Validation of a Lower-limb Musculoskeletal Model for the Estimation of Hip Joint Contact Forces using an Energy-based Cost Function

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ABSTRACT

The present work aims to determine the musculoskeletal loading conditions during gait for two studied patients and compare these findings with *in vivo* data and literature. The relative contribution of three muscular energy consumption processes incorporated in an energy-based cost function for solving the redundant muscle force sharing problem are evaluated using *in vivo* data.

In a context of multibody dynamics, a three-dimensional biomechanical model for the lower limb based is presented. The biomechanical model consists in a lower limb representation for the human motion analysis with small influence of the upper limbs, such as gait. The anatomical articulations are approximated by ideal mechanical joints and the muscles are included in the system as two-point actuators.

Gait analyses are conducted using the kinematic and kinetic data for two patients using instrumented hip prosthesis that measure *in vivo* contact forces. The muscle and joint contact forces are calculated using inverse dynamic optimization. A static optimization technique is used to find the solution for the redundant muscle force sharing problem. The optimization consists on the minimization of a cost function that represents a physiological criterion.

The relative contribution of the energy-related terms included is the energy-based criterion is evaluated by using the *in vivo* measurements of hip contact forces (HCF). The contribution of each term is discussed so that the optimization can lead to a closer match between the model obtained forces and the experimental measurements. The new identified weight factors result in improvements of the model HCF. The muscle forces and activations patterns are also evaluated and compared with literature. This comparison attempts to evaluate the accuracy of the biomechanical model and to identify what alterations can be made to obtain more accurate predictions of HCF.

Keywords

Musculoskeletal Model, Hip Contact Forces, Inverse Dynamics, Metabolic Energy Rate, Gait Analysis.

1. INTRODUCTION

Biomechanics is defined as the science that describes, analyses and assesses the physiology of living structures and animals using the laws of mechanics. The human motion is one of the objects of study in biomechanics (Winter, 2009). Important biomechanics research tools that helps to understand how the human body works include biomechanical models, consisting on a mathematical reproduction of the musculoskeletal biological systems in which the bones, articulations and muscles are included in the form of mechanical elements (Horsman, 2007). Musculoskeletal models can be applied not only to investigate the theoretical principles of the motion and control of biological systems but equally to applied research.

The human locomotion system is able to perform a wide variety of movements and, for every motion, the central nervous system selects a combination of muscles to activate in order to rotate the bones around the articulations (Carbone, 2016) to achieve the desired action. The knowledge of musculoskeletal loading is still limited (Yamaguchi et al., 1995; Carbone, 2016) i.e. the actual forces occurring *in vivo* are hardly accessible, since these forces arise from a complex interaction between the central nervous and musculoskeletal systems, owing to the redundancy of the muscle apparatus (Silva and Ambrósio, 2003). Computational biomechanical models combined with proper optimization techniques allow solving the musculoskeletal force redundancy and offer tools to estimate *in vivo* forces during motion (Yamaguchi et al., 1995; Heller et al., 2001; Praagman, 2008).

The preferred approach to solve the muscle-force sharing problem is an inverse dynamic analysis, where external forces and motion trajectories are the inputs of the optimization process. Therefore, kinematic and kinetic data must be collected beforehand using three-dimensional motion capture systems and force platforms. An important requirement to perform an inverse dynamic analysis is the definition of a cost function which best represents the physiological criteria adopted by the central nervous system to generate the muscular activation patterns needed to achieve a given motion (Rasmussen et al., 2001). Different cost functions have been proposed in the literature (Tsirakos et al., 2017). As expected, the optimal solution found must also satisfy the equations of motion applied for the biomechanical system (Silva and Ambrósio, 2003). The development of more refined optimization criteria that better represents the *in vivo* process is still an ongoing field of research. Several cost functions have been proposed in the literature (Tsirakos et al., 2017), most of which are mechanical cost functions based on muscle force (Collins, 1995; Crowninshield and Brand, 1981). However, more recently, an energy-related cost function representing the two major energy-consumption processes in the muscles was proposed by Praagman (2008).

The meaningfulness of the results of the computational biomechanical models in a key issue, as most of the results cannot be measured experimentally. The *OrthoLoad* project (Bergmann, 2008) provides a comprehensive dataset containing HCF measured *in vivo* for a number of daily activities, as well as kinematics and ground reacting forces. This data repository allows to evaluate the model accuracy by comparing the forces obtained computationally, when using the measured kinematics and GRF as an input, with *in vivo* measurements (Bergmann et al., 2016; Fregly et al., 2012).

