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Ten steps to becoming a musculoskeletal simulation expert: A half-century of progress and outlook for the future

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Abstract

Over the past half-century, musculoskeletal simulations have deepened our knowledge of human and animal movement. This article outlines ten steps to becoming a musculoskeletal simulation expert so you can contribute to the next half-century of technical innovation and scientific discovery. We advocate looking to the past, present, and future to harness the power of simulations that seek to understand and improve mobility. Instead of presenting a comprehensive literature review, we articulate a set of ideas intended to help researchers use simulations effectively and responsibly by understanding the work on which today's musculoskeletal simulations are built, following established modeling and simulation principles, and branching out in new directions.

Introduction

Simulations complement experimental approaches to understanding complex systems in nearly all areas of science and engineering. Simulating musculoskeletal dynamics is a powerful method for understanding the biomechanics of movement. A musculoskeletal simulation is generated by computing the motion of a musculoskeletal model that is governed by the laws of physics and the behavior of the biological system. Simulations may be driven by experimental data, a hypothesis about how an individual moves, an optimization problem, or a combination of these.

The use of simulation in biomechanics has greatly expanded over the past several decades (Fig. 1). Musculoskeletal simulations have enriched our knowledge of sport

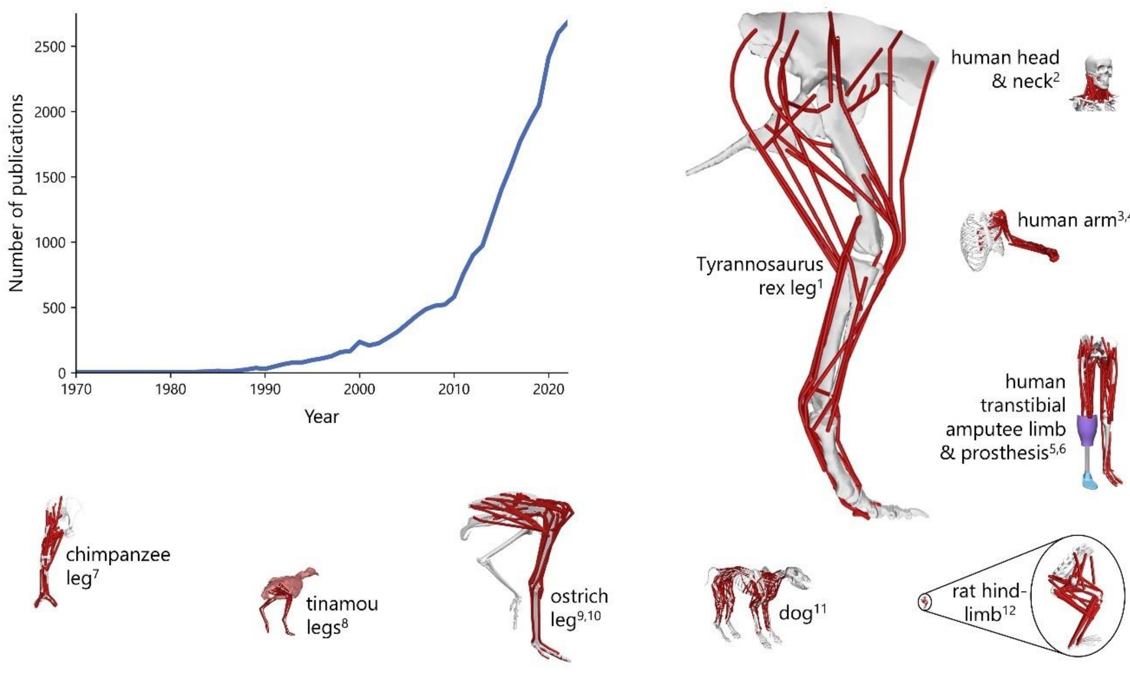

Figure 1. Growth of musculoskeletal modeling and simulation. Annual PubMed publications in "(musculoskeletal simulation) OR (musculoskeletal model*)" have grown by three orders of magnitude since 1970. Over the past two decades, many musculoskeletal models have been developed and shared publicly on SimTK.org for use in simulation research. Examples of shared models, shown to relative scale, have been provided by [1]Hutchinson et al. (2005), [2]Mortensen et al. (2018), [3]McFarland et al. (2019), [4]Saul et al. (2015), [5]Rajagopal et al. (2016), [6]Willson et al. (2020), [7]O'Neill et al. (2013), [8]Bishop et al. (2021b), [9]Hutchinson et al. (2015), [10]Rankin et al. (2016), [11]Stark et al. (2021), and [12]Johnson et al. (2008).

performance (Vanlandewijck et al., 2001), workplace ergonomics (Chaffin, 2001, 1969), vehicle collisions (Bose et al., 2010), and even dinosaur running (Hutchinson et al., 2005). Simulations have become so important in biomechanics that we suggest that all researchers in our field develop expertise in this area.

This article outlines ten steps to becoming a musculoskeletal simulation expert as we celebrate the 50th anniversary of the International Society of Biomechanics in this Special Issue. Several reviews of musculoskeletal modeling and simulation have recently been published (de Groote and Falisse, 2021; Ezati et al., 2019; Febrer-Nafría et al., 2022; Roupa et al., 2022). Thus, rather than provide another review of the literature, our goal is to outline a set of steps intended to help researchers hit the ground running with simulation research. In the first section—Look back: Know your history—we recommend three steps to understand the work upon which today's musculoskeletal simulations are built. In the second section—Look inside: Be a strong simulator—we outline three steps that every researcher should take to define and analyze their musculoskeletal simulations, even as simulation techniques advance. Finally, in the third section—Look forward: Invent the future—we offer four steps the field can take to forge new paths in musculoskeletal simulation and create lasting impact. We focus on human locomotion, but the ten steps apply to other types of human and animal movement and to musculoskeletal modeling and simulation in general.

Look back: Know your history

Step 1: Study early simulations

Modern musculoskeletal simulation began about fifty years ago, at roughly the same time the International Society of Biomechanics was founded. Posed with the difficulty of measuring muscle forces in vivo, researchers turned to musculoskeletal simulations to estimate muscle forces and the motions they produce. Static and dynamic optimizations of human movement were introduced in the 1970s (Chow and Jacobson, 1971; Hatze, 1976; Seireg and Arvikar, 1973). At the time, the equations of motion were derived and programmed by hand, and simulations representing just 0.5 seconds of movement could require more than twenty hours of computation by computers that filled a room. The methods used in early simulations were relatively simple compared to modern techniques, yet they paved the way for today's musculoskeletal simulations.

