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Combined probabilistic and principal component analysis approach for multivariate sensitivity evaluation and application to implanted patellofemoral mechanics

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ABSTRACT

Many aspects of biomechanics are variable in nature, including patient geometry, joint mechanics, implant alignment and clinical outcomes. Probabilistic methods have been applied in computational models to predict distributions of performance given uncertain or variable parameters. Sensitivity analysis is commonly used in conjunction with probabilistic methods to identify the parameters that most significantly affect the performance outcome; however, it does not consider coupled relationships for multiple output measures. Principal component analysis (PCA) has been applied to characterize common modes of variation in shape and kinematics. In this study, a novel, combined probabilistic and PCA approach was developed to characterize relationships between multiple input parameters and output measures. To demonstrate the benefits of the approach, it was applied to implanted patellofemoral (PF) mechanics to characterize relationships between femoral and patellar component alignment and loading and the resulting joint mechanics. Prior studies assessing PF sensitivity have performed individual perturbation of alignment parameters. However, the probabilistic and PCA approach enabled a more holistic evaluation of sensitivity, including identification of combinations of alignment parameters that most significantly contributed to kinematic and contact mechanics outcomes throughout the flexion cycle, and the predictive capability to estimate joint mechanics based on alignment conditions without requiring additional analysis. The approach showed comparable results for Monte Carlo sampling with 500 trials and the more efficient Latin Hypercube sampling with 50 trials. The probabilistic and PCA approach has broad applicability to biomechanical analysis and can provide insight into the interdependencies between implant design, alignment and the resulting mechanics.

1. Introduction

Uncertainty is present in many aspects of biomechanics and orthopaedics; factors, such as patient geometry, kinematics and joint loading, implant alignment and clinical outcomes, are all variable in nature. Sensitivity analyses, typically involving perturbations of individual parameters, provide important insights into changes in performance but do not consider interaction effects that may exist between parameters. Probabilistic analysis represents uncertain parameters with a distribution in order to predict bounds of performance and is often used in conjunction with sensitivity analysis to gauge the robustness of mechanical or kinematic outputs to variability in specific parameters. By perturbing multiple input parameters in each trial, probabilistic analysis considers the potential interaction effects between parameters. Biomechanical studies have used probabilistic analysis to characterize the effect of variability in parameters like component alignment, ligament attachment site location and geometric variation (Dopico-González et al., 2010; Baldwin et al., 2009a; Laz et al., 2006). In the probabilistic framework, sensitivity is evaluated for each performance measure individually, and relationships between performance measures throughout a motion cycle are not considered.

Alternatively, principal component analysis (PCA) can be applied to represent the variability across all parameters (including multiple inputs and their outcome measures) by identifying key relationships in the data. Establishing common modes of change among the parameters, PCA is a mathematical technique that reduces the dimensionality of a data set with a large number of variables to a small number of variables that retain a pre-defined portion (e.g. 95%) of the overall variation present in the data set (Jolliffe, 2002). PCA has been applied in biomechanics to account for subject to subject variability in gait kinematics (Deluzio et al., 1997) and geometry with statistical shape modeling (Cootes et al., 1995, Bryan

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et al., 2009, Fitzpatrick et al., 2008; Barratt et al., 2008; Shim et al., 2008; Rajamani et al., 2007). For example, Stindel et al. (2002) applied PCA techniques to develop a computed assisted surgery (CAS) system that morphed generic bony knee morphology to a patient-specific representation based on inter-operatively digitized geometry.

The objective of the current study was to develop a combined probabilistic and principal component analysis technique to characterize coupled relationships in multivariate orthopaedic analyses. With large numbers of parameters, traditional sensitivity analysis becomes cumbersome and difficult to interpret as the relationship between parameters must be evaluated