The objective of the work now presented is to:

1. Validate the Lisbon Lower Limb Model (LLEM), a model based on the comprehensive dataset published by Horsman (2007).
2. Evaluate the relative contribution of the muscular energy consuming processes included in a muscle load sharing cost function proposed by Praagman et al. (2008).

The aim is to estimate the relative contribution of the processes included in the cost function, i.e. ion pumping and cross-bridges cycling, that can lead to a closer match between hip forces predicted by the model obtained forces and the experimental measurements. The musculoskeletal model is solved in an optimization environment to find the solution for the so-called “redundant muscle force sharing problem”, using an inverse dynamics approach. The model HCF predictions for gait motion of two *OrthoLoad* patients are compared with the respective *in vivo* measurements. Also, the muscle activations patterns and the forces developed are evaluated and compared with those presented in the literature. This comparison attempts to evaluate the accuracy of the biomechanical model and to identify upgrades that can be implemented to obtain more accurate predictions of HCF.

2. METHODS

2.1. The musculoskeletal model

The lower limb model used is based on the dataset of Horsman (2007) whose measurements were performed on a right lower extremity of a male cadaver at the age of 77, with weight 105 kg and height 1.74 m. Data for the left lower extremity is obtained by mirroring the data from the right lower extremity. The biomechanical model proposed is composed of 11 segments, including the pelvis and 5 segments for each lower limb, i.e. femur, patella, tibia, foot and hallux, assumed as rigid bodies. The rigid bodies for the unilateral model are connected by 5 mechanical joints, namely the hip, ankle, femur-patella, ankle and metatarsophalangeal, and 1 inextensible ligament between the patella and tibia. The hip is modelled as a spherical joints meaning that the connected bodies have 3 degrees of freedom (DOF). The knee, ankle and metatarsophalangeal joints are modelled as revolute joints with one DOF. The patella is connected to the tibia by the patellar ligament, assumed to be inextensible, and to the femur in the form of a revolute joint, representing the approximate circular path of the patella around the femur.

A total of 38 muscles were measured by Horsman (2007). Because some muscle lines of action have a large curvature, due to underlying bones and high muscular volume, two methods are used to describe the change in muscle force directions. Bony contours which characterise mathematically the geometry of underlying structures (van der Helm et al., 1992) are used to define the muscle line of action of the gastrocnemius around the femur condyle and the iliopsoas around the pubis of the pelvis. For 19 muscles, via points are used to split the muscles in a series of shorter muscle segments (Delp et al., 1990) as an attempt to better reproduce the muscle path and the different muscle sections behaviour. The 38 muscles are divided in 57 parts, containing up to 6 bundles, resulting in a total of 163 muscle elements, as proposed in the Horsman (2007) dataset.

2.2. Kinematics

The Charité in Berlin (Bergmann, 2008) measured the loads developed in human joint directly by using instrumented implants in several anatomical joints of different individuals, with hip or knee implants on those related to gait. These measurements were done for a number of daily activities, including gait. *OrhoLoad* (Bergmann, 2008) supplies not only the *in vivo* loads but also the kinematic data and the ground reaction forces. Table 1 summarizes the general anthropometric characteristics of the studied subjects.

Table 1: General anthropometric data of the two studied patients

Patient	Gender	Affected Leg	Age (year)	Weight (kg)	Height (cm)	Time post op. (months)
H2R	male	right	62	78	172	12
H1L	male	left	55	73	178	13

The kinematic data provided consists on the trajectory of reflective markers placed on the subject skin, following the recommendations of the International Society of Biomechanics (Wu et al., 2002). A total of 18 markers are used to track the lower limb motion. From the positions of bony landmarks, each anatomical segment coordinate frame is computed following the recommendations of the International Society of Biomechanics (Wu et al., 2002). The evolution of the angles between anatomical segments associated with the DOF of the biomechanical system are measured by processing the reflective markers acquired kinematics. Subsequently, the angles measured are prescribed in the LLEM by using rotational drivers. To ensure total consistency, the kinematic constraints of the system must be satisfied:

$$\mathbf{\Phi}(\mathbf{q},t)=\mathbf{0} \tag{1}$$

where $\mathbf{\Phi}$ represents the assemblage of all the constraint equations relative to the joints of the biomechanical model, $\mathbf{q}$ is the global positions vectors and t is time. The driving angles prescribed for the simulation are comparable with those published in the literature (Arnold and Delp, 2011; Kadaba et al., 1990).

