Title: Benchmarking the predictive capability of human gait simulations.

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Author contributions: MA processed the experimental data, performed the analysis and drafted the manuscript. MA, FDG and DK were involved interpreting the simulation results. All authors discussed the results and contributed to the iterative process of writing the final manuscript.

Abstract

Physics-based simulation generate movement patterns based on a neuro-musculoskeletal model without relying on experimental movement data, offering a powerful approach to study how neuro-musculoskeletal properties shape locomotion. Yet, simulated gait patterns and metabolic powers do not always agree with experiments, pointing to modeling errors reflecting gaps in our understanding. Here, we systematically evaluated the predictive capability of simulations based on a 3D musculoskeletal model to predict gait mechanics, muscle activity and metabolic power across gait conditions. We simulated the effect of adding mass to body segments, variations in walking speed, incline walking, crouched walking. We chose tasks that are straightforward to model, ensuring that prediction errors stem from shortcomings in the neuro-musculoskeletal model.

The simulations predicted stride frequency and walking kinematic with reasonable accuracy but underestimated variation in metabolic power across conditions. In particular, they underestimated changes in metabolic power with respect to level walking in tasks requiring substantial positive mechanical work, such as incline walking (27% underestimation). We identified two possible errors in simulated metabolic power.

First, the Hill-type muscle model and phenomenological metabolic power model produced high maximal mechanical efficiency (average 0.58) during concentric contractions, compared to the observed 0.2–0.3 in laboratory experiments. Second, when we multiplied the mechanical work with more realistic estimates of mechanical efficiency (i.e. 0.25), simulations overestimated the metabolic power by 84%. This suggests that positive work by muscle fibers was overestimated in the simulations. This overestimation may be caused by several assumptions and errors in the musculoskeletal model including its interacting with the environment and/or its many parameters.

This study highlights the need for more accurate models of muscle mechanics, energetics, and passive elastic structures to improve the realism of human movement simulations. Validating simulations across a broad range of conditions is important to pinpoint shortcomings in neuro-musculoskeletal modeling.

Author summary: (non-technical summary of the work)

Our research focuses on understanding how humans walk by using computer simulations. These simulations are based on detailed models, i.e. mathematical descriptions, of skeleton, muscles, joints, and control system. By comparing our simulations to actual experiments where people walked under different conditions—such as carrying extra weight, walking faster or slower, or moving uphill or downhill—we evaluated how well the simulations could predict real-life movement and energy use.

We found that while the simulations performed well in predicting the walking pattern, they underestimated metabolic energy used by the body, especially in tasks like walking uphill. Errors in simulated metabolic power likely stem from two issues. First, the metabolic power model resulted in unrealistically high mechanical efficiency compared to experiment. Second, positive work (and as a result also net negative work) by muscle fibers was overestimated in the simulations.

These findings highlight the need to improve the models so they can more accurately reflect the complexity of human movement and energy use. Ultimately, better models will help us design devices like exoskeletons and prosthetics and improve treatments for people with movement difficulties.

Introduction

Human gait is remarkably stereotypical considering the large kinematic redundancy, i.e. the large number of possible gait patterns people can select to move forward. It is often assumed that the central nervous system exploits this redundancy to select gait patterns that are efficient and robust. However, despite decades of valuable research, it is not yet fully understood how the central nervous and musculoskeletal systems interact during walking. Physics-based simulation is a powerful approach to explore the interaction between the central nervous and musculoskeletal systems and hence to study the principals of human locomotion (1,2). Physics-based simulations rely on a neuro-musculoskeletal model, i.e. a mathematical description of the neural and musculoskeletal systems. Such simulations allow exploring hypothetical scenarios, such as the effect of adding mass to body segments or muscle weakness on human gait (3,4). Differences between simulated and measured gait kinematics and energetics in these scenarios are especially interesting, as such differences point to knowledge gaps and can lead to identification of errors in the neural control or musculoskeletal models. In this study, we simulated a broad range of walking conditions (e.g. walking with added mass, walking at various speeds, walking on a slope) with a state-of-the art musculoskeletal model and compared simulated to measured gait outcomes. We specifically chose conditions that are straightforward to model, ensuring that prediction errors stem from shortcomings in the musculoskeletal and neural control models, rather than inadequate modeling of the intervention itself. By contrasting simulations with experiments we aimed to identify knowledge gaps in current gait simulations.

Physics-based simulations typically assume that humans select a gait pattern, from the redundant set of kinematic trajectories, that minimizes a cost function representing the cost to the human of achieving a task (1). The cost function typically compromises terms related to muscle fatigue (e.g. maximum muscle activations (5)), signal-dependent motor noise (e.g. activations squared (6)), musculoskeletal loading (e.g. contact forces (7)), movement smoothness (e.g. joint accelerations (8)), and metabolic power (9). Under this assumption, simulations of human movement can be formulated as optimization problems, i.e. find muscle excitations (1,10) or (the parameters defining the) control policy (11) that minimize a cost function for a given musculoskeletal model and task constraints (e.g. moving forward at a given speed).

Metabolic power is frequently included in the cost function and is an important outcome for various applications (e.g., exoskeleton design (12)) but the accuracy of muscle energy models is still debated. Muscle mechanics (13) and energetics (14,15) are typically described by phenomenological models. Metabolic energy models phenomenologically relate Hill-type muscle states to metabolic power via heat (maintenance, activation and shortening/lengthening heat) and mechanical work, based on experiments conducted with small bundles of isolated animal muscle fibers. The mathematical models and coefficients derived from these lab experiments have been incorporated into whole-body simulations (16). However, significant discrepancies remain between whole body metabolic power estimated using model-based simulations and measured through indirect calorimetry (17). These discrepancies may arise from multiple modelling simplifications and errors. First, phenomenological energy models might be inaccurate for the muscles' operating conditions during walking. Converting heat rate coefficients from controlled lab experiments on single muscle fibers to whole-body human movement introduces uncertainty as the vast number of possible combinations of muscle activity, fiber length, and velocity observed during human movement are difficult to replicate in controlled lab experiments. Furthermore, it is often unclear whether these models account for both initial heat (contraction coupling efficiency) and recovery heat (phosphorylation coupling efficiency, ATP synthesis). Second, energy models are based on muscle states that are modeled using phenomenological

Hill-type models, which are also based on measurements in controlled environments that do not capture how the muscle operates during walking. In addition, muscle parameters (e.g. isometric force, tendon stiffness, ..) are typically obtained by scaling a generic model that might not well represent a specific person. Finally, rigid-body assumptions, errors in segment masses and lengths, joint definitions and interaction with the environment can all contribute to errors in simulated walking pattern and thus the underlying muscle states and energetics.

Musculoskeletal models are simplifications of the physiological system but the implications of the underlying assumptions on their ability to predict a variety of walking conditions is not well understood. Many model parameters, e.g. the weights of the different terms in the cost function, are not directly measurable. One approach to limit the effect of model errors on the simulated movement pattern, has been to add a tracking term (4,18) minimizing the difference between simulated and experimental kinematics and kinetics to the cost function. However, the reliance on experimental data confounds predictions. Another approach is to estimate parameters that cannot be measured by fitting simulations to experimental data (10,19). This might equally well confound predictions in case of overfitting, i.e. when the data used for fine-tuning these parameters does not contain sufficient information. Hence, such approaches require extensive validation based on independent datasets. Although most studies have validated their simulations to some extent (e.g. (10,20)), a comprehensive validation across a broad range of walking conditions is still lacking.

In this study, we systematically evaluated the capability of simulations based on a muscle-driven 3D musculoskeletal model to predict walking kinematics, kinetics, muscle activity and metabolic power in various experimental conditions without adapting simulation parameters. Specifically, we simulated the effect of adding mass to different body segments, variations in walking speed, walking uphill or downhill, and crouched walking and compared this to experimental data. These tasks were chosen because they are relatively simple to model and introduce variations in average muscle activity (crouched walking), net mechanical muscle work (walking uphill or downhill), and in positive and negative mechanical muscle work (walking speed, added mass), offering insight into potential modeling errors. This systematic approach provides a benchmark for assessing the predictive accuracy of physics-based simulations. We used a previously published trajectory optimization workflow and 3D musculoskeletal model with 31 degrees of freedom driven by 92 Hill-type actuators (21). Gait patterns are calculated by minimizing a multi-objective cost function. Cost function weights were hand-tuned to obtain physiologically plausible walking kinematics, kinetics, and muscle activations at 1.3 m/s (10). Here, we performed a comprehensive evaluation of this simulation approach. We think that results of our evaluation are of broader interest as many modeling choices (e.g. linear muscle actuators, phenomenological Hill-type muscle models, assumption of optimality) are common in physics-based simulation of human motion.

Methods

In order to identify knowledge gaps in human gait simulations, we systematically compared the simulated and measured effect of simple mechanical interventions on gait kinematics, kinetics and energetics.

Musculoskeletal model

Simulations were based on the 3D musculoskeletal model presented in (21). In short, the model is based on an OpenSim musculoskeletal model with 31 degrees of freedom (dof; pelvis as floating base 6 dof,

3 dof hip, 1 dof knee, 2 dof ankle, 1 dof toes, 3 dof lumbar joint, 3 dof shoulder and 1 dof elbow) and 92 muscles actuating the lower limb and lumbar joints, eight ideal torque motors actuating the shoulder and elbow joints, and six contact spheres per foot (10,22). We added passive exponential stiffness and linear damping to the lower limb and lumbar joints to model ligaments and other soft tissues spanning the joint. Muscle-tendon paths and moment arm of the OpenSim model were approximated by polynomial functions (muscle-tendons length and moment arms as a function of joint angles) to improve computational speed (23). We used Raasch's model to describe muscle excitation-activation coupling (24) and a Hill-type muscle model to describe muscle-tendon interaction and the dependence of muscle force on fiber length and velocity (25). We modeled skeletal motion with Newtonian rigid-body dynamics and we used a smooth approximation of the Hunt-Crossley foot-ground contact model (26). The relation between muscle states and metabolic power was modeled as in Bhargava et al. (14), as this energy model had the highest correlation with experimental data in a previous simulation study (17). More details about the musculoskeletal model can be found in a previous publication (21).

