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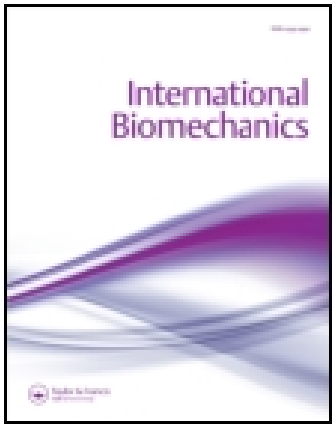

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Subject-specific scaling of cadaver-based musculoskeletal models is important for accurate musculoskeletal analysis within multiple areas such as ergonomics, orthopaedics and occupational health. We present two procedures to scale 'generic' musculoskeletal models to match segment lengths and joint parameters to a specific subject and compare the results to a simpler approach based on linear, segment-wise scaling. By incorporating data from functional and standing reference trials, the new scaling approaches reduce the model sensitivity to assumed model marker positions. For validation, we applied all three scaling methods to an inverse dynamics-based musculoskeletal model and compared predicted knee joint contact forces to those measured with an instrumented prosthesis during gait. Additionally, a Monte Carlo study was used to investigate the sensitivity of the knee joint contact force to random adjustments of the assumed model marker positions (+/− one marker diameter). The model based on linear scaling showed the highest variation in the knee joint contact force of 1.44 body weight (BW) around contra-lateral heel strike, and a variation in root mean square deviation (RMSD) of 0.36 BW. The proposed methods reduced the variation to 1.0 BW (RMSD 0.26 BW) for the anatomical landmark based method and 0.47 BW (RMSD 0.06 BW) for the functional based method. Variation in model predictions due to uncertainty in marker positions is a trait of all marker-based musculoskeletal modelling approaches. The presented methods solve part of this problem and rely less on manual identification of anatomical landmarks in the model. The work represents a step towards a more consistent methodology in musculoskeletal modelling.

Keywords: Musculoskeletal models; scaling; subject specific

Introduction

Subject-specific musculoskeletal models have the potential to assist in many clinical problems within rehabilitation and orthopaedics (Erdemir et al. 2007). Despite the potential, and the growing expectations of what computer models can achieve, clinical adoption of musculoskeletal models has been slow. Many barriers remain before models can achieve their full potential and, in recent years, increasing emphasis has been placed on the fidelity of musculoskeletal models and the assumptions upon which models rely (Lund et al. 2012).

The studies published in a recent special issue on musculoskeletal modelling of the lower limb in *Journal of Engineering in Medicine* are good examples of this trend (Bull & Cleather 2012). Eight of nine papers deal with validation issues and fidelity of models. However, none of these papers were concerned with the sensitivity of musculoskeletal models to modeller decisions. The dependency on the operator is especially relevant in the context of general musculoskeletal modelling packages such as LifeMOD (Lifemodeler Inc 2010), SIMM (Musculographics Inc 2013), AnyBody (Damsgaard et al. 2006) and OpenSim (Delp et al. 2007). Such modelling systems and their associated models have a host of parameters that require manual calibration before they can be applied to specific subjects or in specific applications (Lund et al. 2012).

The possibility of manual adjustment is a deceptive trait in a model. It allows experts to improve models, but it also carries the risk of transforming model calibration into model tuning, thus hiding the true uncertainty of the model. This can lead less experienced musculoskeletal modellers to incorrect conclusions. Models with a large dependency on implicit modeller decisions could, therefore, represent a risk.

It remains technically unfeasible to construct a musculoskeletal model directly from magnetic resonance (MR) images of a given subject. Musculoskeletal models are, therefore, based on cadaver data, which are scaled to match a specific subject using relatively simplistic linear scaling laws that do not change the joint orientations (Rasmussen et al. 2005). In inverse dynamics-based (Damsgaard et al. 2006) musculoskeletal models, the modeller typically has to manually scale each body segment and in some approaches also place the skin markers on the model in the locations corresponding to the placement on the subject during a motion capture experiment. Alternatively, optimisation can be used to compute the segment lengths and skin marker locations for a

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subset of the markers (Andersen et al. 2010), but the remaining markers have to be placed manually.

Many of these limitations do not exist in more traditional gait analysis where models are only used to analyse joint kinematics, moments and powers. For those models, both functional and anatomical scaling approaches are well established in literature. Unfortunately, the same methods have not been generally applied to musculoskeletal modelling, which are still relying on linear scaling techniques. Our work tries to bridge the gap between these fields by incorporating the functional and anatomical methods from traditional gait analysis into musculoskeletal modelling.

The purpose of this work was, therefore, (1) to show that simple linear scaling laws together with the modeller dependency may lead to important differences in the predictions of the model and (2) present two approaches that eliminate part of this problem by scaling cadaver-based musculoskeletal models to match both segment lengths and joint parameters of a specific subject based on either (i) the marker locations in a standing reference trial and regression equations for hip joint centre predictions or (ii) the marker locations in a standing reference trial and functional joint trials.

The study illustrates the linear scaling technique and the two proposed methods in three examples of inverse dynamics analysis to predict the knee joint contact force during gait. The predictions were validated against simultaneously recorded knee contact forces measured with an instrumented knee prosthesis.