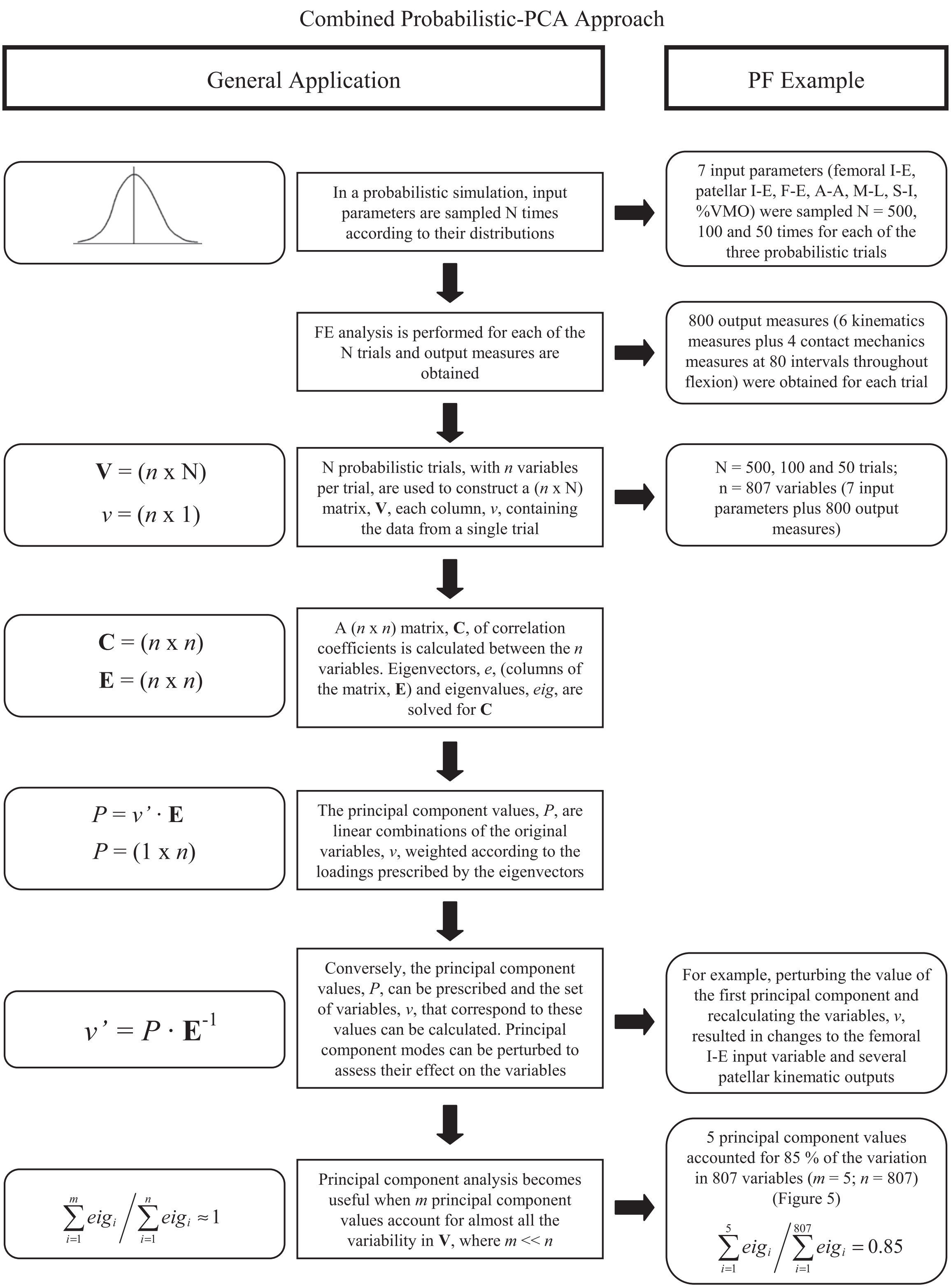

Fig. 1. Schematic of the coupled probabilistic and principal component analysis (PCA) approach to develop relationships between input parameters and output measures. Shown for general application and an example: patellofemoral (PF) mechanics.

individually. In the combined probabilistic and PCA approach, a probabilistic Monte Carlo analysis was used to construct a data set incorporating variability in all parameters and then PCA was applied to investigate the modes of variation relating input parameters and output measures. Sensitivity predictions based on the principal component (PC) values were compared to traditional sensitivity factors. The coupled probabilistic and PCA implementation is notably different from other probabilistic PCA (PPCA) studies (Tipping and Bishop, 1999; Chen et al., 2009), which contrastingly attempt to develop probabilistic representations of the principal components to account for noise or uncertainty in collected data.

The benefits of the combined approach were demonstrated in an application to characterize the effect of implant alignment and loading on the resulting patellofemoral (PF) joint mechanics in a total knee replacement (TKR). The PF application was selected because relative alignment of patellar and femoral components has been identified as an important factor impacting the kinematics, contact mechanics and functional performance of the PF joint and ultimately, the success of the TKR (Kawano et al., 2002; Chan and Gill, 1999; Lee et al., 1999; Berger et al., 1998; Singerman et al., 1997). Numerous cadaveric studies have evaluated changes in clinically relevant parameters to assess their impact on kinematics, load transfer and the surrounding structures, including evaluation of patellar thickness (Ghosh et al., 2009), patellar resection angle (Kawano et al., 2002), patellar component medial-lateral (M–L) and superior-inferior (S–I) placement (Lee et al., 1999; Yoshii et al., 1992) and femoral internal–external (I–E) rotation (Singerman et al., 1997; Anouchi et al., 1993; Rhoads et al., 1990). Experimental studies, however, are constrained in the number of evaluations that can feasibly be performed. Experimentally verified computational models are ideally suited to assess sensitivity of PF mechanics with parameter perturbations. Previous computational studies have