Optimal control simulations

We predicted human movement based on the assumption that humans select a muscle excitation pattern that minimizes a cost function. As a result, we formulated simulations as optimal control problems. We identified muscle excitations and the gait cycle duration that minimized a cost function subject to constraints describing muscle and skeleton dynamics, that limbs cannot cross each other and task constraints, i.e. walking speed, left-right symmetry, and additional constraints for some of the gait conditions (see below). Similar as in previous publications (10,21), our cost function consisted of the time-integral of a weighted sum of squared metabolic power ($\dot{E}$), muscle activations (a), joint accelerations ($\ddot{q}$), passive torques (T_p), and excitations of the ideal torque motors at the arm joints (e_a):

$$J = \frac{1}{d}\int_0^{t_f} \left(w_1\dot{E}^2 + w_2 a^2 + w_3\ddot{q}^2 + w_4 T_p^2 + w_5 e_a^2\right)dt \;\; eq.1$$

To avoid singular arcs (27), we added penalty for slack controls (sum of squared time derivatives of normalized muscle forces and muscle activations) with a small weight (0.001) to the cost function. We used the weights (w1- w5) as published in (21). More details about the optimal control problem formulation can be found in previous work (21). We performed simulations in our PredSim framework that relies on OpenSim to derive skeleton dynamics and uses MatLab and CasADi (28) to formulate the optimal control problem (29). We applied direct collocation using a third order Radau quadrature collocation scheme, used algorithmic differentiation to compute derivatives, and solved the resulting nonlinear programming problem with IPOPT (30).

Modeling experimental walking conditions

In short, we ran simulations replicating a broad range of experimental studies on human locomotion that studied the effect of added mass (31–33), walking uphill or downhill (17,34–37), variations in imposed walking speed ((35,38), table 1) and crouched walking (34) (i.e. walking under a virtual ceiling). We simulated the effect of added mass at the feet, ankles, shanks, knees, thighs, pelvis and trunk on human walking. We modeled the added mass as a point mass that is rigidly attached to the specific segment by adapting the segment's mass, center of mass location, and inertia. We simulated walking on a slope by rotating the direction of gravity in the simulation environment. Walking speeds were imposed by constraining the average forward speed of the pelvis. We also simulated walking on slopes and crouched walking to replicate an experimental study that provided insight in the relative importance of minimizing metabolic power versus minimizing muscle activity (34). In that experiment,

crouched walking was achieved by instructing the participants to walk with an upright trunk and avoid contact with a virtual ceiling at 93% body height. We implemented this in our simulations by constraining the maximal pelvis vertical coordinate to be below 93% of the maximal value in the unconstrained simulation. In our simulations, we did not impose a specific form of locomotion, allowing the model to freely determine the gait pattern (walking, grounded running, running). This contrasts with the experiments by Abe et al., where participants were instructed to walk at treadmill speeds of 2.02 m/s and below and to run at speeds of 2.4 m/s and above (35). Similarly, in the study by Van der Zee et al., participants were constrained to walking at speeds up to a maximum of 2 m/s (38).

Normalization of data

To facilitate comparison between studies, experimental data were converted to non-dimensionless units. We used body mass (m), leg length (l), and gravitational acceleration g = 9.81 m/s^2 for normalization. Step frequency was normalized by $\sqrt{g/l}$, joint moments by mgl, ground reaction forces by mg, and (metabolic) power by $mg^{1.5}l^{0.5}$. Note that in most studies, individual data were not provided and therefore we used the average body mass and height for normalization. We then computed the corresponding non-normalized values for a model with a body mass of 62 kg and stature of 1.70m – the mass and length of our model - to facilitate interpretation of the results.

Comparison of simulations and experimental observations

To evaluate the predictive capability of the simulations, we compared simulated and measured stride frequencies, joint angles and moments, ground reaction forces, and metabolic powers. For studies that published raw data, we used addbiomechanics (39) to extract joint angles and moments. When raw data was unavailable in the experiments, we digitized stride frequency and metabolic power from published figures.

Our evaluation is largely based on relative changes in metabolic rate when comparing walking conditions (i.e. change metabolic power with respect to a reference condition) because differences in accounting for the resting metabolic rate across studies hinder comparison of absolute values of metabolic power. For most comparisons, we chose level walking at 1.1 m/s without added mass and without any constraints on stride frequency as the reference condition and reported the change in metabolic power with respect to this condition. If level walking at 1.1 m/s was not included in the experiment, we selected the condition closest to this walking speed as the reference. To evaluate the effect of added mass on the metabolic power, we chose a different reference, i.e. level walking at the same speed without added mass. The reader should therefore carefully interpret metabolic energy results. Absolute values of measured and simulated metabolic powers can be found in the appendix (Figure S8).

We simulated walking on slopes and crouched walking to replicate an experimental study that provided insight in the relative importance of minimizing metabolic power versus minimizing muscle activity (34). We evaluated if the simulation model could predict the changes in metabolic power and average activity of a subset of muscle (in the experiment based on electromyography) when increasing the slope or when walking in crouch. Additionally, based on the value of the cost function in the simulation of uphill and crouch walking, we evaluated whether the simulation model would also prefer tasks that avoided overburdening muscles (crouch walking) at the expense of higher metabolic power (i.e. lower cost function value indicates that the task is preferred by the simulation model).

Table 1: description of all studies we replicated in simulation.

study	***subjects***	***slope***	***added mass [kg]***	***walking speed***	***Measurement metabolic power***	***Mean body mass [kg]***	***Mean height [m]***	***Mean age [years]***	***method data extraction***
Gomenuka et al.	*10*	*0 % 7% 8%*	*25% body mass, backpack*	*2, 3, 4, 5, 6 km/h*	*O2 and CO2 metabolic rate standing subtracted*	*71.6*	*1.78*	*23*	*digitized figures*
Browning et al.	*5*	*0%*	*foot (4, 8) tibia (4, 8) femur (8, 16) pelvis (4, 8, 16 kg)*	*1.25 m/s*	*O2 and CO2 metabolic rate standing subtracted*	*74.16*	*1.82*		*digitized figures*
Schertzer et al.	*8*	*0%*	*ankle (1, 2, 4) knee (1, 2, 4) back (2, 7.1, 10.1, 16.1, 22.1)*	*4-5-6 km/h*	*based on gas exchange but details not described*	*74.88*	*1.78*	*27*	*digitized figures*
Huang et al.	*8*	*0%*	*6.8 kg - 20.4 kg backpack*	*1.25 m/s*	*O2 and CO2 metabolic rate standing subtracted*	*71.1*	*[0.99 leg length]*	*19-26 years*	*based on regression equation*
Koelewijn et al.	*12*	*level, 8% and -8%*		*0.8 and 1.25 m/s*	*O2 and CO2 metabolic rate standing subtracted*	*70*	*1.73*	*24*	*based on raw data processed with addbiomechanics*
Van Der Zee et al.	*10*	*level*		*0.7 - 0.9 - 1.1 - 1.25 - 1.4 - 1.6 -1.8 - 2 m/s*	*no*	*73.5*	*1.76*	*24*	*based on raw data published in addbiomechanics dataset*
McDonald et al.	*10*	*level, 6%, 12%, 18% and 24%*		*1 m/s*	*O2 and CO2 metabolic rate standing subtracted*	*69.6*	*1.70*	*31*	*based on raw data*
Abe et al.	*11*	*level, -5 % and 5 %*		*0.67, 0.86, 1.06, 1.25 ,1.44, 1.64, 1.83, 2.03, 2.42, 2.62, 2.81, 3 m/s*	*VO2 measurement, Standing VO2 Computed CO2 rate and computed metabolic energy*	*58.9*	*1.70*	*20*	*digitized from figures*
Strutzenberger et al.	*15*	*-12, -6, 0, 6, 12%*		*1.1 m/s*		*73.1*	*1.77*	*25*	*based on table 1*

We quantified the relation between simulated and measured changes in stride frequency and gait cycle average metabolic power (referred to as metabolic power) across different walking conditions by computing the explained variance (R^2), root-mean square error (RMSE), and slope of the relation using

a linear least squares fit. For trajectory outcomes (joint kinematics and kinetics) we discussed qualitatively the differences between experiments and simulations.

Mechanical efficiency of the metabolic energy model

The efficiency of net mechanical work done in the gait simulations was computed as the net mechanical work by muscle fibers divided by the net metabolic energy in one gait cycle. The net metabolic energy is the total metabolic energy minus the basal metabolic energy. The efficiency of positive mechanical work was computed as the positive mechanical work done by muscles fibers divided by the net metabolic energy. Mechanical work done by fibers is the time integral of muscle fiber power. Muscle fiber power was computed as a product of the velocity of the muscle fiber and its force. As the efficiency of net and positive mechanical work was unrealistically high compared to experiments (16) we also computed the maximal mechanical efficiency of muscle fibers in our model. We did this by computing muscle fiber power and metabolic power in isokinetic contractions at different fiber velocities while the muscle fiber was maximally activated and when the muscle fiber was at the optimal length. In addition, due to the unrealistic mechanical efficiency obtained with the Bhargava metabolic energy model, we also evaluated simulations using a model that only accounts for the energy cost of mechanical work and assumes concentric work has an efficiency of 0.25 and eccentric work has an efficiency of -1.2 (Margaria model (40)). We used this energy model to analyze the metabolic power in the default simulations (14) (i.e. post processing the simulation results with cost function (eq 1)). In addition, we also ran new simulations with metabolic power computed with this energy model in the cost function instead of the Bhargava model (14).

Results

Simulations capture differences in stride frequency between walking conditions

Our simulations captured the effect of most walking conditions on stride frequency (Figure 1). The simulations captured changes in stride frequency for variations in walking speed (R^2 = 0.99, 10% over estimation, rmse = 0.03 Hz) and variations in added mass (R^2 = 0.99%, 30% underestimation, rmse = 0.03 Hz). The simulations predicted that walking on a slope had a negligible effect on stride frequency (R^2 = 0.03, underestimation 90%, rmse = 0.04 Hz). Moreover, the simulation not only predicted the changes in stride frequency in the different gait conditions but also captured the absolute values (Figure S1).

