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Original article

# **Sensitivity Analysis of Human Lower Extremity Joint Moments due to Changes in Joint Kinematics**

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## Abstract

Despite the widespread applications of human gait analysis, causal interactions between joint kinematics and joint moments have not been well documented. Typical gait studies are often limited to pure multi-body dynamics analysis of a few subjects which do not reveal the relative contributions of joint kinematics to joint moments.

This study presented a computational approach to evaluate the sensitivity of joint moments due to variations of joint kinematics. A large data set of probabilistic joint kinematics and associated ground reaction forces were generated based on experimental data from literature. Multi-body dynamics analysis was then used to calculate joint moments with respect to the probabilistic gait cycles. Employing the Principal Component analysis (PCA), the relative contributions of individual joint kinematics to joint moments were computed in terms of sensitivity indices (SI).

Results highlighted high sensitivity of (1) hip abduction moment due to changes in pelvis rotation (SI=0.38) and hip abduction (SI=0.4) , (2) hip flexion moment due to changes in hip flexion (SI=0.35) and knee flexion (SI=0.26), (3) hip rotation moment due to changes in pelvis obliquity (SI=0.28) and hip rotation (SI=0.4) , (4) knee adduction moment due to changes in pelvis rotation (SI=0.35) , hip abduction (SI=0.32) and knee flexion (SI=0.34), (5) knee flexion moment due to changes in pelvis rotation (SI=0.29) , hip flexion (SI= 0.28) and knee flexion (SI=0.31) , and (6) knee rotation moment due to changes in hip abduction (SI=0.32), hip flexion and knee flexion (SI=0.31).

Highlighting the “cause-and-effect” relationships between joint kinematics and the resultant joint moments provides a fundamental understanding of human gait and can lead to design and optimization of current gait rehabilitation treatments.

**Keywords:** Gait modification, Rehabilitation, Sensitivity analysis, Joint moments, Multi-body dynamics

## 1 **1. Introduction**

2 Human gait studies have been one of the most attractive and challenging areas of biomechanics with  
3 different applications for musculoskeletal disorder diagnosis [1-5] , therapeutic interventions[6-9] and  
4 functional evaluations of different treatments[10-13]. Multi-body dynamics (MBD) analysis has been widely  
5 used to study human gait. From a technical point of view, two different approaches of MBD analysis can be  
6 found in literature: inverse dynamics and forward dynamics. Inverse dynamics analysis has been mainly used  
7 to calculate joint moments, muscle forces and body torques from known joint kinematics [14-18] . On the  
8 other hand, forward dynamics analysis has been employed to determine the joint kinematics from known joint  
9 moments and muscle forces [19-21].

10 These studies however have major limitations, which prohibit a holistic understanding of human gait;  
11 first, MBD cannot provide a systematic investigation of the causal interactions between joint kinematics and  
12 the resultant joint moments. Typical gait analyses reveal the effects of joint kinematics on the joint moments  
13 and vice versa. However, the relative contributions of individual kinematics to joint kinetics cannot be well  
14 evaluated by MBD alone. Second, gait studies often do not accommodate the role of inter-patient variability.  
15 Large inter-patient variations have been reported in joint kinematics and kinetics [22, 23]. However, gait  
16 studies are often evaluated for a few numbers of subjects due to the cost and time required for experimental  
17 gait measurements.

18 Due to the cost of experimental data acquisition, principal component analysis (PCA) has been widely  
19 used to computationally generate a large population of probabilistic database from a small experimental data  
20 set. PCA outlines a database through its underlying principal patterns and then enlarges the database via  
21 randomizing its major patterns. For example, PCA has been used to generate large probabilistic inter-patient

22 databases of geometry [24], elastic modulus [25] and joint kinetics [26]. Considering the inherent capability of  
23 PCA to discriminate and extract the underlying fundamental patterns of a data space, PCA has been also  
24 employed to extract and interpret the complicated interactions between highly coupled variables. For example,  
25 the relative contributions of joint alignments and loadings to joint mechanics have been investigated through  
26 PCA [27]. These two unique capabilities of PCA, enlarging a small experimental database and analyzing the  
27 causal interactions, may be hired to address the aforementioned limitations of previous MBD studies. We  
28 hypothesized that PCA can computationally produce a large probabilistic database of inter-patient joint  
29 kinematics that can be then imported to MBD to compute the corresponding joint moments. In order to  
30 perform MBD however, ground reaction forces and moments (GRF&M) , related to these probabilistic  
31 kinematics, must be first estimated . Previous studies have successfully used artificial neural network (ANN)  
32 to calculate GRF&M [34].

33 ANN is an efficient surrogate model with the ability to learn a nonlinear relationship [28-31]. Once a set  
34 of inputs (e.g. kinematics) and corresponding outputs (e.g. GRF&M) are presented to the network, the  
35 network learns the causal interactions between inputs and outputs. Given a new set of inputs, the trained  
36 neural network (surrogate model) can generalize the relationship to produce the associated outputs. A neural  
37 network therefore can be of significant advantage, especially when the outputs cannot be directly measured  
38 for all sets of inputs. We hypothesized that a trained ANN can be used to estimate the GRF&M related to a  
39 probabilistic database of joint kinematics that have been computationally generated through PCA. It is  
40 expected that a combination of these computational techniques can address the aforementioned limitations of  
41 the previous human gait studies.

42 This study developed a combined computational framework to provide a thorough quantitative insight  
43 into the essential relationships between joint kinematics and joint kinetics. Accordingly (1) a large data set of  
44 probabilistic gait cycles was created based on experimental data in literature for which (2) the qualitative  
45 contributions of individual joint kinematics to joint moments and (3) the quantitative sensitivity indices of  
46 joint moments due to kinematic variations were investigated. The aim of this study was to understand the  
47 relationships between joint kinematics and the resultant joint moments with the long term aim of optimizing  
48 current rehabilitation methods.