Materials and methods

Experimental data

Data used in the examples come from a subject with an instrumented knee implant. The dataset was made public for the ASME 2012 Summer Bioengineering Conference as part of the third 'Grand Challenge Competition to predict In-Vivo Knee Loads' (Fregly et al. 2012). The subject was a 68-year-old woman (height 1.63 m, body mass 68 kg) with a left total knee replacement. The dataset provides a wealth of different data; see Fregly et al. (2012) for further details of the experimental protocol and set-up. However, this study only used the motion-related recordings of five trials of normal gait, as well as a standing reference and functional joint trials exercising the hip and ankle joint. This included recorded tibial implant forces, skin marker-based photogrammetric recordings and ground reaction forces from three force plates. Motion was recorded at 120 Hz with a 10-camera motion capture system (Vicon Corp., Oxford, UK). A Cleveland Clinic marker set-up was used with extra markers on the trunk and feet. Ground reaction forces were recorded at 1000 Hz with three force plates (Type 2, Bertec Corp., Columbus OH, US). Knee forces were measured at 50 Hz using an instrumented tibial prosthesis capable of measuring all six components of the tibial load (Kirking et al. 2006). The experiment was approved by the institutional review board, and subject had given informed consent to both data collection and public distribution.

Model overview

Models were developed in the AnyScript modelling language and compiled to run simulations with the AnyBody Modeling System V. 6.0.2 (AMS) (AnyBody Technology, Denmark). The three scaling methods were applied to the same musculoskeletal dataset serving the role of a generic template of the subject's anatomy. The template musculoskeletal model is based on measurements of a cadaver specimen (Klein Horsman et al. 2007), which has been implemented in AnyScript. For the sake of simplicity, a simple muscle model that neglects contraction dynamics was used. The only other change to the default implementation was a 35% reduction in strength of the knee extensor and flexor muscles in the leg with the knee prosthesis (left side). This choice was made since total knee arthroplasty patients are known to exhibit reduced knee flexor and extensor strength (Silva et al. 2003).

Although the two new methodologies presented in this study are substantially different from the traditional approach of linearly scaling musculoskeletal models, the actual implementation shares the same basic two-step structure: Firstly, the kinematic analysis uses an over-determinate kinematic solver (Andersen et al. 2009) to track the experimental markers in a least-squares sense. Secondly, the resultant set of joint angle trajectories were used to drive the inverse dynamic analysis model that computed the joint moments, muscle forces and joint reaction forces using the sum of cubed muscle activities as the muscle recruitment criterion.

Scaling methods

The flow diagrams of Figure 1 outline the structure of the three different scaling approaches: the *Linearly scaled model* (Figure 1(A)), the *Anatomical landmark scaled model* (Figure 1(B)) and the *Kinematically scaled model* (Figure 1(C)).

Linearly scaled model

The *Linearly scaled model* (Figure 1(A)) used a traditional approach in musculoskeletal modelling, where each segment was scaled linearly. This is currently the standard method for the gait model examples included in the user-contributed model repository (the AnyBody Managed Model Repository (AMMR)) accompanying