Several advancements have since enabled more accurate musculoskeletal simulations and deeper study of the ways in which muscles produce movement (Fig. 2). Quantitative anatomy and muscle architecture experiments in the early 1980s enabled researchers to improve model accuracy. From cadaveric limbs, Brand et al. (1982) identified three-dimensional lower-limb muscle origin and insertion coordinates. These measured coordinates were great improvements over those previously estimated from drawings in anatomy textbooks. Shortly after, Wickiewicz et al. (1983) measured lower-limb muscle properties, including muscle fiber lengths and physiological cross-sectional areas. These important studies resulted in more accurate musculoskeletal models, including the lower-extremity model developed by Hoy et al. (1990).

Through the 1980s, musculoskeletal simulations, particularly those employing dynamic optimization, were limited by barriers in computation and model development. Kane's method (Kane and Levinson, 1985) offered efficient algorithmic determination of the equations of motion and enabled the first 3D dynamic simulation of part of the gait cycle in 1990 (Yamaguchi and Zajac, 1990). Around the same time, Delp et al. (1990) developed an open-source musculoskeletal model and an interactive computer graphics interface that enabled users to manipulate musculoskeletal model parameters. This open-source model has been used in

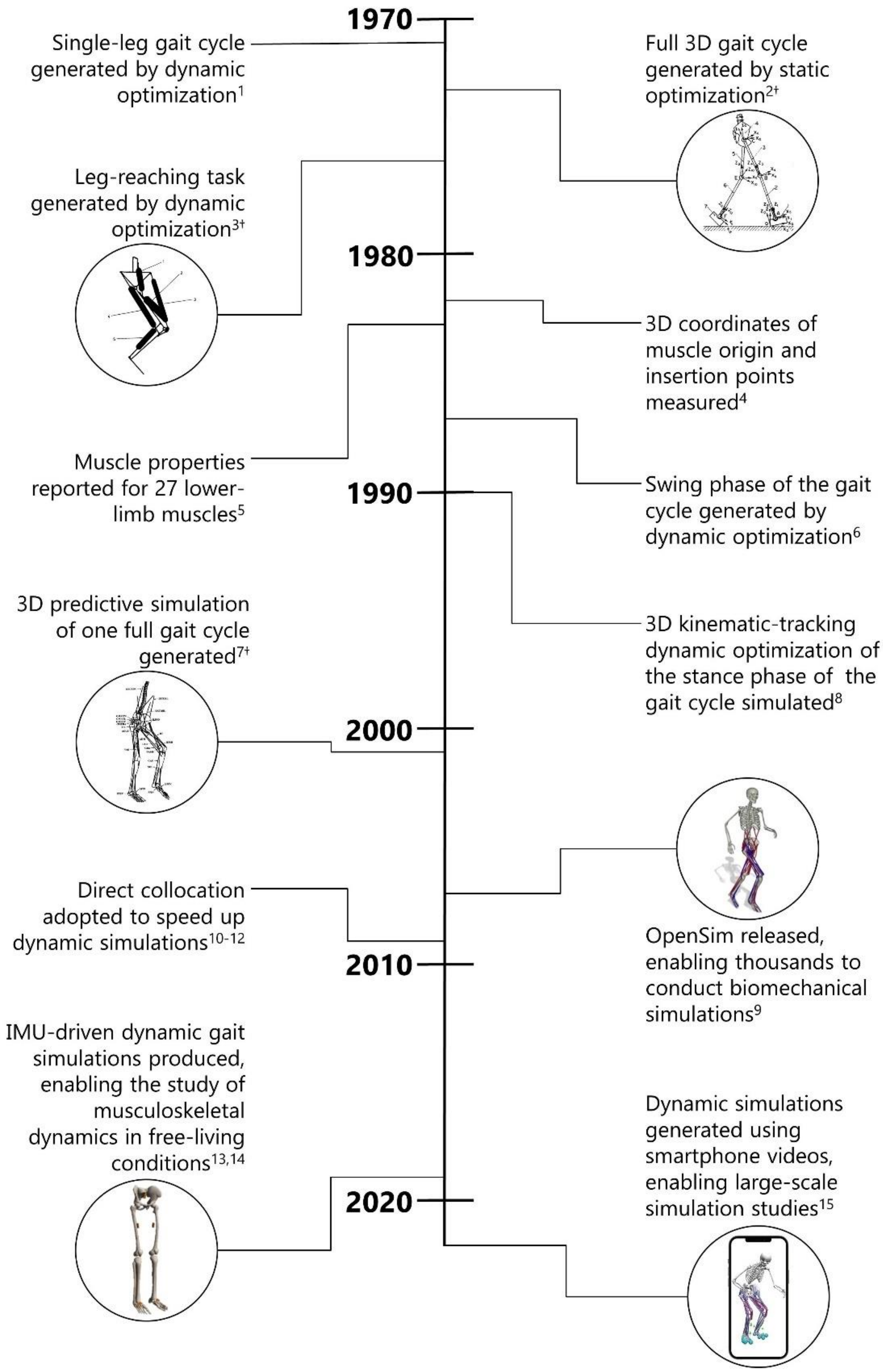

Figure 2. Some of the key advancements in musculoskeletal simulation over the past 50 years. [1]Chow and Jacobson (1971); [2]Seireg and Arvikar (1973); [3]Hatze (1976); [4]Brand et al. (1982); [5]Wickiewicz et al. (1983); [6]Davy and Audu (1987); [7]Yamaguchi and Zajac (1990); [8]Anderson and Pandy (2001); [9]Delp et al. (1990); [10]Ackermann and van den Bogert (2010); [11]de Groote et al. (2009); [12]Kaplan and Heegaard (2001); [13]Dorschky et al. (2019); [14]Karatsidis (2016); [15]Uhlrich, Falisse, and Kidziński et al. (2022). [†]Figures reprinted with permission.

thousands of research studies, including in the groundbreaking 2001 paper describing the first 3D predictive dynamic optimization of a full cycle of walking gait (Anderson and Pandy, 2001).

