



In silico Computation of Knee Muscle Forces tailored to a Novel Multi-Motion *in vitro* Knee Simulator's Constraints

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Abstract

In vitro physiological knee joint simulators have been proven to be valuable tools for characterizing knee joint biomechanics, complementing *in vivo* measurements. However, many simulators only allow simulations of squatting motions. This is partly due to the lack of a tailored approach to efficiently identify the required simulator input parameters for accurate investigation of other frequently performed activities of daily living (ADL). Therefore, we aimed to develop a novel *in vivo*-based computational approach which uniquely integrates multiple constraints from a novel *in vitro* knee simulator to determine the required muscle forces during various ADLs.

During a motion capture study, six healthy subjects performed squatting, sit-stand-sit and gait motions. Subject-scaled musculoskeletal models were adapted to include constraints of the knee joint simulator by including only quadriceps and hamstring muscle actuators, down-scaling ground reaction forces and applying constant hamstring force. Subsequently, muscle forces were computed for each motion using the Concurrent Optimization of Muscle Activations and Kinematics algorithm.

Afterwards, the *in silico*-based squatting results were retrospectively compared with previously performed *in vitro* experiments using the knee joint simulator, which actively controlled the quadriceps and bilateral hamstrings to maintain a constant vertical ground reaction force of 110N during squatting. Resulting *in silico* computed and simulator-measured forces during squatting showed similar magnitudes and high correlations. This indicates robustness of the proposed *in vivo*-based computational approach. Accordingly, its application to stance phase of gait initiated quasi-static *in vitro* simulations of this additional motion, further demonstrating its feasibility.

1 Introduction

As the largest load-bearing joint, the knee joint is susceptible to injuries or disorders, causing discomfort and dysfunction¹. Interventions performed to restore joint function still fail to achieve patient satisfaction in up to 25% of the cases². Therefore, improved understanding of knee joint biomechanics pre- and postoperatively is crucial.

Complementing *in vivo*-based approaches, *in vitro* knee joint simulators allow to investigate biomechanical parameters during dynamic motions using invasive measurement techniques under well-controlled conditions³. Most existing simulators are limited to simulating squatting motion to reduce the complexity of their control strategy and mechanical design^{4,5}. However, implementing frequently performed activities of daily living (ADL) is essential towards a comprehensive understanding of knee biomechanics.

Although some studies have implemented such ADLs, a standardized approach is currently unavailable⁶⁻⁹. Therefore, we aim to develop a novel *in vivo*-based computational approach, incorporating constraints of a novel knee simulator. This approach involves the computation of physiological muscle forces as required input parameters for the *in vitro* simulator. Additionally, we will validate this approach by comparing the *in silico* computed kinetics to *in vitro* simulated outputs during squatting. Upon successful validation, the approach will be applied to quasi-static gait simulator experiments as a proof-of-concept.

2 Materials and Methods

Six fresh-frozen cadaveric lower limbs were mounted into a novel knee simulator, allowing independent, tri-directional control of ankle assembly translations, as well as quadriceps and bilateral hamstring muscle groups (Figure 1). Subsequently, specimens were subjected to a squatting motion (35°-100°) while actively controlling quadriceps and bilateral hamstrings (50N each) to maintain a constant vertical ground reaction force (GRF) of 110N¹⁰. During experiments, muscle forces and GRFs were obtained directly from the simulator, while kinematics were based on reflective markers rigidly attached to the femur, tibia and patella, and spatially tracked using a six-camera motion capture system (Vicon).

After ethical approval, six healthy volunteers participated in a motion capture study (s56093) including squat, sit-stand-sit and gait in triplicate¹¹. The collected skin-mounted marker trajectories and GRFs served as input for muscle force calculations using the Lenhart2015 musculoskeletal model in OpenSim 4.0^{12,13}. To ensure physiological knee contact, a custom Python script was used for model scaling towards the subjects' anthropometry and mass as measured during a static trial.

Subject-tailored models were subsequently adapted to incorporate knee simulator constraints. Specifically, input GRFs were down-scaled towards a mean vertical component of 110N (i.e. a previously defined safety margin to protect the simulator and specimen from mechanical overload¹⁰) and only quadriceps and medial and lateral hamstrings were included, with the latter prescribed to produce a constant 50N force each during squatting and sit-stand-sit.