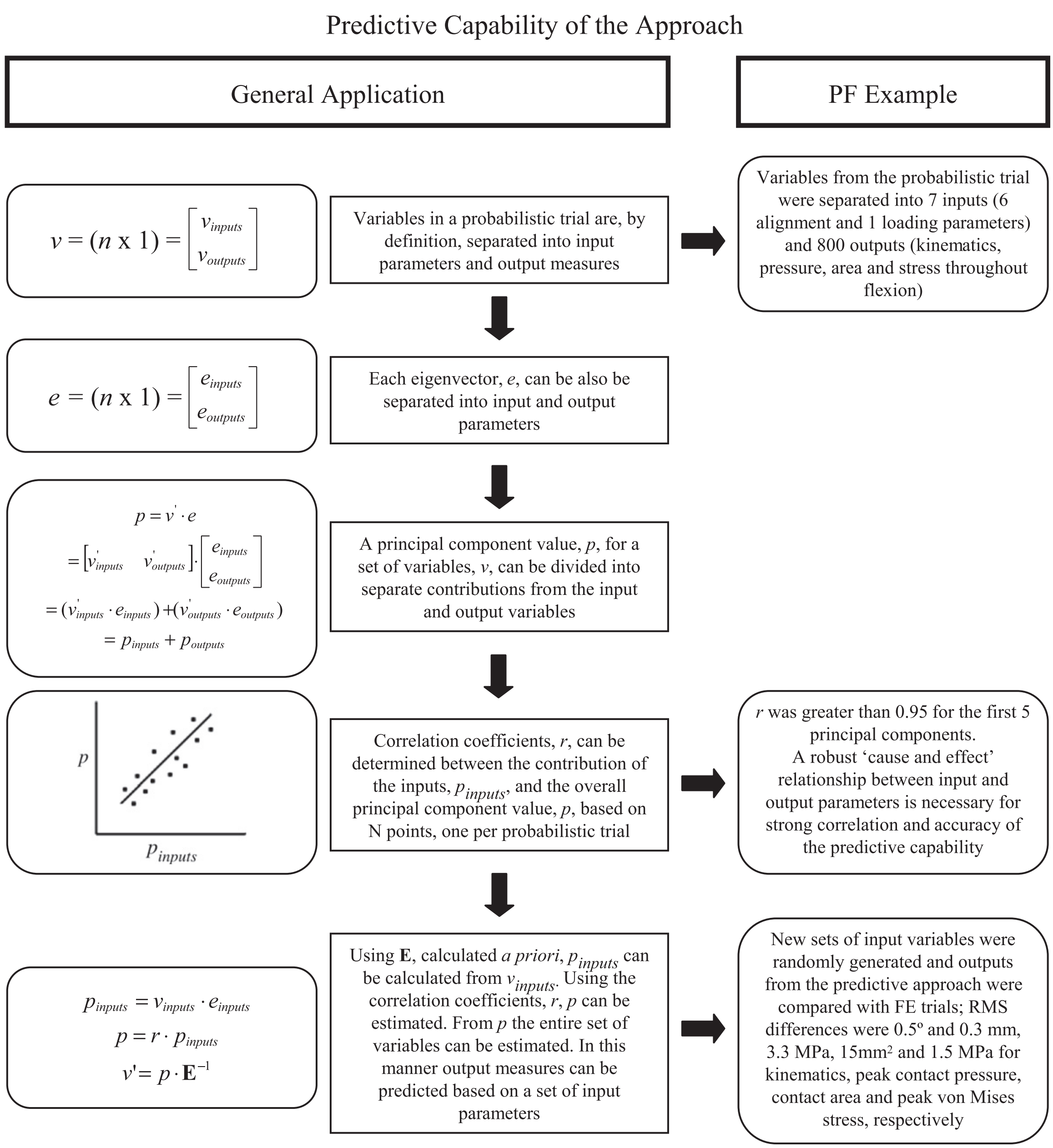

Fig. 2. Schematic of application of the probabilistic and principal component analysis (PCA) approach to predict output measures from a set of input parameters. Shown for general application and an example: patellofemoral (PF) mechanics.

considered the effect of femoral component I–E positioning, M–L patellar component positioning and quadriceps load distribution on predicted PF kinematics and contact forces (Kessler et al., 2008; D'Lima et al., 2003; Elias et al., 2006; Dhaher and Kahn, 2002). These studies, however, have typically altered a single parameter in isolation, thus interactions between alignment and loading variables were not considered.

Using the probabilistic and PCA approach in this application established relationships between alignment and loading conditions and PF mechanics. The ability of these relationships to predict performance, without performing additional analyses, for a new set of input parameters was also evaluated. Quick and reliable predictions of joint mechanics for a TKR subject based on implant placement have the potential to aid in implant design, alignment fixtures and inter-operative decision support applications.

2. Methods

2.1. Probabilistic and PCA approach

The combined approach applies PCA to a data matrix constructed from perturbed parameters and outcome measures from probabilistic trials performed with a Monte Carlo simulation (Fig. 1). Monte Carlo simulation accounts for variability in the input parameters by repeated random sampling of the parameters according to their distributions in order to populate a distribution of performance. Each input parameter is defined by a distribution type and parameters, for example, mean and standard deviation for a normal distribution. While Monte Carlo simulation is often referred to as the "gold standard", it should be noted that the accuracy of the results are dependent on the number of trials. Traditional Monte Carlo sampling results in more trials near the mean and fewer trials covering the entire sample space. Alternatively, Latin Hypercube sampling attempts to ensure an even coverage of the sample space by partitioning it such that the associated probability of each partition is equal (McKay et al., 1979). Larger partitions exist at the tails of the distributions and more partitions near the mean, thus reducing the risk of clustering of samples. The result is a good spread of data over the sample space in a smaller number of trials than traditional sampling.

Sensitivity is commonly evaluated in probabilistic analysis (Dopico-González et al., 2010; Easley et al., 2007; Laz et al., 2006) to identify the factors that have the most significant effect on the resulting outputs. Several different types of sensitivity measures are commonly used. Traditionally, sensitivity assesses the change in performance when a specific variable is perturbed and has been computed in design-of-experiment (DOE) studies. Alternatively, in Monte Carlo analyses, correlation coefficients serve as a measure of the strength of the relationship between a particular input parameter and output measure. These linear measures can be computed for a performance measure at an instant in an activity or can be averaged over a cycle or portions of a cycle, for an output to provide indications of relative rank. Sensitivity measures computed with DOE and probabilistic analyses can consider changes in multiple input variables but are dependent on the perturbation levels utilized. In general, as they are based on a single performance measure, sensitivity measures do not consider the complex interdependencies between multiple input and output parameters throughout a cycle.