In 2001, simulation of this single gait cycle required 10,000 hours of total CPU time. Efficient optimal control methods like direct collocation (Hargraves and Paris, 1987) were adopted in biomechanics in the 2000s (Ackermann and van den Bogert, 2010; de Groote et al., 2009; Kaplan and H. Heegaard, 2001). Today, researchers can perform predictive dynamic optimizations of walking in less than one hour (Dembia and Bianco et al., 2020; Falisse et al., 2019).

Advancements in quantitative anatomy, increased computational speed, and the introduction of open-source models and tools have broken barriers in musculoskeletal simulation, allowing researchers today to focus on important biomechanical questions.

Step 2: Understand what can be learned from simulations

Muscle-driven simulations extend the insights gained from experiments. For example, it is possible to measure muscle activity, ground reaction forces, and joint motions in experiments, but it is not possible to determine how each muscle contributes to ground reaction forces and body motions with experiments alone. Muscle-driven simulations reveal the forces and motions caused by muscles and provide powerful tools for understanding muscle actions during movement. We can also leverage simulations to predict how the body responds to disease (Knarr et al., 2013; Steele et al., 2012a), surgery (Delp and Zajac, 1992), or altered muscle activations (DeMers et al., 2014). These capabilities allow us to design surgeries (Delp and Zajac, 1992) and assistive devices (Bianco et al., 2022b; Dembia et al., 2017) or simulate dangerous events, such as falls or injuries (DeMers et al., 2017).

To provide a specific example, muscle-driven simulations have revealed how muscles generate forces that support the body’s weight and regulate forward progression during the stance phase of walking. We can quantify a muscle’s contribution to body-weight support by determining how the muscle affects the vertical acceleration of the center of mass. Similarly, we can investigate how a muscle contributes to forward progression by analyzing its role in generating accelerations of the center of mass in the fore–aft direction (Liu et al., 2008; Neptune et al., 2001).

The same muscles that provide body-weight support during walking also regulate forward progression. For example, the vasti and gluteus maximus make important contributions to support during early stance while the vasti also reduce the body's forward velocity (Fig. 3; Liu et al., 2008). The gluteus medius provides support during midstance and, in the second half of stance, contributes to forward acceleration. The soleus and gastrocnemius contribute to vertical

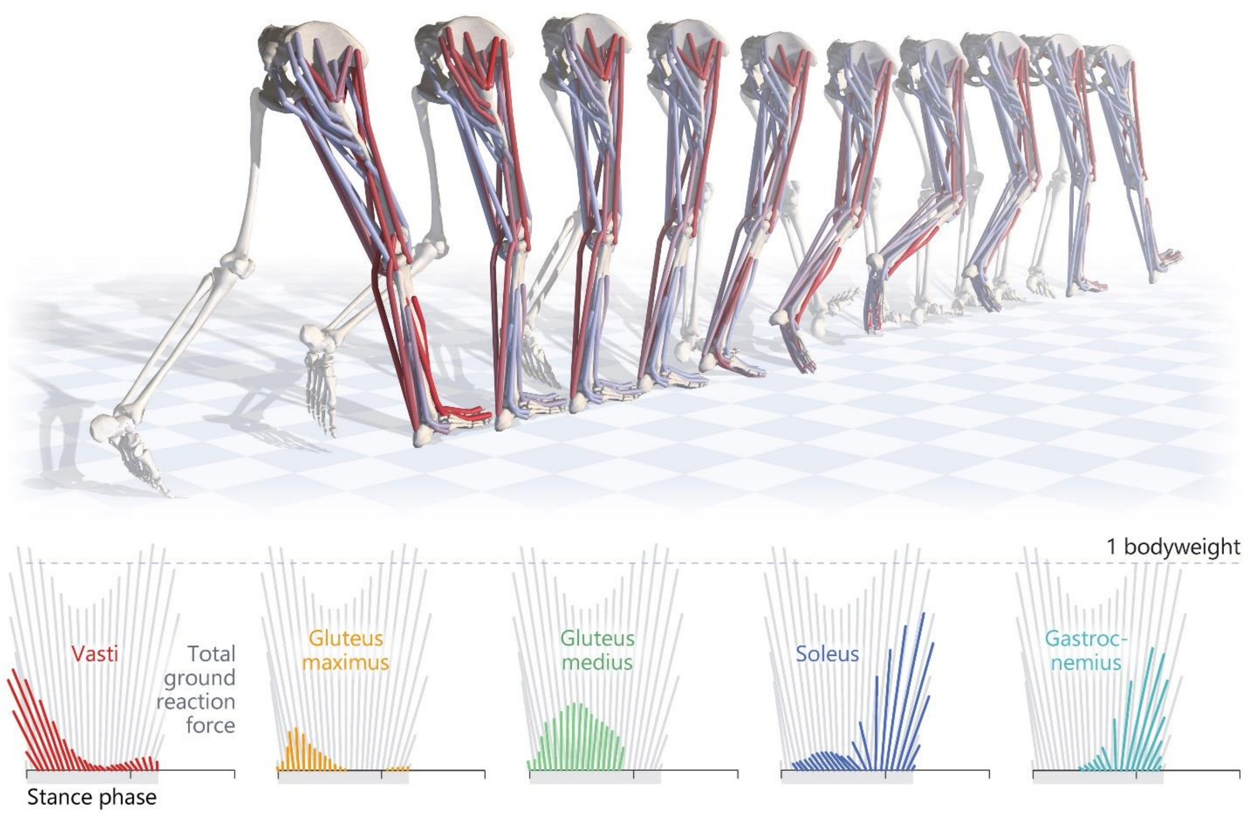

Figure 3. Top. Visualization of a muscle-driven simulation of walking. The colors of the muscles indicate their level of activation ranging from inactive (blue) to highly active (red). **Bottom.** Contributions of muscles to center-of-mass accelerations during the stance phase of walking. The vasti accelerate the center of mass upward and backward during early stance, while the plantarflexors accelerate the center of mass upward and forward during late stance. The gluteus maximus and gluteus medius also contribute to body-weight support. Data from Liu et al. (2008) and Dembia et al. (2017).

and forward acceleration in late stance. The contributions to body-weight support from the soleus and gastrocnemius are so important that weakness or contracture of these muscles may lead to crouch gait (Ong et al., 2019; Steele et al., 2012b). For this reason, crouch gait can be improved in some cases by wearing an ankle brace that generates a plantarflexion moment (Rosenberg and Steele, 2017).