## 49 **2. Material and methods**

50 A published repository of experimental gait cycles was adopted for the present study (section 2.1). A  
51 large data set of probabilistic kinematics was then created from experimental gait cycles using PCA (section  
52 2.2). Associated GRF&M were computed using ANN technique (section 2.3). MBD analysis was then  
53 employed to calculate joint moments based on the probabilistic joint kinematics and computed GRF&M  
54 (section 2.4). Once again, PCA was used to determine the contributions of joint kinematics to joint moments  
55 (section 2.5). It should be noted that PCA was used for a twofold purpose: (1) randomizing the joint  
56 kinematics and (2) extracting the interactions between kinematics and joint moments. Figure 1 shows the  
57 schematic diagram of the proposed methodology.

### 58 **2.1. Experimental gait data**

59 A subject pool consisted of four different participants (three males, one female; height:  $168.3 \pm 2.6$  cm;  
60 mass:  $69.2 \pm 6.2$  kg) was adopted from a published repository (<https://simtk.org/home/kneeloads>). This  
61 repository included three dimensional GRF&M (Force plate, AMTI Corp., Watertown, MA, USA) , recorded

62 with a frequency of 1000 Hz and marker trajectory data (10-camera motion capture system, Motion Analysis  
63 Corp., Santa Rosa, CA, USA) recorded at a frequency of 200 Hz for a total number of 144 gait trials. A  
64 modified Cleveland Clinic marker set was used with extra markers on the feet and trunk. These subjects  
65 walked with a variety of different patterns which provided sufficient diversity in this repository. A complete  
66 description of this data set is provided in Fregly et al (2012) [32]. A gait cycle was defined as the time interval  
67 between foot strike of one leg to the following foot strike of the same leg [33]. Subsequently, two complete  
68 gait cycles were picked up from each trial using the associated vertical GRF, leading to a total number of 288  
69 experimental gait cycles (144 trials  $\times$  two gait cycles). Joint kinematic waveforms and segmental motions  
70 were then computed using a three dimensional musculoskeletal model, implemented in MBD analysis (section  
71 2.4). In the present study, “segmental motion” refers to “displacement” and “acceleration” of human body  
72 segments.

## 73 **2.2. PCA-based statistical model**

74 In the traditional scenario of random sampling, input parameters are perturbed independently whereas the  
75 interactions between input parameters are often ignored. Therefore, the conventional randomizing techniques  
76 (e.g., Monte Carlo, Latin hyper cube sampling, etc.) cannot be used to randomize human gait patterns since  
77 joint kinematics are highly coupled to each other and cannot be randomized separately. In other words,  
78 correspondence should be preserved between joint kinematics in order to generate a valid randomized  
79 database. To create a large database of probabilistic joint kinematics from a small experimental database, PCA  
80 was used[26]. The main idea behind this technique is to map the “inter-dependent” variables (joint kinematics)  
81 into a reduced number of corresponding “independent” variables (principal component values) that can be  
82 randomized separately. Randomized independent variables were then inversely mapped into their original

83 inter-dependent variables. For a more detailed study of PCA technique, see [34]. Probabilistic joint kinematics  
84 were generated following the steps below:

85 (1) A total of 288 experimental gait cycles were arranged in a matrix X such that :

$$86 \quad X = [x_1, x_2, x_3, \dots, x_{288}] \quad (1)$$

87 Where  $x_i$  is a single “experimental” gait cycle:

$$88 \quad x_i = [PR_x \ PR_y \ PR_z \ HA \ HF \ HR \ KF \ AF \ SE] \quad 1 \leq i \leq 288 \quad (2)$$

89 In the above equation ,  $PR_x$  is pelvis tilt,  $PR_y$  is pelvis obliquity,  $PR_z$  is pelvis rotation , HA is hip  
90 abduction/adduction, HF is hip flexion/extension , HR is hip rotation, KF is knee flexion/extension , AF is  
91 ankle flexion/extension and SE is subtalar eversion/inversion.

92 (2) Using PCA, a total of nine eigenvectors and the corresponding eigenvalues, associated with the above  
93 nine kinematic variables, were computed for the experimental database (X). The importance of  
94 eigenvectors was ranked with respect to the associated eigenvalues. Higher eigenvalues meant the  
95 associated eigenvectors were more essential and descriptive for the database (X) and the lower  
96 eigenvalues referred to the less-important features that might be caused by noise.

97 (3) The first six important eigenvectors which explained 95% of variance in X were arranged in the matrix E.  
98 The experimental data set (X) was then transformed into principal component (PC) values without  
99 significant loss of information:

$$100 \quad PC \text{ value} = X_{288 \times 9} \times E_{9 \times 6} \quad (3)$$

101 In other words, matrix X, consisted of nine inter-dependent kinematic variables, was transformed into a

102 reduced number of six secondary independent variables (PC values) that can be randomized separately.

103 (4) For the computed PC values, row-wise mean (m) and standard deviation (d) were computed over all the  
104 288 experimental gait cycles. Each PC value was randomly sampled from a normal distribution with a  
105 mean value of m and a standard deviation value of  $\pm 2d$ . Randomized PC values ( $\bar{P}$ ) were then mapped  
106 into their original variables (joint kinematics) resulting in a probabilistic population of joint kinematics (Y)  
107 while the correspondence between coupled kinematics was preserved:

$$108 \quad Y = \bar{P} \times E^{-1} \quad (4)$$

109 in the above equation,  $E^{-1}$  represents the inverse of matrix E.

### 110 **2.3. Ground reaction force and moment computation**

111 A number of computational techniques have been developed to calculate GRF&M only based upon  
112 kinematic waveforms [17, 35, 36]. Oh et al (2013) [35] showed feasibility of calculating ground reaction  
113 forces and moments based on joint kinematics using an artificial neural network. They proved the feasibility  
114 of using ANN-based computed GRF&M to calculate joint moments. This technique was adopted to calculate  
115 the GRF&M, related to the probabilistic joint kinematics. The methodology can be outlined as below:

116 (1) Using MBD software, segmental motions were calculated from probabilistic kinematics.

117 (2) For the single support phase, GRF&M were calculated by subtracting the gravitational acceleration from  
118 segmental acceleration regarding each human body segment (Newtonian mechanics-second law)[37].