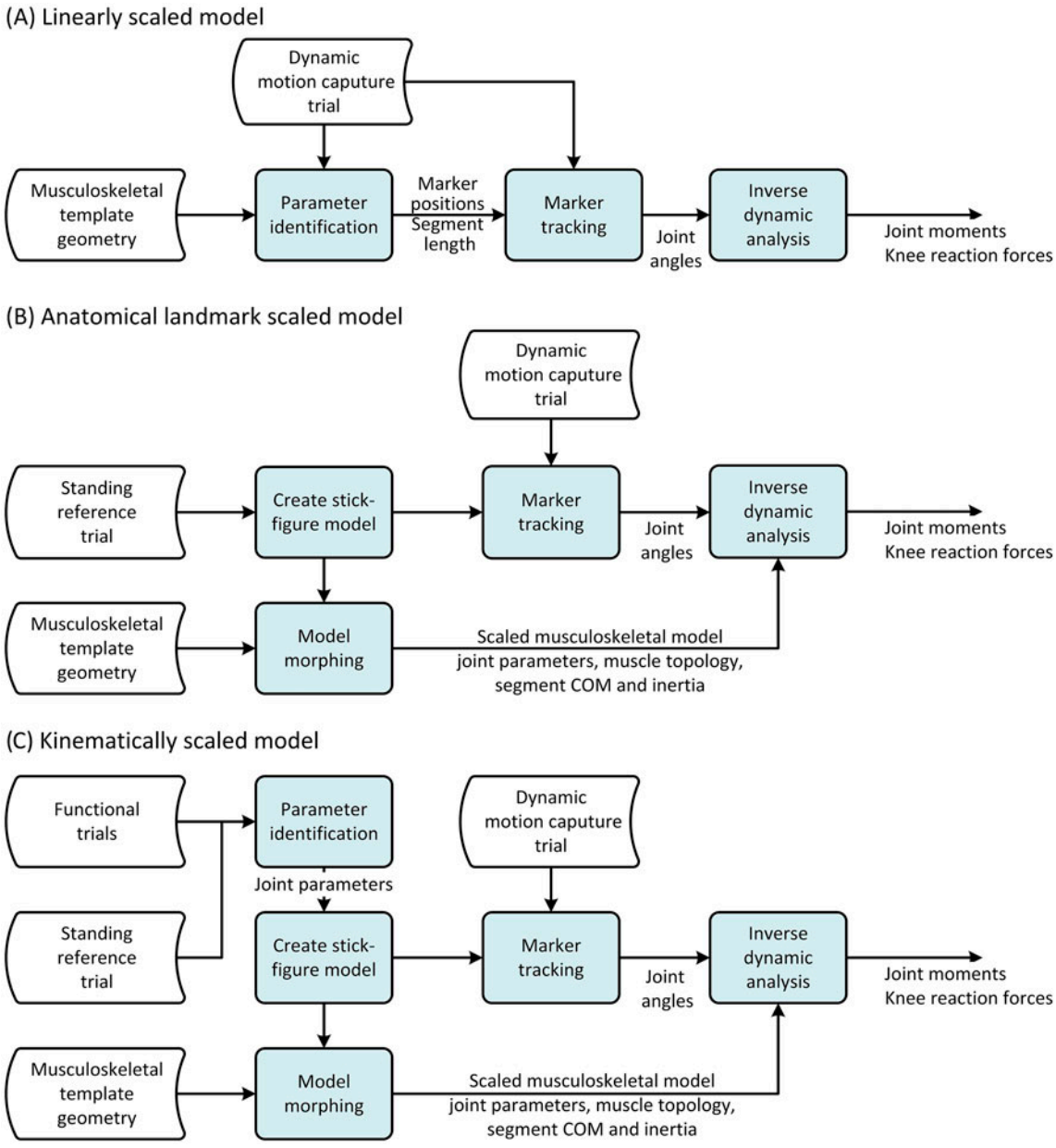

Figure 1. Schematic overview of the three models. (A) The *Linearly scaled model* relies on the dynamic trial itself to linearly scale the segments and calibrate marker positions. (B) The *Anatomical landmark scaled model* uses an additional standing reference as input. (C) The *Kinematically scaled model* uses an additional set of functional trials to obtain a subject-specific kinematic model.

the AnyBody Modeling System. The model was scaled based on the gait trial itself. The segment length (see Figure 2(B)) as well as local coordinates of markers not placed on anatomical landmarks were identified in an optimisation routine (Andersen et al. 2010). A more detailed description of the scaling method and the optimised parameters is supplied as supplementary material. The resulting scaled model was applied to track the markers of the gait trial, and the joint angles produced were used in an inverse dynamic analysis to compute muscle and joint reaction forces.

Anatomical landmark scaled model

The first proposed method (Figure 1(B)) relies on a standing reference recording to create a stick-figure model. The joint parameters of the stick-figure model were computed directly from the optical markers placed on anatomical landmarks. The kinematic representation of the subject was then registered to a cadaver-based musculoskeletal dataset. From this registration, a non-linear transformation was created by which the cadaver-based dataset was scaled (morphed) to match the subject-specific joint parameters. The morphing was

implemented using radial basis functions (RBF) to interpolate between the registered points. Thus, given an appropriate marker protocol, this approach directly provides the scaling of the musculoskeletal model without the need for additional inputs from the modeller. A detailed description of the scaling method and RBF interpolation is provided as supplementary material.

Finally, the stick-figure model was applied to track the markers of the dynamic motion capture trial to compute the joint angles over the entire trial. The joint angles and the scaled (morphed) musculoskeletal model were subsequently used in the inverse dynamic analysis.

Kinematically scaled model

The second proposed method (Figure 1(C)) takes this idea a little further and eliminates the dependency on correct marker placement in the experiment. Using a gait trial as a functional trial, this approach finds the subject-specific joint parameters through an optimisation-based method for parameter identification. The result is a kinematic representation of the subject entirely based on functional trials. This is similar to the multi-joint method proposed by Reinbolt et al. (2005) and minimises the least-squares error between model markers and markers from motion capture experiments. The joint parameters, local positions and rotations, of the hip, knee, ankle and subtalar joint were used as design variables. The complete model had 27 design variables for each leg; six for the hip, nine for the knee and 12 for the ankle complex (see Figure 2). Although it is theoretically possible to identify most parameters from a single functional activity, such a single activity trial rarely involves sufficient range of motion of all degrees-of-freedom (DOF) in order to reliably identify all joint parameters. To overcome this problem, extra functional trials exercising the hip and ankle joint complex were used to calibrate the parameters of the hip and ankle joints. A few parameters, for example, the pelvis hip joint position in the sagittal plane, were subsequently used as constraints in the multi-joint parameter identification (see Table 1). The rest of the method is similar to the *Anatomical landmark scaled model* and a detailed description of this method is also provided in the supplementary material.

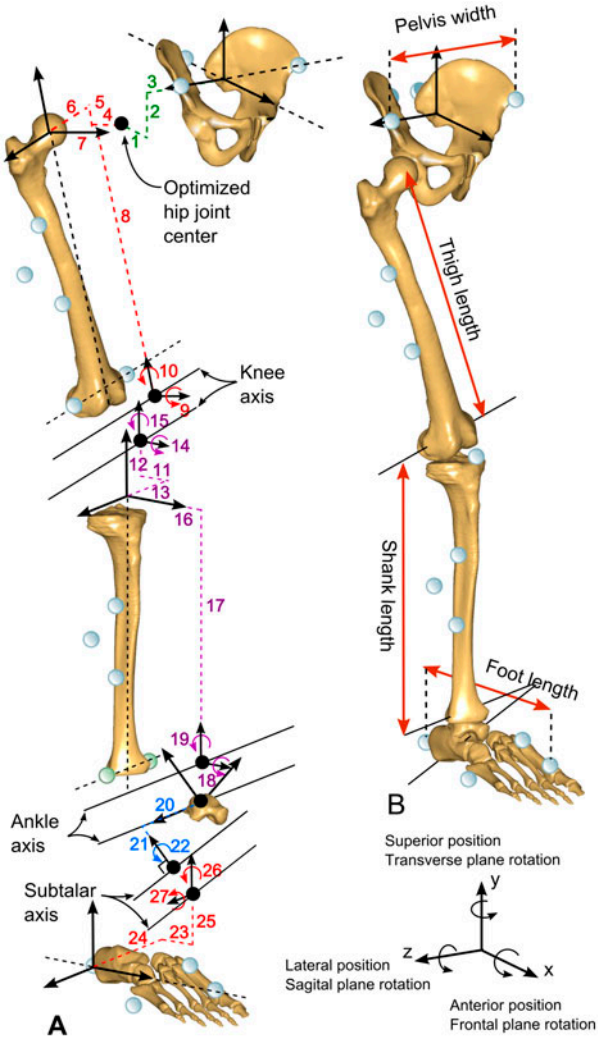

Figure 2. (A) Structure of the *Kinematically scaled model* for one leg. The numbered joint parameters are scaled to minimise marker error, see Table 1 for a list of design variables. (B) Structure of the *Linearly scaled model*. Pelvis width, thigh length, shank length and foot length are optimised along with some markers' local positions (see supplementary material for a detailed list).

