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A screening method to analyse the sensitivity of a lower limb multibody kinematic model ¹

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Abstract

The study presents a screening method used to identify the influential parameters of a lower limb model including ligaments, at low numerical cost. Concerning multibody kinematics optimisation, the ligament parameters (isometric length) were found the most influential ones in a previous study. The screening method tested if they remain influential with minimised length variations. The most important parameters for tibiofemoral kinematics were the skin markers, segment lengths and joint parameters, including two ligaments. This was confirmed by a quantitative sensitivity analysis. The screening method has the potential to be used as a stand-alone procedure for a sensitivity analysis.

Keywords: Sensitivity analysis; Morris method; biomechanics; multibody kinematics optimisation; ligament constraints; joint angles

1. Introduction

In biomechanics, lower limb multibody models have been widely used for gait analysis to estimate the joint angles, joint moments and joint contact forces. Such models may involve a very large number of uncertain parameters defining the joint degrees of freedom (DoFs), body segment masses and inertias, muscle geometry and physiology. Some of these parameters are not influential on the response and can be fixed to a nominal values, whereas the variability of others infers a large variability of the response. The most influential parameters are typically the ones that should be considered subject-specific.

Numerous sensitivity analyses (SA), e.g. [1, 4, 9, 12, 15, 17, 19, 20, 25–27, 29, 35, 36, 41, 43] have been performed in order to determine the influential and non-influential parameters especially with regards to the results of inverse dynamics and musculoskeletal modelling. The sensitivity analyses

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were generally based on a Monte Carlo propagation of uncertainties and different ad hoc sensitivity indices. As far as gait analysis is concerned, the sensitivity is to be assessed at different instants of time and for numerous outputs (e.g., angles, moments) and that is why many indices involved time averages [4, 12, 15, 35, 41] or time integrals [9, 29, 43]. As a matter of fact, these sensitivity analyses have a high numerical cost which may also explain why only first order sensitivity indices, which give the expected reduction in the response variance by fixing one factor [32], have been used although non-linear effects and interactions between parameters can be of high importance [15].

The influence of the parameters defining the lower limb model other than the muscle and inertial parameters has been scarcely analysed, except in terms of uncertainties propagation [22, 30, 40]. Therefore, the most influential parameters of inverse kinematics (also designated as multibody kinematics optimisation [3, 21]) are not clearly identified. Moreover, detailed joint model such as parallel mechanisms, and typically subject-specific models based on medical imaging, are becoming more and more popular [5, 10, 11, 39] while the sensitivity of the model parameters has been scarcely analysed [15, 33].

It is known [15] that the joint models with a limited number of DoFs (i.e., hinge, parallel mechanisms) are more sensitive to the model parameter values than models with a higher number of DoFs (i.e., spherical). Moreover, the model parameters have to be tuned to avoid singular positions of the mechanism [5] which demonstrates the high potential influence of these parameters.

This paper aims to show that it is possible to draw some conclusions for a sensitivity analysis from a screening approach (i.e., with a low numerical cost) in the context of multibody kinematics optimisation. First, the screening method and the lower limb multibody model are presented. The lower limb multibody model analysed in this study corresponds to the most detailed rigid-body kinematic models for which personalization using MRI or biplane radiography is currently under progress [5, 10, 11, 37, 39]. Then, some sensitivity indices are calculated and compared to the total sensitivity indices evaluated with the Sobol method [32], which is widely used in SA and will be the reference method. Finally, a discussion is proposed about the efficiency of the screening method with respect to the Sobol method, and some conclusions on the most influential parameters of the joint model, namely a parallel mechanism with minimised ligament length variation, are drawn.

2. Material and Methods

Many SA methods exist. Some are based on a coefficient that is quite easy to derive (e.g., PEAR, SPEA, SRC, SRRC [32]) but the interpretation is based on assumptions that are difficult to verify (e.g., linearity, monotonicity). Therefore more general methods based on ANOVA [31] are usually preferred. However, as there are based on Monte Carlo simulations, they are not applicable when the number of parameters is high: in that case a screening method is used as a first step in a sensitivity analysis to detect the non-influential parameters. The Morris method [24] is the most popular and efficient screening method [7, 8] as it considers not only the linear but also the non-linear effects and interactions between parameters.

2.1. Morris screening method and sensitivity measures

The first step of the method consists in transforming all the uncertain parameters into a set of normalized parameters, $\{X_i\}_{i=1\dots k}$, which belong to the unit hypercube $[0, 1]^k$, and follow a uniform statistical law: such transformation may be done with the cumulative distribution function [32]. Each normalized parameter X_i has a value that belongs to the set $S_\Delta = \{0, \Delta, \dots, (p-2) \times \Delta, 1\}$, where $\Delta = 1/(p-1)$ with p a given number of points chosen to define a “ p -level-grid” [24]. Δ^* is then defined as a multiple of Δ such that $\Delta^* < 1$. Morris suggests considering the number of levels, p , as an even number and choosing $\Delta^* = (p/2)\Delta$, which will be the case in the following. In most of the publications $p = 4$ or 6 (e.g., [24]).