119 (3) For the double support phase, a three-layer ANN with 14 inputs (displacements and accelerations of  
120 skeletal segments), three hidden neurons and six output nodes (GRF&M) was constructed (Table 1). For a

121 detailed description of this neural network, see [35]. This structure was trained based on two-thirds of the  
122 experimental kinematics (inputs) and the corresponding measured GRF&M (outputs) obtained from the  
123 experimental repository (section 2.1) and was validated for one-third of the remaining experimental  
124 kinematics [38]. In fact, the experimental repository was divided into three main subsets: train (70%),  
125 validation (15%) and test (15%). Once the network was trained and validated, its prediction ability was  
126 tested for those inputs that were not included in the training procedure (test subset). The trained neural  
127 network was then employed to predict the GRF&M corresponding to the double support phase of  
128 probabilistic kinematics.

129 (4) The cubic spline function was applied to assemble the GRF&M of single support phase (obtained from  
130 Newtonian second law) with the GRF&M of double support phase (obtained from ANN) and reconstruct  
131 the GRF&M of a complete gait cycle. All of the above computations were implemented in MATLAB  
132 (version 2009, The MathWorks, Inc., MA, USA).

#### 133 **2.4. Multi body dynamics analysis**

134 A three dimensional musculoskeletal model was implemented in MBD software AnyBody Modeling  
135 System (version 6.0, AnyBody Technology, Aalborg, Denmark). This model was constructed based on the  
136 University of Twente Lower Extremity Model (TLEM). The TLEM model was a detailed cadaver-based  
137 model which has been previously validated to calculate muscle forces and joint moments[39]. The skeleton  
138 included thorax, trunk, pelvis, thigh, patella, shank and foot segments. Hip joint was modeled as a sphere joint  
139 with three degrees of freedom (DOF): flexion-extension, abduction-adduction and internal-external rotation.  
140 Knee joint was modeled as a hinge joint with only one DOF for flexion-extension and universal joint was  
141 considered for ankle-subtalar complex. The musculoskeletal model also contained 160 muscle-tendon

142 actuators. The musculoskeletal model was scaled to the average anthropometric characteristics of four  
143 participants and was then used in the MBD analysis at three different stages:

144 First, MBD analysis was employed to calculate the joint kinematic waveforms and segmental motions related  
145 to the experimental gait trials (published repository, section 2.1).

146 Second, MBD analysis was also used to calculate the segmental motions related to the probabilistic kinematic  
147 waveforms (section 2.2).

148 Third, the probabilistic kinematics (section 2.2) and the associated GRF&M (section 2.3) were imported into  
149 an inverse dynamics simulation to calculate joint moments.

## 150 **2.5. PCA-based sensitivity analysis**

151 Traditional sensitivity analysis often discards the potential dependencies between input variables and  
152 therefore is not applicable to study human gait with highly inter-dependent joint kinematics. Instead, a  
153 principal component-based technique was adopted following Fitzpatrick et al (2011) [27]. A data matrix (T)  
154 was constructed from probabilistic joint kinematics (section 2.2) and resultant joint moments (section 2.4):

$$155 \quad T = [\text{joint kinematic variables}, \text{joint kinetic variables}] \quad (5)$$

156 PCA was applied to calculate the eigenvectors and eigenvalues for the probabilistic gait cycles (T). Here,  
157 each eigenvector consisted of two separate parts: one part was related to the “joint kinematic variables” and  
158 the other part was related to the “joint kinetic variables”. The “*kinematic*” part represented how the coupled  
159 joint kinematics varied together and the “*kinetic*” part explained how the resultant joint moments were  
160 changed accordingly. In other words, eigenvectors represented the relative contributions of joint kinematics to

161 the variations of joint kinetics. Sensitivity indices were then calculated to “rank” the above contributions  
162 within two steps:

163 (1) The data matrix T was transformed into a secondary orthogonal data space of PC values:

$$164 \quad \text{PC value} = T \times E_T \quad (6)$$

165 In the above equation,  $E_T$  is the feature matrix which contained all eigenvectors of matrix T. PC values  
166 were in fact the secondary independent variables for primary inter-dependent variables (joint kinematics and  
167 kinetics).

168 (2) The average PC values, over all probabilistic gait cycles, contained two separate parts associated with the  
169 “kinematic” and “kinetic” variables. The proportions of the PC values corresponding to the “joint kinematic  
170 variables” to the PC values associated with the “joint kinetic variables” were considered as the sensitivity  
171 indices (SI) of joint moments due to the joint kinematic variations.

## 172 **3. Results**

### 173 **3.1. Generating the probabilistic gait cycles**

174 The PCA-statistical model was randomly sampled and a total number of 500 probabilistic gait cycles  
175 were created. The sampled gait cycles were similar in pattern to the original experimental kinematics (Figure  
176 2). Regarding each set of probabilistic joint kinematics, the trained ANN was used to estimate the GRF&M of  
177 double support phase. Figure 3 shows the average performance of the ANN. Results show that ANN could  
178 accurately predict the GRF&M of double support phase for all three subsets. All of the Pearson correlation  
179 coefficients ( $\rho$ ), between network predictions (y axis) and experimental data (x axis), were above  $\rho=0.98$ .  
180 Figures (3-a) and (3-b) show that the network learned the nonlinear relationship between kinematics and

181 GRF&M ( $\rho=0.98$ ) and Figure (3-c) implies that the network could generalize the relationship and predict the  
182 GRF&M for new kinematics which were not included in the network training ( $\rho=0.97$ ). The overall patterns  
183 of estimated GRF&M were well-consistent with the experimental GRF&M (Figure 4). Computed joint  
184 moments were also similar (in terms of the overall patterns) to those joint moments which were computed  
185 based on “experimental” kinematics and “measured” GRF&M (Appendix, Figure A.1). This in turn approved  
186 the validity of the ANN-based computed GRF&M.

### 187 **3.2. Relative contributions of joint kinematics**

188 Eigenvectors are presented to demonstrate the relative contributions of individual joint kinematics to the  
189 variations of joint moments (Figure 5). For the hip joint, results indicate that the first eigenvector (the most  
190 important mode of variation) of the hip abduction moment was mainly attributed to changes in the pelvis  
191 rotation and hip abduction whilst the second eigenvector (the second important mode of variation) was highly  
192 attributed to changes in the hip joint rotation combined with knee joint flexion. PCA demonstrates the higher  
193 contributions of the pelvis rotation and hip joint abduction over the lesser contributions of other kinematics to  
194 the hip abduction moment. For hip flexion moment, first eigenvector demonstrates the higher contributions of  
195 hip flexion and knee flexion kinematics to hip flexion moment whilst the second eigenvector implies that hip  
196 flexion moment was also influenced by pelvis rotation and pelvis tilt. Similarly, hip rotation moment was  
197 mainly affected by changes in the pelvis rotation, pelvis obliquity and hip rotation.