Data analysis and model comparison

The three model approaches were applied to the same five gait trials of normal walking available in the dataset. The results of the three modelling approaches were compared at different steps in the modelling process. The joint parameters, the joint angles and marker errors were extracted from the kinematic analysis. The joint moments were extracted from the inverse dynamic analysis and compared between the three modelling approaches. The knee joint reaction force in the superior direction of tibia was also extracted and compared with the total contact knee force measured experimentally by the instrumented knee prosthesis. Differences between models were assessed using root mean square deviations (RMSD) and the coefficient of determination (R^2).

Joint coordinate systems

To ensure comparability between joint angles of the three modelling approaches, identical marker-based anatomical reference frames (ARFs) were added to every segment in the models. The ARFs were added in post-processing by loading the scaled models with the photogrammetric data

Table 1. Summary of the joint parameters of the three models.

Segment/Joint	Variable name	Design var. #	Unit	*Anatomical landmark scaled model*	*Kinematically scaled model*		*Linearly scaled model*	
					Single joint trials (hip & ankle)	Multi-joint functional trials		
Pelvis/Hip	Anterior pos.	1	mm	−64	−105	←	−92	(0.8)
	Superior pos.	2	mm	−88	−89	−84 (2.1)	−81	(0.5)
	Lateral pos.	3	mm	−114	−94	←	−90	(0.4)
Thigh/Hip	Anterior pos.	4	mm	0	−80	−31 (1.6)	−34	(0.9)
	Superior pos.	5	mm	0	−16	14 (3.0)	5	(0.4)
	Lateral pos.	6	mm	14	37	20 (1.3)	28	(0.2)
Knee	Anterior pos.	7	mm	0		9 (0.8)	5	(0.4)
	Superior pos.	8	mm	−422		−426 (2.1)	−446	(0.8)
	Lateral pos.		mm	–		–	−4	(0.2)
	Frontal plane rot.	9	°	0		7 (1.2)	1	(0.0)
	Transverse plane rot.	10	°	0		−8 (0.8)	−3	(0.2)
Shank/Knee	Anterior pos.	11	mm	0		10 (0.8)	3	(0.5)
	Superior pos.	12	mm	0		−7 (1.3)	−25	(0.8)
	Lateral pos.	13	mm	6		5 (0.4)	4	(0.2)
	Frontal plane rot.	14	°	−6		3 (1.1)	−6	(0.0)
	Transverse plane rot.	15	°	5		0 (0.9)	2	(0.2)
Ankle	Anterior pos.	16	mm	0	−16	1 (3.1)	−7	(0.1)
	Superior pos.	17	mm	−423	−423	←	−419	(0.2)
	Lateral pos.		mm	–	–	–	6	(0.1)
	Frontal plane rot.	18	°	0	−8	←	−10	(0.0)
	Transverse plane rot.	19	°	0	−7	←	15	(0.2)
Talus/Ankle	Anterior pos.		mm	–	–	–	−2	(0.2)
	Superior pos.		mm	–	–	–	8	(0.1)
	Lateral pos.		mm	–	–	–	6	(0.1)
	Frontal plane rot.		°	–	–	–	5	(0.1)
	Transverse plane rot.		°	–	–	–	17	(0.1)
Subtalar	Anterior pos.		mm	–	–	–	−4	(0.2)
	Superior pos.	20	mm	−10	−4	←	−13	(0.1)
	Lateral pos.	21	mm	0	7	←	1	(0.1)
	Frontal plane rot.		°	–	–	–	0	(0.2)
	Transverse plane rot.	22	°	−15	−18	−27 (0.7)	−13	(0.1)
Foot/Subtalar	Anterior pos.	23	mm	81	81	79 (3.0)	81	(0.1)
	Superior pos.	24	mm	22	32	32 (0.8)	17	(0.2)
	Lateral pos.	25	mm	0	−1	4 (0.4)	1	(0.1)
	Transverse plane rot.	26	°	−25	−29	←	−16	(0.0)
	Sagital plane rot.	27	°	42	30	←	48	(0.1)

Note: Joint parameters are relative to the reference frames defined by the standing reference markers. For the *Anatomical landmark scaled model* and the *Kinematically scaled model,* all parameters marked with '-' indicate values that default to zero due to the definition of the reference frame. Parameters marked with '←' under multi-joint trials are constrained to the values obtained during single joint optimisation. The values with appended parentheses indicate the mean value and standard deviation (mean (std.)), when applying the scaling procedure to all five gait trials.

from the standing reference. First, the over-determined kinematics were solved for a single time step to align the model markers with the experimental markers in the standing reference. Secondly, the ARFs were defined based on the measured skin marker positions and registered to the scaled musculoskeletal model. ARFs were added proximally and distally of each joint. For the hip joint and the ankle joint complex, the ARFs follow the recommendation of the International Society of Biomechanics (ISB) (Wu et al. 2002). In the lack of standardised recommendations for the knee joint, a definition following the same principles as the ISB recommendations was used. The precise definitions are provided in the supplementary material.

Knee force sensitivity to model marker positions

The manual placement of the skin markers on the *Linearly scaled model* has a direct effect on the resultant kinematics and the joint moments for those markers that are not optimised. This is not the case for the *Anatomical landmark/Kinematically scaled models*, because the manual step of locating the markers with respect to the joint parameters has been eliminated.