The algorithm consists in [24]:

1. Draw a point $\mathbf{X}_0(X_1, \dots, X_k)$ that belongs to the p -level grid,
2. Initialise an index $j = 0$,
3. Initialise a set of indices $I = \emptyset$,
4. repeat until $j = k$:
 - (a) Draw a sign ϵ where $\epsilon = +1$ or $\epsilon = -1$,
 - (b) Draw an index i such that $i \in \{1, \dots, k\} \setminus I$,
 - (c) Define a new point $\mathbf{X}_{j+1}$ from $\mathbf{X}_j$ by varying the i -th element X_i by $\epsilon\Delta^*$ such that $\mathbf{X}_{j+1}$ stays on the grid (if not, change the sign of ϵ),
 - (d) Calculate elementary effect d_i of the i -th parameter: $d_i = \frac{Y(\mathbf{X}_{j+1}) - Y(\mathbf{X}_j)}{\epsilon\Delta^*}$ where $Y()$ is an output of the model (note that $Y(\mathbf{X}_j)$ and $Y(\mathbf{X}_{j+1})$ are evaluated with the same parameters except for the i -th parameter),

- (e) Update the set of index $I = I \cup \{i\}$,
- (f) Increment the index $j = j + 1$.

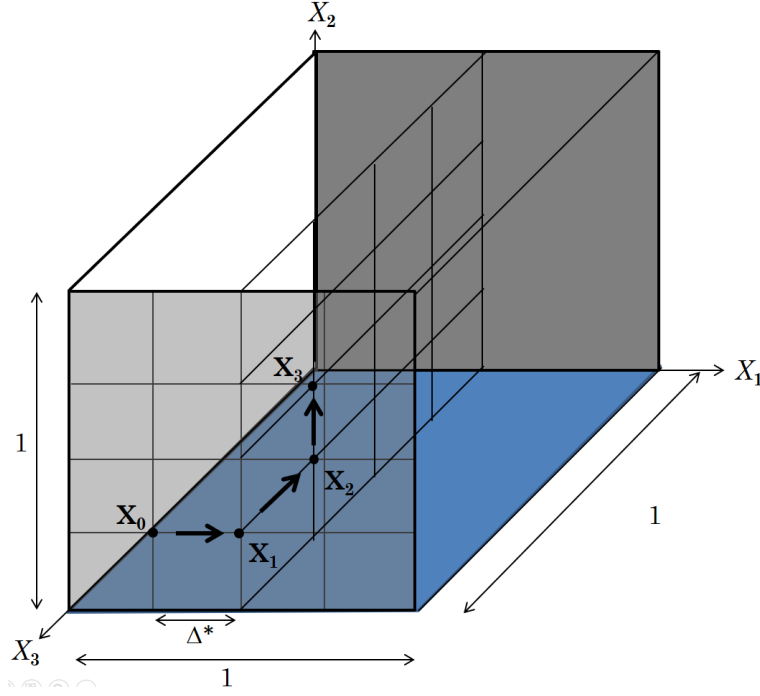


Figure 1: Principle of the screening method: points $\mathbf{X}_0, \dots, \mathbf{X}_k$ define a trajectory of $k + 1$ points where the model is evaluated to calculate the elementary effect of each parameter.

This way, points $\mathbf{X}_0, \dots, \mathbf{X}_k$ define a trajectory of $k + 1$ points in the p-level-grid (see Figure 1) and the model is evaluated at each $\mathbf{X}_j$, that is $k + 1$ times. This process is repeated r times and a collection of r values for each elementary effect d_i is obtained. The number of model evaluations is : $n = r \times (k + 1)$.

The mean over the r repetitions of the absolute value, μ_i^* , and the standard deviation, σ_i , of the elementary effects d_i are then computed for all indices $i \in \{1, \dots, k\}$ [7, 24]. Hence, each model parameter has two sensitivity measures, μ_i^* and σ_i , and the results are provided as a graph (μ_i^*, σ_i) allowing for the ranking of the parameters (see Figure 2). The points close to the σ_i -axis (small μ_i^* values) correspond to factors that have a negligible overall influence on the model outputs. The points close to the μ_i^* -axis (small σ_i values) correspond to parameters that have a linear effect on the model outputs, whereas the other points correspond to parameters that have either a non-linear effect or an interaction with other parameters. The ranking is mainly qualitative and the two sensitivity measures μ_i^* and σ_i do not represent quantitative indices. Usually, after having selected the unimportant model

parameters from the screening, a proper sensitivity analysis is to be performed with unimportant parameters set to their nominal value.

2.2. Sensitivity analysis and Sobol indices

The Sobol method is one of the most used methods of quantitative global sensitivity analysis: this is why it is chosen as the reference method for the SA in this study. It consists in analysing the variance of the model outputs by evaluating the so-called Sobol indices, such as first order sensitivity indices S_i and total sensitivity indices S_{Ti} (see Appendix) [31]. The total sensitivity indices S_{Ti} can quantitatively sort the parameters with respect to their influences (including non-linear effects and interactions between parameters) on the model outputs. Similarly to the sensitivity measure μ_i^* , the parameter i with the highest index S_{Ti} , is the most influential one.