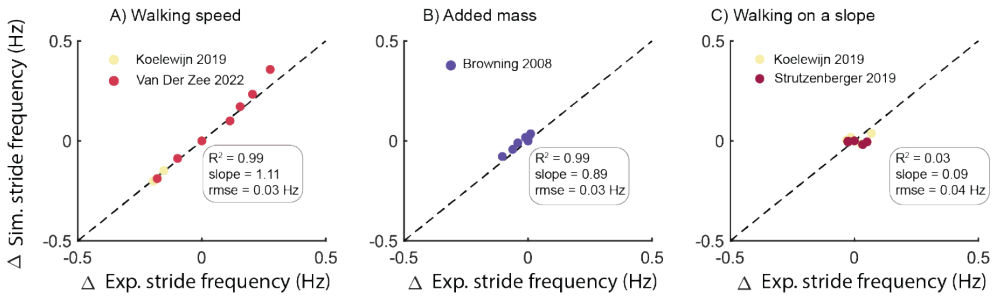

Figure 1: Predicted changes in stride frequency from level walking at 1.1-1.2 m/s with changes in walking speed (A), added mass at various locations on the body (B), and walking on a slope (C). Experimental data were converted to non-dimensionless units and subsequently converted for the anthropometry of the simulation model.

Simulation capture some, but not all, effects of walking conditions on joint kinematics and kinetics

We evaluated if the simulation could predict measured joint kinematics and kinetics for walking at various speeds (38) and walking on a slope (17). The predicted joint kinematics and kinetics are reasonably accurate for walking at 1.3 m/s (i.e. condition that was used to fine-tune the weights in the cost function (10)) except for the ankle joint kinematics during stance which underestimated the dorsiflexion during midstance and plantarflexion at push-off (Figure S2). As we were mainly interested in the experimental conditions that were not used to fine-tune the weights in the cost function, we focused on evaluating whether simulations capture alterations with respect to walking at self-selected speed.

For walking at various speeds, the simulations captured changes in kinematics for speeds between 0.7 and 1.6 m/s. The simulation adequately predicted the increase in ankle plantarflexion angle at push-off and knee flexion at initial stance with increased walking speed (Figure S2). However, the simulation overestimated changes in ankle and knee kinematics when gait speed was further increased to 2 m/s. In contrast with the experiments, the simulations predicted a more crouched position at push off at higher gait speeds (Figure S2). The observed increase in hip flexion moment and extension moment with faster walking was predicted accurately (Figure S3). The simulations failed to capture the increase in plantarflexion moment at push-off with increasing gait speed (Figure S3). Instead, they predicted large changes in knee moments at the highest gait speeds that were not observed experimentally. The discrepancies between experiments and simulations may partly stem from the transition to a (grounded) running gait in simulations at speeds of 1.8 m/s and above, in contrast to the imposed walking gait at all evaluated speeds (up to 2 m/s) in the experiment by Van der Zee et al. (38). Additional details on the walk-to-running transition are provided in Figure S15.

For walking on a slope, the model captured the changes in ankle, knee and hip kinematics reasonably well for walking on a positive or negative slope (Figure S5). Similar to experimental data, the simulations showed increased plantarflexion angle at stance-swing transition in uphill walking, increased knee flexion at initial stance and more hip flexion in general. The model also captured most changes in joint kinetics for walking on a slope (Figure S6) with increased hip flexion moment for downhill walking and increased hip extension moment for uphill walking. The model failed to capture the increase in knee flexion moment during early stance in downhill walking.

Simulations underestimate changes in metabolic power due to changes in walking conditions

We evaluated the simulations' ability to predict changes in metabolic power across various conditions. In general, simulations underestimated the changes in metabolic power compared to walking at 1.1 m/s (R^2 = 0.91, 15% underestimation, rmse = 57W). The simulations predicted the effect of varying gait speed on metabolic power with reasonable accuracy (R^2= 0.92, 10% underestimation, rmse = 53.9 W). The simulations particularly underestimated the increase in metabolic power at high gait speeds (Fig. 2C). The simulations underestimated the increase in metabolic power due to added mass (R^2 = 0.81, 21% underestimation, rmse = 17.3 W). The model underestimated the effect of slope on metabolic power both for positive and negative slopes (R^2= 0.93, 27% underestimation, rmse = 59 W).

We also compared the absolute values of the simulated and measured metabolic powers across conditions (Figure S8). Experimentally reported measures of metabolic power for a given walking condition (e.g. level walking at 1.1 m/s) varied between experimental studies, indicating that differences

in measurement equipment or protocol (e.g. subtraction of basal metabolic power) confound this analysis. This complicated the interpretation of the simulations results and might explain why we found, depending on the experimental study, an over- or underestimation of the simulated metabolic power for a given gait condition.

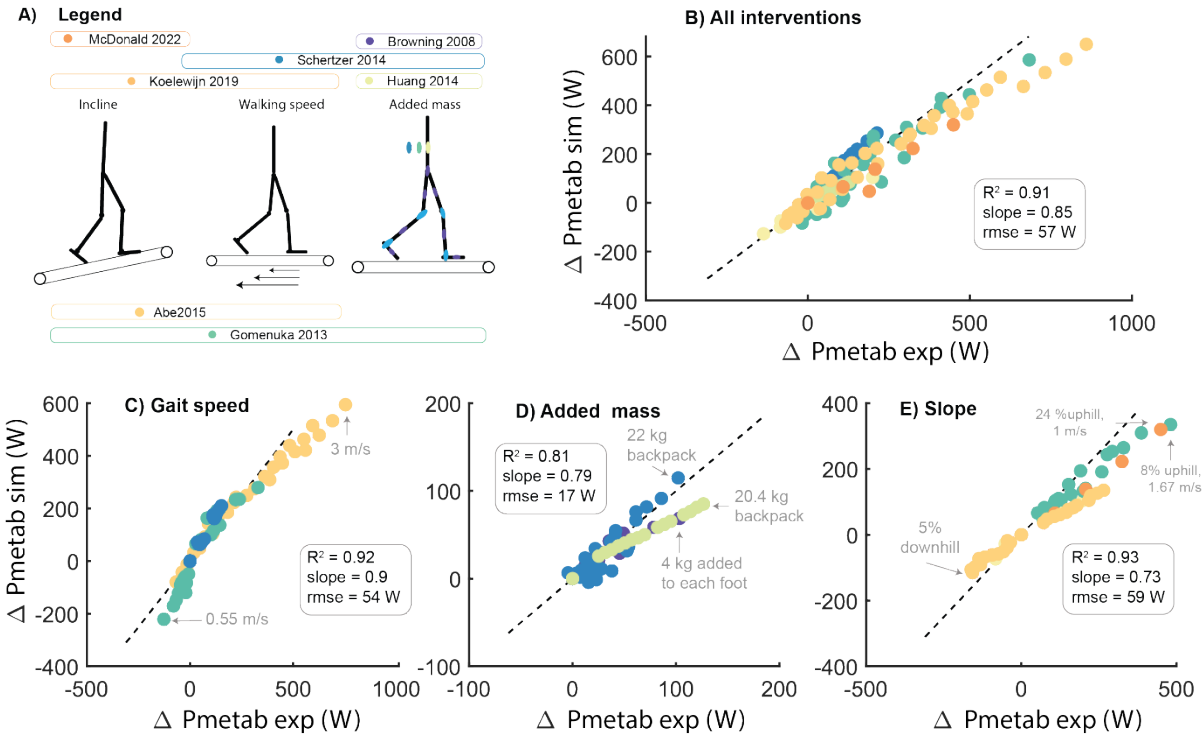

Figure 2: Predicted changes in gait cycle average metabolic power (Pmetab) from level walking at 1.1-1.2 m/s with changes in walking speed (C), mass added to different body segments (D) and walking on a slope (E). The colors represent the subject-mean data reported in the different studies (A). Experimental data were converted to non-dimensionless units and subsequently converted to the anthropometry of the simulation model.

<u>Simulations capture the activation, but not the energetic cost of walking</u>

We simulated walking on a slope and in crouch to determine whether our simulations capture the experimentally observed trade-off between increased muscle activity (walking in crouch) and metabolic power (walking on a steep slope) (34). We first compared the simulated and measured changes in metabolic power and activation cost (i.e. the average activity of a subset of muscles reported by (34)) for crouch walking and walking on a slope. We found that the simulations substantially underestimated the increase in metabolic power with increased slope and crouch (Figure 3B). However, unlike the metabolic power predictions, the activation cost was simulated with reasonable accuracy for both walking conditions (Figure 3C).

Next, we examined the cost function value across gait conditions to assess whether the simulations captured the preference of participants for crouch over slope walking for a slope gradient above 12%-18%. We found that the cost function value of crouch walking was lower than for slope walking across all gradients tested (6%, 12%, 18%, 24%) (Figure 3D). The metabolic power component of the cost

function was lower for crouched walking than for slope walking (Figure 3E). Interestingly, we also observed that the muscle activation component in the cost function for crouch walking was lower than for slope walking, which seemingly contradicts the simulated activation cost calculated from the subset of muscles (Figure 3F). The discrepancy between the activation cost computed from a subset of muscles and the activation term in the cost function, suggests that the activation cost of a subset of muscles might not be representative for all muscles. The simulation did not account for the total activated muscle volume, which could have influenced the results (Figure 3 G).

