Modeling and Simulation Workflow Using Open Knee(s) Data

Model Calibration Protocol Deviations

Cleveland Clinic Approach

Document created on December 6 2019; last updated on November 10, 2020.

Document prepared by

Ariel Schwartz, BSc – schwara2@ccf.org, +1 (216) 445 0373

Department of Biomedical Engineering and Computational Biomodeling (CoBi) Core, Lerner Research Institute, Cleveland Clinic, 9500 Euclid Avenue (ND20), Cleveland, OH 44195, USA

Snehal K. Chokhandre, MSc – chokhas@ccf.org, +1 (216) 445 3555

Department of Biomedical Engineering and Computational Biomodeling (CoBi) Core, Lerner Research Institute, Cleveland Clinic, 9500 Euclid Avenue (ND20), Cleveland, OH 44195, USA

*__Ahmet Erdemir, PhD –__ erdemira@ccf.org, +1 (216) 445 9523

Department of Biomedical Engineering and Computational Biomodeling (CoBi) Core, Lerner Research Institute, Cleveland Clinic, 9500 Euclid Avenue (ND20), Cleveland, OH 44195, USA

**For correspondence.*

Table of Contents

Cite this document as

> Schwartz A, Chokhandre, SK, Erdemir, A, *Modeling and simulation workflow using Open Knee(s) data: model calibration protocol deviations – Cleveland Clinic approach*, 11/10/2020, Cleveland Clinic, Cleveland, Ohio, USA.

Contributions to this document by Ariel Schwartz, Snehal Chokhandre, and Ahmet Erdemir were supported by the National Institute of Biomedical Imaging and Bioengineering, National Institutes of Health (R01EB024573; *Reproducibility in simulation-based prediction of natural knee mechanics*; Principal Investigator: Erdemir) and in part by the National Institute of General Medical Sciences, National Institutes of Health (R01GM104139; *Open Knee(s): virtual biomechanical representations of the knee joint*, Principal Investigator: Erdemir).

Synopsis

This document describes protocol deviations to the model calibration specifications[1], which were aimed for generating a calibrated model of the knee joint based on an initial working model[2–4] and an existing, additional joint testing data set from the Open Knee(s) project[5], which was acquired for the same specimen. The documentation is in response to *Model Calibration* phase[6] of the project *Reproducibility in simulation-based prediction of natural knee mechanics,* a study funded by the National Institute of Biomedical Imaging and Bioengineering, National Institutes of Health (Grant No. R01EB024573)[7]. The decisions for protocol deviations represent those of the Cleveland Clinic team, who launched and has been maintaining the Open Knee(s)[8]. These deviations were in response to unforeseen challenges during the calibration of the model and aim to provide previously missing information. They also facilitated the delivery of a pragmatic, yet comprehensive, calibration of an anatomically and mechanically detailed and extensible knee joint model incorporating its major tissue structures. The document follows the outline of the previously disseminated model calibration specifications[1], augmenting information related to the burden of activities and listing protocol deviations in detail.

Initial Working Model

There is no additional information to report for this section. One can refer to the original model calibration specifications[1] for details.

Data Utilized

There is no additional information to report for this section. One can refer to the original model calibration specifications[1] for details.

Overview of Modeling and Simulation Processes

The broad description of the modeling and simulation processes does not have any major changes. More details can be found in the original model calibration specifications[1]. At a more granular level, the changes to the modeling and simulation workflow should be inferred from the rest of this document.

Detailed Modeling and Simulation Outputs

The outline of modeling and simulation processes did not change in a significant way. More details can be found in the original model calibration specifications[1]. Any specific changes in the type of outputs, file formats, etc. should be inferred from the rest of this document.

Workflow

General Deviations

These deviations are not specific to any particular calibration protocols, however they reflect general changes that were important to note.

By Ariel Schwartz on February 21 2020 –This deviation should have been included in the model development phase protocol deviations[3]. In contacts between rigid and deformable tissues, FEBio[9] requires that the deformable body be defined as the master surface. Our original model specifications listed the opposite relationship – this was a typo. The disseminated models included the correct master/slave definitions.