In the Sobol method [31], the number of model evaluations is $n = (k + 2) \times n_s$ where n_s is the number of samples of each model parameter drawn from its statistical distribution used to perform the Monte Carlo simulation. A latin hypercube sampling method [23] can be used to evaluate the Sobol indices with a reduced number of evaluations. Typically, n_s ranges from 200 to 10000 [1, 4, 15, 17, 20, 22, 25, 26, 40].

In the present study, the sensitivity measure μ_i^* was compared to total Sobol indices to verify if the screening method could be sufficient for determining the most influential model parameters. Indeed previous studies [7, 8] have shown that the Morris sensitivity measures are interesting indicators of the total sensitivity of a parameter, while they require far fewer model evaluations.

2.3. Lower limb kinematic model and gait data

The same lower limb kinematic model and gait data as in [15] were analysed except for the joint modelling. The model was made of 5 segments (foot, shank, patella, thigh, and pelvis) and 4 joints (ankle, tibiofemoral, patellofemoral, and hip). In the present study, the ligament length variation was minimised with a penalty-based method [18] for all the ligaments of the ankle, tibiofemoral and patellofemoral joints. Regarding the gait data, the trajectories of 14 skin markers were recorded during one gait cycle at comfortable speed of one healthy (i.e. without orthopaedic problems or previous surgery) subject (50 years old, height 1.85 m, body mass 90 kg).

Multibody kinematics optimisation, which consists in minimising the sum of the squared distances between measured and model-derived skin marker positions [3], was performed to compute the joint kinematics. The numerical cost was quite low, namely less than 2 s per model evaluation on a

conventional computer (i.e., Intel^R CoreTM i7-6700/3.4GHz). The total number of model parameters was $k = 129$. The complete description of the model parameters and their role in the multibody kinematics optimisation (i.e. driving, kinematic and rigid body constraints) can be found in [15]. The model outputs were the 3 joint angles (flexion-extension, adduction-abduction, and internal-external rotation) per joint and the tibiofemoral anterior-posterior, proximal-distal and lateral-medial displacements evaluated at each n_t -th instant of time (n_t varies from 1 to 130 in the analysed gait cycle): for one model evaluation, each response is therefore calculated n_t times. Only the six tibiofemoral DoFs were analysed in the present study. A detailed definition of the segment and joint coordinate systems can be found elsewhere [14, 15]. The definition follows the ISB recommendations [42] with the X , Y , Z axes in the anterior, superior and left directions, respectively. The uncertainty associated to each model parameter was modelled as a normal distribution. As in [15], the mean values were derived from the gait data and the standard deviations were set to 2.5 cm for all the segment parameters (position of the skin markers with respect to the segment coordinate systems, length of the segments). These positions and lengths were averaged over the gait cycle. Other mean values were derived from the literature [13, 16, 34] and the standard deviations were set to 2.5 mm and 5° for all the joint parameters (position of joint centres, orientation of joint axes, position and orientation of joint planes, position of centre and radius of joint spheres, position of origins and insertions and length of ligaments)

3. Results

3.1. Morris screening method

With $r = 10$ repetitions and 129 parameters, the model was therefore evaluated $n = 1300$ times with the screening method. The sensitivity measures were then calculated at each of the n_t time steps of a gait cycle as shown in Fig. 3. In order to rank the parameters, averaged sensitivity measures over the values obtained for the n_t time steps are also calculated. The graph $(\bar{\mu}_i^*, \bar{\sigma}_i)$ of the averaged sensitivity measures are presented in Figure 2. Similar tests were carried out with $r = 20$ and $r = 50$ repetitions (not presented here). The results were the same, showing a convergence of the results from $r = 10$.

For each DoF of the tibiofemoral joint kinematics, the parameters with $\bar{\mu}_i^* > 0.75 \max_i(\bar{\mu}_i^*)$ are considered as the most influential.