Step 3: Know what tools are available

Powerful musculoskeletal modeling and simulation tools are available to today's biomechanists. Some researchers produce fantastic individual contributions to the field by writing custom programs for their simulations. These programs can be fast when optimized for just one or a few applications (e.g., Mansouri and Reinbolt, 2012; van den Bogert et al., 2013). Developing custom software encourages researchers to understand every element of their code and simulations and thus requires great effort. Fortunately, since general-purpose simulation tools exist, custom software is rarely required for simulation research.

On the other end of the simulation-tool spectrum is commercial software. Commonly used commercial software in musculoskeletal modeling include the AnyBody Modeling System (AnyBody Technology, Aalborg, Denmark; Damsgaard et al., 2006), multibody dynamics simulation tools like Adams (Hexagon AB, Newport Beach, CA), and finite element tools like Abaqus (Dassault Systèmes, Vélizy-Villacoublay, France). Most motion capture companies also offer software capable of performing inverse dynamic analyses. Commercial biomechanics packages are intended to support a variety of applications. They are well tested and well suited for commercial applications, with technical support available to users. In many cases, researchers cannot access or modify the software and methodological details, which can be limiting in research.

Between custom and commercial software lies open-source software. Open-source tools in musculoskeletal simulation include OpenSim (Delp et al., 2007; Seth, Hicks, and Uchida et al., 2018) for dynamic simulations, the Calibrated EMG-Informed Neuro-musculoskeletal Modelling Toolbox (CEINMS; Pizzolato et al., 2015) for electromyography-informed simulations, Simulated Controller OptimizatioN Environment (SCONE; Geijtenbeek, 2019) for predictive simulations, and Finite Elements for Biomechanics (FEBio; Maas et al., 2012) for finite element modeling. These freely available tools invite involvement from a worldwide community of biomechanics researchers and enable reproducibility while making the underlying code available and modifiable.

It is important to know what research question you are asking so that you can determine which custom, commercial, or open-source software will provide the best answer.

Look inside: Be a strong simulator

Step 4: Ask the right question

A research question is the driving force behind a scientific study. To quote Carl Jung, “to ask the right question is already half the solution of a problem.” Research questions that are specific and stated directly (e.g., “Does a model with weakness or contracture in the ankle plantarflexor muscles walk more slowly?” [Ong et al., 2019]) provide more direction than those that are posed more generally or are not questions at all (e.g., “The effect of muscle weakness on gait”). A good research question should also be novel, important, and interesting. Research questions in biomechanics are often posed to improve our fundamental understanding of movement (e.g., Farris and Sawicki, 2012; Umberger, 2010); to improve prevention, diagnosis, or treatment of an injury or pathology (e.g., Alentorn-Geli et al., 2009; Piazza, 2006); to enhance function and quality of life (e.g., Shull et al., 2014); to develop and disseminate analytical tools (see Section 3); and, frequently, as combinations of these (Hicks et al., 2015).

A good research question must also be answerable. Depending on the question, it may be more appropriate to perform human experiments, computer simulations, or some combination of these. One may need to collect motion data to answer the question. Alternatively, the data may already be available and can simply be aggregated from medical records (Hicks et al., 2011) or large sets of unlabeled data (Ratner et al., 2017) and analyzed to discover new insights without recruiting a single human subject. For a research question to be answerable, the study must also be feasible given the available resources, including experimental equipment, study participants, physical prototypes, musculoskeletal simulations, software, algorithms, or computational resources.

Although curiosity-driven exploration can ultimately lead to insight, scientific “dead-ends” may be avoided from the outset by imagining the goal: Supposing the desired experiments or simulations were completed, what plots would you generate and what numbers would be most important? Having a clear vision of the outcome will help to guide the study and reveal limitations in the planned approach that could be addressed by adjusting the study design. Importantly, a vision of the outcome will help to ensure that all the necessary data are collected during experiments and that any musculoskeletal models used are sufficiently detailed where the detail matters. We’ll look at this in the next section.

Step 5: Use the right tool for the job

The design of a study is driven by the research question. Inverse dynamic simulations can provide deeper understanding of experimental observations. An inverse dynamic simulation determines the values of variables in a musculoskeletal model (e.g., joint angles, net joint moments, or muscle forces over time) that best explain the observations (e.g., motion capture marker trajectories, ground reaction force data, or electromyography). Inverse dynamic simulations have been used in many human movement studies to estimate quantities that cannot be measured directly. In contrast, forward dynamic simulations use physics-based models to compute the motions that result from a set of muscle excitation patterns. For example, numerical optimization can be used to discover the muscle excitations that cause a musculoskeletal model to move to achieve a desired objective, such as minimizing metabolic cost or jumping as high as possible. Forward dynamic simulations can be useful when experimental data are unavailable—for example, when studying the locomotion of extinct animals (Bishop et al., 2021a; Hutchinson et al., 2005), potentially injurious motions (Shin et al., 2007), and assistive devices that have not yet been built (Dembia et al., 2017; Uchida et al., 2016).

All musculoskeletal simulations require a musculoskeletal model. A model is a description of reality that explains and predicts some phenomena of interest within a required precision. Any model, whether physics-based or data-driven, should be as simple as possible while capturing all the information necessary for the model to be useful (Fig. 4). Increasing