In order to develop further insight into the interdependent relationships between input and output parameters, PCA is applied to the probabilistic data (Fig. 1). The eigen-based PCA determines a series of modes characterizing common changes in the data with the first mode representing the largest amount of variation. In each mode, the eigenvalue represents the amount of variation explained and the eigenvector or principal component defines how each of the parameters is changed. PC values are calculated as linear combinations of the variables from the probabilistic trials, weighted according to the eigenvectors. PCA has been used to create statistical shape models describing multivariate data sets with a small number of shape parameters without significant loss of information (Reed et al., 2009; Cootes et al., 1995). While PCA has been applied to analyze variability in biomechanics data, e.g. gait kinematics (Deluzio et al., 1997), it has not been used previously to identify key relationships between input and output parameters.

To assess the effect of changes in a specific mode of variation, the PC value can be perturbed, resulting in a corresponding new set of variables that can be used to assess the effects of the perturbation on input and output parameters (Fig. 1). This approach is analogous to computing a traditional sensitivity factor (change in output due to change in input) while noting that a mode of variation is perturbed instead of a specific variable. The level of perturbation for each principal component mode was based on the variability observed in the probabilistic data. For each probabilistic trial, PC values were determined and a standard deviation was computed over all trials. The perturbation for each mode was set equal to 2 standard deviations of the PC values.

The analysis described above maps PC values to their constituent variables, which consist of both inputs and outputs. A PC value for a set of variables can be divided into separate contributions from the input and output variables. If a sufficiently robust 'cause and effect' relationship exists between input parameters and output measures, correlations may be established between modes of variation of the overall PC value and the contribution of the inputs only (Fig. 2). This has an applicability in predicting output measures from the knowledge of input parameters. To evaluate the predictive capability of the approach, a particular PC value was estimated from inputs and subsequently used to predict output measures. Using this approach, performance can be quickly predicted for a new set of input parameters as an alternative to performing an additional analysis.

2.2. Application to patellofemoral mechanics

To demonstrate the approach, the probabilistic analysis was performed using a finite element (FE) model of the isolated PF joint based on Baldwin et al. (2009b). The subject-specific knee model, developed in Abaqus/Explicit (Simulia, Providence, RI), was implanted with an anatomic TKR and a deep knee bend activity

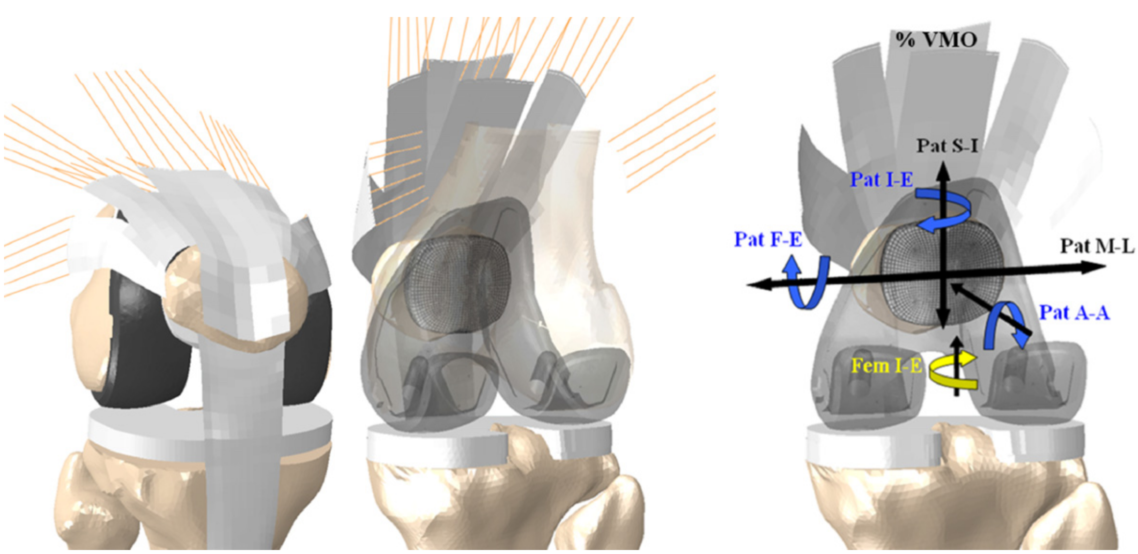

Fig. 3. Left: frontal view of the finite element model of the patellofemoral joint, including the patellar ligament, vasti complex and rectus femoris of the extension mechanism in flexion. Center: posterior view of the FE model including femoral and patellar components. Right: probabilistic alignment parameters: femoral I–E alignment, patellar I–E, F–E and A–A alignments, M-L and S–I translations and distribution of the quadriceps load (%VMO).

was simulated. The tibial, femoral and patellar bones and articular cartilage were extracted from magnetic resonance scan data from a healthy normal subject. Patellar and femoral cruciate retaining components were sized and positioned by a surgeon in a neutral alignment (Fig. 3). The patellar ligament, rectus femoris (RF) and vasti tendons were represented by deformable hyperelastic 2D membrane elements, with uni-axial tension characteristics matching literature values (Atkinson et al., 1997; Stäubli et al., 1999). A 2000 N load was distributed among the heads of the RF and vasti (separated into lateralis longus (VLL), lateralis obliquus (VLO), intermedius (VI), medialis longus (VML) and medialis obliquus (VMO)) structures proportional to their physiological cross-sectional areas (Farahmand et al., 1998). Penalty-based contact was defined between all soft-tissue structures and relevant bony and articular surfaces for wrapping. Kinematic predictions from the FE model were validated by comparisons with experimental results from the Kansas knee simulator (Baldwin et al., 2009b).