2.3. Inverse Dynamic Analysis

An inverse dynamic analysis consists in obtaining the joint reaction and driving forces that the biomechanical model must produce to be mechanically consistent with a pre-defined dynamics response, i.e. a given motion under the action of externally applied forces. The ground reaction forces together with the gravitational forces, represent the externally applied forces in the biomechanical system during normal gait. In a dynamic analysis the equations of motion must be fulfilled, written as:

$$\mathbf{M}\ddot{\mathbf{q}}+\mathbf{\Phi}_q^T\boldsymbol{\lambda}=\mathbf{g} \tag{2}$$

where the matrix $\mathbf{M}$ denotes the global mass matrix, $\ddot{\mathbf{q}}$ is the vector of global accelerations, $\mathbf{g}$ is the vector of externally applied forces, $\mathbf{\Phi}_q^T$ is the Jacobian matrix and $\boldsymbol{\lambda}$ is the vector of Lagrange multipliers, each associated with a reaction force developed to satisfy to the respective kinematic constraint, which are the only unknowns of Equation (2) when performing an inverse dynamic analysis.

Being the HCF one of the results of the inverse dynamic analysis, the major advantage of the *OrthoLoad* data is to allow the comparison of these findings with the measured contact joint forces, provided for the captured and reconstructed motion of the subject. This comparison can determine if the predicted HCF are within the range of those found *in vivo* and help validating the lower limb model. In addition, they also serve as a reference to identify improvements in inverse dynamics optimization, when assessing the related parameters.

The muscles are included in the musculoskeletal model as one or several two-point actuators. The muscle is modelled as a mechanical element that simulates the muscular contraction dynamics using the Hill-type model presented in Silva and Ambrósio (2003). The dynamic properties of force-length and force-velocity relationships of the muscle tissue are included in the modelling. However, the activation dynamics was neglected for the sake of computational efficiency since it is expected to have low influence on the results (Anderson and Pandy, 2001). In force of the motion scenarios considered in this work the elasticity of the tendons of the lower limb are neglected, since the simulation of tendon elasticity strongly increases the computational time (Quental et al., 2018). Note that most studies also neglect tendon elasticity, supporting the suitability of this assumption.

The muscles of the leg under study, that is, the leg comprising the instrumented prosthesis, are considered two-point actuators in order to estimate correct hip joint reaction forces. In the contralateral leg, joint rotational drivers are considered for the sake of computational simplicity. The upper limb musculoskeletal structure is disregarded. The contribution of each muscle is added to the system as a constraint equation. Because the number of muscles is much larger than the number of DOF, the problem becomes indeterminate. From a biological point of view, the indeterminacy means that any given movement can be achieved by recruiting different combinations of muscles, sets of muscles, or by applying different activation levels. The muscle recruitment criteria is controlled by the central nervous system which, depending on the motion or posture to be achieved, selects the appropriate activation patterns.

2.4. Redundant Muscle Force Sharing Problem

The indeterminate problem described, usually referred in literature as ''the redundant muscle force-sharing problem'' (Yamaguchi et al., 1995), is generally solved using optimization procedures. This solution minimizes a given cost function while satisfying the equations of motion and other physiological constraints. A static optimization procedure is selected to solve the problem, meaning that the muscle load sharing problem is solved for each frame individually.

The optimization problem described can be formulated as (Quental et al., 2015):

$$\begin{gathered} \text{minimize } J_E = \sum_{i=1}^{n} \dot{E}_{mi} \\ \text{subject to } f_{mt} = \left(\mathbf{M}\ddot{\mathbf{q}} + \mathbf{\Phi}_{\mathrm{q}}^{\mathrm{T}}\boldsymbol{\lambda} - \mathbf{g}\right)_t = \mathbf{0} \\ 0 \leq a \leq 1 \end{gathered} \tag{3}$$

The objective function is a mathematical expression that attempts to simulate the muscle recruitment criteria adopted by the central nervous system. In the present work the muscle recruitment criterion adopted is an energy-related cost function based on physiological parameters proposed by Praagman (2008). This function, expressed in Equation (4), considers two biological processes that are assumed to be the major energy consuming mechanisms in the muscles: (1) the cross bridges detachment and (2) the calcium re-uptake.

$$\dot{E}_m = l_m F_m + wf_1 V_m a(t) + wf_2 V_m (a(t))^2 \tag{4}$$

The first term the is related to the distribution of attached cross-bridges in relation to the cross-bridge length. The second and third terms are related with the absorption/reabsorption of calcium ions in by a calcium pump and is proportional to the product of the total muscle volume and the active state. The energy required for the calcium re-uptake is not exactly known, but it is assumed to be a non-linear relationship with muscle force generation. Thus, a polynomial approximation is applied, resulting in one-linear term and a quadratic term. The constants wf_1 and wf_2 are weight values that determine the contribution of each term in the process.