By Ariel Schwartz on March 5 2020 – Abduction-Adduction axes were labeled backwards in all the model development phase outputs[2,3]. This included the labeling of axes in the model files, and any outputs including graphs, csv[10] files, etc. This error has been fixed in all calibration phase outputs.

Mesh Convergence

Burden

Mesh convergence for oks003 was completed by Ariel Schwartz. The activity required 3 weeks of full time effort.

Deviations

Geometry Generation Procedures

By Ariel Schwartz on December 9 2019 – smoothing procedures used in model development phase[2,3] were not reproducible, and caused holes in some meshes. Instead of using the raw stl and performing smoothing, the smoothed meshes from the initial working model were iso parameterized, and re-meshed at the desired mesh densities. Some additional smoothing and manual editing was required after the remeshing step. This means that any loss of volume or detail in the meshes in the initial working model were carried over into the mesh convergence phase.

Mesh Generation Procedures

By Ariel Schwartz on December 13 2019 – a Python[11] script was created to transfer tie and contact groups from an existing MED[12] file, to a newly generated mesh of the same tissue, it is:

transfer_med_groups.py – in house script to transfer groups from an existing MED[12] file, to a new mesh of the same tissue geometry. To be used with Python[11] and SALOME[13], source code available at https://simtk.org/svn/openknee/app/KneeHub/src/

Model Generation Procedures

By Ariel Schwartz on December 16 2019 – For all cartilage and menisci compression models, intended prescribed displacements of 2mm were too high, causing unrealistic reaction forces. The following adjustments were made to the prescribed displacements to produce reasonable reaction forces:

-Patella Cartilage, Tibial Cartilage, Medial and Lateral Meniscus models prescribed displacements were reduced to 1 mm.

-Medial Tibia Cartilage, Femoral cartilage prescribed displacements were reduced to 0.2 mm

By Ariel Schwartz on December 16 2019 –Contact penalty was increased from 0.1 to 1 to reduce penetration in all the compression models.

By Ariel Schwartz on December 16 2019 – In the meniscus compression models, Tibia was included in the model to tie the ends of the meniscus.

Mesh Convergence Procedures

By Ariel Schwartz on December 26 2019 – Medial Tibial cartilage – although the criteria for convergence was 5 % change in force, a 7.6 % criteria was used for this tissue, as the computational cost increased significantly by increasing the mesh density past this point.

By Ariel Schwartz on December 26 2019 – Medial meniscus – all models run had less than 5% change in force, however upon inspecting the fiber stretch maps, there were unexplained inconsistencies in the models re-meshed at sampling rates of 6, and 8, so a sampling rate of 10 was chosen as the converged mesh.

By Ariel Schwartz on December 26 2019 – Lateral meniscus – model re-meshed at sampling rate of 10 gave unexplained results in fiber stretch, as well as reaction forces, so that model was ignored, and convergence was found at a sampling rate of 8.

Confirmation of Material Properties

Burden

Material properties confirmation for oks003 was completed by Ariel Schwartz. The activity required 2 weeks of full time effort.

Deviations

KNOWN LIMITATIONS OF CONSTITUTIVE MODELS

By Ariel Schwartz on September 4 2020- After experiencing difficulties with calibration of in situ strains for the Natural Knee model[14–17], more investigation was done which uncovered several limitations of the constitutive models used here. Although these issues did not arise in the current model, they should be noted here as they may influence model behavior that has not yet been tested on the current model.

- Ligaments and meniscus are modeled as uncoupled transversely isotropic Mooney Rivlin materials. Material properties were initially assumed from literature, and ligament models were tested in tension for structural response, and calibrated for the fiber modulus as noted in the calibration specifications[1]. However, the remaining material properties (bulk modulus, ground substance properties) were not changed from what was provided in literature. Under further inspection, we found that the ground substance was generating reaction forces when the ligaments were loaded under compression, as well as contributing significantly to the overall material stiffness. Therefore, adjustment of other material properties is likely necessary in order to ensure accurate structural behavior of the tissues under diverse loading scenarios.
- Further investigation is needed to determine what the appropriate material properties are, and the workflow that should be used to calibrate the material properties, including ground substance properties and bulk modulus for all ligaments and meniscus.