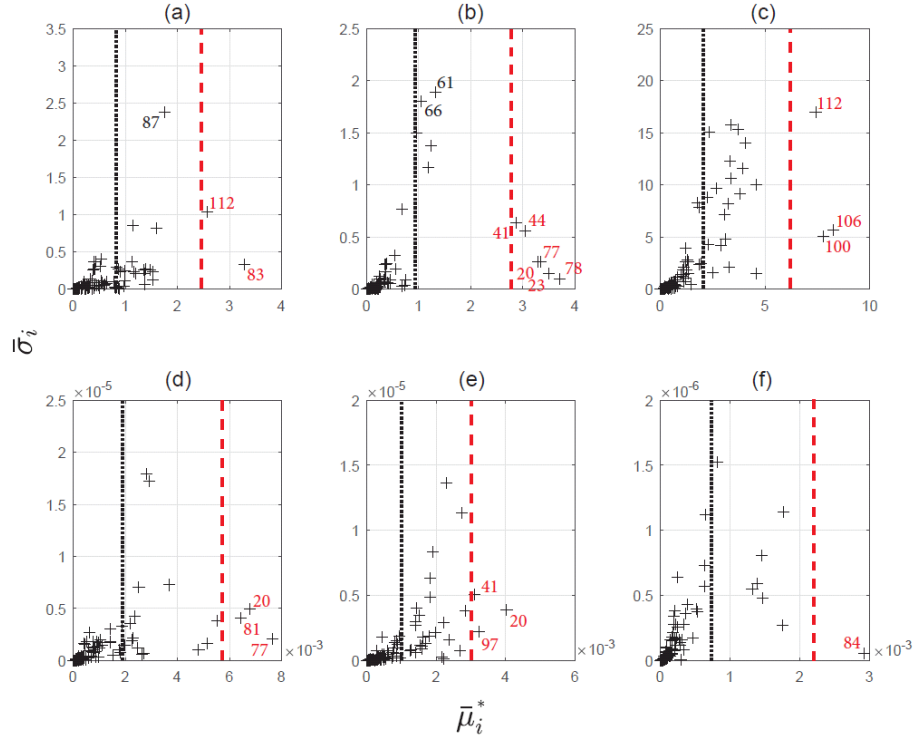


Figure 2: Graph $(\bar{\mu}_i^*, \bar{\sigma}_i)$ of the averaged sensitivity measures over the gait cycle. Vertical black and red dotted lines represent the two thresholds of $\bar{\mu}_i^* < 0.25 \max_i(\bar{\mu}_i^*)$ and $\bar{\mu}_i^* > 0.75 \max_i(\bar{\mu}_i^*)$, respectively. Indices in red are for the most influential parameters according to the model output: flexion-extension (a), adduction-abduction (b), and internal-external rotation (c) angles, and lateral-medial (d), anterior-posterior (e) and proximal-distal (f) displacements of the tibiofemoral joint.

For flexion-extension (Figure 2a), the most influential parameters are the foot length ($i = 83$) and the X -coordinate of lateral epicondyle marker ($i = 112$) while another parameter, the pelvis length ($i = 87$), demonstrates high non-linear effects or interactions with others parameters. For adduction-abduction (Figure 2b), the most influential parameters are the radius of lateral condyle ($i = 78$), the Y -coordinate of lateral plateau ($i = 23$), the radius of medial condyle ($i = 77$), the Y -coordinate of medial plateau ($i = 20$), Y -coordinate of lateral condyle ($i = 44$), and the Y -coordinate of medial condyle ($i = 41$). Two other parameters, the X -component of normal to medial plateau ($i = 61$) and the Z -component of normal to lateral plateau ($i = 66$), demonstrates high non-linear effects or interactions between parameters. For internal-external rotation (Figure 2c), the most influential parameters are the X -coordinate of lateral malleoli marker ($i = 106$), the X -coordinate of fibula head marker ($i = 100$), and the X -coordinate of lateral epicondyle marker ($i = 112$). On this DoF, the X -coordinate of lateral epicondyle marker ($i = 112$) is also the parameter with the highest non-linear effects or interactions between parameters.

For lateral-medial displacement (Figure 2d), the most influential parameters are the radius of medial condyle ($i = 77$), the Y -coordinate of medial plateau ($i = 20$), and the length of the medial collateral ligament ($i = 81$). For anterior-posterior displacement (Figure 2e), the most influential parameters are the Y -coordinate of medial plateau ($i = 20$), the X -coordinate of the tibia tuberosity marker ($i = 97$), and the Y -coordinate of medial condyle ($i = 41$). For proximal-distal displacement (Figure 2f), only one parameter, the shank length ($i = 84$), is considered as most influential. For all the tibiofemoral joint displacements, the values of $\bar{\sigma}_i$ are all very low with respect to $\bar{\mu}_i^*$, suggesting very limited non-linear effects or interactions between parameters.

Conversely to the most influential parameters, the parameter with $\bar{\mu}_i^* < 0.25 \max_i(\bar{\mu}_i^*)$ were considered as the least influential. Accounting for all the DoFs of the tibiofemoral joint kinematics, they represented 85 parameters out of the 129. These least influential parameters were set to their mean values during the quantitative sensitivity analysis.

3.2. Sobol sensitivity analysis

A Sobol sensitivity analysis has been also performed to evaluate the total Sobol indices. With $n_s = 10000$ samples for each of the 129 model parameters, the model should have been evaluated $n = 1\,310\,000$ times for the entire sensitivity analysis. Tough, with the 85 model parameters set to their mean values according to the screening method, the number of model evaluation was reduced to $n = 460\,000$.