2.5. Energy-Based Cost Function Identification

Although the energy comsuming processes are thoroughly described in Equation (4), the rational for selecting the weights of each one of them, wf_1 and wf_2, are not reported. To explore this option an analysis of the influence of each function term is conducted by comparing the forces predicted by the model to the *in vivo* forces measured by instrumented prostheses. The aim is to estimate the relative contribution of the processes included in the cost function, that can lead to a closer match between hip forces predicted by the model and the experimental measurements.

Because the first term of the objective function is much larger than the remaining terms, a scaling factor of 10^6 is considered to allow all terms to present similar orders of magnitude. Thus, in the following sections, for simplicity, the contributions of ω_1 and ω_2 are discussed, instead of the non-scaled weight factors wf_1 and wf_2, where:

$$wf_{1,2} = \omega_{1,2} \cdot 10^6$$

To quantify the similarities between the numerical HCF curve shape and that measured *in vivo*, three indicators are used: (1) root mean square error (RMSE), (2) relative deviation between force peaks (RDP), equivalent to the difference between the numerical and measured HCF at maximum peaks, and (3) the *Fréchet* distance (FD), which is another measure of similarity between two curves.

The first approach to the problem is done by analysing the individual contribution of each term, by running simulations where the cost function used is composed by only one of the three cost function terms at a time.

Next, the muscle force sharing problem is solved for different combinations of the weight factors by performing a grid search where the parameters are varied within a selected range. The weight factors ω_1 and ω_2 are varied between 0.01 and 100, considering a logarithmically spaced vector of 50 values, resulting in a *50x50* grid, i.e. 2500 weight factor combinations.

Considering a two-level optimization approach new weight factors are sought by minimizing the error between the computational and experimental HCF. The optimization of the weight factors is done using the *patternsearch* algorithm available in *MATLAB*. The algorithm consists on a numerical optimization method that does not use gradients for finding local minima. The objective of the optimization is only the minimization of the RMSE. The search was performed in the range of [0.01 100] by creating upper and lower bound constraints. Due to possible existence of local minima, the pattern search is run 10 times, starting from different initial conditions, i.e. different initial weight values, chosen arbitrarily.

3. RESULTS

3.1. Individual Contribution of the Weight Factors

The HCF estimated by these simulations are presented in Figure 1 and the goodness-of-fit indicators are presented in Table 2. The results show that when considering only one of the linear terms, i.e. either the first or the second term of Equation (4), the force predictions are similar, presenting only minor deviations. The individual contribution of these terms seems therefore to represent similar muscle recruitment criteria. The non-linear term leads to more unrealistic force predictions, which is especially highlighted by the over-estimation of the second peak of the HCF.

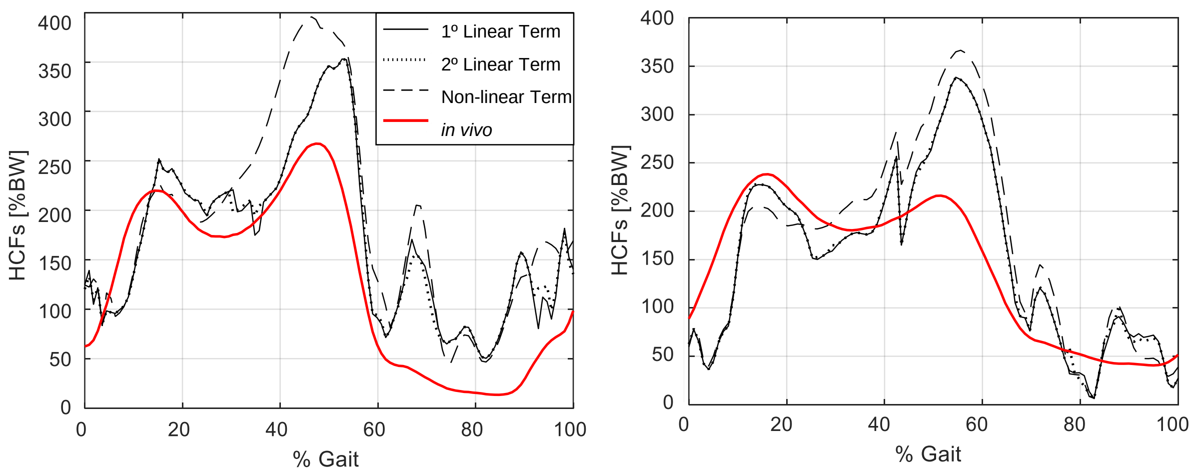

Figure 1: HCF considering individually each term of the energy-based cost function for (a) H2R patient and (b) H2R patient. The solid, dotted, and dashed lines represent the data obtained considering the first linear term, the second linear term and the non-linear term, respectively.