Probabilistic analyses were carried out with Monte Carlo simulation using standard sampling with 500 and 100 trials and Latin Hypercube sampling with 50 trials. The accuracy of the predictions was compared for the varying number of trials and sampling methods, with a maximum sampling error of 1.9% on the 5% and 95% bounds with the 500 trial Monte Carlo simulation (Haldar and Mahadevan, 2000). The analyses included seven independent input parameters reported to affect PF mechanics: femoral I–E alignment, patellar I–E, flexion–extension (F–E) and adduction–abduction (A–A) alignment, patellar M–L and S–I translations, as well as percentage of the quadriceps load on the VMO tendon (Fig. 3). Each parameter was assumed to be normally distributed, with means and standard deviations based on variability quantified in experimental studies (Lee et al., 1999, 2004; Nagamine et al., 2001; Chan and Gill, 1999; Akagi et al., 1999; Anouchi et al., 1993; Gomes et al., 1988) or assessed in computational studies (Kessler et al., 2008; D'Lima et al., 2003; Heegaard et al., 2001) (Table 1). The probabilistic analysis predicted the 5% and 95% bounds of six-degree-of-freedom PF kinematics, contact mechanics (area and pressure), von Mises stress and M–L contact force at 80 intervals throughout the flexion cycle. For comparison with the PCA results, correlation coefficients were computed between each input and output parameter and averaged over the flexion cycle.

PCA was performed on the data matrix consisting of the Monte Carlo trials; data from each probabilistic trial comprised the seven alignment and loading parameters plus resultant output mechanics (six-degree-of-freedom kinematics, contact pressure and area, von Mises stress, M–L force) through the flexion cycle. By varying PC values, relationships between changes in alignment and loading and PF mechanics could be characterized (Fig. 1).

Lastly, the capability of the PCA model to accurately predict performance was assessed. Using linear regression relationships relating the contribution of the input parameters to the overall PC value, 10 randomly generated sets of alignment and loading parameters were mapped to their representative PC values, which were subsequently mapped to PF mechanics outputs (Fig. 2). The PCA-based mechanics predictions were compared with outputs from an FE model.

Table 1
Probabilistic input parameters.

Component	Degree of freedom	Standard deviation
Patellar	Medial–lateral (M–L)	1 mm
	Superior–inferior (S–I)	1 mm
	Flexion–extension (F–E)	3.3°
	Internal–external (I–E)	3.3°
	Adduction–abduction (A–A)	5.0°
Femoral	Internal–external (I–E)	1.6°
Percentage of the quadriceps load on the vastus medialis obliquus (VMO) tendon		3.3%

3. Results

Results are presented for the PF application to demonstrate the combined probabilistic and PCA approach. The 5% and 95% bounds of the probabilistic analysis evaluated the robustness of the

