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Neuromusculoskeletal modeling in health and disease

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ABBREVIATIONS
EMG Electromyograms

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ABSTRACT
This opinion paper provides an overview of musculoskeletal modeling, revealing insights into muscle-tendon kinematics, forces, and joint contact forces during dynamic movements, thereby advancing our understanding of biomechanics. While subject-specific modeling poses challenges, emerging software tools enable rapid personalization of musculoskeletal geometry and motor control, enhancing physiological accuracy. Advanced predictive simulations and multi-scale modeling expand clinical applications, facilitating surgery outcomes prediction and movement modification for joint diseases. Collaborative interdisciplinary efforts are essential for overcoming challenges, refining workflows, and ultimately enhancing clinical treatment outcomes.

KEYWORDS: Biomechanics | Musculoskeletal modeling | Gait analysis

BACKGROUND

Musculoskeletal modeling is a powerful tool for simulating and analyzing the intricate functioning of the musculoskeletal system. By integrating a musculoskeletal model with an individual's movement data—such as marker trajectories obtained from a 3D motion capture system—it becomes possible to estimate in-vivo muscle-tendon kinematics, muscle forces, and joint contact forces during dynamic movements. These variables, otherwise challenging to directly measure non-invasively, offer a comprehensive understanding of biomechanics. Computational musculoskeletal models also enable predictive simulations of movement (Fig. 1), which do not rely on experimental data [1]. These simulations generate novel movements based on optimization of a performance criterion, which typically involves several terms such as metabolic energy rate and muscle activity. They allow addressing 'what-if' questions that are beyond the reach of traditional experimental methods.

VIEW OF THE PAST

Musculoskeletal modeling has been refined over the last 50 years (summarized in two recent reviews [2,3]). Initially, 2D simulations were performed, and muscles were modelled as ideal actuators. The Hill-type muscle model was developed in the 1970s and has since become the standard muscle model for the majority of simulations [2]. Over the years, musculoskeletal properties in generic models have been updated based on novel experimental data, mainly from cadaver and medical imaging studies. With advancements in computational methods and increased processing power, it is now possible to simulate whole-body movement in 3D within minutes.

In the initial stages of clinically-oriented musculoskeletal modeling studies, the primary emphasis was on examining walking impairments in children with cerebral palsy. Amongst others, it has been shown that femoral geometry influences walking capabilities [4,5], crouch gait requires more knee extensor and less hip abductor strength compared to unimpaired gait [6], and Botulinum Toxin injections have a minor impact on dynamic muscle forces [7]. While enabling mechanistic insights, most simulations were still based on generic models, neglecting subject-specific musculoskeletal geometry and motor control.

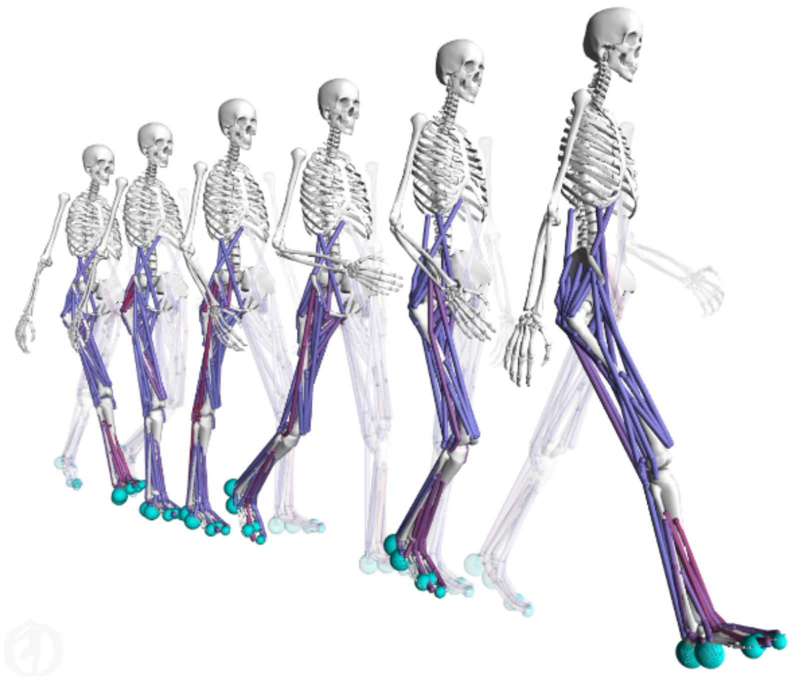

Figure 1. Predictive simulation of human walking. Blue spheres represent contact geometries. Muscles turn red when active (image adapted from De Groote and Falisse[1] with permission).

CURRENT STATE

Personalized musculoskeletal modeling has significantly advanced over the last two decades. Models with subject-specific musculoskeletal details can be created either directly from 3D medical images (e.g., magnetic resonance imaging or computer tomography) or by modifying existing models. Medical imaging-based models offer the potential to accurately represent the specific musculoskeletal geometry of participants. Yet, challenges remain for creating a complete personalized model from medical images; critically, defining muscle origin and insertion points from medical images is a laborious, time-consuming, and, error prone-process. Consequently, software tools [8–10] that enable pre-existing models to be personalized in a rapid way have been developed (Fig. 2).