In silico computations of the three different motions were performed with inverse kinematics and GRFs serving as input for muscle force calculations using Concurrent Optimization of Muscle Activations and Kinematics (COMAK)¹⁴. After validating our approach based on squatting data, *in silico* computed quadriceps and hamstring forces of stance phase were quasi-statically applied to one simulator-mounted fixated cadaveric leg (Figure 1). The first 8% of stance phase were excluded from cadaver experiments to avoid a gimbal lock near peak knee extension, which could potentially damage the simulator or specimen.

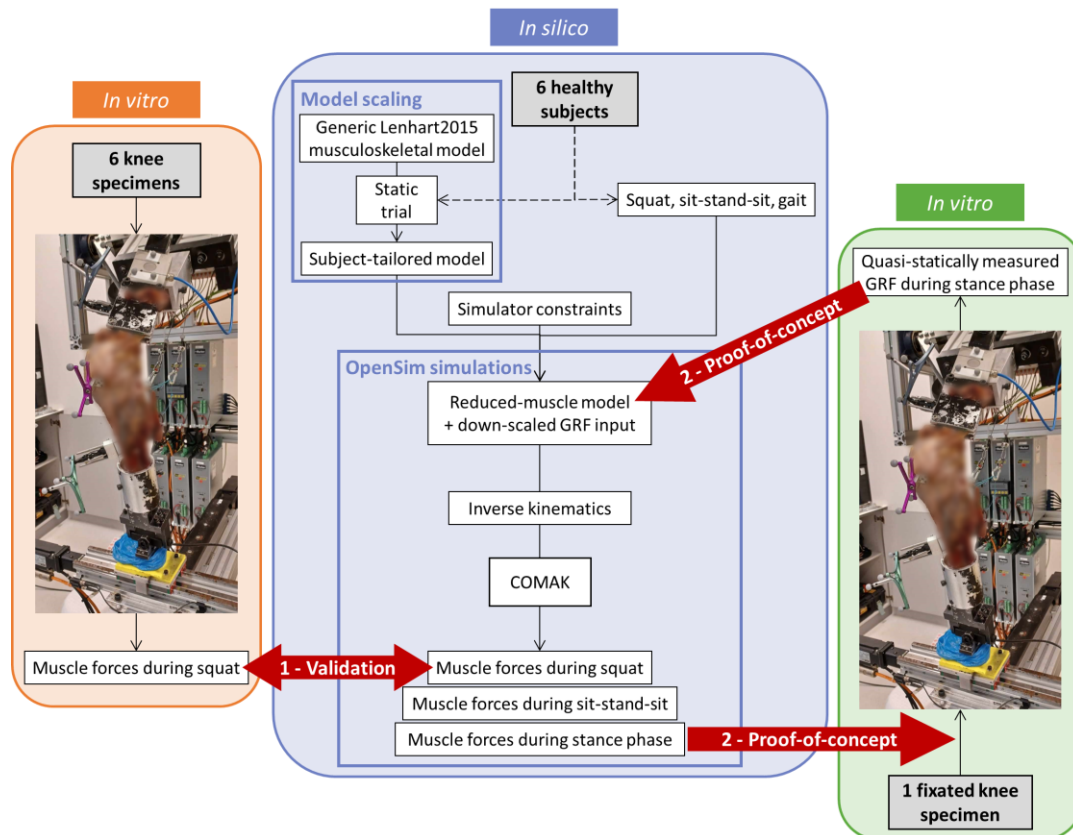


Figure 1: Workflow of the entire methodology. 1-Validate approach by comparing muscle forces during squat. 2-Proof-of-concept by comparing the vertical GRF during stance phase.

Comparison of *in silico* with simulator squatting was performed with a generalized mixed-model and Tukey Post Hoc tests ($p < 0.05$), as well as Pearson correlation coefficients (R) within common flexion angles (35° - 77°).

Due to remaining *in vivo* versus *in vitro* differences in this proof-of-concept, vertical GRF values of *in vitro* and *in silico* gait simulations were qualitatively compared after zeroing the offset between both curves at the *in vitro* starting position.

3 Results

Mean differences between vertical GRF parameters of simulator and *in silico* squatting (Figure 2) were not significant ($p > 0.16$), while their correlation was low ($R = 0.76$). Similarly, mean differences between quadriceps forces of both simulations remained insignificant ($p > 0.17$).