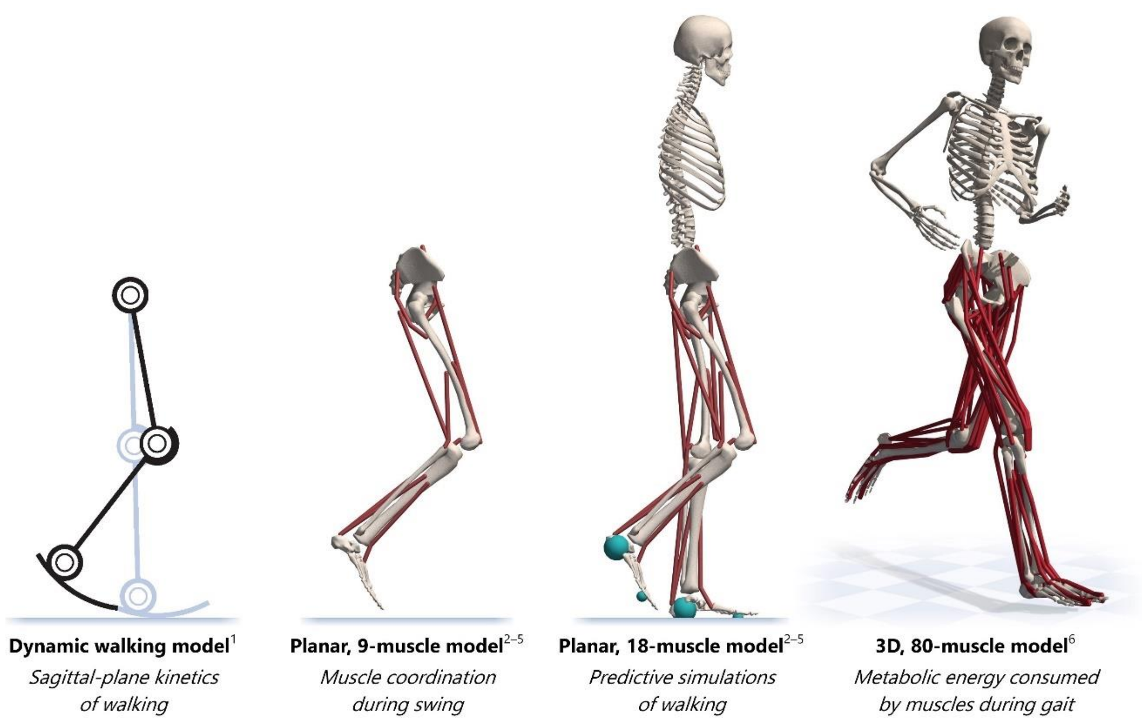

Figure 4. Four gait models of increasing complexity and an example of a study for which each model might be appropriate. The research question dictates the requirements for a musculoskeletal model. [1]Kuo and Donelan (2010); [2]Delp et al. (1990); [3]Yamaguchi and Zajac (1989); [4]Anderson and Pandy (1999); [5]Anderson and Pandy (2001); [6]Rajagopal et al. (2016).

model complexity can introduce new parameters and uncertainties, increase computation time, and obscure the information required to answer the research question. On the other hand, overly simple models may embed assumptions that lead to inaccurate conclusions. Whether computational or “purely” experimental, nearly every biomechanics study uses a model of some kind. For example, calculation of the knee flexion angle during gait may use a model that makes assumptions about the possible motions of the knee or the relationships of motion capture markers to the underlying bones. Some typical questions to consider when choosing or developing a model to answer a research question include which degrees of freedom the model should have, whether muscles are required, and how contact will be represented (e.g., using measurements, kinematic constraints, a contact model, or machine learning). Many musculoskeletal models have been built, validated, and openly shared for the biomechanics community to use (Fig. 1).

Step 6: Preserve a healthy skepticism

To quote Carl Sagan, “extraordinary claims require extraordinary evidence.” This so-called “Sagan standard” reminds us to aspire to be skeptical, unbiased scientists. From simulations, we often seek general conclusions about human movement. The robustness of these conclusions must be tested by exploring simulation results over a range of operating conditions, performing sensitivity analyses, and evaluating conclusions with real-world data. Uncertainties in the variables of interest should be evaluated and reported. The most reliable conclusions are those that have been found consistently using many datasets, models, simulation strategies, and software packages.

Models and simulations must be verified and validated. Verification tests ensure that simulation results satisfy known relationships, such as energy conservation and Newton’s laws. Validation tests ensure that simulation results agree with real-world observations. For example, even if a simulation passed verification tests, a result indicating that the cost of transport decreases as walking speed increases from self-selected speed would contradict established principles of human locomotion. Hicks et al. (2015) provide an overview of verification and validation for modeling and simulation studies as well as recommendations.

It is important to be aware of the limitations of models and simulation tools that you employ. Modelers should identify and quantify the largest sources of error in their analyses and evaluate how these errors affect the outputs of interest. For example, OpenSim uses residual actuators to ensure that Newton's second law is satisfied despite dynamic inconsistencies between measured forces F, estimated segment masses m, and measured accelerations a. The Residual Reduction Algorithm in OpenSim aims to minimize the "residual forces" F_{residual}:

$$F + F_{\text{residual}} = ma$$

Some, but not all, software tools quantify and report the errors in the underlying models. Whether reported or not, modeling errors always exist and must be considered when drawing conclusions. It is also important to know the limitations of the musculoskeletal model you are using to ensure the model is operating within the range for which it has been validated. Additional validation may be required to ensure the model is suitable for your study. For example, the gait model developed by Rajagopal et al. (2016) was extended by Lai et al. (2017) to model movements involving substantial hip and knee flexion. Errors also appear during simulations—for example, integration tolerances and interpolation between data points pollute calculations with numerical error. Convergence analyses can be used to determine simulation parameters such as integration tolerances and termination criteria for iterative algorithms that maintain sufficiently small errors.

Look forward: Invent the future

Step 7: Embrace new techniques

Leveraging technical advances from other fields can catalyze progress in musculoskeletal simulation. For example, direct collocation, which originated in aerospace engineering (Hargraves and Paris, 1987), has made it far easier to generate predictive simulations using complex musculoskeletal models (Falisse et al., 2019). Another emerging trend is applying machine learning to biomechanics problems (Halilaj et al., 2018). Understanding when to apply physics-based models versus machine learning models and devising clever ways to combine the two are becoming important skills in computational biomechanics.

Physics-based simulations are usually more generally applicable and interpretable than machine learning models. If we have a good model, we can estimate unmeasurable quantities based on established physical laws. Improvements to the fidelity of these models (e.g., through the Knee Grand Challenge [Fregly et al., 2012; Kinney et al., 2013]) can have widespread benefits for other modeling problems. Two drawbacks of the physics-based approach are that the questions we can answer are limited by how well we model the physical system, and our results can be sensitive to assumptions, some of which may be difficult to test.

Machine learning models are well suited to approximate phenomena for which we lack good physical models, enabling accurate predictions when given input data that are within the distribution of the training dataset. For example, machine learning has been used to predict fall risk (Tunca et al., 2020), recognize intent for prosthesis control (Labarrière et al., 2020), and detect freezing of gait in Parkinson's patients (O'Day, Lee, and Seagers et al., 2022). Common drawbacks of this approach are that models typically require large amounts of training data, are often not interpretable, struggle to generalize beyond the distribution of the training dataset, and do not take advantage of our knowledge of the physical system.