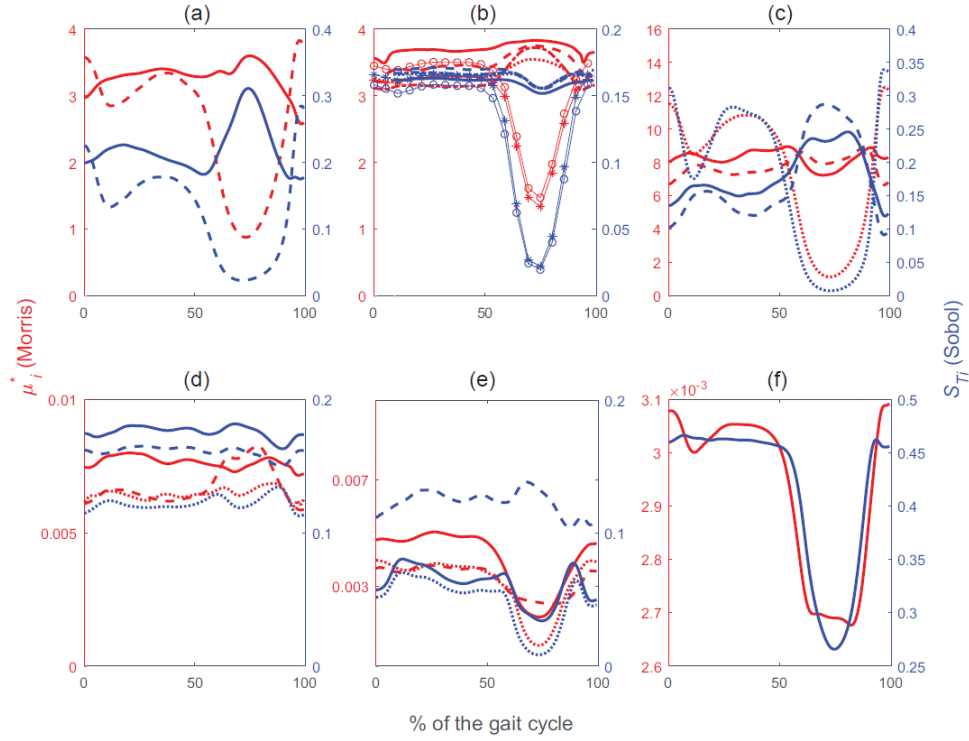


Figure 3: Evolution of the sensitivity measures μ_i^* (red lines) and Sobol indices S_{Ti} (blue lines) over the gait cycle for the most influential parameters. If existing, solid, dashed, dotted, dashed-dot, o-marked, and *-marked lines are respectively related to the first, second, third, fourth, fifth and sixth most influential parameter according to the model output: flexion-extension (a), adduction-abduction (b), and internal-external rotation (c) angles, and lateral-medial (d), anterior-posterior and proximal-distal (f) displacements of the tibiofemoral joint.

For the most influential parameters according to the screening methods, the sensitivity measures μ_i^* were plotted over the gait cycle together with the corresponding Sobol indices S_{Ti} (Figure 3).

On the whole, the ranking obtained with sensitivity measures μ_i^* are confirmed with the Sobol indices S_{Ti} . However, some exceptions are observed. For adduction-abduction (Figure 3b), the second most influential parameter according to μ_i^* (Y-coordinate of lateral plateau, $i = 23$), is ranked the first influential parameter according to S_{Ti} . Similarly, for anterior-posterior displacement (Figure 3e), the second most influential parameter according to μ_i^* (X-coordinate of the tibia tuberosity marker, $i = 97$), is ranked the first influential parameter according to S_{Ti} .

More details on the ranking according to both μ_i^* and S_{Ti} of all the parameters except the ones that the Morris method definitively considered as unimportant ($\bar{\mu}_i^* \geq 0.25 \max_i(\bar{\mu}_i^*)$) can be found in Figure 4.

Plotting μ_i^* and S_{Ti} over the gait cycle together also reveals that some parameters remain almost equally influential while others become less influential in the swing phase (61%-100% of gait cycle)

with respect to the stance phase (1-60% of gait cycle). For instance, the third most influential parameter for internal-external rotation (X -coordinate of lateral epicondyle marker, $i = 112$) becomes non-influential at mid-swing (Figure 3c). Without becoming non-influential, both μ_i^* and S_{Ti} for the second most influential parameter for flexion-extension (X -coordinate of lateral epicondyle marker, $i = 112$), the fifth and sixth most influential parameters for adduction-abduction (Y -coordinate of lateral condyle, $i = 44$, and the Y -coordinate of medial condyle, $i = 41$), and the most influential parameter for proximal-distal displacement (the shank length, $i = 84$) seem to decrease as the flexion-extension angle (not displayed here) increase. A variation up to 85 % was observed for the sensitivity measures or indices of these parameters.

4. Discussion

4.1. Screening method and Sobol sensitivity analysis

This study reports a comparison between a qualitative (Morris method) and a quantitative sensitivity analysis (Sobol method) [24, 31]. It can be interesting to examine how both approaches perform in a problem where the number of model parameters is high (i.e., $k = 129$). The screening method allows qualitatively ranking the parameters from the most significant to the less significant at an affordable numerical cost. In the present study, the number of model evaluation for screening is $n = 1300$ compared to $n = 460\,000$, and this number for the quantitative sensitivity analysis has been highly reduced by setting the 85 non-influential parameters to their mean values. Identifying these non-influential parameters before completing the quantitative sensitivity analysis is exactly the purpose of a screening method. However, Figure 4 shows that there is strong agreement between average Morris sensitivity measure $\bar{\mu}_i^*$ and average total Sobol index $\bar{S}_{Ti}$ that confirms the ranking illustrated in Figure 3, where the evolution of μ_i^* and S_{Ti} are on the whole comparable over the gait cycle. Accordingly, the present results suggest that the screening method may be used as a stand-alone sensitivity analysis.