Compartmental Modeling of Structural Tissue Behavior

By Ariel Schwartz on December 21 2019 – a Python[11] script was written to read the model outputs from an FEBio[9] logfile, and fit a line to the final 1/3 of the force displacement curve to determine linear stiffness.

StiffnessFromLog.py – in house script to determine linear stiffness from FEBio[9] model results. To be used with Python[11], source code available at https://simtk.org/svn/openknee/app/KneeHub/src/

Ligaments and Tendons

By Ariel Schwartz on December 21 2019 - The PCL stiffness was not converging as expected. Changing the fiber modulus failed to bring the linear stiffness into the desired range. It was determined through trial and error of different material properties that this issue was geometry-specific and not having to do with other material properties. Instead of assigning a single fiber direction for all elements, an element-wise fiber direction was determined for the PCL. This solved the problem, and fiber modulus was then adjusted so that the stiffness was in the desired range. Element wise fiber directions were determined by:

a) finding the vector along the shortest edge of the oriented bounding box of the ligament geometry

b) for each element finding the nearest surface element normal

c) taking the cross product between that normal and the shortest edge vector

By Ariel Schwartz on December 27 2019 - For the PCL tensile test, total ligament stretch was increased to 5 mm, because the force displacement curve was still not in the linear region after 3mm displacement.

Cartilage

By Ariel Schwartz on January 14 2020 - using prescribed force caused instability in the model, and it failed to converge. Instead, a prescribed displacement was used, such that the reaction force was approximately 0.5 N. The stiffness was measured using the force displacement results.

Registration for Specimen-Specific Calibration

Burden

Registration for oks003 was completed by Ariel Schwartz. The activity required 1 weeks of full time effort.

Deviations

By Ariel Schwartz on February 4 2020 – a Python[11] script was written to fit spheres to the digitized registration markers, and the segmented registration markers, and find the transformation from experiment to image coordinate system using singular value decomposition between sphere centers. Digitized anatomical landmarks are then transformed from the experiment coordinate system to the image coordinate system. It is:

Register_probed_points.py – in house script to transform the digitized anatomical landmarks to the image coordinate system. To be used with Python[11], source code available at https://simtk.org/svn/openknee/app/KneeHub/src/

Specimen-Specific Kinematics-Kinetics Data Processing

Burden

Data Processing for oks003 was completed by Ariel Schwartz. The activity required 2 weeks of full time effort.

Deviations

General Notes

By Ariel Schwartz on February 7 2020 – a Python[11] script was written to process the oks003 tdms[18] data and provide it in a form amenable for simulations with the full knee model, it is:

tdms_processing_oks.py – in house script to process the tdms[18] files provided with Open Knee(s)[5] experimental data. To be used with Python[11], source code available at https://simtk.org/svn/openknee/app/KneeHub/src/

Passive Flexion Data

By Ariel Schwartz on February 12 2020 - cropping kinematics and kinetics on off-axis loading channels was done with cutoffs of 3 N and 0.3 Nm, as cropping at 1.0N, 0.1 Nm removed too much data. This changes the assumption that the flexion is purely passive. For true comparison of passive flexion to the experimental condition, experimental loads will need to be applied in addition to flexion angle.

By Ariel Schwartz on February 12 2020 - threshold for resampling the data at 5 degree increments was increased from 0.1 degrees, to 1.25 degrees, to include enough data for 90 degree passive flexion. Prior to increasing the range, too many data points were missing.

Laxity Data

By Ariel Schwartz on February 17 2020 - kinematics were cropped so the flexion angle was within 1 degree of the average flexion angle, as opposed to within 1 degree of the intended flexion angle. For example, for the 30 degree flexion file, the average flexion angle was closer to 29 degrees, so the data was cut off from 28 to 30 degrees. This prevented loss of data when the average flexion angle was more than 1 degree difference from the intended flexion angle.

By Ariel Schwartz on February 17 2020 - cropping kinematics and kinetics on off-axis loading channels was done within 1.5 N for force, as cropping within 1.0 N removed significant data. This change is unlikely to have a significant impact on the assumption of pure laxity.

By Ariel Schwartz on July 23 2020 - Note: a bug was found in the processing script which lead to errors in the movements of experimental kinetics from Tibia origin to the Femur origin. The bug was fixed, and lead to having to re-run the in situ strain calibration and all the models. This is not a protocol deviation, however it is important to note as it had an influence on future phases of model calibration, specifically the burden required.