198 The knee joint adduction moment was found to be sensitive to the pelvis rotation, hip abduction, and  
199 knee flexion. Eigenvectors also highlight the substantial contributions of the pelvis rotation and knee flexion  
200 (first eigenvector) to the knee flexion moment compared to the lesser contributions of the hip flexion and hip  
201 rotation (second eigenvector). Knee rotation moment was heavily influenced by hip abduction and knee

202 flexion in the first mode of variation (first eigenvector) as well as by hip flexion in the second mode of  
203 variation (second eigenvector). For the ankle joint, results show the key relationships between knee and ankle  
204 joints flexion and ankle flexion moment. Eigenvectors also reveal that ankle joint rotation moment was highly  
205 influenced by the hip joint rotation and subtalar joint eversion.

### 206 **3.3. Sensitivity indices of joint moments**

207 Sensitivity indices (SI) of joint moments due to changes in joint kinematics are presented in Figure 6.  
208 Results highlight that hip joint abduction moment was significantly more sensitive to variations in pelvis  
209 rotation (SI=0.38) and the hip abduction (SI=0.4) than to variations in other kinematics. Hip flexion moment  
210 was noticeably sensitive to sagittal-plane kinematics including pelvis tilt (SI=0.23), hip flexion (SI=0.35),  
211 knee flexion (SI=0.26), and ankle flexion (SI=0.17). Hip rotation moment was slightly more sensitive to  
212 pelvis obliquity (SI=0.28), pelvis rotation (SI=0.22) and hip rotation (SI=0.4). Three dimensional knee joint  
213 moments (adduction, flexion and rotation components) were mainly sensitive to changes in hip and knee  
214 joints flexion (SI $\cong$ 0.3). Both adduction and rotation components of the knee joint moment were highly  
215 influenced by the hip joint abduction (SI =0.32). In addition, both adduction and flexion components of the  
216 knee joint moment were sensitive to changes in pelvis rotation (for knee adduction moment: SI =0.35; for  
217 knee flexion moment: SI =0.28) but fairly insensitive to changes in pelvis tilt, pelvis obliquity and subtalar  
218 eversion. Similarly, ankle flexion moment was more sensitive to the variations in leg flexion including hip  
219 flexion (SI=0.3), knee flexion (SI=0.29) and ankle flexion (SI=0.44) while ankle rotation moment was mainly  
220 affected by the hip joint rotation (SI=0.39) and subtalar joint eversion (SI=0.29). In general, varying the  
221 kinematics of an individual joint not only changed the moment about that joint, but also could yield to  
222 substantial changes in the moments of adjacent joints. For example, hip joint abduction could noticeably affect

223 the hip abduction moment as well as adduction and rotation components of the knee joint moment. Similarly,  
224 changes in the knee flexion led to substantial changes in three dimensional knee joint moments as well as  
225 abduction and flexion components of the hip joint moment.

## 226 **4. Discussion**

### 227 **4.1. Relative contributions and sensitivity indices**

228 In the conventional sensitivity analysis, a single input is perturbed while other inputs are kept constant.  
229 The individual contribution of each input to an output measure therefore can be easily perceived. This  
230 technique however cannot be employed to discriminate between different contributions of dependent inputs  
231 where all inputs are simultaneously involved to alter an output measure. For example, the overall variation in  
232 a joint moment is the result of simultaneous changes in all joint kinematics. Fitzpatrick et al (2011) [27]  
233 suggested using PCA as an alternative to interpret the “cause-and-effect” relationships between dependent  
234 inputs and outputs (section 2.5). Eigenvectors of the data space (i.e. probabilistic joint kinematics and the  
235 resultant joint moments), provided a qualitative comparison between the contributions of different kinematics  
236 (see section 3.2). For a quantitative “ranking” of the overall contributions of different joint kinematics,  
237 eigenvectors were further used to transform the inter-dependent joint kinematics and joint moments into an  
238 orthogonal data space. In the orthogonal data space, inter-dependent variables were treated as independent  
239 variables (PC values). The ratios of “joint kinematic” PC values to “joint kinetic” PC values were interpreted  
240 as sensitivity indices (see section 3.3).

## 241 **4.2. Validity of the results**

242 The fact that the patterns of probabilistic gait cycles and the computed joint moments are similar to the  
243 patterns of experimental data reassures and builds confidence in the results. Although, it cannot be guaranteed  
244 that human body replicates these patterns, our findings are well consistent with previously published clinical  
245 reports in literature. For example, our results highlight the influence of hip joint abduction and rotation  
246 kinematics on hip abduction moment which is in agreement with the study of Kraus et al (2012)[40]. PCA  
247 findings also highlight the sensitivity of knee adduction moment to changes in pelvis rotation, hip  
248 abduction/flexion/rotation, and knee flexion. Likewise, Fregly et al (2007)[41] and Barrios et al (2010)[6]  
249 demonstrated the influence of pelvis rotation, hip adduction and hip internal rotation and leg flexion on knee  
250 adduction moment. Moreover, PCA demonstrated the concurrent influence of pelvis rotation, hip flexion, hip  
251 rotation and knee flexion kinematics on knee flexion moment and knee adduction moment components (see  
252 Figure 5). Walter et al (2010)[42] and Creaby et al (2013)[43] also reported that kinematic modifications  
253 which decrease knee adduction moment may adversely increase knee flexion moment. These clinical  
254 observations can be justified according to the aforementioned multi-effect kinematics which were found to be  
255 shared between flexion and adduction components of the knee joint moment.

## 256 **4.3. Applications in gait rehabilitation**

257 Clinical biomechanics has revealed the importance of gait modification strategies in pre- and  
258 post-surgical stages [44-49]. Gait modification aims to alter joint loading distributions and decrease load on an  
259 affected limb through minor changes in the human gait pattern. Majority of the studies, concerned with the  
260 gait modification designs, are established based on conventional MBD analysis [6, 41, 50]. However, MBD  
261 alone does not provide a systematic investigation of joint kinematics that influence rehabilitation outcome.