In all three approaches, the choice of model marker positions influences the muscle moment arms. This happens because the position of the pelvis markers and foot markers in the experiment must be registered to their counterparts on the musculoskeletal template dataset

Table 2. Summary of knee contact force predictions.

			Monte Carlo study			
			Best result		Worst result	
Scaling method	RMSD	R^2	RMSD	R^2	RMSD	R^2
Linearly scaled model	0.36	0.89	0.27	0.82	0.62	0.92
Anatomical landmark scaled model	0.64	0.73	0.48	0.71	0.74	0.78
Kinematically scaled model	0.28	0.90	0.25	0.88	0.31	0.91

Note: Difference between predicted and experimental values is given as RMSD [BW] and coefficient of determination (R^2). The simulation that provided the best and worst RMSD value in the Monte Carlo study is also shown.

(see Section 1.2.2 in the supplementary material for additional details).

The sensitivity of manual marker placements on the knee contact force was quantified with a Monte Carlo study. The entire analysis of a single gait trial was repeated 1000 times for each of the three examples. To simulate the effect of different choices of model marker positions, a random offset of +/− one marker diameter (10 mm) was added to the model markers. This involved six markers for each side of the body for the *Linearly scaled model* and five markers in the case of the *Anatomical landmark/Kinematically scaled model*.

Results

Joint parameters

A summary of the joint parameters with respect to the ARFs is listed in Table 1. A notable difference was the optimised hip joint positions in the thigh ARF that deviated 59 mm between the unloaded hip functional trial and the loaded gait trial used for functional optimisation. Here, the hip joint centre from the loaded multi-joint trial was placed more anteriorly and closer to the regression-based hip joint centre of the *Anatomical landmark scaled model*. Another noteworthy difference was the hip joint position in the pelvis segment, where the joint centre was located 41 and 28 mm more anteriorly compared with the *Kinematically scaled model* and *Linearly scaled model*, respectively.

The *Design var* numbers in Table 1 indicate the parameters, which were optimised in the *Kinematically scaled model*, see also Figure 2(A). The results of multi-joint optimisation are listed as mean values and standard deviations to provide an indication of the reliability of repeating the modelling procedure using any of the five gait trials as the dataset for parameter identification. No uncertainty information is provided for the single joint functional trials, since the dataset did not contain multiple repetitions of these trials. The highest uncertainty was observed for the anterior/posterior position of the ankle joint centre with a standard deviation of 3.1 mm in the shank segment (parameter 16) and 3.0 mm in the foot segment (parameter 23). The corresponding highest uncertainty for the rotational parameters was 1.2° for the frontal plane orientation of the knee joint axis in the thigh segment (parameter 9 on Figure 2(A)). The uncertainty in the parameters of the *Linearly scaled model* was generally smaller with largest positional and rotational standard deviation being 0.9 mm and 0.2°, respectively.

Marker errors

The marker errors (+/− 1 standard deviation) for the three models are compared in Figure 3. The *Anatomical landmark scaled model* (Green) had the highest average marker error of 6.8 (SD 3.0) mm. The *Linearly scaled model* (Blue) and the *Kinematically scaled model* (red) had similar average marker errors of 4.5 (SD 2.8) mm and 4.9 (SD 2.9) mm, respectively.

Joint angles and joint moments

Joint kinematics were similar between the three models for the major DOF; hip flexion, knee flexion and ankle

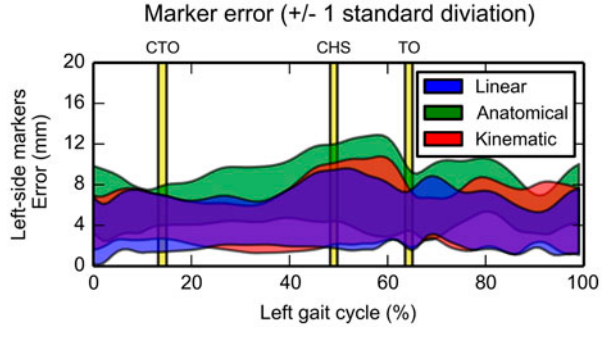

Figure 3. Marker errors (+/− one standard deviation) for the left gait cycle over all five gait trials. Data only display marker error for the left side. Vertical bars represent the timing of the gait events. CTO: Contra-lateral toe-off. CHS: Contra-lateral heel-strike. TO: Toe-off.

dorsi flexion, see Figure 4. Differences that are more notable occur for the remaining DOF such as hip abduction, ankle internal rotation and ankle inversion. Joint moments are also similar for most DOF. Noteworthy differences were a decreased hip flexion moment and an increased hip abduction moment for the *Anatomical landmark scaled model*, as well as different values of the first peak of the knee flexion moment for all three examples.

Knee forces and sensitivity to changes in model marker positions

The knee contact force sensitivity to marker positions in the modelling process is illustrated for the left leg with a single gait trial in Figure 5. The figure shows the total joint contact force as well as the corresponding force recorded by the instrumented knee implant. Ranges indicate the minimum and maximum forces obtained in 1000 Monte Carlo repetitions of each of the three model-