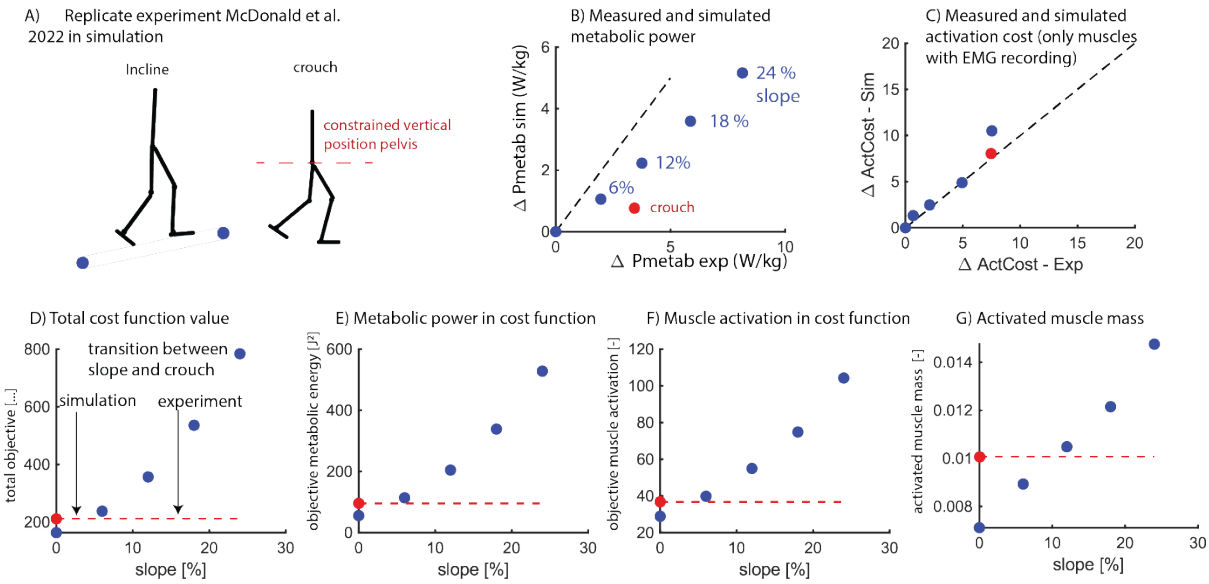

Figure 3: Predicted changes in gait cycle average metabolic power (Pmetab) and activation cost (ActCost) for crouched walking (red) and walking on a slope (blue). The simulations underestimated the increase in average metabolic power for slope and crouch walking (B) and estimated the increase in activation cost for slope and crouch walking with reasonable accuracy (C). The cost function in the simulation could not capture the observed transition from slope to crouch walking (D). Similar as in experiments, the average metabolic power of crouch walking was smaller compared to the average metabolic power of walking on a slope (E). It was harder to compare the activation related component of the cost function between experiments and simulations as a subset of muscles was used in the experiment to compute activation related costs and all muscles were used in the simulation. We found that the activation related cost in simulations was not higher for crouch walking compared to walking on a slope (F). This was slightly different when evaluating activated muscle mass (G).

Unrealistically high mechanical efficiency of muscle contraction

We evaluated the mechanical efficiency of the muscle model to better understand the underestimation of changes in metabolic power across all walking conditions. The simulated ratio of positive fiber work to metabolic energy was close to 0.5 for some conditions of fast and uphill walking (Figure 4A). The simulated ratio of net muscle work to metabolic energy was up to 0.38 for some conditions of uphill walking and walking with added mass (Figure 4B).

To investigate the maximal mechanical efficiency of the modeled muscles for positive and negative work, we conducted additional single-muscle simulations where simulated metabolic power and mechanical work was evaluated for muscle contractions at optimal fiber length with maximal activation and with varying contraction velocities (Figures 4 C-F). The maximum mechanical efficiency for

positive mechanical work ranged from 0.47 to 0.64, with an average maximal efficiency of 0.58 across all muscles (Figure 4 C-D). The minimal mechanical efficiency of negative mechanical work, which reflects the energetic cost of dissipating mechanical energy, ranged from $-2 \cdot 10^4$ to $-0.5 \cdot 10^4$ (Figure 4 E-F).

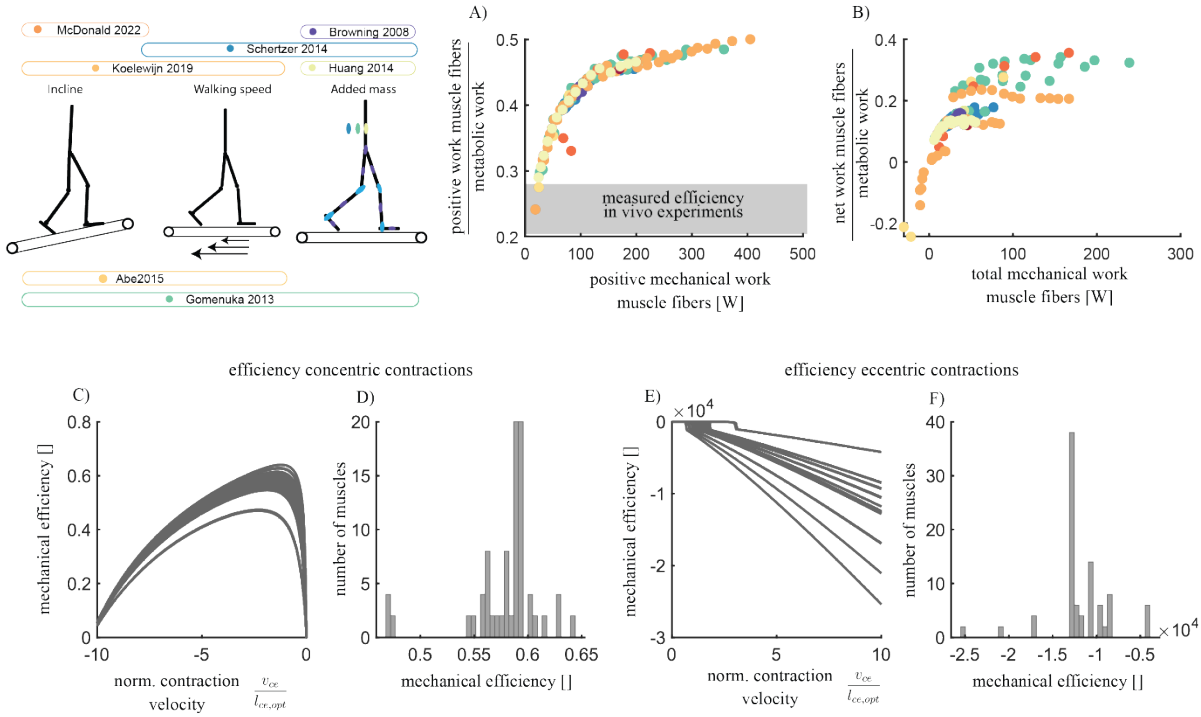

Figure 4: The Bhargava metabolic energy model has an unrealistically high maximal mechanical efficiency. The ratio of total simulated positive muscle fiber work and simulated metabolic energy was up to +/- 0.5 in the simulated walking conditions (A) and the ratio of simulated net muscle work and metabolic energy was up to +/- 0.35 (B). In single-muscle simulations where simulated metabolic power and mechanical work was evaluated for muscle contractions at optimal fiber length ($l_{ce,opt}$) with maximal activation and with varying contraction velocities (v_{ce}), we found mechanical efficiencies of up to 0.6 for concentric contractions (C-D) and -20000 for eccentric contractions (E-F).

<u>Metabolic energy models are too efficient in performing mechanical work</u>

Given the high mechanical efficiency observed in our muscle energy model, we explored if an alternative metabolic energy model with mechanical efficiency based on in vivo experiments can improve the prediction of metabolic power (Margaria model) (40). This model assumes that muscle fibers have an efficiency of 0.25 when performing positive mechanical work (concentric contraction) and -1.2 efficiency when performing negative mechanical work (eccentric contraction) (40). First, we used the Margaria model to evaluate whether this model resulted in more realistic metabolic powers for the simulated walking motions (with cost function eq. 1). Second, we predicted new walking motions with a cost function based on the Margaria instead of the Bhargava energy model to evaluate whether this resulted in more realistic walking motions and simulated metabolic powers.

When post-processing the simulations with the Margaria energy model, we found that it overestimated the increase in metabolic power with changes in walking speed (R^2 = 0.9, 100% overestimation, rmse = 266 W, Figure 5 B). However, we found reasonably accurate estimates of the increase in metabolic

power due to added mass (R^2 = 0.83, 23% overestimation, rmse = 22 W) and walking on a slope (R^2 = 0.95, 48% overestimation, rmse = 103W, Figure 5-C and 5-D).

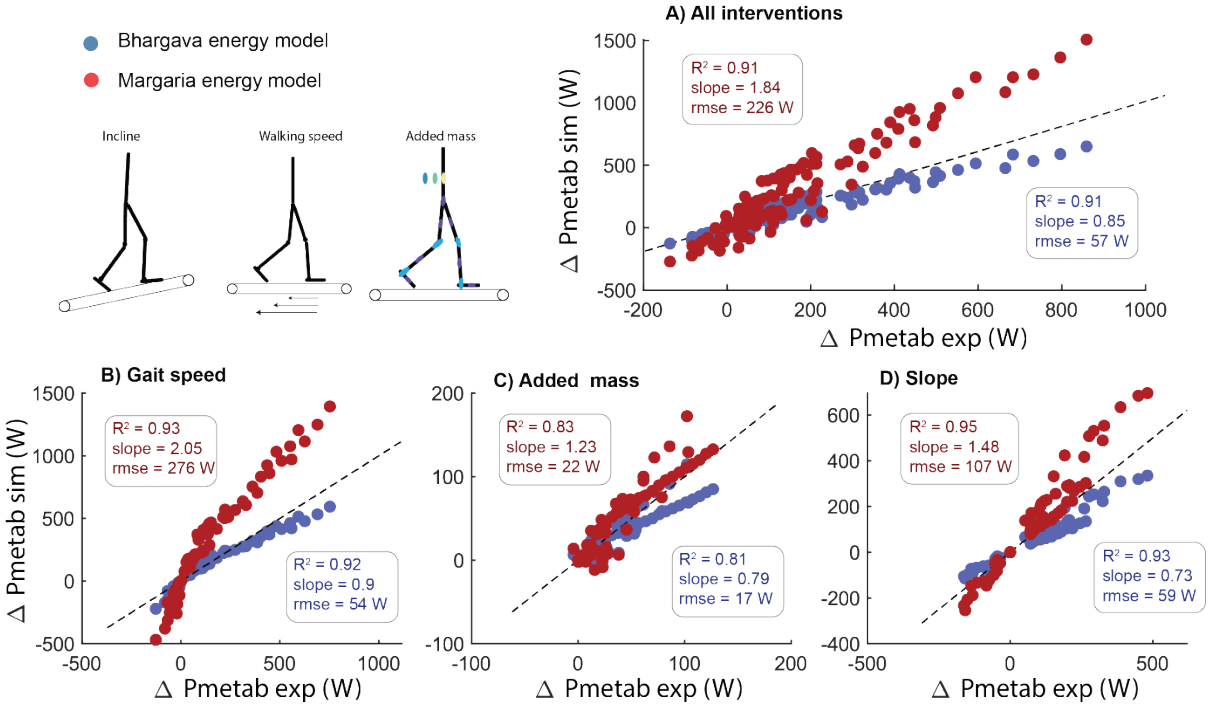

Figure 5: Postprocessing the simulations with the Bhargava energy model (blue) or Margaria energy model that only accounts for the metabolic power of mechanical muscle fiber power (red) has a large influence on the predicted change in metabolic power. The Bhargava energy model systematically underestimated the change in metabolic power, while the Margaria energy model systemically overestimated the change in metabolic power with variations in walking conditions.

