activation-Maintenance power coefficient (per mass) for slow twitch fibers. Contributed to A+M	25.0	Umberger
CoefActMaintPowerFast	Activation-Maintenance power coefficient (per mass) for fast twitch fibers. Contributed to A+M	128.0	Umberger
CoefSLPowerEcc	Shortening-Lenghtening heat rate coefficient For eccentric terms. Contributed to S.	0.3	Umberger

Journal of Biomechanical Engineering. Received April 07, 2023;
Accepted manuscript posted October 06, 2023. doi:10.1115/1.4063640

CoefActMaintPowerAer	Activation-Maintenance power coefficient, that tune the model to whether the activity is mostly anaerobic or aerobic. Umberger proposes a range from 1.0 to 1.5 (from anaerobic to aerobic). The default value fitts the fully aerobic work case. Contributed to A + M	1.5	Umberger
HeatPowerMinPerMass	Lower threshold for the combined heat production power per muscle mass [W/kg]. Contributes to B.	1.0	Umberger
MuscleDensity	Muscle density [kg/m^3]	1059.7	Umberger
AddMusclePowerForEcc	Switch for whether to add to prroduce external power of the muscle (the muscle power) to the heat production in the eccentric case.	Off	Umberger
AddMusclePowerForEccCoef	Fraction to the muscle power to add when 'AddmusclePowerForEcc' is 'on'. Default is '1.0' like in the paper. A Values of '-1.0' will subtract the negative eccentric muscle power, i.e. add a positive value	1.0	Umberger