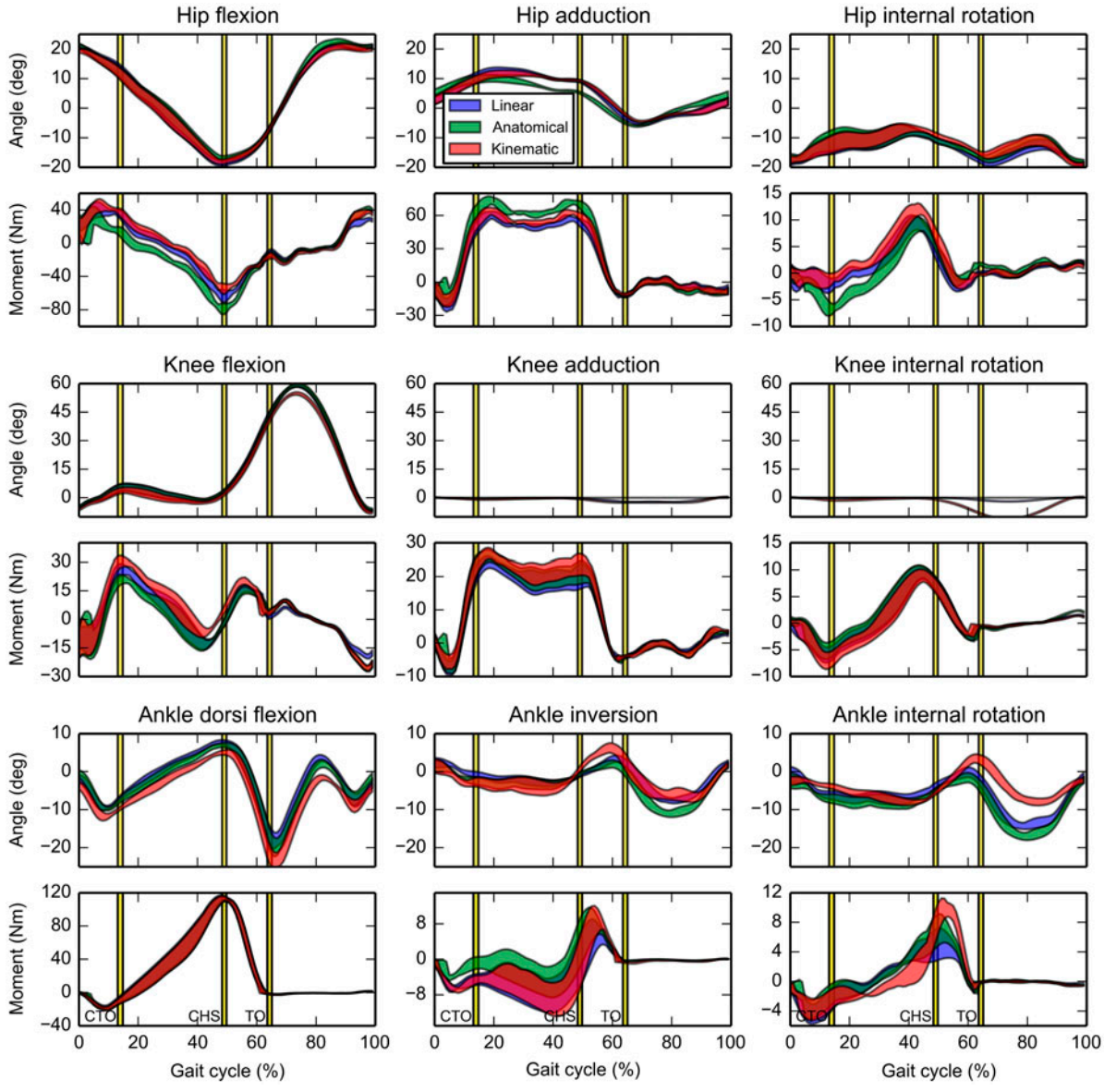

Figure 4. Left leg joint angles and moments for the hip joint, knee joint and ankle joint complex. Ranges indicate the minimum and maximum values from the five gait trials. All models have revolute knee joints, thus knee adduction and knee internal rotation are purely kinematic cross-talk (please refer to the Discussion). Note that the joint moments are expressed as projections of the joint moment vector onto the three rotation axes. Vertical bars represent the timing of the gait events. CTO: Contra-lateral toe-off. CHS: Contra-lateral heel-strike. TO: Toe-off.

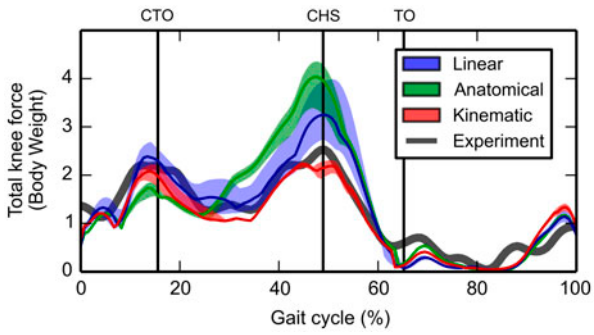

Figure 5. Sensitivity of the knee joint contact force to adjustment of marker positions in the modelling process. The result is illustrated for a single gait trail and compared with the measured force (bold solid line) from the instrumented knee implant. The thin lines indicate that the model-predicted knee force and the shaded area are minimum/maximum values from the Monte Carlo study. Monte Carlo results were generated by repeating the modelling process 1000 times with a uniform random offset (+/− one marker diameter, 10 mm) to the tunable marker positions.

ling processes. In all three examples, the computed muscle force and joint reaction force were sensitive to the choice of model marker positions. The highest range of knee forces was observed in the *Linearly scaled model* around the peak force at contra-lateral heel strike. The force varied by 1.44 body weight (BW) from 2.53 to 3.97 BW. The corresponding variation in the *Anatomical landmark scaled model* was 1.03 BW (3.21–4.24 BW) also at contra-lateral heel strike. For the *Kinematically scaled model*, the highest variation was 0.47 BW (1.63–2.11 BW), which occurred around the first peak at contra-lateral toe-off.