Table 2: Goodness-of-fit indicators for the HCF obtained for standard and individual contribution of each cost function term.

Subject	Term	RMSE [%BW]	RDP [%Exp.Peak]	FD [%BW]
H2R	First Linear Term	62,7	24,2	85,6
	Second Linear Term	63,4	24,3	86.0
	Non-linear Term	83,9	32,4	128,4
H1L	First Linear Term	58,1	29,6	107,4
	Second Linear Term	58,0	29,6	107.3
	Non-linear Term	73,5	35,0	134,3

3.2. Grid Search

The combinations of the weight factors associated with the best goodness-of-fit measurements differ from those originally recommended in the literature, resulting in improvements of the hip joint force predictions. However, no unique combination exists, i.e., different goodness-of-fit indicators may point towards different combinations, as shown in Figure 2. Moreover, note that for a given range of weight factors, differences between solutions are negligible, suggesting that many different weight factor combinations may lead to similar HCF predictions. Note that, in Figure 2, the dark blue area embraces multiple combinations of weight factors, for both patients. The results for both subjects seem to point towards the same direction. Overall, a small weight factor ω_2, lower than 20, and always smaller than ω1, leads to more realistic force predictions. For the H2R patient, weight factors ω_2 smaller than 10 are not satisfactory as well. The HCF prediction curves, illustrated in Figure 3, are under-estimated during initial stance and over-estimated during the late stance and swing phases for both patients. A high peak, much greater than *in vivo*, is observed at 50% of the gait cycle, i.e. at the end of the stance phase. Despite impacting the solution of the load sharing problem, the variation of the weight factors did not vary much the prediction of HCF, as highlighted in Figure 3. Note that the grey shadowed region represents the variation in HCF resulting from the application of the different weight factors considered. In any case, the optimization of the weight factors still leads to better force predictions.

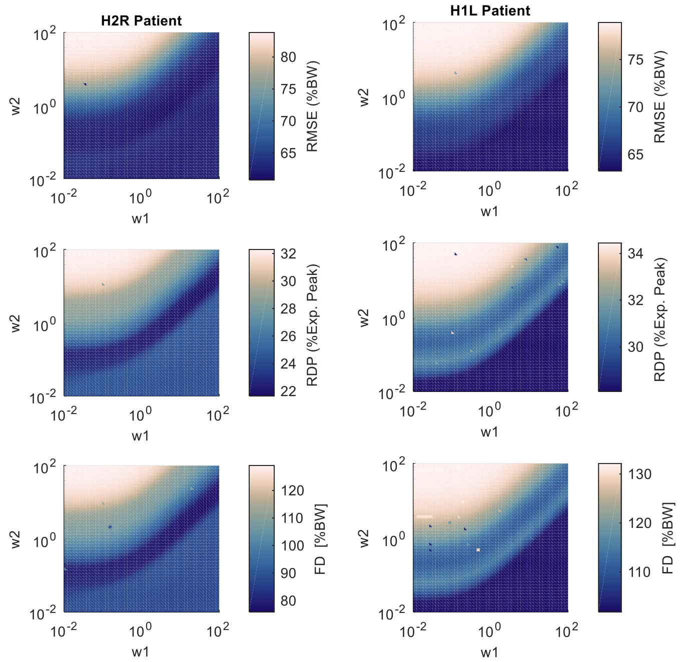

Figure 2: Grid search results for the three indicators of similarity between *in vivo* and numerical forces. The results for (a) patient H2R and (b) H1L. The colour map depicts the value of the indicator (RMSE, RDP and FD) in the respective weight factors combination, where dark blue means best fit.