When we incorporated the Margaria energy model, instead of the Bhargava energy model, into our multi objective optimization, the model accurately predicted changes in metabolic power with varying walking speeds (Figure 6 A-B). However, the simulations no longer captured experimentally observed stride frequency and joint moments (Figure D-I).

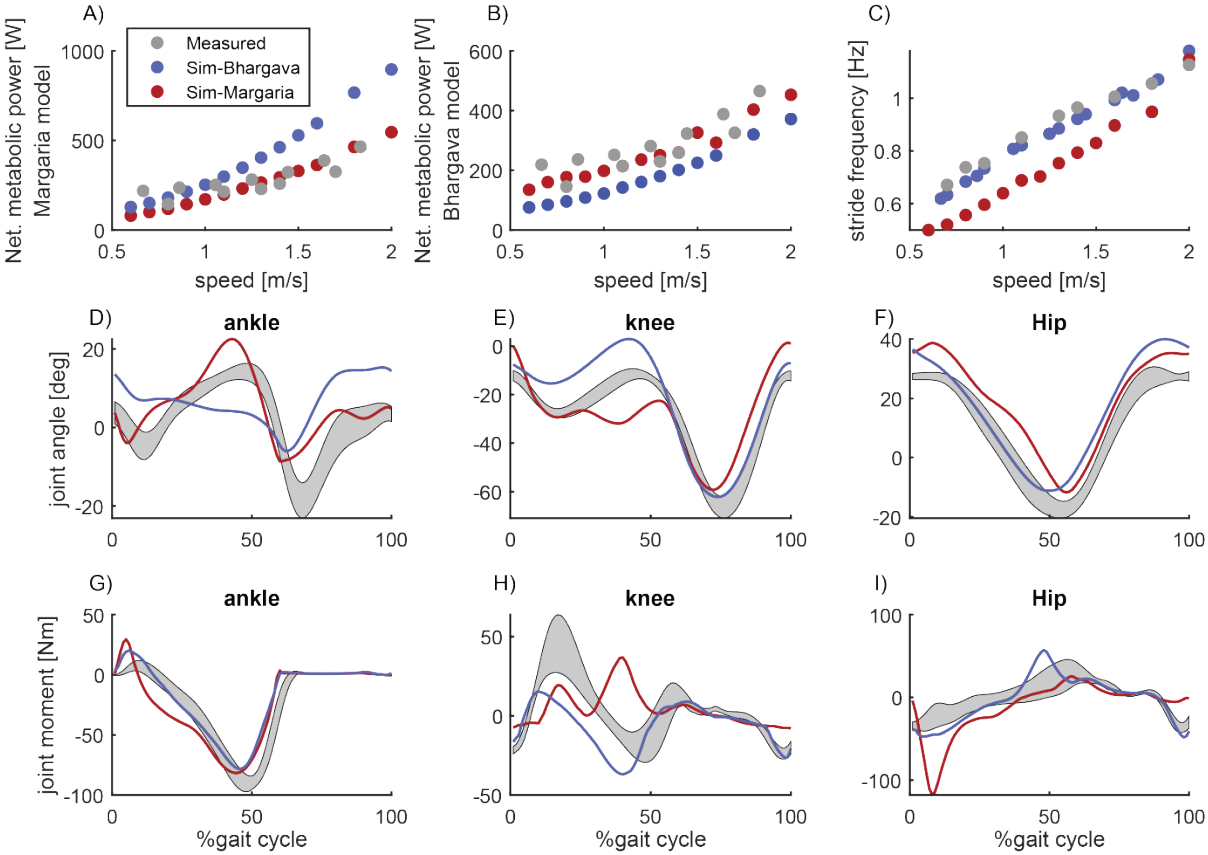

Figure 6: Simulated gait with the Bhargava energy model (blue) or the Margaria energy model in the (multi objective) cost function. The simulations with the Bhargava energy model overestimated the effect of walking speed on metabolic power computed with the Margaria energy model but not with the Bhargava energy model. While the simulations with the Margaria energy model in the cost function resulted in realistic metabolic powers for both energy models, the walking simulations deviated strongly from measured kinematics and kinetics (D-I, data walking at 1.3 m/s).

Discussion

This study evaluated the capability of physics-based simulations to predict human gait across various conditions, including variations in speed, slope and added mass, to gain insight in limitations in our current understanding of the mechanics and energetics of human walking. While the simulations reasonably predicted changes in spatio-temporal parameters, joint kinematics and kinetics under varying conditions (Figure 1), they underestimated the changes in gait cycle average metabolic power (Figure 2). Errors in metabolic power predictions are not solely due to errors in the metabolic energy model since the simulated muscle mechanical powers would yield unrealistically high metabolic power estimates when assuming realistic muscle efficiencies (Figure 5). This demonstrates that while physics-based simulations can reasonably predict variations in human walking joint mechanics, substantial limitations exist in the prediction of metabolic power.

The underestimation of metabolic power, particularly in conditions with added mass and for incline walking (Figure 2), appears related to the unrealistic mechanical efficiency of muscles in the phenomenological Hill-type and energetics models (Figure 4). The Hill-type muscle models that we used in our simulations have maximum (instantaneous) mechanical efficiencies for isokinetic concentric contractions between 0.47 and 0.64 averaging 0.58. While these values align with previous modeling studies (15,41) and are similar to other energy models that model heat rate (Figure S14, (42)),

they are significantly higher than the maximal 0.2-0.3 efficiency observed in laboratory experiments on small bundles of muscle fibers (16) and task-average efficiencies in whole-body exercises predominantly involving positive muscle fiber work such as cycling (43,44). This discrepancy explains the underestimation of metabolic cost for uphill walking in the simulations, where net positive mechanical work due to gravity is substantial. The model's high mechanical efficiency might result from errors in converting heat rate coefficients derived from in vitro experiments to simulations with hill-type muscles. Moreover, the high mechanical efficiency might also stem from only modelling initial heat and ignoring the energy cost of recovery heat (i.e. ATP resynthesized via oxidative pathways, with a phosphorylating coupling efficiency of 0.5-0.6 (16,45)). Assessing metabolic power during single-joint tasks with variable mechanical power and contraction forces could provide data for estimating heat rate coefficients for in vivo human muscle function (46).

While muscle mechanical efficiency in humans has never been reported to exceed 0.25, this value is mainly based on experiment with isolated muscle fibers (16) or derived from whole-body exercises with supposedly predominantly positive work (47). This raises the question whether 0.25 efficiency is also applicable for muscle contractions during whole-body movements. Isolated muscle fiber experiments are typically done in very specific conditions (i.e. operating at specific length and velocity of muscle fibers, stimulation patterns, temperatures) with tetanic activation. The stimulation amplitude and frequency in most muscle fiber experiments are different from those generated by the nervous system, potentially leading to an underestimation of maximal efficiency (45). The accuracy of mechanical efficiency estimates derived from whole-body movements with predominantly positive mechanical work (e.g. cycling) can also be questioned. The mechanical efficiency of 0.22-0.23 in cycling, computed as the net mechanical work at the crank divided by the (net) metabolic energy, does only account for the net mechanical work done by muscles fibers. This implicitly assumes that during cycling no negative muscle work is performed. Recent simulation work shows that this assumption may very well not be correct, and that actual mechanical efficiency is higher than the efficiency measured. Furthermore, mechanical work for other tasks, for example by the heart and respiratory muscles to increase blood and air circulation, is not accounted for in these analyses. In addition, the estimates based on cycling experiments should be interpreted as the task-average rather than maximal efficiency of muscles as it is unlikely that muscles perform work at the energetically most efficient length and velocity during the full cycling motion. Not accounting for all mechanical work has most likely a small influence on the estimated mechanical efficiency (i.e. in the order of a few percent) as the mechanical power for increased blood and air circulation when cycling is in the order of 10W and average mechanical power at the crank is in the order of 200W. Hence, the maximal mechanical efficiency of concentric contractions might be slightly higher than 0.25, but the reported 0.58 maximal efficiency in our model and 0.4 efficiency in uphill walking simulations remains implausibly high.

The inaccuracies in predicting metabolic power appear to stem not only from errors in the energy model but also from inaccuracies in modelling the musculoskeletal dynamics. The Margaria model that is based on mechanical efficiencies for concentric contractions derived from in vivo experiments overestimated the metabolic power in the simulated gait patterns although it did not account for the cost of isometric contractions (i.e. due to cross-bridge cycling and calcium transport). This suggests that positive work (and as a result also negative work) by muscle fibers was overestimated in the simulations, particularly at higher walking speeds. For instance, in our simulation of level walking at 1.3 m/s, positive fiber work was 101 J/stride and negative fiber work was -56 J/stride (details in Figure S13), resulting in an estimated cost of transport (COT) of 5.02 J/kg/m, which is substantially higher than the experimentally measured 3.0-3.5 J/kg/m (17,32,35). The overestimation of mechanical energy is not specific for the simulation approach used in this study but has also been reported in previous forward

(41,48) and inverse simulations (17). The implausibly high positive and negative muscle fiber work likely arises from a combination of assumptions and inaccuracies in the musculoskeletal model. In the following sections, we discuss some contributors that we consider likely, although this list is certainly not exhaustive.

Excessive energy dissipation in ground contact and rotational dampers might contribute to the over-estimation of negative (and hence positive) muscle fiber work. Energy dissipation in the ground contact model was higher in simulation compared to estimates from experiments (30 J/stride in simulation versus 7.6 J/stride in experiments (49)). Similarly, energy dissipation in rotational dampers in the simulation was also higher compared to estimated soft tissue energy dissipation in experiments (17 J/stride in simulation versus ~10 J/stride in experiments (50)). Even with a less compliant ground contact model (51), which reduced dissipation to 15 J/stride, the simulation still predicted unrealistic mechanical work, with an estimated COT of 6.46 J/kg/m with the Margaria energy model for level walking at 1.3 m/s.