Table 2 shows the RMSD in BW and coefficient of determination (R^2), when comparing the predicted knee contact force with the force measured by the instrumented tibial implant. The *Kinematically scaled model* performed far best with a RMSD value of 0.28 BW and an R^2 value of 0.90. The table also shows the two simulations from the Monte Carlo study that gave the best and worst RMSD values, which showed the smallest span for the *Kinematically scaled model*.

Discussion

The purpose of the present investigation was (1) to show that simple linear scaling laws together with modeller decisions may lead to important differences in the predictions of the model and (2) present two approaches that eliminate part of this problem by scaling cadaver-based musculoskeletal models to match both segment lengths and joint parameters of a specific subject. The two scaling methods use either a standing reference trial or a standing reference trial together with functional joint trials. The three scaling approaches were applied to an inverse dynamic analysis-based musculoskeletal model and used to estimate joint angles, moments and joint contact forces. The influence of the scaling method on the motion reconstruction as well as the sensitivity of the knee contact force to manual adjustments of model marker positions was quantified.

Identification of joint parameters

The definition of reference frames must be kept in mind when comparing the results, e.g. the numbers in Table 1. The reference frames of the *Anatomical landmark scaled model* were used for reporting results of all methods. The axis definitions depend on the placement of markers on external anatomical landmarks. Thus, many of the joint parameters are by definition zero for the *Anatomical landmark scaled model*, and part of the deviation of joint parameters in the other methods may be attributed to inaccurate placement of markers in the experimental set-up. However, differences in joint parameters were also seen between the single and multi-joint trials for the *Kinematically scaled model*. Especially, the hip joint position in the thigh ARF changed by almost 6 cm. This could indicate that soft tissue artefacts (STA) affect the joint parameters differently in the functional hip trial compared with the multi-joint trial that is based on gait. However, single joint functional trials are necessary to identify some joint parameters, because gait as a functional trial does not provide sufficient articulation of all DOF.

The reliability of different joint parameter identification methods has already been addressed in the literature. Della Croce et al. (2005) provide an extensive review of the precision and potential pitfalls of anatomical landmark-based methods. The performance of functional methods has also been investigated in the literature although to a lesser extent, since these methods are still evolving (Besier et al. 2003; Pohl et al. 2010). No studies have reported the accuracy of multi-joint optimisation. Neither does this study, but it provides a clue to the repeatability of the multi-joint methods, since each of the five gait trials in the dataset could serve the role of a functional trial. However, since the markers were not re-attached to the subject between the trials, the repeatability error is likely underestimated. The single highest standard deviation in the positional joint parameters for the multi-joint trials was 3.1 mm for the anterior/posterior position of the ankle joint in the shank reference frame. With the exception of the ankle, the highest variations were observed for parameters related to the superior/inferior direction.

The *Linearly scaled model* had a noteworthy lower standard deviation in the joint parameters. This is not surprising as the uncertainty was distributed over twice

as many parameters, i.e. all of the coordinates of the anatomical frames. At the same time, the number of DOF in scaling the model was lower (seven parameters, one per segment), while the multi-joint optimisation included 36 parameters. With fewer DOF for scaling, the method is less prone to over-fitting and capturing the artefacts in the data, thus reducing standard deviation.

Marker errors

Marker error was a result of two distinct phenomena: (i) mismatch between the subject's true joint mechanics and the model representation and (ii) STA of the markers moving relative to the bone. In terms of the latter, attempts have been made to investigate the sensitivity of joint parameter optimisation to random noise in the marker data (Reinbolt et al. 2005). However, Andersen et al. (2012) recently demonstrated that marker error caused by STA is neither random nor independent and 95% of the cumulative marker error caused by STA during gait could be modelled with a linear model containing only four parameters. Therefore, it is not completely evident that the lower error exhibited by the *Linearly scaled model* and the *Kinematically scaled model* (Figure 3) was a result of the model's ability to capture the underlying subject-specific kinematics. It could be that the optimisation-based parameter identification techniques simply reduced the marker error by over-fitting the model to the data. The three models' mutual ability to track the subject-specific kinematics can only be investigated using more complex experimental studies that establish a gold standard to compare against, such as bone-pin or fluoroscopy experiments. Here, we should again mention that the kinematic errors seen in the *Anatomical landmark/Kinematically scaled model* are the same as those in traditional gait analysis and a large amount of the literature committed to validation of these methods are directly applicable (Besier et al. 2003; Della Croce et al. 2005; Pohl et al. 2010). For the *Linearly scaled model*, the same validation studies do not apply and care should be taken using a linearly scaled approach in the cases, where the subject's joint parameters differ in a non-linear manner from the joint parameters of the template geometry.

Joint angles and joint moments

The joint angles and moments in Figure 4 reveal that the three models showed the same overall trends for the major DOF, and the inter-trial variation was small. Please notice that non-zero articulations for knee adduction and internal rotation occurred for the *Linearly* and *Kinematically scaled model* only because joint reference frames were based on the ARFs, which did not align with the joint axis, i.e. these are purely kinematic cross-talk.

With measured external forces, the joint moments depend closely on the distance between joint centres and the applied external force vectors. The hip joint centre was located more lateral for the *Anatomical landmark scaled model*, which explains the higher hip adduction moment. Similarly, the knee joint moments at contra-lateral toe-off varied among all three methods. Differences agree with the anterior/posterior position of the knee joint (see Table 1, parameter 7, and 11). The *Kinematically scaled model* exhibited the highest knee external joint moment and had a more anteriorly located knee joint axis. This also illustrates the high sensitivity of all three modelling approaches to changes in joint parameters.