Calibration of In Situ Ligament Strains

Burden

In situ strain calibration for oks003 was completed by Ariel Schwartz. The activity initially required 1 week of full time effort in script preparation and troubleshooting, and 1 week of computation time. A bug in the processing of experiment kinetics was found, leading to re-running of calibration which took an additional 4 days of computation time.

Deviations

By Ariel Schwartz on February 19 2020 – a Python[11] script was written to update a full knee model in FEBio[9] to replicate experimental conditions. Experimental kinetics are applied as external femur loads, and experiment flexion angle is prescribed to the extension-flexion joint.

experiment_to_model.py – in house script to apply experimental conditions to a full knee model in FEBio[9]. To be used with Python[11], source code available at https://simtk.org/svn/openknee/app/KneeHub/src/

By Ariel Schwartz on February 25 2020 – a Python[11] script was written to update the in situ strain of the target ligament in the FEBio[9] model file, to read simulation results (displacement and load in dominant degree of freedom), to implement a scalar (one-dimensional) optimization that will minimize the sum of squared differences between model predicted and experimental loading response in the dominant degree of freedom, and to write optimization results in a text file.

InSituOptimization.py – in house script to perform in situ strain optimization for the target ligaments. To be used with Python[11], FEBio[9]. Source code available at https://simtk.org/svn/openknee/app/KneeHub/src/

By Ariel Schwartz on March 9 2020 – An initial shifting of the femur during the in situ strain step was noticed, due the tied contact between the MCL and medial meniscus attempting to fill a gap between the two surfaces. The tied contact was replaced by springs connecting each node in the contact group on the MCL to the nearest node in the contact group on the medial meniscus. The springs were assigned a spring constant of 1000 N/mm each, essentially creating a rigid connection between each set of nodes. This eliminated the issue, as the springs were set such that the initial length is equal to the distance between the connected nodes, leading to zero forces in the initial positions of the MCL and medial meniscus.

Summary of in final situ strain optimization results:

Test Name	**Anterior Laxity**	**Posterior Laxity**	**Varus Laxity**	**Valgus Laxity**
Ligament of interest	ACL	PCL	LCL	MCL
Experiment kinetics (for generation of models)	Laxity_0deg_AP1_kinetics_in_TibiaCS.csv	Laxity_0deg_AP2_kinetics_in_TibiaCS.csv	Laxity_0deg_VV2_kinetics_in_TibiaCS.csv	Laxity_0deg_VV1_kinetics_in_TibiaCS.csv
Experiment kinematics (for calculation of rms error)	Laxity_0deg_AP2_kinematics_in_JCS.csv	Laxity_0deg_AP2_kinematics_in_JCS.csv	Laxity_0deg_VV2_kinematics_in_JCS.csv	Laxity_0deg_VV1_kinematics_in_JCS.csv
Initial In Situ Stretch guess	1.016	1.0	1.027	1.034
Optimized In Situ Stretch	**1.079**	**0.931**	**1.062**	**0.985**
RMS error on dominant loading axis	**0.093 mm**	**0.463 mm**	**0.528 deg**	**0.444 deg**

Customized Full Models

Burden

Generation of customized full models was completed by Ariel Schwartz. The activity required 1 day of full time effort for script preparation.

Deviations

By Ariel Schwartz on April 29 2020 -Experimental loading cases were generated using in house script **experiment_to_model.py**, described above.

<u>Customization for Test Simulation Case</u>

By Ariel Schwartz on May 19 2020 –One additional staged model was added to the list. First the mcl-mns tie was swapped for springs, so that an assessment could be made on how that change affects the model kinematics-kinetics.

<u>Customization for Experimental Loading Cases</u>

By Ariel Schwartz on May 19 2020 –Additional experimental loading model was added to the list – F90, to replicate the experimental passive flexion with kinetics. This model was initially exclude due to the assumption that the passive flexion test simulation case was sufficient for comparison to experimental passive flexion. However, as noted in data processing protocol deviations the experimental passive flexion loading cannot be considered true passive flexion due to loading on other axes, thus this model was added to replicate the experimental conditions for passive flexion, including kinetics.