Whatever the approach used to identify the influential parameters, it seems important to analyse the evolution of the sensitivity measures or indices over the gait cycle as they may be different between the stance and swing phases or may vary with the joint amplitude, as it appears in the present study, depending on the knee flexion-extension. Some previous sensitivity analyses of a lower limb models have reported time averages [4, 12, 15, 35, 41], time integrals [9, 29, 43] as well as correlation coefficients [17, 25, 26, 38] or root mean square differences [1] computed on the whole

gait cycle. One study has reported partial derivatives of the output with respect to the parameters (calculated using a finite-difference approximations) at each instant of time of the gait cycle [36] and demonstrated varying influence of some parameters on the lower limb joint moments.

The objective is to have an indicator of all the contributions of one parameter on the variability of the response: these contributions can be linear, nonlinear or an interaction with other parameters. This explains the importance of computing the total sensitivity indices rather than first order indices, as the former ones account for all the contributions. Moreover, the effect of multiple parameter variations could be inferred by a linear combination of the single effect if the contribution is assumed linear (which is implicitly the case if only first order indices are analysed). The same cannot be said if the contribution of the parameters on the variability of the response is not linear. All the studies previously mentioned except one [41] reported first order sensitivity indices only. The screening method [24] allows for a specific sensitivity measure (σ_i) of the non-linearities and interactions, and, most importantly, μ_i^* is a good proxy of the total indices [7, 8]. Using this sensitivity measure, it appears that the tibiofemoral joint displacements, as opposed to the joint angles, are not affected by non-linear effects or interactions between parameters.

The numerical cost of a SA mainly depends on the number of model evaluations. Therefore, deriving the Sobol indices for all the parameters would have required 1310000 model evaluations, that is about 1000 time the number of model evaluations of the Morris method (1300). Thanks to the screening step, the Sobol indices required “only” 460000 model evaluations, which is still 350 time the model evaluation number with the Morris method. The numerical cost ratio between both methods is the same, which explains the interest of the Morris method if it is not necessary to perform another sensitivity analysis after the screening.

4.2. Most influential parameters of model-derived tibiofemoral joint kinematics

With minimised length variations in the joints, it was expected that the ligament parameters were not the most influential ones. This turns out to be partially true. Indeed, for the six DoFs of the tibiofemoral joint kinematics, the most influential parameters are the position of skin markers (lateral epicondyles, lateral malleoli, fibula head, tibia tuberosity), the segment lengths (foot, shank), and the joint parameters (position of condyles and plateaus, condyle radii, and ligaments lengths). Nevertheless, compared with the model with ligament length constancy [15], only two ligaments, the medial collateral and anterior cruciate ligaments, are identified as the most influential. Moreover,