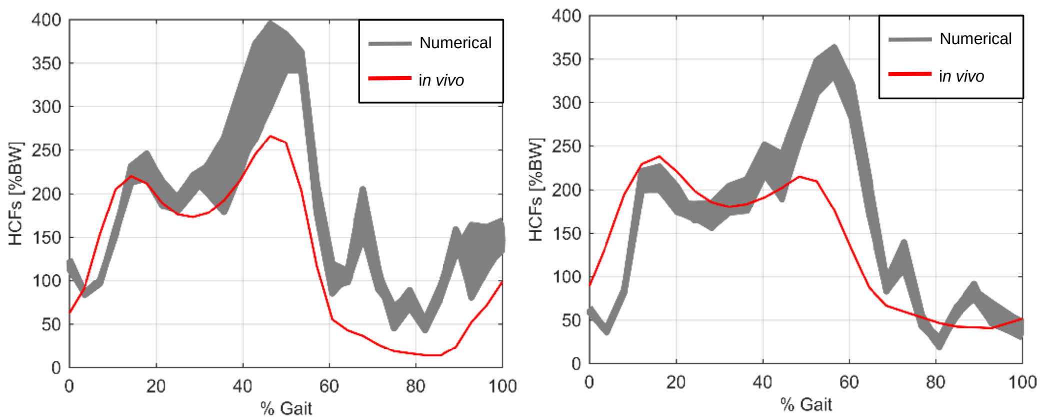

Figure 3: HCF for the (a) patient H2R and (b) patient H1L. The shaded grey area represents the range of the HCF predictions for all grid search simulations

3.3. Two-level Optimization

For the H2R patient, the 10 simulations converge to close combinations of the weights factors, presenting only slight variations, but the RMSE value is identical, within the given tolerance. The simulations carried for the H2R converged to different local minima, presenting slight different values of RMSE for the HCF predicted. Table 3 presents the minimum found for the 10 simulations.

Table 3: Optimal weight factors and respective RMSE. The results for the standard weight factors are also presented for comparison

Subject		**W1**	**W2**	**RMSE [%BW]**
H2R	Standard	0,33	0,66	63,3
	Optimal Weight Factors	87,40	11,09	60,8
	Relative Deviation			3,9%
H1L	Standard	0,33	0,66	68,8
	Optimal Weight Factors	47,7	0,04	63,3
	Relative Deviation			8,0%

4. DISCUSSION

The identification of the optimal objective weights is not straightforward. The goodness-of-fit indicators point towards different solutions, even though all of them resulted in improvements in relation to the standard weight factors. For some different combinations of weight factors, differences between HCF predictions are negligible. The cost function weights considered in the muscle load force sharing problem have a low influence on HCF. When evaluating the relative contribution of the linear terms, it is challenging to draw clear conclusions. The individual contribution of the two linear terms of the cost function, one related with the detachment of cross bridges and another with calcium pumping, lead to similar HCF predictions. This suggests that the solution for minimum energy consumption might the similar for the two energy terms, and one of the linear terms may possibly be disregarded without compromising the HCF predictions.

Nonetheless, a clear conclusion can be drawn: for both subjects, the error associated with the HCF predicted increased when increasing the non-linear term, ω_2. Similar results were obtained by Nikooyan et al. (2013). Pragmaan (2008) reports that introducing a non-linear term in the cost function should lead to more physiologically realistic results since only-linear cost functions predict sequential muscle recruitment instead of force sharing. In other words, the non-linear term leads to synergy (Crowninshield and Brand, 1981). In the present work, the non-linear term does lead to muscle synergy: for higher contributions of ω_2, the number of active muscles for each stride phase increased. The lower contributions of ω_2, cause sequential recruitment: the muscle with minimum cost tends to be activated, and the other muscles are only activated when the first reaches his maximum force. This can be observed in Figure 4, where the lower contributions of ω_2, lead to continuously maximum activation of some muscles.

The model overestimates the HCF for late stance and swing phase, especially for the second peak of the HCF. For higher contributions of the non-linear term of the cost function, the synergism between muscles increases, and so does the magnitude of the calculated HCF. The parameters that minimize the error between numerical and experimental forces, lead to low muscle synergy. The muscle synergy is not advantageous for the purpose of this work and results in worse predictions of the HCF. Nevertheless, muscle synergism is important for a correct simulation of the muscle recruitment criteria and should be included. The human motion is achieved via co-activation of muscles, instead of activating each muscle independently. This result, i.e. optimal parameters having low contributions of the non-linear term, suggests that there are other aspects limiting the contribution of this term to the result. One example is the incorrect modelling of some muscles, such as the gluteus muscles, which are introducing errors in the HCF prediction.