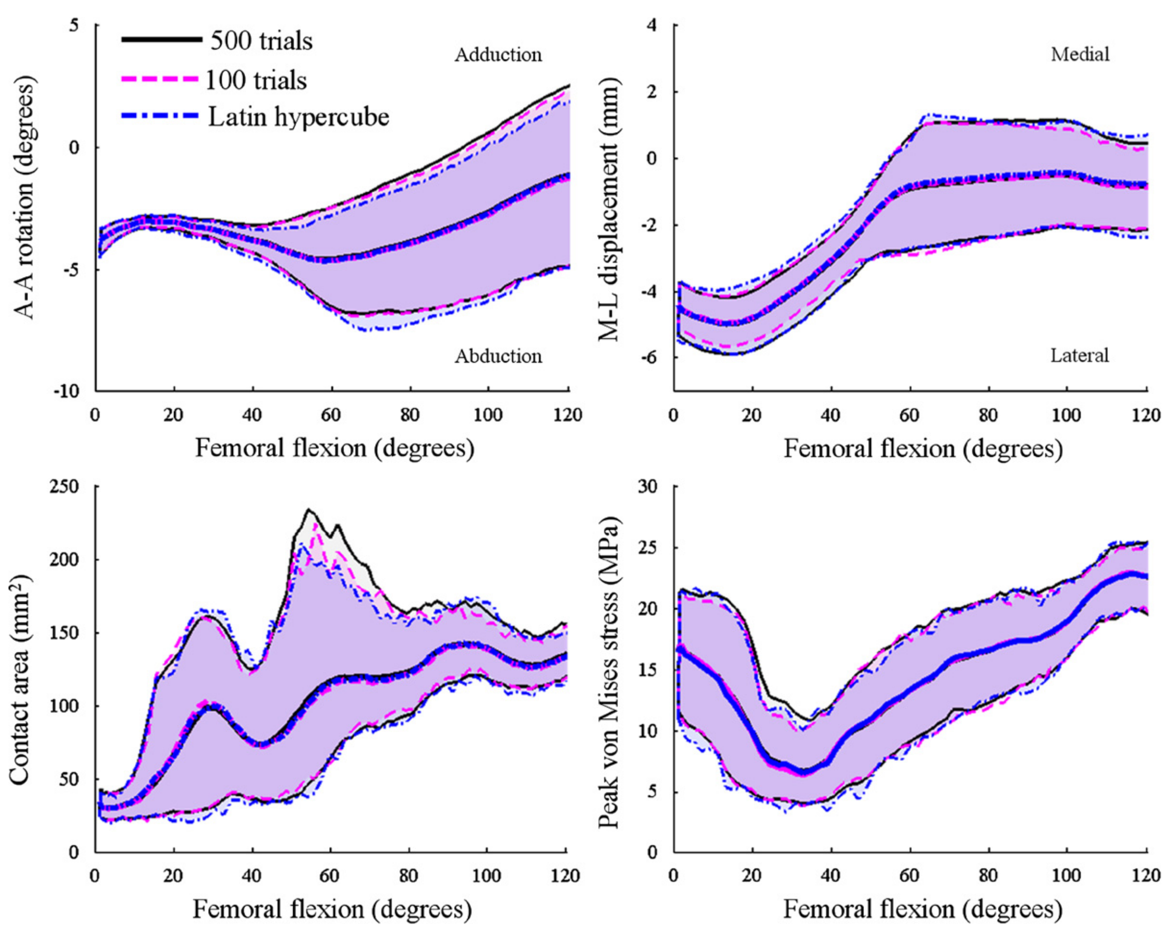

Fig. 4. Probabilistic bounds (5–95%) for each of the three Monte Carlo simulations (500 trials, 100 trials and 50 trials with Latin Hypercube sampling) shown for patellar A–A rotation, M–L displacement, contact area and peak von Mises stress.

anatomic component to alignment variability and how this varies with flexion angle (Fig. 4). In early flexion (less than 40°) changes in alignment had relatively little influence on kinematics, whereas in later flexion component placement had a more substantial effect, with a range (5–95%) in A–A rotation and M–L displacement of 6° and 4 mm, respectively, at 90° flexion. Similarly, contact mechanics were heavily influenced by initial alignment, particularly in mid-flexion. Contact area and peak contact pressure had a range (5–95%) of 180 mm^2 and 23 MPa at 50° flexion. Comparing the 500 trial Monte Carlo analysis with the 100 trial Monte Carlo and Latin Hypercube sampling (50 trials), both sets of analyses were found to effectively reproduce the variability predicted by the more computationally intensive analysis; root-mean-square (RMS) differences in kinematics, contact pressure, area, von Mises stress and M–L force were within 0.6° and 0.25 mm, 1.3 MPa, 9 mm^2, 0.6 MPa and 12 N, respectively, compared to the 5% and 95% bounds of the 500 trial simulation (Fig. 4).

Using correlation coefficients, traditional sensitivity analysis can highlight some of the key relationships between alignment parameters and mechanics. Reported correlations were averaged over the flexion cycle. Patellar spin was influenced by femoral I–E alignment ($r=0.86$). Patellar flexion and S–I translation were sensitive to F–E alignment ($r>0.7$). Patellar I–E rotation was sensitive to initial patellar I–E alignment ($r=0.85$) and to a lesser extent femoral I–E alignment ($r=0.42$).

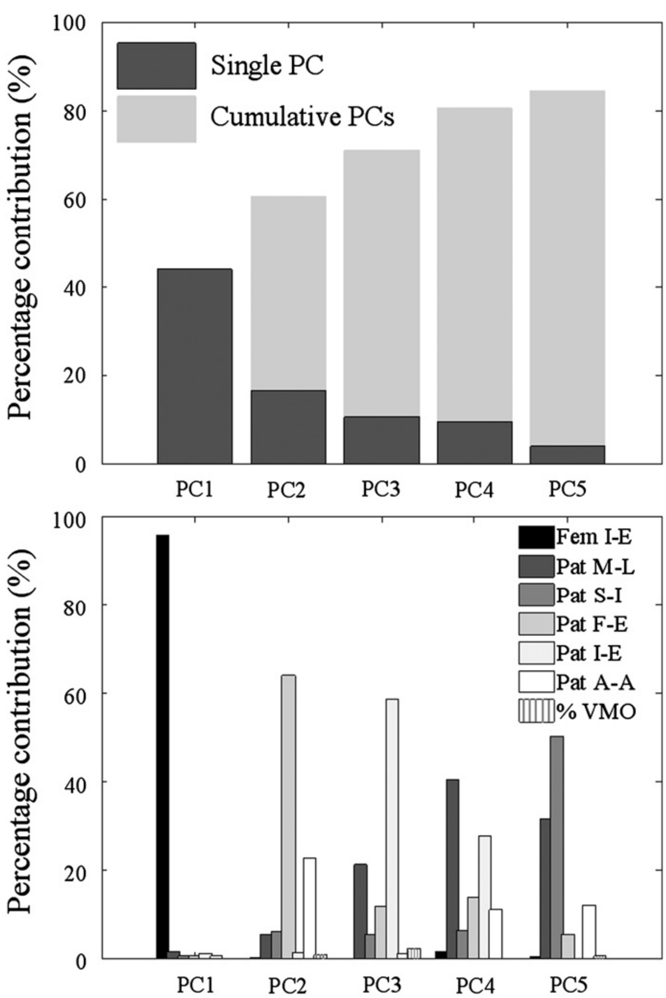

Fig. 5. Top: contributions of the first five principal components (modes of variation) to overall variation, as well as the cumulative variation explained. Bottom: contributions of each alignment parameter to the first five principal components.