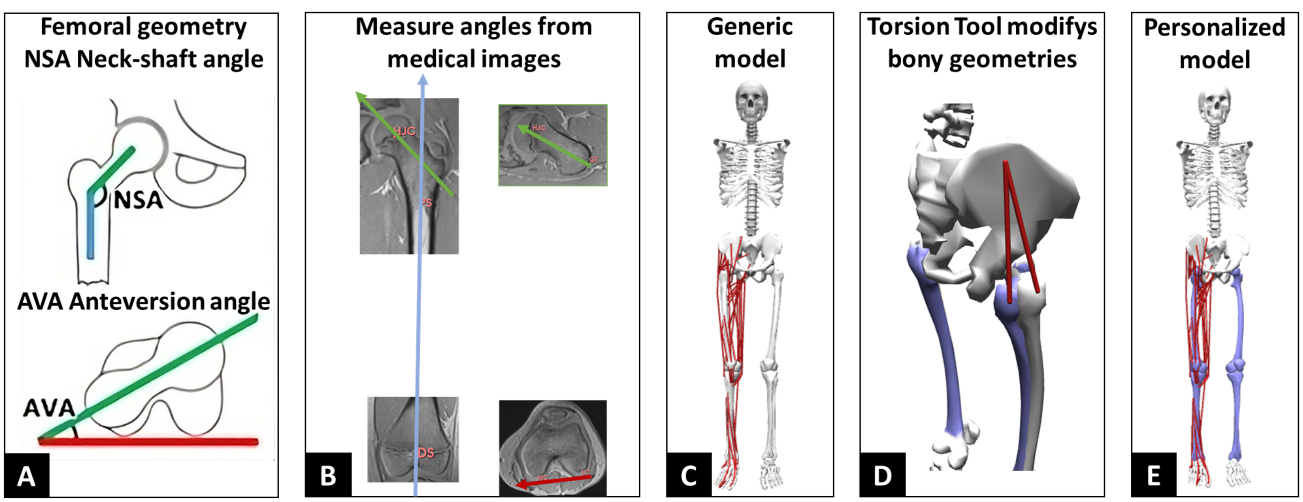

Figure 2. Morphological features of the femur (**A**) that have a big impact on muscle and joint contact forces estimated from musculoskeletal models [23] angles can be measured from medical images (**B**) and used in freely available tools, e.g., the Torsion Tool [9], (**D**) to modify the geometry of a pre-existing generic model (**C**), resulting in a more personalized model (**E**). In (**D**), two muscle lines-of-action, representing the middle parts of the gluteus medius, are depicted, emphasizing how manipulating the bony geometry with the Torsion Tool leads to alterations in muscle paths.

Personalizing muscle properties and motor control has become an essential part for state-of-the-art musculoskeletal modeling. Due to muscle redundancy, the same movement can be performed using different muscle recruitment strategies, which may vary among individuals and pathological populations [11–13]. Electromyograms (EMG), which are electrical potentials associated to muscle contraction and coordination, can be combined with musculoskeletal modeling to calibrate muscle-tendon parameters and simulate the effect of individual-specific motor control on the muscle forces and joint contact forces [14]. These EMG-informed simulations account for potential co-contraction, which is common in various populations such as individuals with osteoarthritis, thereby enhancing the physiological plausibility of the simulation results [12].

Predictive simulations based on musculoskeletal models can reveal principles of locomotion by elucidating cause-effect relationships. Recent advancements in computational methods have enabled the generation of 3D muscle-driven simulations of walking in less than 30 minutes, promising broader applications [15]. Combining personalized musculoskeletal models with predictive simulations allows for the assessment of cause-effect relationships between specific impairments and a patient's gait pattern. This facilitates the identification of primary treatment targets tailored to individual patients [16]. However, further refinement and validation of the modeling workflow are necessary before predictive simulations can be routinely employed in clinical practice.

Multi-scale models integrate musculoskeletal simulations with finite element analysis, facilitating the estimation of tissue loads. These cutting-edge modeling approaches have been used to estimate subject-specific stresses on growth plates, thereby advancing our understanding of pathological bone growth [17,18]. Additionally, sophisticated multi-scale simulations have enabled real-time estimation of stresses on the Achilles tendon [19], paving the way for various clinical applications such as load monitoring during rehabilitation. However, the widespread clinical application of these approaches is currently hindered by several factors. Firstly, it demands expertise across various biomechanical disciplines. Additionally, it requires comprehensive and expensive data collection, including medical images and 3D motion capture data. While some of these challenges are being tackled by the adoption of wearable sensors and computer vision approaches [20], further work is required to facilitate the broader adoption of multi-scale musculoskeletal modeling approaches in clinical settings.

FUTURE PERSPECTIVE

Current research endeavors are dedicated to advancing musculoskeletal modeling and its clinical applications on multiple fronts. Among ongoing developments, two emerging 'hot topics' hold promise for potential breakthroughs in the coming decade. One focuses on predicting surgery outcomes, where personalized modeling and comprehensive experimental data collections may bring us closer to this goal. The other area involves using musculoskeletal modeling to inform movement modification for joint diseases, potentially offering non-invasive interventions [21]. Personalized simulations could pinpoint how small adjustments to a person's gait can alleviate joint loads, reduce pain, and slow the progression of degenerative diseases [13]. Integration of subject-specific models with real-time simulations using smart garments [22] may enable real-time quantification of individual internal loads in the future.

In summary, musculoskeletal modeling has evolved into a cornerstone of biomechanics, experiencing a significant surge in popularity over the past two decades. Numerous research groups are actively developing new models and tools, sharing their advancements with the community, thereby fostering rapid progress. With the increasing ease of model personalization and simulation, collaborative research efforts involving multidisciplinary teams are crucial to address challenges, refine modeling workflows, validate simulation results, facilitate clinical integration, and ultimately enhance clinical treatment outcomes.

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