By Ariel Schwartz on July 27 2020 –all experimental loading models were re-generated due to a change in experimental kinetics processing when a bug was found in the processing script. Control setting were changed to speed up the model run-times. During the first run through of the experimental loading models (before the bug was found), more efficient control setting were discovered and these were applied in the second round of models. Some requested must points were removed in the in situ strain and initial loading stages, so the model could take larger steps when the loading increment was small. Min_residual in the control section was increased to 0.01, to assist in convergence when loading increment was small.

Simulations

Burden

Simulations were completed by Ariel Schwartz and Ahmet Erdemir. The activity required 4 days of computational time, plus approximately 2 weeks full time effort troubleshooting models that failed to converge (exact time is unknown, this issue was revisited several times over the course of 3 months). After discovery of a bug in experimental kinetics processing, all models were re-generated and re-run. The second round of simulations were completed by Ariel Schwartz. The activity required 2 days of computation time plus 3 days of full time effort troubleshooting models that failed to converge. Improvements in control settings and better understanding of troubleshooting methods lead to decreased computation time and less difficulty solving convergence errors.

Deviations

<u>Test Simulation Case</u>

By Ariel Schwartz on March 25 2020 – Test Simulation passive flexion case after changing to confirmed material properties failed to converge fully. Model error outputs indicated negative jacobians at certain elements on the MCL, located near the edge of the tied region to the femur bone. Those problematic elements were removed from the tied group, and the model successfully converged. The kinematics of the two models were compared, and the removal of the elements was found to have a negligent effect on the kinematics. These nodes were permanently removed from the input file for all test simulation models moving forward.

By Ariel Schwartz on August 12 2020 – Test Simulation passive flexion case after changing to calibrated in situ strain values failed to converge fully. Model error outputs indicated negative jacobians at elements in the MCL-MNS-M ties region (connected by springs). Some springs were removed, and then the model failed to converge due to negative jacobians in elements at the PCL to FMB tie region. Some nodes were commented from that area, and then the model converged fully.

<u>Experimental Loading Cases</u>

By Ariel Schwartz on July 2 2020 – during troubleshooting the first round of experimental loading models, some lessons were learned about successfully troubleshooting a failed model, which contributed to the “art” of modeling in the second round of models. For this reason, we have included here some notes and what knowledge was gained from the first round which lead to decisions made in the second round when troubleshooting models that failed to converge.

- When a model indicates negative jacobians at a region where a soft tissue is tied to the bone, releasing some nodes from the tied region in the problematic area often gives the model the flexibility it needs to converge fully.
- When a model indicates negative jacobians at elements near the tied region between the MCL and meniscus, reduction of the spring constant in the springs between the MCL and meniscus sometimes solved the issue. Kinematics were compared between models with a spring constant of 1000, and 333, and the difference is negligent.
- When a model indicates that max number of stiffness reformations was reached, changing the max_refs to 50 (from 25) in the control settings may help.
- When the model is attempting to take small time steps and the loading increment is small, increasing min_residual to 0.01, and removing some of the must points to allow the model to take larger steps may be successful.

- When a model indicates a negative jacobian in a single cartilage element in an unloaded region of the cartilage, simply removing that element may lead to convergence.

Note: Specifics on which nodes and elements were excluded from each model can be found in the model files included in the calibration phase outputs packages.

By Ariel Schwartz on July 29 2020 – F60_AT, F90_ER ,F60_VR, F90_VR, F60_VL failed to converge with initial settings. Model outputs indicated negative jacobians in elements located in the ACL-FMB tie. Some nodes in the ACL to FMB tie were excluded from the group, the models converged fully. These nodes were excluded in all future models described in protocol deviations below to avoid the potential for the same issue to appear.

By Ariel Schwartz on August 4 2020 – F90 failed to converge with initial settings. Model outputs indicated negative jacobians in elements located in the MCL-FMB tie. Some nodes in the MCL-FMB were excluded, and the model converged fully. These nodes were excluded in all future models described in protocol deviations below to avoid the potential for the same issue to appear.