The relationships established by the PCA resulted in a similar ranking of importance of alignment parameters but also provided an understanding of the interconnected nature of alignment parameters and their impact on PF mechanics (Figs. 5 and 6). The PCA results highlighted the importance of alignment over the lesser contribution of VMO at its current variability level. The first mode of variation (varying the value of the first PC) was attributed to changes in femoral I–E alignment (Fig. 5) and resulted in external rotation, abduction and lateral shift of the patella with external femoral alignment (Fig. 6). The second mode (varying the value of the second PC) was attributed to changes in patellar F–E combined with A–A alignment. Anterior positioning of the superior pole of the anatomic patella in the sagittal plane in conjunction with medial positioning of the superior pole in the coronal plane resulted in substantially higher contact area and lower contact pressure mid-cycle (Fig. 6). The third mode (varying the value of the third PC) was a combination of patellar I–E alignment and M–L position, primarily affecting kinematics. Internal alignment and lateral positioning of the patellar component resulted in external rotation and medial translation of the patella (Fig. 6).

The predictive analysis was based on the first five PC values, which accounted for 85% of the total variation. Correlation coefficients between the overall PC value and a PC value based on the contribution of the input parameters were greater than 0.95 for these five modes. Comparing the PCA predicted results with the FE results (Fig. 7), kinematic differences across the 10 new sets of input parameters averaged RMS differences of less than 0.5° and 0.3 mm throughout flexion. RMS differences between the PCA-predicted and FE results throughout flexion averaged to 3.3 MPa for peak contact pressure, 15 mm^2 for contact area and 1.5 MPa for peak von Mises stress for the 10 input sets. There were no statistically significant differences in RMS values between the three probabilistic methods (Monte Carlo with 500 trials, 100 trials and 50 trials with Latin Hypercube sampling) in either kinematics or contact mechanics.

4. Discussion

The current study details the development of a novel, coupled, probabilistic PCA approach to perform holistic multivariate assessments of relations between input parameters and output measures. The combined approach performs PCA on the results of probabilistic Monte Carlo trials and identifies the modes of variation which reveal dependencies between multiple input and multiple output parameters. The approach was applied to characterize relationships in PF mechanics considering component alignment and loading variability utilizing a subject-specific FE model (Baldwin et al., 2009b). The PCA results highlighted the importance of femoral I–E alignment (Mode 1), which is emphasized in the current surgical procedure (Sharkey et al., 2002; Berger et al., 1998; Anouchi et al., 1993). Traditional sensitivity analysis indicated correlation between femoral I–E alignment and patellar spin and I–E rotation, but the combined approach additionally highlighted a relationship between femoral I–E alignment and patellar M–L shift. The combined impact of patellar F–E and A–A alignment (Mode 2) in influencing the contact area and pressure mid-flexion demonstrated the effectiveness of the approach in identifying interdependencies between alignment parameters. As the modes of variation fully defined PF mechanics profiles throughout flexion for the specified alignment, they provide additional insight beyond single parameter perturbation studies.