262 Therefore, the synergistic joint kinematic changes, required for joint offloading, would be very challenging to  
263 determine by typical MBD.

264 Our findings highlighted the importance and contributions of different joint kinematics to joint moments.  
265 The most effective and ineffective joint kinematics with significant influence on joint moments were  
266 documented. Moreover, joint kinematics with simultaneous effects on adjacent joint moments were also  
267 highlighted leading to a preference or avoidance about specific kinematics to be involved in a targeted  
268 rehabilitation. These quantitative understandings therefore, can provide significant benefits in design and  
269 optimization of an objective gait retraining strategy. Considering the relative importance of kinematics, an  
270 objective rehabilitation can be designed through the most influential kinematics.

#### 271 **4.4. Limitations of the study**

272 This study developed a computational framework to provide a quantitative understanding of the  
273 “cause-and-effect” interactions between joint kinematics and joint moments. To accommodate the inter-patient  
274 variability, PCA was employed to create a large probabilistic database of joint kinematics. Perhaps the main  
275 limitation of the developed framework was that the primary experimental database contained a small number  
276 of four participants. However, these subjects were quite different in anthropometric characteristics, preferred  
277 walking velocity, and shoe type. Moreover, each subject completed a variety of different walking trials  
278 ranging from normal gait to exaggerated rehabilitation patterns. Accordingly, it is expected that the present  
279 repository accommodated sufficient diversity. The second limitation was that the knee joint was modeled as a  
280 hinge joint in MBD analysis with only one DOF for flexion-extension. Nevertheless; the proposed  
281 methodology will be equally applicable for more numbers of subjects and a MBD analysis with higher DOFs.

## 282 **5. Conclusion**

283 This study provided a quantitative understanding of the interactions between joint kinematics and the  
284 resultant joint moments. A computational framework was developed to (1) generate a large database of  
285 probabilistic gait cycles, (2) assess the contributions of individual joint kinematics to the joint moments and (3)  
286 evaluate the relative sensitivity indices of joint moments due to joint kinematic variations. Results highlighted  
287 the high contributions of pelvis rotation and hip abduction to hip abduction moment, the importance of hip  
288 and knee joints flexion for hip flexion moment, and the effect of pelvis obliquity, pelvis rotation and hip  
289 rotation on hip rotation moment. Results also revealed the importance of pelvis rotation, hip abduction and  
290 knee flexion for knee adduction moment, the influence of pelvis rotation and knee flexion on knee flexion  
291 moment and the contributions of hip abduction and knee flexion to knee rotation moment. Results also showed  
292 that ankle flexion moment was highly influenced by knee and ankle joints flexion whilst ankle rotation  
293 moment was mainly influenced by hip rotation and subtalar eversion kinematics. It is expected that such  
294 quantitative insights provide potential benefits to direct the rehabilitation design procedure to optimal gait  
295 retraining programs.

### 296 **Conflict of interest statement**

297 The authors have no conflict of interests to be declared.

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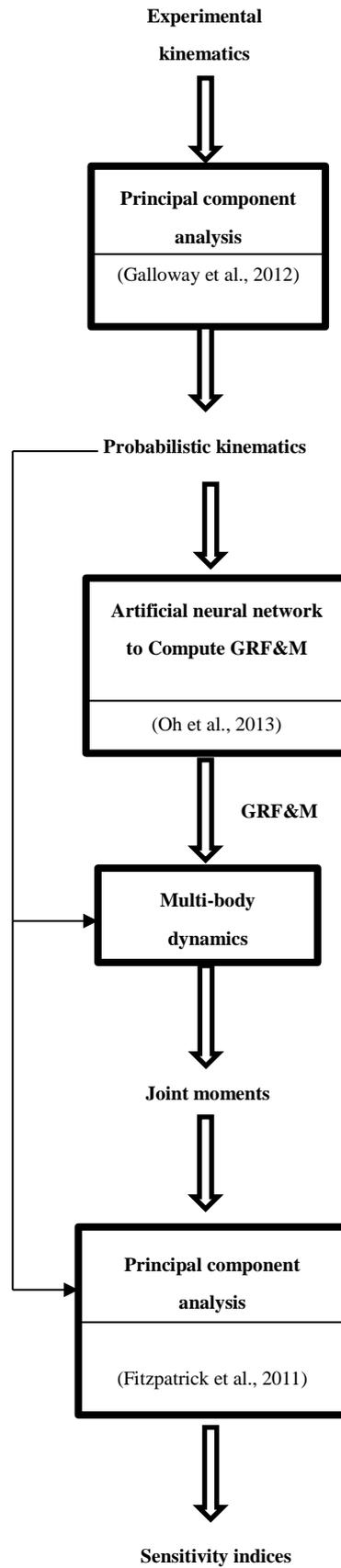


Figure 1 A schematic diagram of the proposed methodology.