The high net positive mechanical work done by muscle fibers in simulation might also be due to errors in modeling muscle-tendon mechanics. Accurately modelling the interaction between the tendon in series with the muscle fiber is essential for estimating muscle fiber work (52). While our model includes compliant tendons, errors in modelling tendon stiffness might lead to an underestimation of energy stored in tendons and an overestimation of muscle work. Recent studies indicate that simulations with a more compliant Achilles tendon produce ankle kinematics more consistent with experimental data (51), suggesting that the Achilles tendon in our model may be too stiff. While ultrasound studies might provide some insight in the errors in modelling the storage and release in tendons, it is challenging to accurately measure tendon and fiber kinematics and forces during human movement. Similar as with tendon compliance, inaccurate modelling of the energy storage and release in the connective tissue (i.e. parallel elastic element) might result in overestimation of mechanical work done by muscle fibers (53). Additionally, certain mechanisms, such as titin's elasticity and residual force enhancement following eccentric contraction (54), are not modeled and may influence muscle fiber mechanical work. Finally, we simplified the complex 3D anatomy of a muscle to a massless 1D actuator with variable pennation angle and constant width. This modelling assumption might also influence the simulated mechanical work.

The optimality assumption and the particular cost function used might also contribute to the errors in simulated mechanical work. The cost function influences the predicted kinematics and kinetics and muscle activation. Inaccurate modelling of co-contraction might also influence the simulated mechanical work by muscle fibers (41). Increased co-contraction increases energy dissipation in antagonistic muscles, which has to be compensated by increased positive work in agonistic muscles. It is however unlikely that high levels of co-contraction cause the large amount of positive and negative mechanical work in our simulation as co-contraction was implicitly minimized in our cost function (activation squared and metabolic energy term).

When using physics-based simulations to predict the effect of an intervention, such as a wearable robotic device, it is crucial to know the accuracy of the simulated walking kinematics, kinetics, and energetics. In some cases, it might be helpful to be able to predict the direction of the change even if the predicted magnitude is not accurate. For example, when designing assistive devices, knowing whether a design choice will increase or decrease step frequency or energy consumption is often more crucial than exact values. In this study, for the range of walking conditions tested, the explained variance in stride frequency and metabolic cost was generally high (Figures 1 and 2), suggesting that the model

correctly captured the direction of the intervention's effects. An important future step is to assess whether simulations can be used for designing better interventions. The simulations presented here rely on a predefined musculoskeletal model and we altered the task constraints. When using simulations for design of interventions, e.g. the stiffness of an orthoses, model parameters become optimization variables. It is unclear whether the accuracy of capturing the effect of different task constraints and different model parameters is comparable. For example, a lower-limb exoskeleton that replaces entire ankle-knee-hip torque would be optimal in our simulations. This is however not observed in experimental studies where submaximal assistance is optimal (55,56). This demonstrates that other modelling assumptions might become critical in designs that have a large impact on the simulated walking motion and/or muscle activity.

In this study, we predicted various walking conditions without explicitly (i.e. part of cost function or as constraints) or implicitly using validation data to tune simulation parameters, apart from walking at 1.3 m/s (10). This systematic approach revealed substantial limitations, particularly in the metabolic energy model and the mechanical work done by muscle fibers. We believe that this benchmarking process should be iterative, preferably incorporating novel data when adapting models or model parameters in the simulation (i.e. weights in cost function, constraints on muscle coordination). This approach would minimize the risk of overfitting the model to a specific walking condition and enhance the model's ability to generalize across various walking conditions.

Conclusion

This study demonstrates that while physics-based simulations can reasonably predict variations in human walking kinematics and spatio-temporal parameters, substantial limitations exist in the prediction of metabolic power. These inaccuracies likely stem from two issues. First, the predicted positive muscle fiber work is unrealistically high, which may be caused by assumptions and errors in the musculoskeletal model including its interacting with the environment and/or its many parameters. Second, the model of metabolic power based on Hill-model states and inputs results in unrealistically high efficiencies (18). This highlights the need for more accurate musculoskeletal and energetics models to improve the predictive capability of human movement simulations. Addressing these limitations through improved modeling and iterative validation will enhance the reliability of simulations, especially in predicting metabolic power during walking. Ultimately, refining these models will be crucial for enabling the use of simulations for the design of assistive devices or for optimal treatment selection.

Acknowledgments

We want to thank all the authors that published their raw data as a supplement or dataset. Without this, or the use of tools like AddBiomechanics, benchmarking predictive simulations would be even more time intensive. I also want to thank Koen Lemaire, Tim van der Zee, and Maarten Bobbert for the insightful discussion on metabolic energy models; Lars D'Hondt for the numerous developments in the predictive simulation code; Keenon Werling for the development and help with AddBiomechanics; Steve Collins, Katie Poggensee and Antoine Falisse for the discussions on simulations with waking with an ankle-foot exoskeleton. The (lack of) validity of these simulations was the basis of this research project.

Data availability statement

Simulation code and experimental data can be accessed through GitHub (https://github.com/MaartenAfschrift/PredSim_gait_conditions) when the paper is published.

Reviewers can access this repository here:
https://drive.google.com/file/d/1pItM7SHJtOCIttX0ED4ee6OkDgF7M4mf/view?usp=sharing

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Supplementary files caption

Appendix.pdf: Appendix with additional simulation results

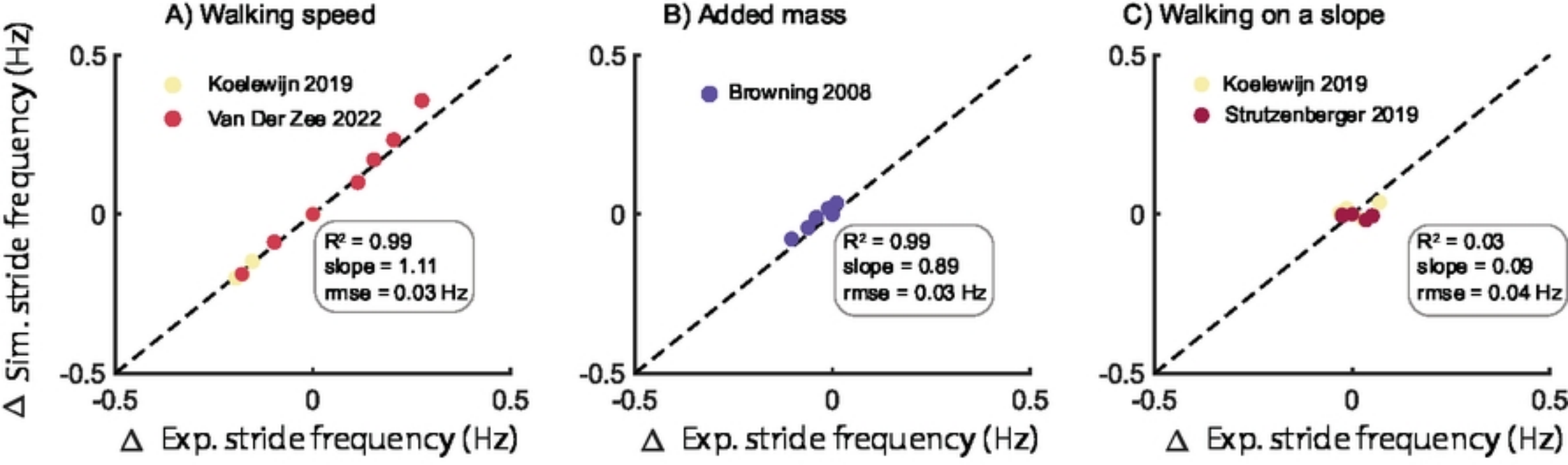
A) Walking speed
Koelewijn 2019
Van Der Zee 2022
R² = 0.99
slope = 1.11
rmse = 0.03 Hz
B) Added mass
Browning 2008
R² = 0.99
slope = 0.89
rmse = 0.03 Hz
C) Walking on a slope
Koelewijn 2019
Strutzenberger 2019
R² = 0.03
slope = 0.09
rmse = 0.04 Hz
Δ Sim. stride frequency (Hz)
Δ Exp. stride frequency (Hz)
0.5
0
-0.5