Knee contact force

The Grand Challenge Competition to Predict In Vivo Knee Loads has shown how difficult it is to accurately predict *in vivo* knee loads. Comparing the results of the competition to the results of this study is unfair, since the modellers in the competition were blinded to the experimental knee forces. However, from the third year of the competition (the same dataset used for this study), the competitors were also asked to provide un-blinded predictions after submitting the blinded results. Even though our study have only computed the total contact force, the RSMD of 0.28 BW, and R^2 of 0.90 for the *Kinematically scaled model* is better than the best-blinded and un-blinded results from the competition (0.34 BW and 0.89) (Kinney et al. 2013). In fairness, the goal in the un-blinded part of the competition was not to predict the total contact, but rather a compromise between the medial and lateral component of the contact force.

The predictions of the *Anatomical landmark scaled model* and the *Linearly scaled model* were not as good as the *Kinematically scaled model* (see Table 2). Figure 5 shows a large over-prediction of the second peak in the gait cycle. The peak occurred at collateral heel-strike just as the knee begins to flex and as the external knee moment changes sign from a knee extension to a knee flexion moment. The magnitude of the knee joint moment and the timing of when it changes sign is closely linked to the position of the knee joint centre. A more anteriorly located knee joint centre, as is the case of the *Kinematically scaled model*, causes the external moment to change sign earlier (see the knee joint moment in Figure 4). This is important because the knee contact force is very sensitive to the knee moment at this point in the gait cycle, because the knee flexion muscles have inefficient moment arms when the knee is fully extended.

The Monte Carlo study showed the minimum and maximum knee contact force from a relatively small

random perturbations of +/− one marker diameter. The shaded areas in Figure 5 indicate the result of the Monte Carlo study and Table 2 summarises them. The high peaks in the knee contact force for the *Linearly scaled model* and the *Anatomical landmark scaled model* were also reflected in the Monte Carlo study. Both models showed the largest differences at this point in the gait cycle. The *Linearly scaled model* had the largest difference in the RSMD values from the Monte Carlo study (0.27–0.65 BW). The *Anatomical landmark scaled model* had a smaller difference of RSMD values (0.48–0.74 BW), and the *Kinematically scaled model* had the smallest difference (0.25–0.31 BW).

Note that the lower limit from the Monte Carlo study of the *Linearly scaled model* (RSMD: 0.27 BW) is considerably smaller than the default result (RSMD: 0.36 BW) produced with our best guess of the model marker positions. It shows two interesting things. Firstly, it is possible to get a relatively good prediction of the total knee contact force using a simplified musculoskeletal model with linear segment-wise scaling, revolute knee joints and neglecting muscle contraction dynamics. Secondly, it shows that despite our best effort to create the best model, we were not manually able to find this optimal combination of marker positions that was generated in the Monte Carlo study.

General findings

With the exception of the general danger of introducing subjective input into the modelling process, the results of this paper cannot support the superiority of one scaling approach over the others. Achieving such a goal would require a more precise statement of purpose of the model. See Oberkampf and Trucano (2008) for a discussion of the special nature of validation experiments.

For general purpose investigations, the scaling methodologies should be applied on a large population of subjects. Doing so would require significantly more data and it was not the goal of this study. The dataset used in the present study was chosen for two important reasons. Firstly, the experimental work was from the beginning designed for benchmarking and validation purposes and not with a particular research question in mind. Secondly, the open nature of the dataset and the fact that other groups have used the same dataset in their work to create musculoskeletal models creates the opportunity to compare results with other published research (Fregly et al. 2012; Chen et al. 2014). Finally, it allows sharing of the models without the ethical or legal problems, often affiliated with human subject data. Thus, the dataset provides an excellent base for presenting and comparing new methods.

Modelling procedures were implemented within the framework of the AnyBody Modeling System, but the basic concepts are generally applicable. Relying on a modelling system (like the AnyBody Modeling System or any other generally available modelling package) to illustrate the scaling concepts implies some limitations to what can be achieved, depending on the possibilities of the chosen framework. Nonetheless, it also has some important advantages. It makes it possible to build upon the works of others, which has been exploited in the current study by taking the existing implementations of the Klein Horsman et al. (2007) cadaver dataset to serve the role of a musculoskeletal template geometry. Most importantly, it allows others to scrutinise the results, extend the work or just reuse ideas. The field of musculoskeletal modelling is still maturing. Thus, models and methodologies are likely to improve and change rapidly, making journal publications an inefficient way to communicate new methods, unless papers are accompanied by supplementary material allowing readers to reuse the methods and recreate the results. All the models used in this paper are, therefore, provided for readers to scrutinise and recreate the results. Furthermore, to allow the models to continuously change and improve over time, we are in the process of adding these new modelling approaches to the user-contributed repository of modelling examples available for the AnyBody Modeling System. Until that happens, the models will be available in an online version control system (https://github.com/AnyBody-Research-Group/LowerExtremity-RBF-scaling).

Conclusion

Variation in model predictions due to uncertainty in marker positions is a trait of all marker-based musculoskeletal modelling approaches. This study presented two approaches to scale musculoskeletal models, which reduce sensitivity to manual adjustments of the assumed model marker positions in the modelling process. This was accomplished by replacing the implicit dependency on manual skin marker placements with data from standing reference and functional trials. This work also illustrates how large the implicit uncertainty may be in models based on linear segment-wise scaling. This kind of scaling approach have been used in numerous published studies that use musculoskeletal models (Rasmussen et al. 2012; Alkjaer et al. 2012; Ali et al. 2014; Oliveira et al. 2013; Chen et al. 2014). To our knowledge, none of these studies have explicitly quantified sensitivity to manual adjustments in the modelling process and care should be taken when interpreting the results.

Conflict of interest disclosure statement

No potential conflict of interest was reported by the author(s).

Supplemental data

Supplemental data for this article can be accessed at http://dx.doi.org/10.1080/23335432.2014.993706.

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