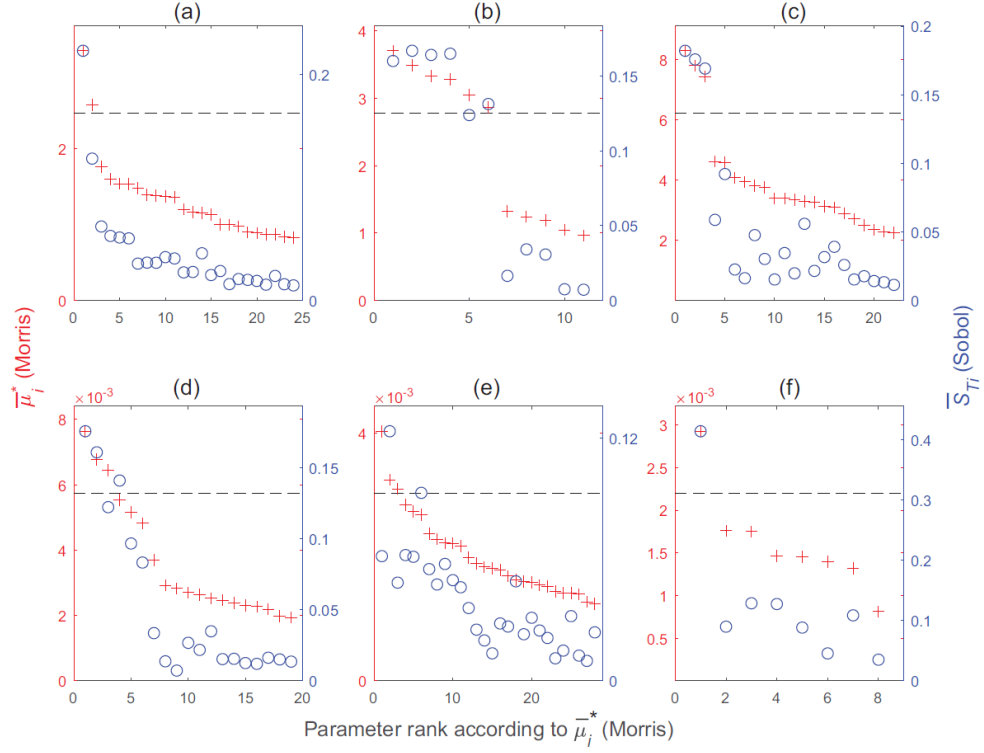


Figure 4: Values of $\bar{\mu}_i^*$ (red markers +) and $\bar{S}_{Ti}$ (blue markers o) averaged over the gait cycle for all parameters but the least influential ($\bar{\mu}_i^* < 0.25 \max_i(\bar{\mu}_i^*)$) according to the model output: flexion-extension (a), adduction-abduction (b), and internal-external rotation (c) angles, and lateral-medial (d), anterior-posterior (e) and proximal-distal (f) displacements of the tibiofemoral joint. Horizontal dotted black line represent the threshold of $\bar{\mu}_i^* > 0.75 \max_i(\bar{\mu}_i^*)$.

the high influence of the medial collateral ligament obtained with the screening method ($\bar{\mu}_i^*$) is not confirmed by the quantitative sensitivity analysis ($\bar{S}_{Ti}$) while the high influence of the anterior cruciate ligament is only obtained with the Sobol indices.

Thus, even if the ligament parameters seem less influential when a minimised ligament length variation is used, the majority of the most influential parameters remain the parameters which define the contact constraints of the tibiofemoral joint (i.e., position of condyles and plateaus, condyle radii). Furthermore, according to the screening method, the parameters with the highest non-linear effects or interactions (i.e., highest $\bar{\sigma}_i$) are the orientations of the plateaus. In other words, it seems opportune to personalise the geometry of the condyles and plateaus in order to obtain an accurate model-derived tibiofemoral joint kinematics (Brito da Luz et al. 2017; Charbonnier et al. 2017; Clément et al. 2015; Smale et al. 2019).

Moreover, when looking at the evolution of the sensitivity measure (μ_i^*) over time it appears that the influence of some model parameters is not consistent over the gait cycle. These parameters are the position of lateral epicondyle marker and the position of medial and lateral condyles. It is important to remind that the model-derived kinematics results from the minimisation of the sum of the squared distances between measured and model-derived skin marker positions. These distances are varying between skin markers and over the gait cycle. From the measurement side, it can be understood that the distance associated to one given skin marker may come to be substantial or negligible because the so-called “soft tissue artefact” [6] is known to be dependent on the knee flexion-extension. From the modelling side, the constraints introduced by the parallel mechanisms are comparable to introducing couplings between the tibiofemoral DoFs [18] and are, therefore, also dependent on knee flexion-extension.

4.3. Limitations

The study is performed on one gait cycle of one subject. This is rather classical in sensitivity analysis studying gait analysis [2, 9, 17, 20, 22, 25, 27–30, 36, 38, 41]. As gait is a very consistent motor task, the authors do not think that having tested more subjects would have changed the main findings of the study: (a) most ligament parameters were rather unimportant when a minimised ligament length variation is used; (b) influence of some model parameters can be inconsistent over the gait cycle; and (c) the screening method has the potential to be used as a stand-alone sensitivity analysis.

The uncertainties associated to the model parameter do not discriminate between the segments or the joints. This choice was already made in the previous study [15] and retained in order to test the hypothesis that, in comparison, the most influential parameters are no longer the ligament parameters. In the present study, the ligament length constancy is replaced by a minimised length variation (i.e., with a penalty-based method). This introduces a new model parameter, namely the penalty factor, the sensitivity of which is not currently evaluated but has been evaluated previously [33].

Concerning the screening method, two arbitrary thresholds have been chosen to identify the most ($\bar{\mu}_i^* > 0.75 \max_i(\bar{\mu}_i^*)$) and least ($\bar{\mu}_i^* < 0.25 \max_i(\bar{\mu}_i^*)$) influential parameters. Obviously, this choice is not easy and always subjective as it is in all SA methods when a decision must be made. When the screening method is typically used to identify the non-influential parameters and set them to their mean values before completing a quantitative sensitivity analysis, such a threshold of 25% of the maximal value is rather classical [24]. In the present study, another threshold of 75% is proposed to determine the most influential parameters using this screening method automatically. Figure 4 shows that this threshold was appropriate for most of the cases (Figures 4(a-d),(f)) and confirmed by the Sobol indices, but in one case (Figure 4(e)) this threshold is too high. However, Figure 4(e) shows that the Morris measure decreases regularly: there is no real gap between the values (except between the first two, which are above the criterion). This suggests this is difficult to set a threshold. As a consequence, it seems mandatory to check the distribution of the sensitivity measure to set a threshold: if there is a doubt, then a further sensitivity analysis should be performed.

As to the quantitative sensitivity analysis performed in this study, the number of samples for each model parameter is set to $n_s = 10000$. This number is already associated to a high numerical cost, but the converged value of the sensitivity indices S_{T_i} may not be reached: probably that a number larger 10000 should have been used, but the numerical cost would have been too high. Yet, $n_s = 10000$ can be considered quite high in comparison to a number of samples in the range [200-3000] more generally used in biomechanics [1, 4, 17, 20, 22, 25, 26, 40].