Applying our *in vivo*-based computational approach to sit-stand-sit (Figure 2) resulted in increased quadriceps forces compared to *in silico* squatting, with a maximum value of 1750N at 77° knee flexion.

Comparing vertical GRF data between simulator and *in silico* stance phase (Figure 2) indicated that the *in vitro* simulation successfully reproduced the physiological double-bump pattern while closely following the prescribed muscle forces from *in silico* computations.

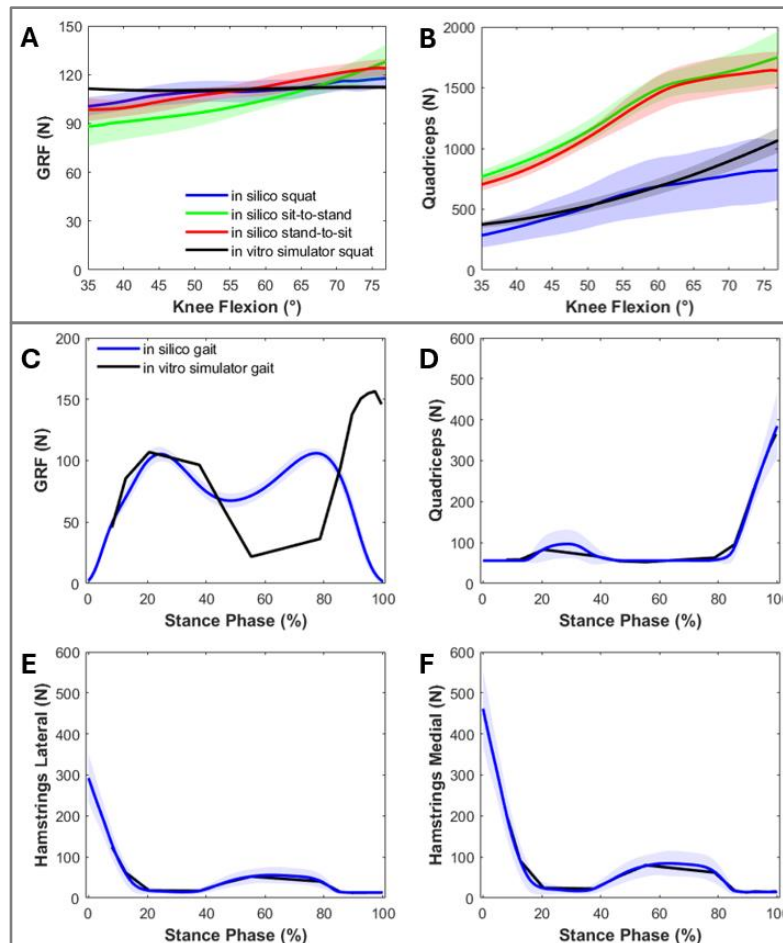


Figure 2: Vertical GRF (A) and quadriceps force (B) as a function of knee flexion angle, shown for simulator (black) and *in silico* (blue) descending squat, as well as *in silico* sit-to-stand (green) and stand-to-sit (red). Vertical GRF (C), quadriceps (D), lateral (E) and medial (F) hamstring muscle force, shown for simulator (black) and *in silico* (blue) gait, as a function of the stance phase cycle. *In silico* computed muscle forces are indicated as the sum of their muscle groups. Variables are presented as mean(solid)+/-standard deviation(shaded area).

4 Discussion

We introduced and validated a novel *in vivo*-based computational approach to implement ADLs into a novel *in vitro* knee joint simulator. To our knowledge, such a methodology has never been introduced before^{6-9,15}.

The low correlation between vertical GRF curves of simulator and *in silico* squatting could be attributed to differences in knee flexion accelerations. Apart from this, no significant differences were observed between quadriceps muscle force and GRF results of both measurements, indicating the validity of our approach.

In silico computed muscle forces for sit-stand-sit and stance phase remained within cadaver loading limits observed in previous simulator experiments, suggesting feasibility of their implementation¹⁰. Although vertical GRF patterns of *in silico* and simulator measurements for stance phase were similar, remaining differences could arise from *in silico* modeling assumptions, simulator constraints, the usage

of a single fixated cadaveric leg, quasi-static implementation, and differences in the GRF measurement location.

In conclusion, the results suggest robustness and feasibility of our *in vivo*-based computational approach, but further experiments including simulator implementation of additional ADLs are required to demonstrate its standardization potential.

5 Acknowledgements

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