Merging physics-based and machine learning approaches can yield more accurate models that are trained on smaller datasets (Fig. 5). One common approach is to use musculoskeletal models to generate training data for machine learning models that use sparse inputs, such as data from a small number of inertial measurement units or acoustic emissions

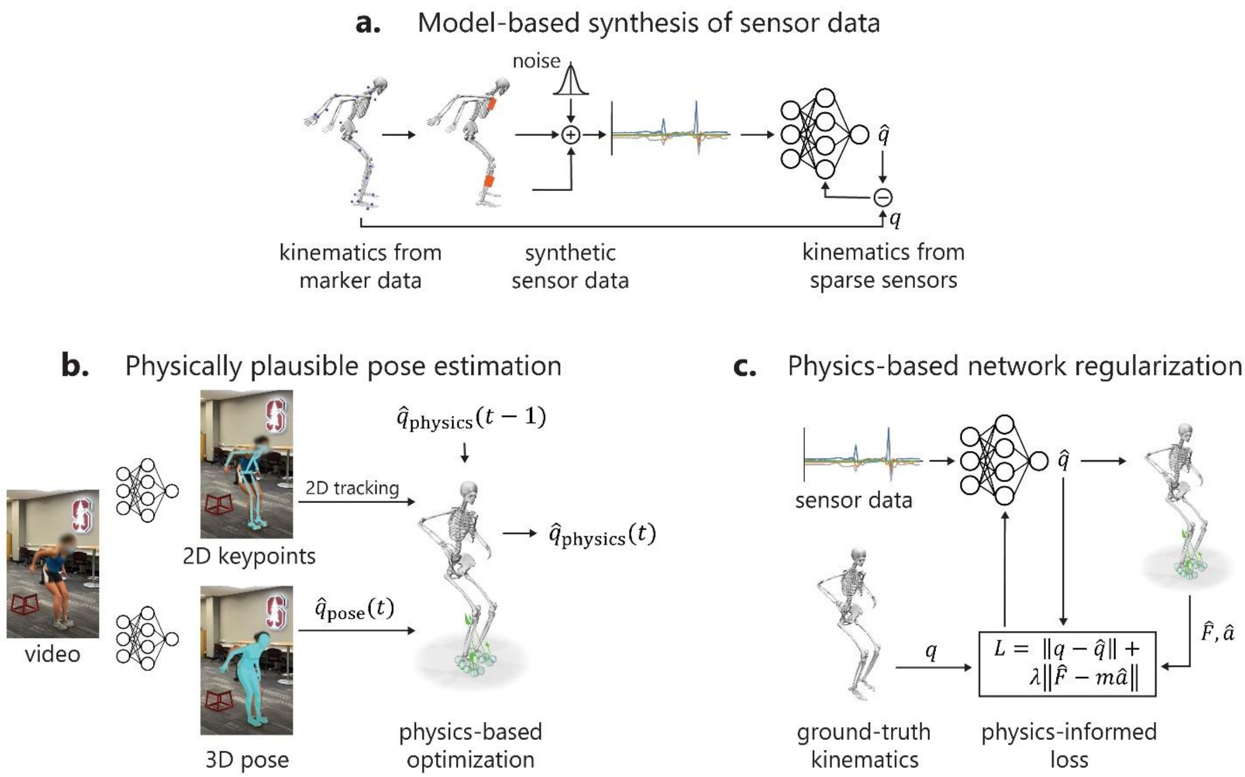

Figure 5. Approaches to combining physics-based modeling and machine learning. **(a)** Musculoskeletal models can be used to synthesize inputs to machine learning models (Jiang et al., 2022; Sharifi Renani et al., 2021; Uhlrich, Falisse, and Kidziński et al., 2022). Here, q and $\hat{q}$ represent the ground-truth and predicted generalized coordinates of a musculoskeletal model. **(b)** Physics-based optimization can improve the accuracy of deep-learning-based pose estimation (Shimada et al., 2020; Yuan et al., 2021). **(c)** Physics terms can regularize the loss function of a deep learning model, helping to reduce overfitting (Zhang et al., 2023). In this simple example, F represents ground reaction forces, a represents center-of-mass accelerations, and λ changes the relative weighting between the tracking error and physics terms in the loss function. Fully connected neural networks are used to depict machine learning models of any architecture.

from a joint (Jiang et al., 2022; Scherpereel et al., 2021; Sharifi Renani et al., 2021; Uhlrich, Falisse, and Kidziński et al., 2022). Another approach is to build elements of the physical system into the machine learning model. For example, physics simulations can improve the accuracy of a deep-learning-based pose estimation model (Shimada et al., 2020; Yuan et al., 2021), and neural networks can be regularized with physics-based terms in the loss function (Raissi et al., 2019; Zhang et al., 2023). Yet another approach is to use physical models for elements of the system that we understand well and to train machine learning models for the remaining elements. Using reinforcement learning, for example, a network can learn a model of sensory-motor control (which is challenging to model mechanistically) that enables a musculoskeletal model to navigate complex environments (Kidziński et al., 2018; Song et al., 2021). Novel methods for combining physics and data into unified models will likely be a popular theme in future biomechanics research.

Step 8: Leverage simulation at scale

Improvements in computational efficiency and the release of easy-to-use software packages continue to expand the community that has access to musculoskeletal simulation (Fig. 1). Despite these advances, most inverse dynamic simulation studies continue to include only a small number of participants, in part due to the time required to collect and process optical motion capture data. Use of optical motion capture and force plates also limits most studies to the controlled laboratory setting. Mobile sensors reduce these barriers to simulation studies that include hundreds of participants. Simulations can be generated from data collected outside the lab using sensors that are orders of magnitude less expensive than marker-based motion capture, such as standard video cameras or inertial measurement units (al Borno and O'Day et al., 2022; Dorschky et al., 2019; Haralabidis et al., 2020; Karatsidis et al., 2016; Slade et al., 2022; Uhlrich, Falisse, and Kidziński et al., 2022). We anticipate that automated pipelines for generating simulations from mobile sensor data will enable large studies with sufficient statistical power to discover movement biomarkers that can be easily measured in the clinic or home.