5. Conclusion

A sensitivity analysis was applied to a lower limb multibody kinematic model, and sensitivity measures were calculated with the Morris method, which is a screening method. The study found

that the ligament parameters were rather unimportant when a minimised ligament length variation is used. It was also highlighted that the condyle and plateau parameters had a strong influence on the results. Therefore, these parameters are worth being personalised for an accurate model-derived tibiofemoral kinematics. Another finding is the influence of some model parameters being inconsistent over the gait cycle. It may be therefore, important to analyse the evolution of the sensitivity measures or indices over the gait cycle.

The presented screening method is usually devised to qualitatively rank the parameters at an affordable numerical cost. A comparison with a well-established global sensitivity analysis, the Sobol method, showed that the Morris method has the potential to be used as a stand-alone sensitivity analysis.

Appendix A. Total Sobol sensitivity indices [31]

Consider response y of an uncertain model, which depends on k random variables, $\{x_i\}_{i=1,\dots,k}$. Consider design of experiment (DoE) matrices X and X' : the j -th column of the DoE matrices is a vector of n_s samples of random variable x_j . A model evaluation is performed for the i -th row of matrix X (resp. X'): the result is denoted by $Y(X_{i1}, \dots, X_{ik})$ (resp. $Y(X'_{i1}, \dots, X'_{ik})$).

The total Sobol SI is

$$ST_i = \frac{VT_i}{V} = \frac{\mathbb{E}_{X_{\sim i}}(\mathbb{V}_{X_i}(Y | X_{\sim i}))}{V} = 1 - \frac{\mathbb{V}_{X_{\sim i}}(\mathbb{E}_{X_i}(Y | X_{\sim i}))}{V} \quad (\text{A.1})$$

where V is the variance of output Y ; VT_i is the total contribution to V of parameter X_i ; $\mathbb{E}$ and $\mathbb{V}$ denote respectively the expectation and the variance taken over parameters specified in the subscript; symbol “ $\sim i$ ” in $\mathbf{X}_{\sim i}$ means that parameter X_i is not concerned.

To estimate these quantities, the Sobol method [31] is based on two $(n_s \times k)$ matrices, $\mathbf{A}$ and $\mathbf{B}$ and two vectors $\mathbf{Y}_A$, and $\mathbf{Y}_B$:

$$\mathbf{A} = \begin{bmatrix} X_{11} & \cdots & X_{1k} \\ \vdots & \ddots & \vdots \\ X_{n_s 1} & \cdots & X_{n_s k} \end{bmatrix} \quad \text{and} \quad \mathbf{B} = \begin{bmatrix} X'_{11} & \cdots & X'_{1k} \\ \vdots & \ddots & \vdots \\ X'_{n_s 1} & \cdots & X'_{n_s k} \end{bmatrix}$$

$$\mathbf{Y}_A = \begin{bmatrix} Y(X_{11}, \dots, X_{1k}) \\ \vdots \\ Y(X_{n_s 1}, \dots, X_{n_s k}) \end{bmatrix} \quad \text{and} \quad \mathbf{Y}_B = \begin{bmatrix} Y(X'_{11}, \dots, X'_{1k}) \\ \vdots \\ Y(X'_{n_s 1}, \dots, X'_{n_s k}) \end{bmatrix}$$

A resampling matrix, $\mathbf{G}_i$, and the corresponding model evaluations, $\mathbf{Y}_{\mathbf{G}_i}$, can be obtained for each parameter X_i :

$$\mathbf{G}_i = \begin{bmatrix} X_{11} & \cdots & X_{1(i-1)} & X'_{1i} & X_{1(i+1)} & \cdots & X_{1k} \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ X_{n_s 1} & \cdots & X_{n_s(i-1)} & X'_{n_s i} & X_{n_s(i+1)} & \cdots & X_{n_s k} \end{bmatrix}$$

$$\mathbf{Y}_{\mathbf{G}_i} = \begin{bmatrix} Y(X_{11}, \cdots, X_{1(i-1)}, X'_{1i}, X_{1(i+1)}, \cdots, X_{1k}) \\ \vdots \\ Y(X_{n_s 1}, \cdots, X_{n_s(i-1)}, X'_{n_s i}, X_{n_s(i+1)}, \cdots, X_{n_s k}) \end{bmatrix}$$

The variances are estimated by

$$V = \frac{1}{n_s - 1} \mathbf{Y}_A^T \cdot \mathbf{Y}_A - \left(\frac{1}{n_s} \mathbf{1} \cdot \mathbf{Y}_A \right)^2 \quad (\text{A.2})$$

$$VT_i = \frac{1}{n_s} \mathbf{Y}_A^T \cdot (\mathbf{Y}_A - \mathbf{Y}_{\mathbf{G}_i}) \quad (\text{A.3})$$

where “ T ” stands for vector transpose.

Conflict of Interest

No potential conflict of interest was reported by the authors.

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