Figure 1

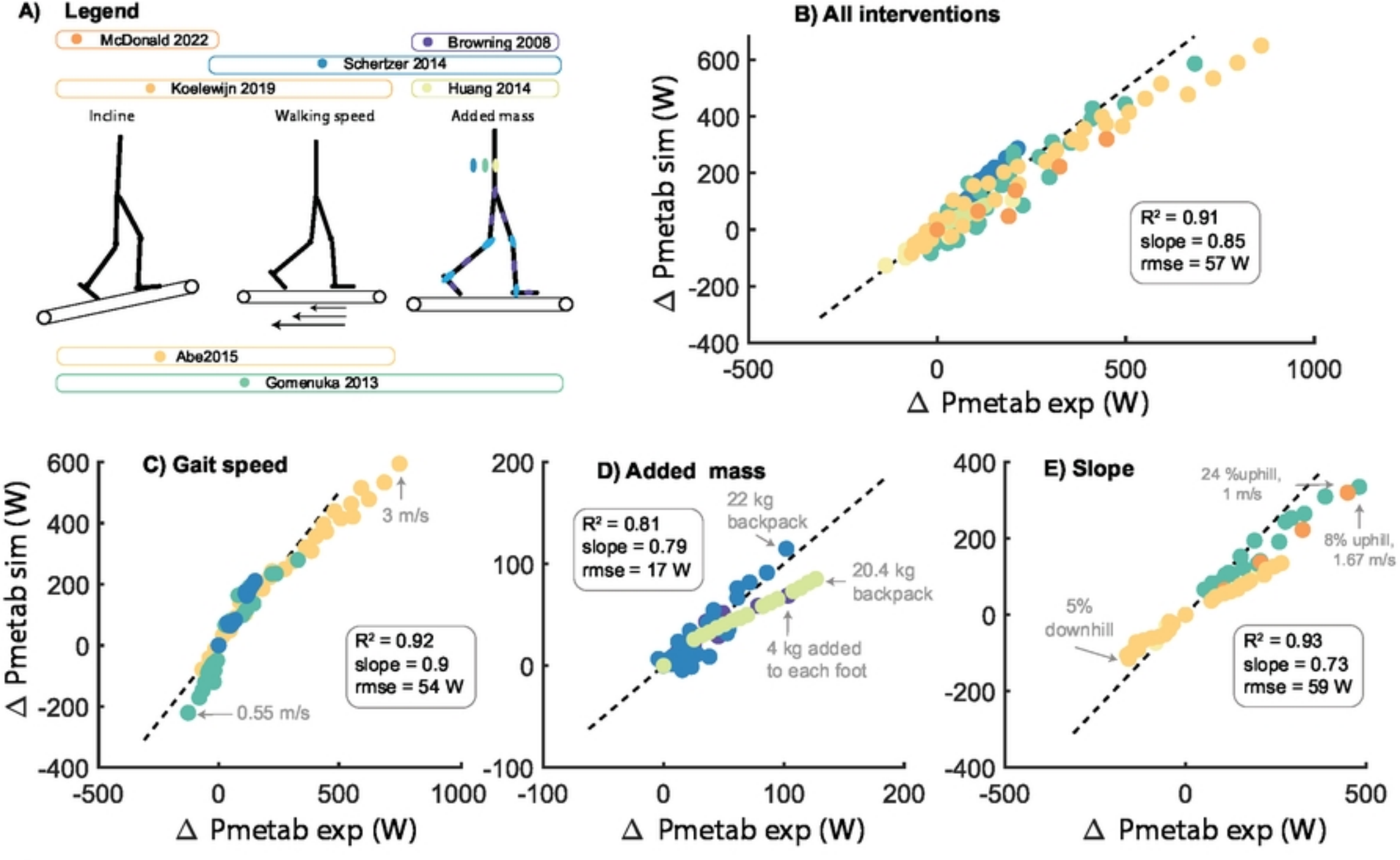
A) Legend
McDonald 2022
Browning 2008
Schertzer 2014
Koelewijn 2019
Huang 2014
Incline
Walking speed
Added mass
Abe2015
Gomenuka 2013
B) All interventions
Δ Pmetab sim (W)
Δ Pmetab exp (W)
R² = 0.91
slope = 0.85
rmse = 57 W
C) Gait speed
3 m/s
0.55 m/s
R² = 0.92
slope = 0.9
rmse = 54 W
D) Added mass
22 kg backpack
20.4 kg backpack
4 kg added to each foot
R² = 0.81
slope = 0.79
rmse = 17 W
E) Slope
24 %uphill, 1 m/s
8% uphill, 1.67 m/s
5% downhill
R² = 0.93
slope = 0.73
rmse = 59 W

Figure 2

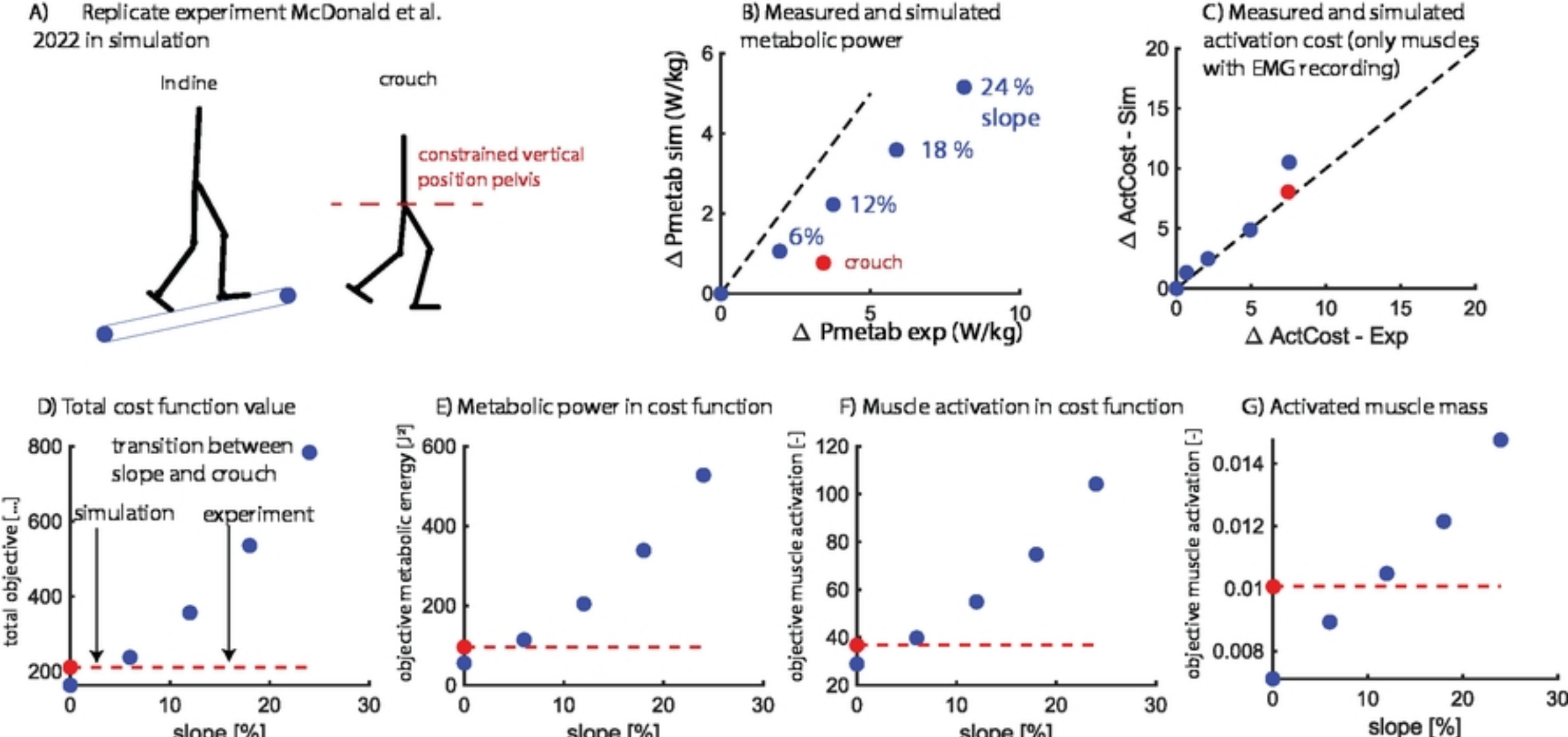
A) Replicate experiment McDonald et al. 2022 in simulation
Indine
crouch
constrained vertical position pelvis
B) Measured and simulated metabolic power
Δ Pmetab sim (W/kg)
Δ Pmetab exp (W/kg)
24 % slope
18 %
12%
6%
crouch
C) Measured and simulated activation cost (only muscles with EMG recording)
Δ ActCost - Sim
Δ ActCost - Exp
D) Total cost function value
transition between slope and crouch
simulation
experiment
total objective [...]
slope [%]
E) Metabolic power in cost function
objective metabolic energy [J²]
slope [%]
F) Muscle activation in cost function
objective muscle activation [-]
slope [%]
G) Activated muscle mass
objective muscle activation [-]
slope [%]

Figure 3

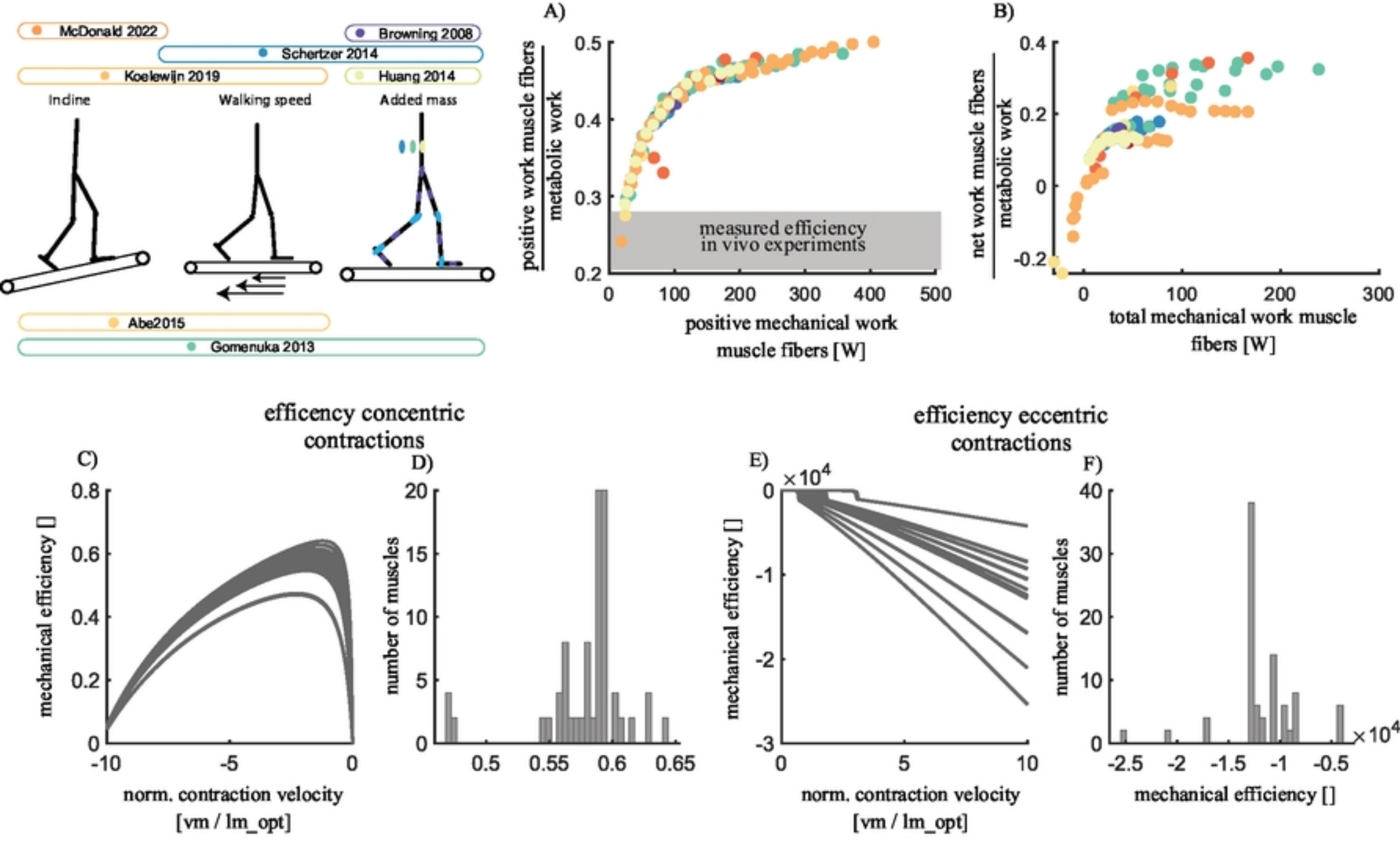
McDonald 2022
Browning 2008
Schertzer 2014
Koelewijn 2019
Huang 2014
Incline
Walking speed
Added mass
Abe2015
Gomenuka 2013
A)
positive work muscle fibers
metabolic work
measured efficiency
in vivo experiments
positive mechanical work
muscle fibers [W]
B)
net work muscle fibers
metabolic work
total mechanical work muscle
fibers [W]
efficency concentric
contractions
C)
mechanical efficiency []
norm. contraction velocity
[vm / lm_opt]
D)
number of muscles
efficiency eccentric
contractions
E)
mechanical efficiency []
norm. contraction velocity
[vm / lm_opt]
F)
number of muscles
mechanical efficiency []