By Ariel Schwartz on August 4 2020 – F90_IR failed to converge with initial settings. Model outputs indicated negative jacobians in elements located in the MCL-MNS-M tie region (connected by springs). The spring constant of the springs connecting the MCL and MNS-M was reduced from 1000 to 333. The model failed to converge due to an unloaded element in the FMC. The problematic element was excluded from the model, and then the model converged fully. The spring constant was reduced, and the FMC element was commented in all future models described in protocol deviations below to avoid the potential for the same issue to appear.

By Ariel Schwartz on August 4 2020 – F60_IR failed to converge with initial settings. Model outputs indicated negative jacobians in elements located in the FMC. To avoid excluding too many elements from the FMC, instead some nodes in the area of the problematic FMC elements were excluded from the FMC to FMB tie. The model fully converged.

By Ariel Schwartz on August 7 2020 – F90_PT failed to converge with initial settings. Model outputs indicated negative jacobians in elements located in the ACL to FMB tie. Some additional nodes were removed from the ACL to FMB tie. The model still failed to converge, indicating negative jacobians in the MCL-MNS-M tie region (connected by springs). Some of the springs were removed in the problematic region, and then the model converged fully.

By Ariel Schwartz on August 13 2020 – F90_AT failed to converge with initial settings. Model outputs indicated negative jacobians in elements located in the ACL to FMB tie. Some additional nodes were removed from the ACL to FMB tie. The model still failed to converge, indicating negative jacobians in the MCL-FMB tie region. Some additional nodes were excluded, and then the model fully converged.

Post-Processing

Burden

Post Processing was completed by Ariel Schwartz. The activity required 1 days of full time effort for script preparations.

Deviations

By Ariel Schwartz on August 17 2020 –Post processing was performed using scripts **LogPostProcessing.py**, described previously, for extracting joint kinematics and kinetics from the model outputs, and an in house script generated to compare kinematics and kinetics between models and experiment. It is:

model_prediction_errors.py – in house script to calculate rms error between models and experiments kinematics-kinetics. Generates graphs and saves as png[19], and rms error are saved to xml[20]. To be used with Python[11], source code available at https://simtk.org/svn/openknee/app/KneeHub/src/

Dissemination

Burden

Dissemination was completed by Ariel Schwartz. The activity took 1 day for file management and uploading.

Deviations

By Ariel Schwartz on November 10 2020 –an internal data management system, MIDAS Platform[21], was used for staging and organization prior to dissemination

Protocol Deviations

Burden

Protocol deviations were completed by Ariel Schwartz. Deviations were reported on an ongoing basis, so exact burden is unknown, however it is estimated that the total amount of time to report deviations was less than 1 day.

Deviations

No deviations.

Overall Burden

Overall burden of the model calibration phase, in regard to data and software, was faithful to the original model calibration specifications[1]. Use of existing, publicly available data, in this case Open Knee(s)[5] data set, negates the burden for data acquisition. Software packages, which were used for model calibration, were in line with specifications. The activity leveraged SimTK[22] as a collaboration infrastructure within the team, e.g. for version control and public dissemination. Required labor, however, was higher than what was anticipated in the model calibration specifications[1]. Overall, the entire calibration process took approximately 15 weeks of full time effort, including computation time from a research engineer with bachelor's degree, mechanical/biomedical background, less than 3 years of research experience, and familiarity to finite element analysis. This effort level includes programming to streamline some of the operations, all data processing and modeling activities, record keeping, and dissemination. Now that the scripting to expedite some of the model calibration operations has been completed and the team has a better understanding of the nuances of model convergence, calibration of another working knee model in the Open Knee(s)[5] data set, with existing experimental data in the same format, will likely be completed in approximately 5 weeks. This estimate includes 3 weeks for mesh convergence and material properties calibration, 1 week for in situ strain optimization computation time, and 1 week for running and troubleshooting models replicating experimental conditions. Mesh convergence and material properties calibration require a significant amount manual intervention from the analyst. The remaining phases require minimal manual intervention, only for troubleshooting when models fail to converge. However, much progress was made during the model calibration phase in understanding how to troubleshoot model convergence issues in a streamlined manner. The overall burden of the model calibration specifications should be evaluated in concert with their desired final outcome – a comprehensive and extensible knee joint model incorporating anatomical and mechanical detail of its major structures, which is capable of reproducing measured specimen-specific response.

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