Figure

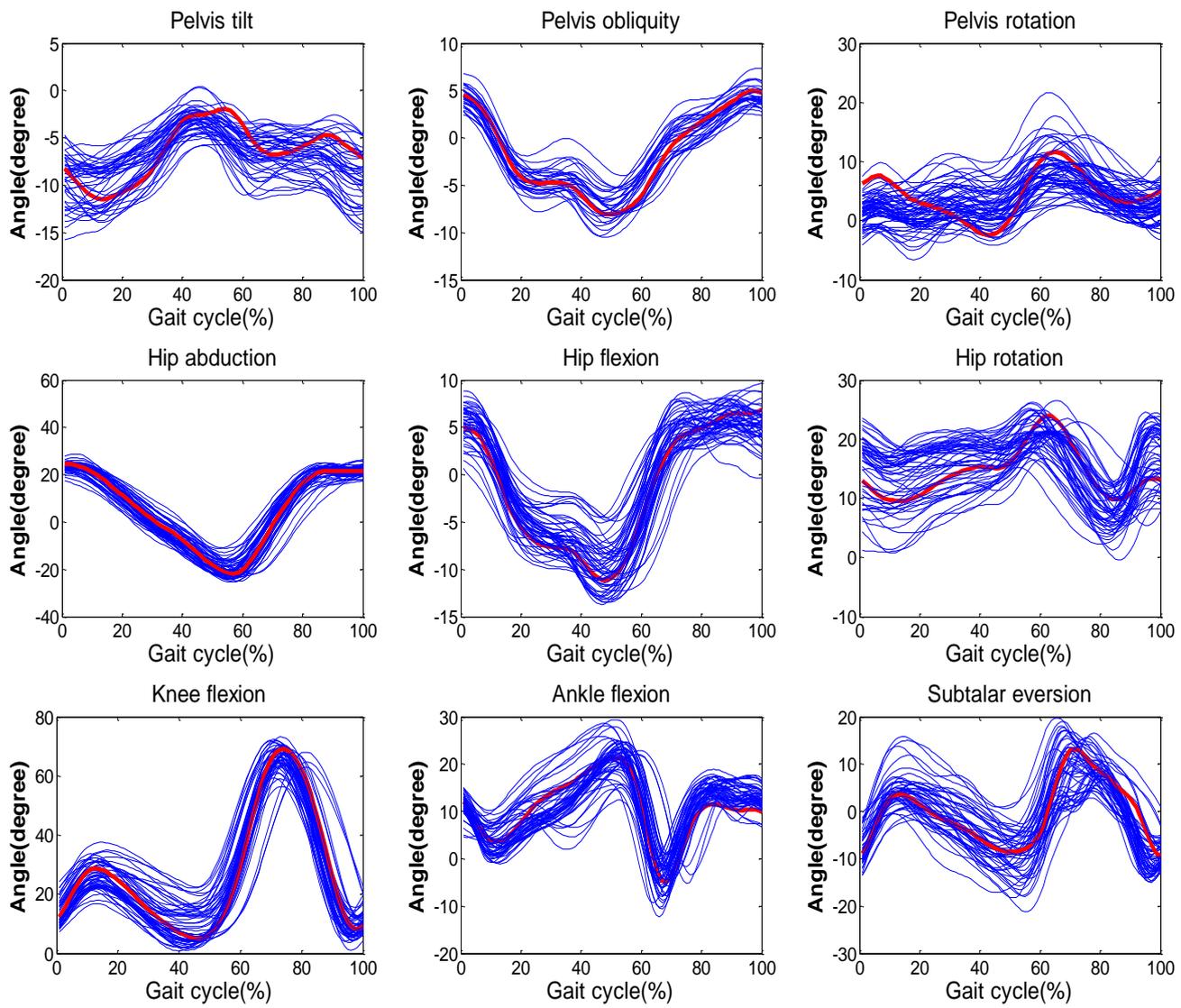


Figure 2 Probabilistic gait cycles (blue) were seen to be similar in pattern to the original experimental kinematics (red).

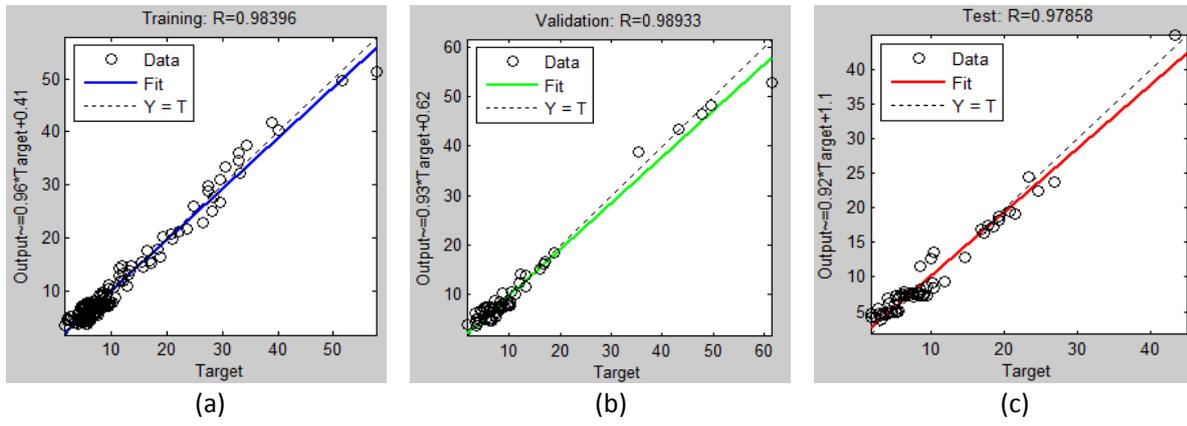


Figure 3 Network predictions (vertical axis) versus experimentally measured GRF&M (horizontal axis) for (a) train (b) validation and (c) test subsets.