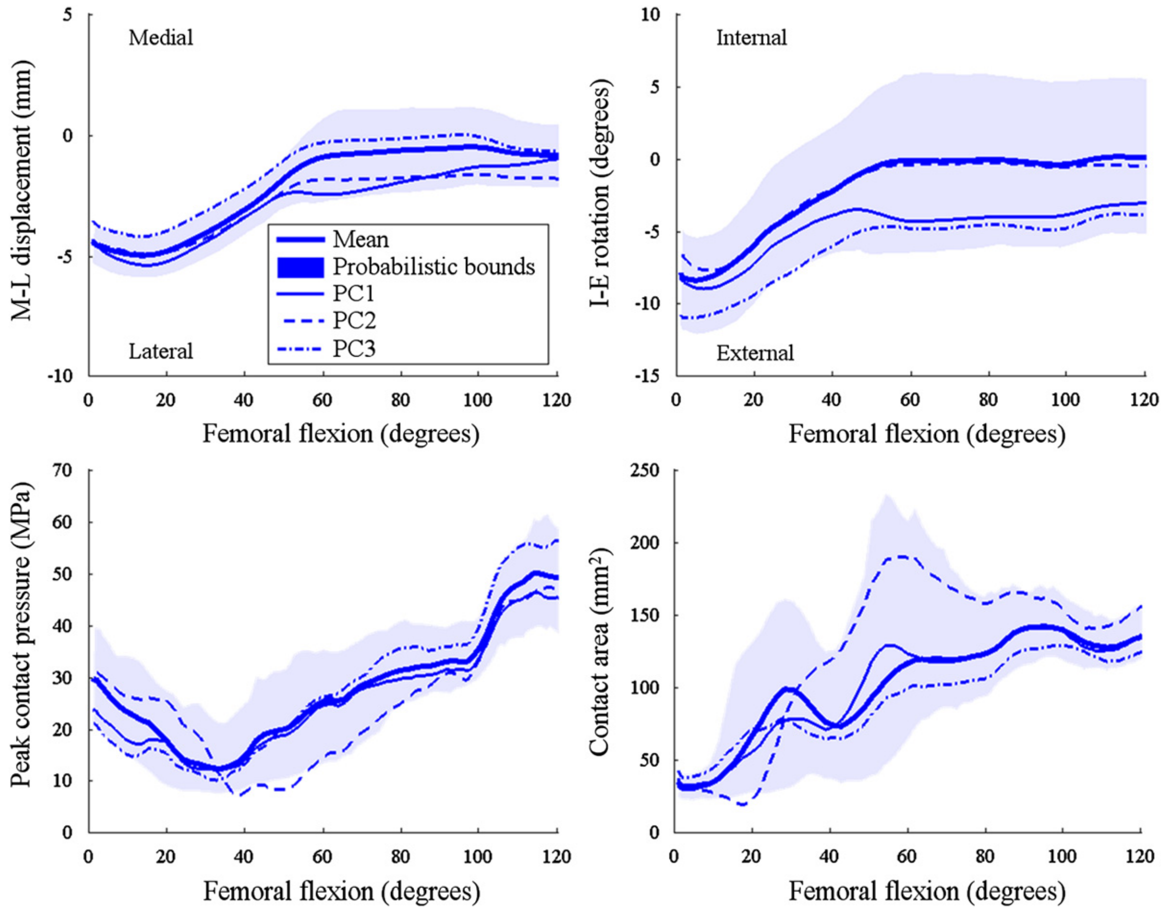

Fig. 6. The effect of varying initial alignment parameters along the modes of variation on patellar M–L displacement, I–E rotation and PF contact mechanics. Results shown as +2 standard deviations for first 3 modes. Shaded region represents probabilistic (5–95%) bounds.

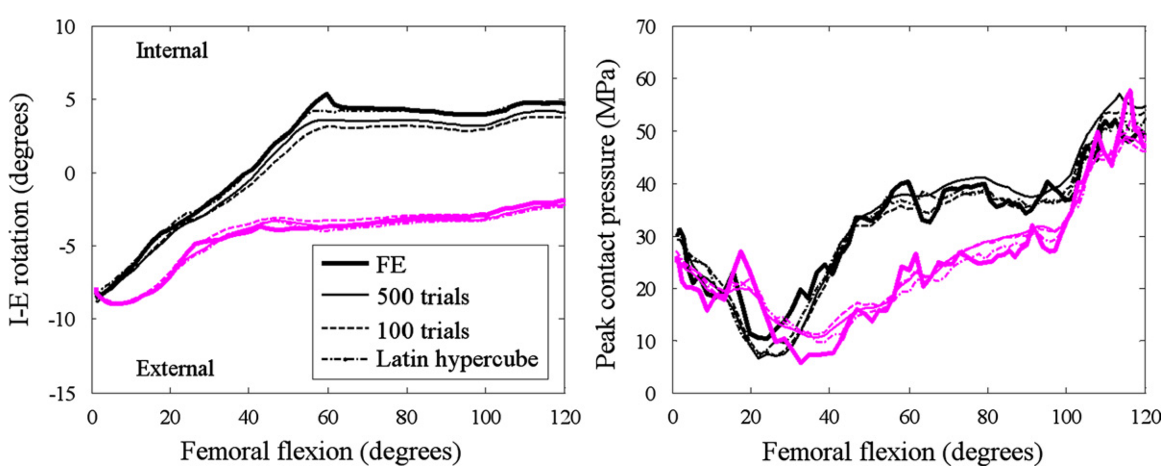

Fig. 7. PF mechanics predictions based on each of the three Monte Carlo simulations (500 trials, 100 trials and 50 trials with Latin Hypercube sampling) compared to the FE model analysis. Patellar I–E rotation (left) and peak contact pressure (right) shown for two of ten randomly generated sets of input parameters.

Broad 5% and 95% probabilistic bounds indicated the sensitivity of PF mechanics to component alignment (Fig. 4). Considering the substantial level of variability in the distribution of performance measures, accurate identification of alignment-mechanics relationships provides insight into the performance of TKR implants. An understanding of the impact of alignment conditions on kinematics and contact mechanics can provide guidance to focus instrumentation design on those parameters of primary concern. The relationships identified in this study, which used anatomic components, are most likely design specific. Application of the approach to dome or modified dome patellar components may reveal design-specific differences in the influence of alignment parameters or relationships between parameters.

In the long term, the predictive capability of the PCA approach has potential to influence decision making in CAS applications. For example, the ability to estimate functional performance of a TKR joint inter-operatively, with interactive feedback to the surgeon as components are positioned, would be a valuable tool in determining optimal component placement. The probabilistic analysis used to establish dependencies between parameters does require a substantial amount of computational time and expertise. However, the good agreement of Latin Hypercube sampling with standard Monte Carlo sampling demonstrated that probabilistic analyses can be performed efficiently without significant loss of information. Additionally, once alignment-mechanics relationships have been established, the PCA-based predictions can be made instantaneously for any new set of inputs. While nonlinearities may be present in the PCA relationships, the good agreement of the predicted results for new component alignments (Fig. 7) indicated that the behavior is appropriately captured with the linear PCA applied.

The combined probabilistic and PCA approach has broad applicability in biomechanics, serving as a means of accounting for various sources of uncertainty, which are common in these applications. It is recognized that many subject-specific factors, apart from alignment and loading in the current study, influence mechanical performance of natural and implanted joints. Because of the probabilistic nature of the approach, it is envisaged that subject-specific geometry could be incorporated using a PCA-based statistical shape model and additional uncertainty in soft-tissue constraint, for example, could be included in the probabilistic analysis. An additional point of discussion is that the current evaluation included all inputs and performance measures to provide an overall assessment; if specific performance measures are of greater interest, PCA can be performed on a subset of measures or a weighted data set, and the resulting ranking of the PC modes and associated alignment parameters may vary.

To highlight the usefulness of the coupled probabilistic and PCA approach, this study demonstrated that it can be used effectively both to isolate and describe interdependencies between input (component alignment and loading) and output (joint mechanics) and as a predictive tool to estimate functional performance of the PF joint based on component placement. It is anticipated that continued development of the approach and the insight it provides have potential benefits to implant design and alignment instrumentation.

Conflict of interest statement

There are no conflicts of interest.

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