The *gluteus* group force results are critical since they are maximally activated during mid and terminal stance, which can be observed in Figure 4, producing forces of about 500N in a stride period in which these muscles are reported not to contribute to any specify gait task *in vivo* (Sheffler and Chae, 2015; Silva and Ambrósio, 2003). The same issue is reported in the literature (Modenese et al., 2011; Modenese and Phillips, 2012) when using biomechanical models based on Horsman (2007) dataset. The *gluteus* are muscles with large attachment areas, that are being included in the LLEM as several independent straight-line units with different origin and insertion points. Modelling these muscles as straight lines may lead to an underestimation of the muscle moment arms with respect to the hip joint center, so that a higher force is needed to equilibrate the intersegmental moments, causing high activation levels. This aspect is further aggravated because these muscles are introducing unrealistic moments in the biomechanical systems that need to be compensated by other muscles, further contributing to over-estimated forces. The modelling of these muscles should be reviewed, and the inclusion of wrapping surfaces might be considered for a more accurate representation. In fact, Carbone et al. (2015) proposes a new comprehensive dataset for biomechanical modelling where wrapping surfaces were added to model the *Gluteus Maximus* to ensure more realistic moment arms. For the same musculoskeletal model, De Pieri et al. (2018) even proposes a different wrapping surface for each *Gluteus maximus* segment.

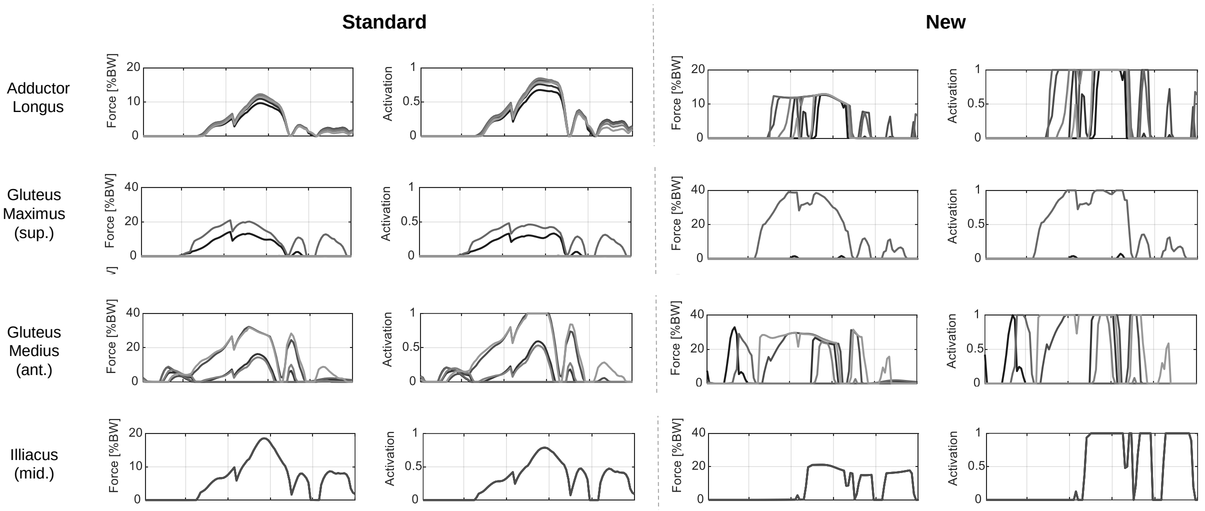

Figure 4: Activation patterns and total muscle forces for four muscles considered relevant during gait. The data were estimated for the H1L patient considering the (a) the standard parameters and (b) the new identified parameters. For some muscles, several lines are plotted because they represent the behaviour of the different muscle bundles into which the muscle is discretized**.**

5. CONCLUSIONS AND FUTURE WORK

The first objective of the present work is to validate the LLEM, a three-dimensional biomechanical model based on the comprehensive dataset published by Horsman (2007). The kinematic and kinetic data provided by OrthoLoad (Bergmann, 2008) for two patients is properly treated and used as input for inverse dynamic analyses. A kinematic analysis is successfully performed, and kinematic consistency was ensured. The driving angles prescribed for the simulation are comparable with those published in the literature (Arnold and Delp, 2011; Kadaba et al., 1990). The redundant muscle force sharing problem is solved using inverse dynamics and musculoskeletal model is shown to allow the prediction of HCF that compare well, both in magnitude and pattern, to those measured *in vivo*, for different weight parameters.