Figure

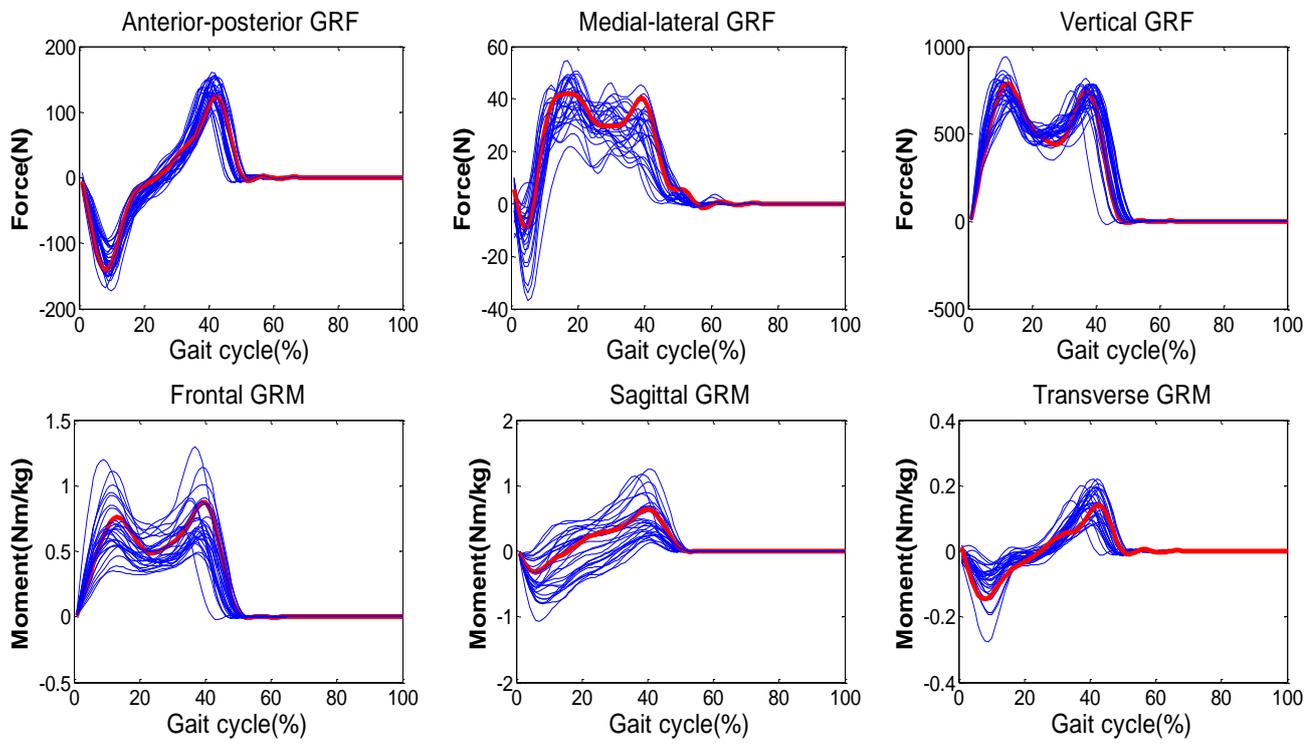
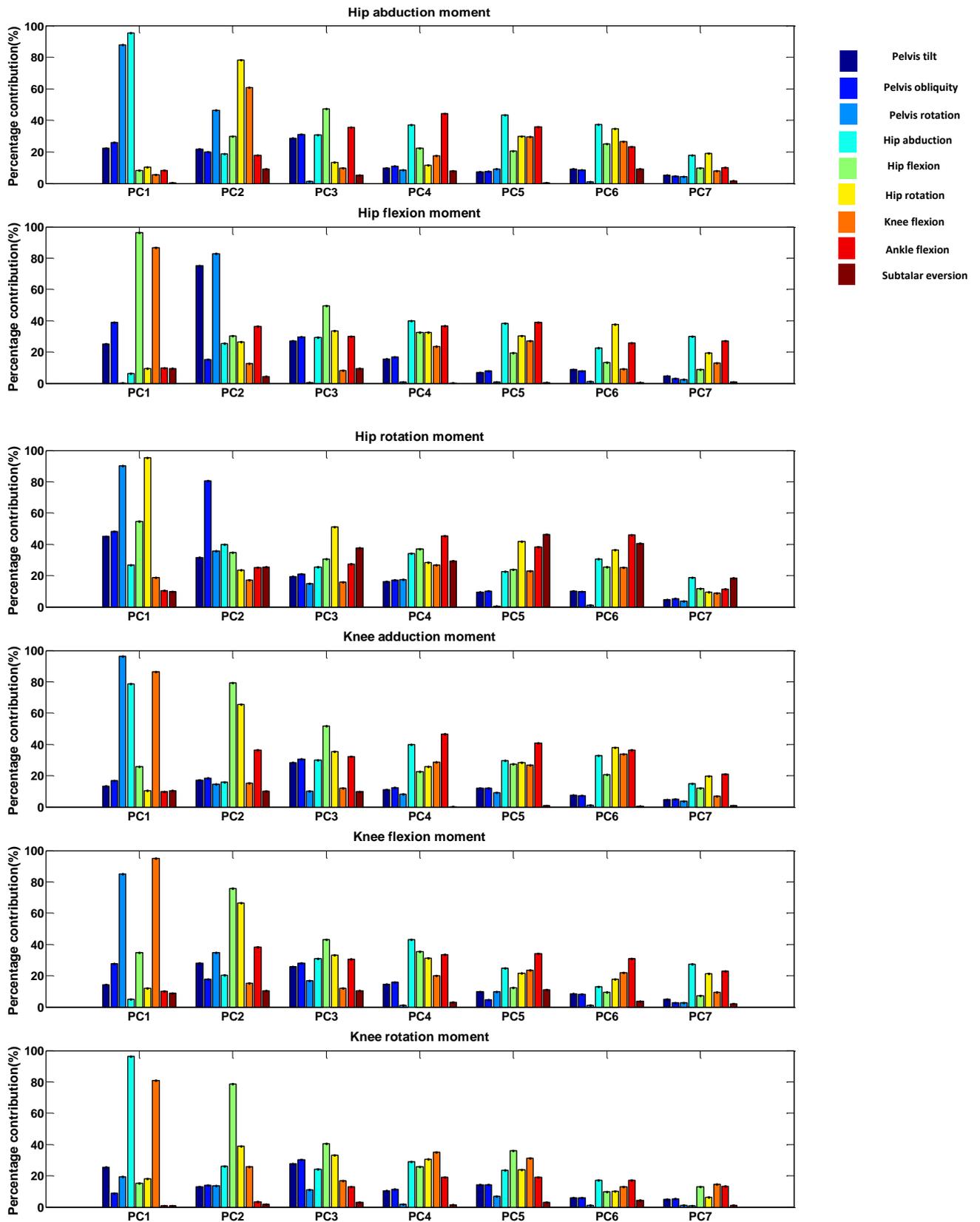


Figure 4 Predicted GRF&M (blue) were seen to match with the experimental GRF&M (red) in terms of the overall patterns.