We envision a future where a digital representation of our musculoskeletal system is continuously monitored, allowing for the prediction and prevention of musculoskeletal injury and disease. Our digital twins (Glaessgen and Stargel, 2012; Pizzolato et al., 2019) will be created passively from videos of us moving through our natural environments or from wearable sensors embedded into our clothing. With these technologies, we will capture the mechanics of events, such as falls and sports injuries, that cannot be captured in a laboratory. With sufficient data, we will then be able to predict these events and deliver just-in-time interventions. For example, sensor-embedded clothing continuously estimating the dynamics of an older adult could predict a future loss of balance and command a balance-restoring exoskeleton torque (Bianco et al., 2022a). Furthermore, inexpensively generated simulations will lead to a better understanding of the role of musculoskeletal mechanics in the onset of movement-related diseases. Large-scale observational studies, such as the UK Biobank or the Osteoarthritis Initiative, will be able to incorporate estimates of musculoskeletal dynamics with the same ease as step counts, which are commonly measured in population health studies. Instead of simulating seconds of movement, future simulations will leverage these rich longitudinal datasets and simulate years into the future, driving the creation of personalized preventative interventions.

Step 9: Tackle the hard problems

Many challenges remain in modeling the neuro-musculoskeletal system. First, we need to integrate better models of neural control into musculoskeletal models. Current optimization-based approaches for estimating muscle excitations can generate realistic motion, but they are insufficient for studying the impact of pain or neurological pathology on motor control and movement. Next, we need better models of temporal changes in neural control and the musculoskeletal system. Improved models of how motor control changes over time will elucidate how humans acquire new skills and adapt to assistive devices. Enhanced models of the interaction between long-duration tissue loading and biological responses will help us study soft tissue injuries, tissue remodeling, and muscle fatigue. More generally, solutions to complex, movement-related health challenges, such as the global inactivity pandemic, will require multidisciplinary collaborations that incorporate biomechanics, psychology, sociology, and environmental factors (Althoff et al., 2017; Crum and Langer, 2007; Hicks et al., 2023; King et al., 2020).

Solving these and other grand challenges will require increasingly multidisciplinary training and teams. Bridging biomechanics, neuroscience, computer science, robotics, and psychology will lead to breakthrough technologies that improve mobility. For example, using musculoskeletal models to inform prosthesis control (Sartori et al., 2018), neural stimulation (Angeli et al., 2018), or rehabilitation robot control (Pizzolato et al., 2019) could lead to dramatic functional improvements for individuals with amputation or neurological injury. Additionally, blurring the boundaries between simulations and experiments will improve our models and help translate simulation-based insights. The design of joint-offloading gait modifications exemplifies this process. Fregly et al. (2007) used a torque-driven simulation to design a gait modification strategy that reduced the knee adduction moment, a surrogate measure of medial knee loading. Walter et al. (2010) tested this gait modification experimentally and found that increases in muscle force (which were not modeled by Fregly et al. [2007]) attenuated the expected reductions in medial knee contact force. These findings inspired the development of simulations to design interventions that reduce the muscle contribution to knee loading (DeMers et al., 2014; van Veen et al., 2019), which were later tested experimentally (Uhlrich et al., 2022). This positive feedback between simulations and experiments will accelerate as real-time simulations become common (Pizzolato et al., 2017; Stanev et al., 2021; van den Bogert et al., 2013).

The ability to solve problems with global impact will be enhanced by creating global teams with diverse members. Since simulation research can be conducted without a laboratory, it is conceivable that the modeling and simulation community could be more globally diverse than experimental domains that require specialized equipment. If this were true, we might expect the OpenSim community to be more representative of the global population than the International Society of Biomechanics (ISB) membership, which includes both computational and experimental researchers. However, both the ISB and OpenSim communities are concentrated in Europe and North America, and researchers from Asia, Africa, and South America are underrepresented in both communities (Fig. 6). While these disparities are multifactorial, open-source code and datasets will continue to lower the barrier to entry for simulation research. In addition, assembling international teams to solve problems of mutual interest will enable bidirectional sharing of expertise (Haelewaters et al., 2021). To this end, we have found “virtual research office hours,” during which we consult with research teams from around the world, to be an effective and inclusive way to disseminate simulation knowledge and to learn from research teams based far from our own.

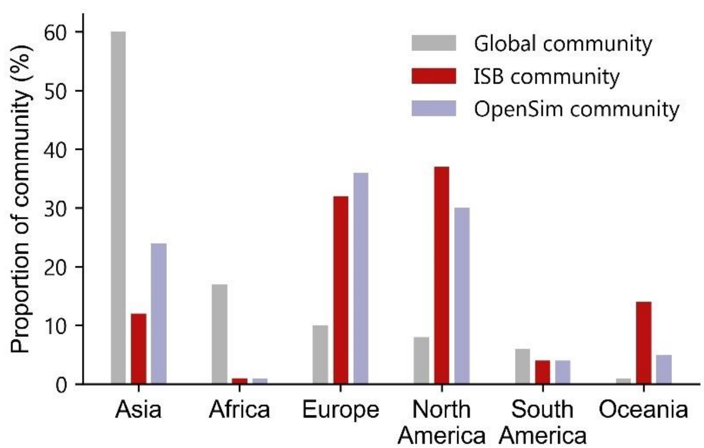

Figure 6. The distribution across continents of the International Society of Biomechanics (ISB) membership and the OpenSim community compared to the global population. Relative to their proportion of the global population, members of ISB and the OpenSim community from Europe, North America, and Oceania are over-represented, while those from Asia, South America, and Africa are under-represented. Data from https://isbweb.org and visits to OpenSim documentation (https://simtk-confluence.stanford.edu:8443/display/OpenSim) as of December 2022.