Figure 4

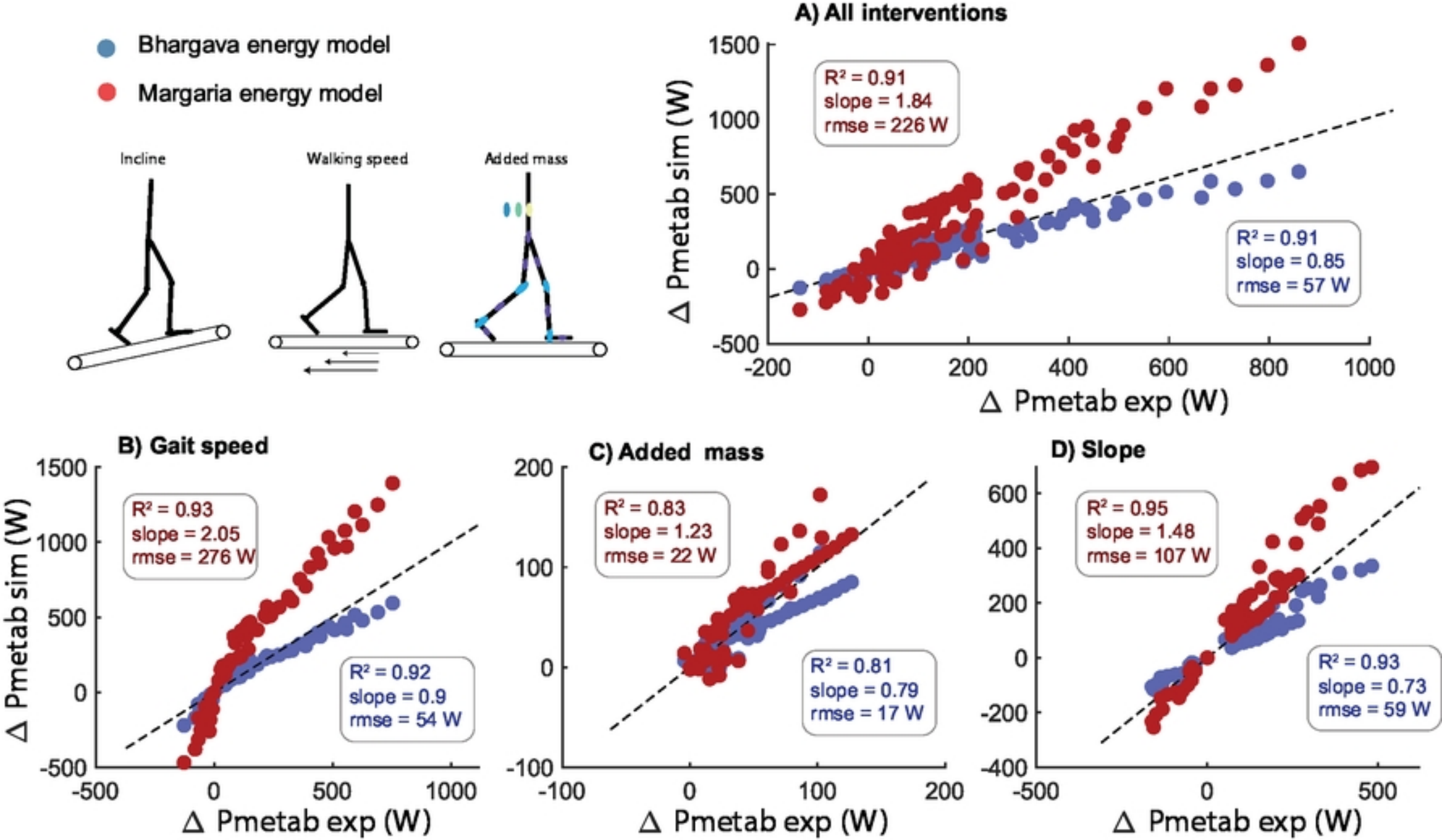
Bhargava energy model
Margaria energy model
Incline
Walking speed
Added mass
A) All interventions
R² = 0.91
slope = 1.84
rmse = 226 W
R² = 0.91
slope = 0.85
rmse = 57 W
Δ Pmetab sim (W)
Δ Pmetab exp (W)
B) Gait speed
R² = 0.93
slope = 2.05
rmse = 276 W
R² = 0.92
slope = 0.9
rmse = 54 W
C) Added mass
R² = 0.83
slope = 1.23
rmse = 22 W
R² = 0.81
slope = 0.79
rmse = 17 W
D) Slope
R² = 0.95
slope = 1.48
rmse = 107 W
R² = 0.93
slope = 0.73
rmse = 59 W

Figure 5

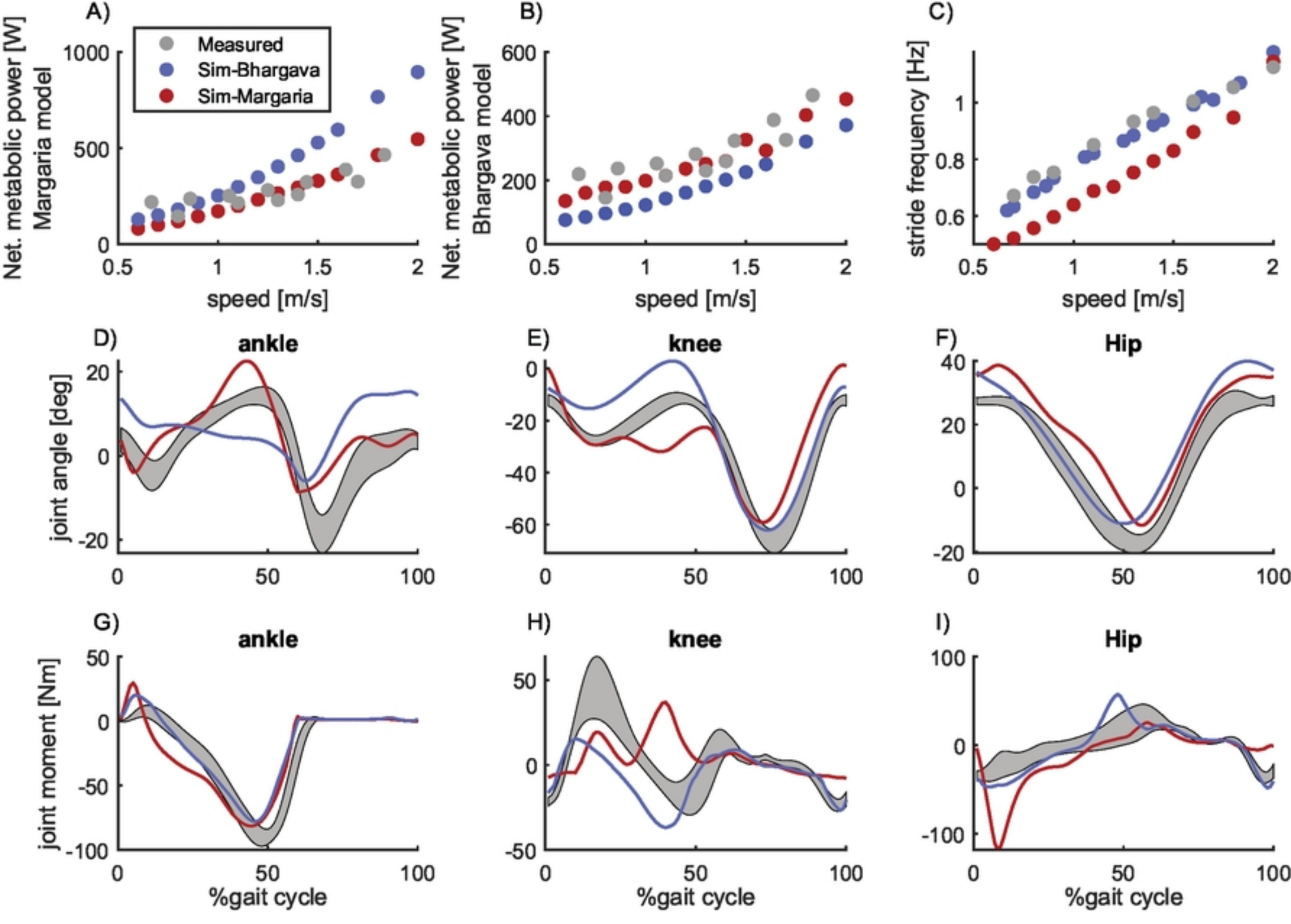
A)
Measured
Sim-Bhargava
Sim-Margaria
Net. metabolic power [W]
Margaria model
speed [m/s]
B)
Net. metabolic power [W]
Bhargava model
speed [m/s]
C)
stride frequency [Hz]
speed [m/s]
D)
ankle
joint angle [deg]
E)
knee
F)
Hip
G)
ankle
joint moment [Nm]
%gait cycle
H)
knee
%gait cycle
I)
Hip
%gait cycle

Figure 6