Figure



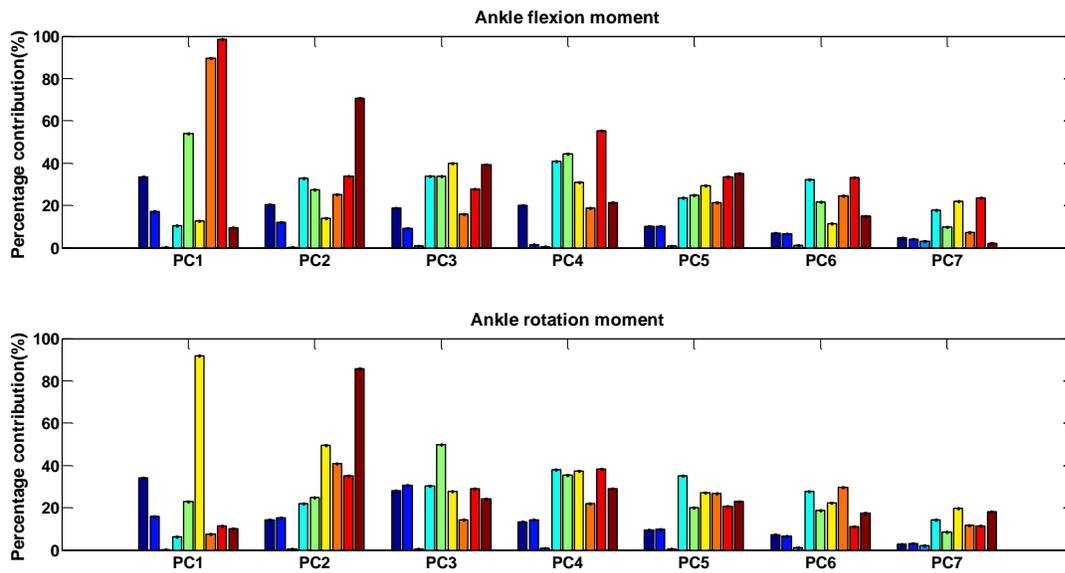


Figure 5 Eigenvectors represented the comparative contributions of individual kinematics to overall variations of the joint moments.

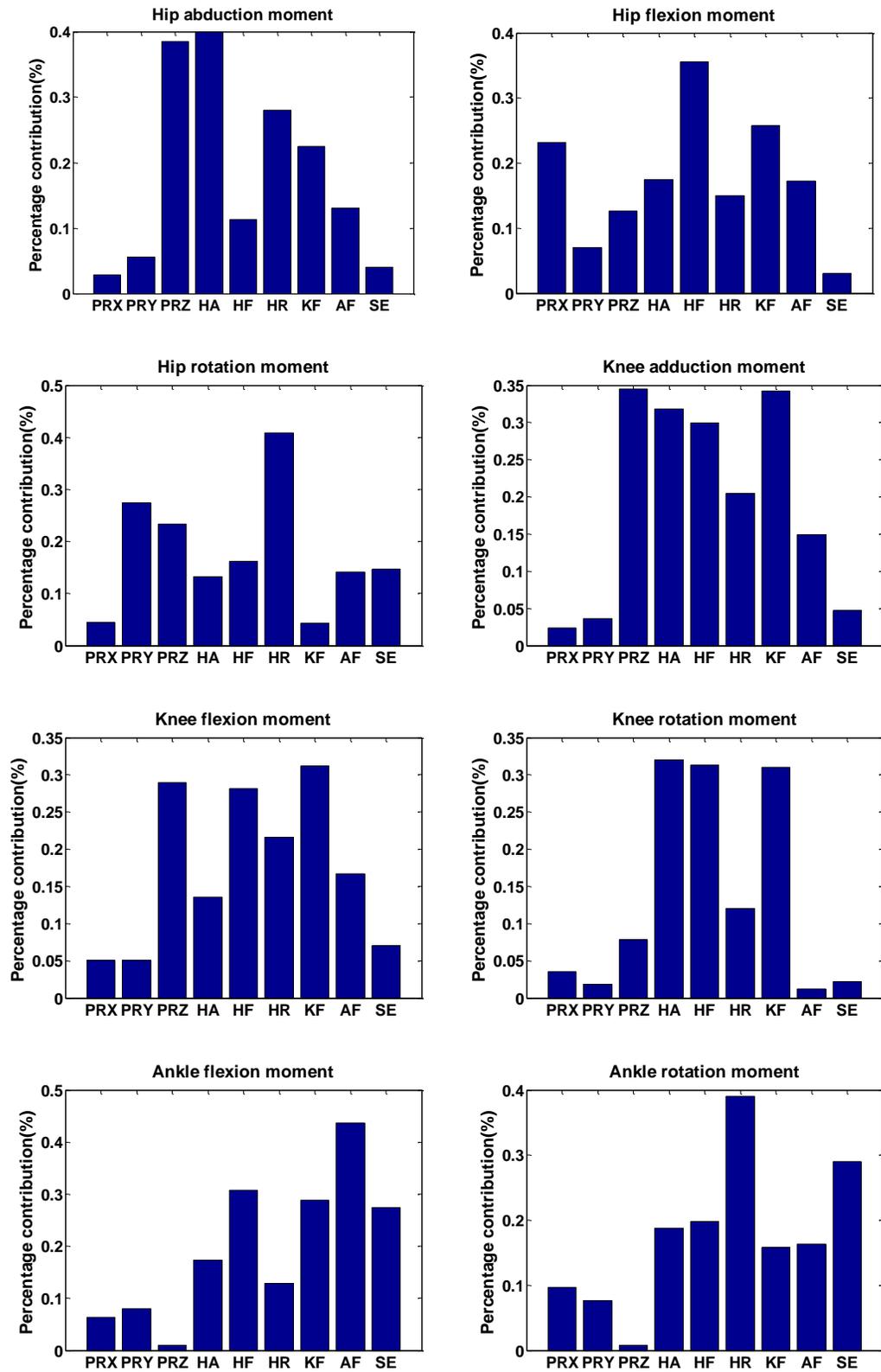


Figure 6 Quantitative sensitivity indices of joint moments due to kinematic variations (obtained from PC values).

Table 1 14 input variables for artificial neural network

<b>Input variable</b>	<b>Description</b>
<b>Displacement</b>	Left knee joint centre in X-axis
	Left hip joint centre inY-axis
	Right ankle joint centre inZ-axis
	Left foot segment mass centre inX-axis
	Pelvis segment mass centre inX-axis
	Left thigh segment mass centre inY-axis
	Right shank segment mass centre in Z-axis
<b>Acceleration</b>	Thorax segment mass centre inY-axis
	Right knee joint centre inZ-axis
	Right shank segment mass centre inX-axis
	Right foot segment mass centre inY-axis
	Right thigh segment mass centre inY-axis
	Left foot segment mass centre inZ-axis
	Pelvis segment mass centre inZ-axis