Step 10: Make an impactful contribution

Simulations have led to clinically relevant research insights in the past two decades, and they will likely have more direct impact on clinical care in the near future (Fig. 7; Killen et al., 2020). Simulations have elucidated general principles that can inform care, such as the relative tissue loads induced by common rehabilitation exercises (Pellikaan et al., 2018; van Rossom et al., 2018). Although simulations rarely inform patient-specific treatment decisions, easy-to-use tools to inform surgical planning with simulation-based insights (Pitto et al., 2019; Rajagopal et al., 2020) and tools to quickly generate simulations using portable sensors demonstrate

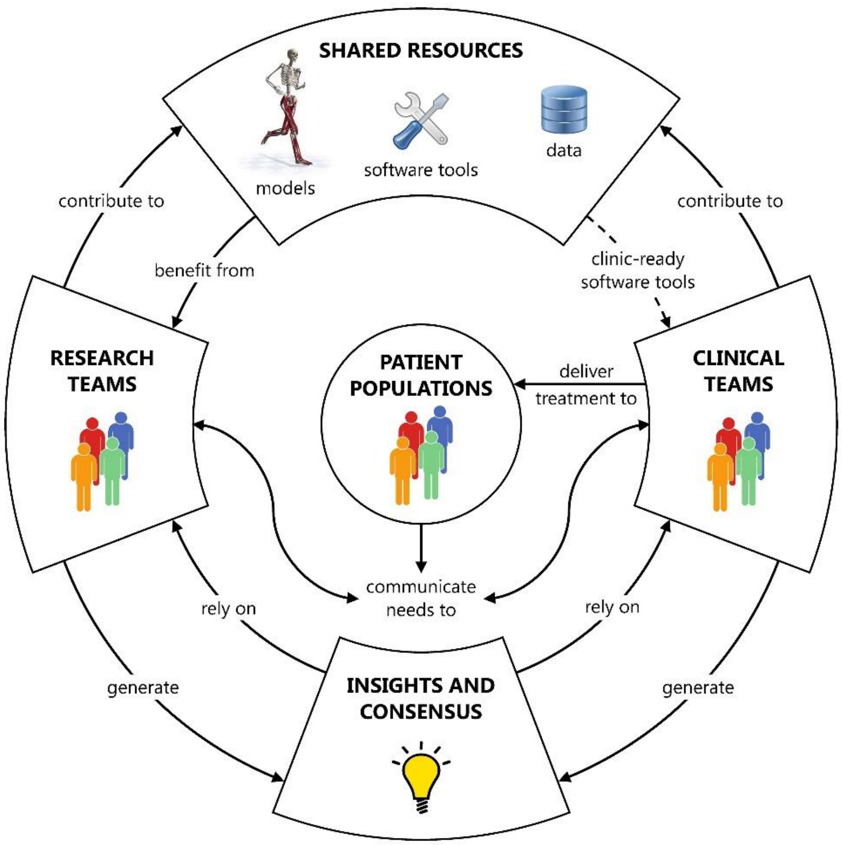

Figure 7. Clinically relevant research questions are driven by the needs of patient populations. Research teams and clinical teams work together to develop shared resources and to arrive at generalizable insights and consensus. In the future, use of software tools to improve clinical treatment (dashed line) will be ubiquitous.

progress toward this long-standing goal (Stanev et al., 2021; Uhlrich, Falisse, and Kidziński et al., 2022). As technical advances facilitate the integration of simulations into clinical workflows, it is critical for researchers to spend time with clinicians and patients to understand unmet needs: Which decisions are data-poor? Which generic treatments have poor outcomes? What are the stakeholder incentives and constraints? As simulations begin to inform device design, intervention design, and treatment decisions, it will be important to demonstrate efficacy through clinical trials. For example, van Rossom et al. (2018) used simulated knee contact forces to propose an ordered introduction of rehabilitation exercises following anterior cruciate ligament reconstruction. A randomized controlled trial demonstrating that this simulation-informed rehabilitation protocol slows the cartilage degeneration that is common after ligament injury (Monu et al., 2017) could lead to rapid clinical adoption.

Sharing code and models along with publications increases impact. Although it is time consuming, preparing code for sharing adds a useful verification step, improves reproducibility, and enhances confidence in results. Others may find errors in your shared code—this advances the field. Making models and simulation software available allows others to build on your work. When possible, building custom algorithms that extend widely used platforms will increase impact (e.g., CEINMS [Pizzolato et al., 2015], SCONE [Geijtenbeek, 2019], or OpenSim Moco [Dembia and Bianco et al., 2020]), but doing so requires maintenance. Increasing funding and career incentives for releasing, documenting, and maintaining open-source software will increase the number of valuable simulation tools available to the field.

Sharing data is another way to have impact. To train generalizable machine learning models, we need publicly available biomechanics datasets that are orders of magnitude larger than what currently exists. ImageNet, a dataset of images that catalyzed profound developments in deep learning, contains 3.2 million samples (Deng et al., 2009). In contrast, AMASS, the largest publicly available motion database, contains only 11,000 motions (Mahmood et al., 2019). The biomechanics community can create large datasets if we (1) make a practice of including data-sharing options in consent documents for experiments involving human subjects, (2) understand the benefits to the field and individual scientists (e.g., higher citation rates [Colavizza et al., 2020]), and (3) leverage tools that simplify data collection and sharing (e.g., addBiomechanics [Werling et al., 2022]). Representing motion data in terms of common musculoskeletal models will help standardize data across sensing modalities.

Conclusions

Early pioneers of musculoskeletal simulation may have found it difficult to believe that, in 50 years, one would be able to download a musculoskeletal model created by a colleague across the world and run a dynamic simulation in less than an hour without writing a single equation. Today's biomechanists have access to dozens of validated models and software tools to generate forward and inverse dynamic simulations. The volume of movement data available to biomechanists is increasing rapidly. Identifying clever ways to integrate our biomechanical knowledge of the neuro-musculoskeletal system with data-driven approaches will be key to developing models that predict and improve health.

Biomechanists of the 1970s also likely did not predict that a telephone would be able to generate input data for a simulation. Technical advances in the next 50 years are sure to surprise us, but even today's technology is poised to have great impact. By the 100th anniversary of the International Society of Biomechanics, we predict that insights from simulations will have contributed to solving today's pressing healthcare challenges, such as reducing the incidence of falls; improving mobility following a stroke, an amputation, or a spinal cord injury; reducing rates of injuries; and reducing the prevalence of osteoarthritis.

We live in an exciting time of musculoskeletal simulation research. By leveraging insights from the decades of previous work in the field, following established research principles, and adopting open, forward-thinking mindsets, discoveries in biomechanics will continue to improve our lives.

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Conflict of interest statement

The authors have no conflicts of interest to disclose.