The muscle recruitment criteria is simulated by an energy related cost function proposed by Praagman et al. (2008). The second objective of the present work is to evaluate the relative contribution of the muscular energy consuming processes included in muscle load sharing cost function. The aim is to estimate the relative contribution of the processes included in the cost function, i.e. ion pumping and cross-bridges cycling, that can lead to a closer match between hip forces predicted by the model and the experimental measurements. For that, the inverse dynamic simulation is repeated for a variety of different combinations of weight factors. Also, new parameters are identified using a two-level optimization approach, where the objective is to find the combination of weight factors that lead to a lower RMSE. Also, the muscle activations and the forces developed are evaluated to assess the accuracy of the biomechanical model and to identify upgrades that can be implemented to obtain more accurate predictions of HCF.

In the context of this work (i.e. predict the joint contact forces as close as possible to *in vivo*), a higher contribution of the non-linear term is not advantageous since the forces are more over-estimated, increasing the error. Nevertheless, the muscle synergism is important for a correct simulation of the muscle recruitment criteria and should be included. Even though the non-linear term leads to synergy, the accuracy of the muscular agonist/antagonistic activity is not guaranteed.

The *in vivo* coordination of the agonist and antagonist muscles is still an ongoing field of research (Lundberg et al., 2016; Yoo et al., 2016). Hurwitz et al. (2003) showed that the level of agonistic/antagonistic muscle activity affects the HCF prediction of biomechanical models. The muscle synergy predicted by the model did not lead to a correct HCF prediction since the numerical contact forces are mostly over-estimated. A possible limitation to correct synergy performance may be linked to incorrect representation of some of the muscles. Future studies should focus on including an accurate representation of the muscle synergy. For example, a constraint could be added in the muscle load sharing problem to ensure that the agonist/antagonism pairs must be active at the same time.

A set of new weight factors is identified for each subject, based on a two-level optimization approach. This newly identified parameters result in improvements in the model numerical HCF, but the new weight factors differ for the two subjects. Considering that local minima exist in the problem formulated, further investigation is necessary to find if a common set of parameters is possible to be defined for different subjects.

The force over-estimation may be related with the inappropriate description of some muscles. More precisely, the gluteus muscle group presents activation patterns that do not compare well with literature. The modelling of these muscle should be reviewed, and the use of additional wrapping surfaces might have to be considered. Note that the present model only presents wrapping surfaces for two muscles: gastrocnemius and iliopsoas. Recently, Carbone et al. (2015) proposed a lower limb model including wrapping surfaces for eight muscles (including the *Gluteus maximums*), and, based on this model, De Pieri et al. (2018) proposed more wrapping surfaces for another three muscles.

An analysis of the muscle moment arms developed in the biomechanical model should be performed to identify the critical muscles that are introducing inconsistent forces in the system (responsible for the over-estimation of the HCF). The geometry and modelling of the identified muscles should be modified to allow a better representation of the muscle apparatus.

A series of studies used different criteria for solving the muscle load sharing problem. The use of different criteria resulted in different activation patterns, especially when comparing linear to non-linear criteria (Pedersen et al., 1987). Nonetheless, differences in predicted contact forces are limited, which is in agreement with the study of Stansfield et al. (2003) who stated that the criterion considered in the muscle load sharing problem has an effect on muscle loading but a less obvious influence on joint contact forces. This suggests that identifying the relative contribution of the energy terms based on the reproduction of joint contact forces may not be the best approach. The optimization should also include muscle information.

When simulating the motion of the biomechanical model, the measured driving angles for the subjects performing a gait cycle were directly prescribed. However, a scaling procedure to adapt the model to the individual patient anatomy should be considered. A number of linear and non-linear scaling procedures have been proposed in the literature (Correa and Pandy, 2011; Lund et al., 2015; Nolte et al., 2016) to enable subject-specific simulations and increase the accuracy of the biomechanical model.

The present work showed that the HJC prediction has a considerable impact on HCF prediction. Two studied predictive methods positioned the HJC in dissimilar distances, which led to considerable differences in the numerical HCF. Previous studies have also shown that changes in hip joint geometry and location have a high influence on the HCF predictions of the biomechanical system (Lenaerts et al., 2008). Therefore, further investigation on how to accurately track the HJC is fundamental.

The predicted contact forces present some peak irregularities that do not occur in vivo, but that are also found in other computational studies in the literature (Dumas et al., 2014; Fraysse et al., 2009; Heller et al., 2001; Modenese et al., 2011; Rane et al., 2019; Stansfield et al., 2003). Although different simulations were performed to gain insight into the possible origin of these irregularities, no clear conclusions could be drawn. Consequently, further analyses are required.

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