

REVIEW

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Biomechanical models in the lower-limb exoskeletons development: a review

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Abstract

Lower limb exoskeletons serve multiple purposes, like supporting and augmenting movement. Biomechanical models are practical tools to understand human movement, and motor control. This paper provides an overview of these models and a comprehensive review of the current applications of them in assistive device development. It also critically analyzes the existing literature to identify research gaps and suggest future directions. Biomechanical models can be broadly classified as conceptual and detailed models and can be used for the design, control, and assessment of exoskeletons. Also, these models can estimate unmeasurable or hard-to-measure variables, which is also useful within the aforementioned applications. We identified the validation of simulation studies and the enhancement of the accuracy and fidelity of biomechanical models as key future research areas for advancing the development of assistive devices. Additionally, we suggest using exoskeletons as a tool to validate and refine these models. We also emphasize the exploration of model-based design and control approaches for exoskeletons targeting pathological gait, and utilizing biomechanical models for diverse design objectives of exoskeletons. In addition, increasing the availability of open source resources accelerates the advancement of the exoskeleton and biomechanical models. Although biomechanical models are widely applied to improve movement assistance and rehabilitation, their full potential in developing human-compatible exoskeletons remains underexplored and requires further investigation. This review aims to reveal existing needs and cranks new perspectives for developing more effective exoskeletons based on biomechanical models.

Keywords Assistive device, Biomechanical model, Exoskeleton, Lower-limb, Neuromuscular model

Introduction

Lower-limb exoskeletons offer a variety of applications. They could significantly improve mobility and the quality of life for individuals with lower-limb impairments, while also offering benefits such as augmented strength and reduced effort for unimpaired users [1]. The design and development of these devices require a multidisciplinary approach, with biomechanical modeling as a helpful

conceptual framework. Biomechanical gait models help to better understand and analysis human locomotion, the interaction between the human body and assistive devices, and optimization of the design and control parameters to achieve optimal performance [2].

In the realm of biomechanical models, two main categories are commonly used: conceptual models and detailed models [3]. By conceptual models, we refer to computational models that provide an abstract representation of human movement patterns, e.g., the overall motion behavior of a whole limb, using basic mechanical elements and possibly minimalistic control circuitry. Detailed models include more intricate mathematical formulation to address different biomechanical details of human movement systems like musculoskeletal structure, actuation on muscle level and neural control. Both

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have been employed in the development of lower-limb assistive devices, offering valuable insights and contributing to advancements in the field [2, 4].

Several studies reviewed selected aspects of exoskeletons for gait assistance [1, 5] and biomechanical models of gait [6–9]. However, the potentials of biomechanical models have not yet been considered systematically enough in the development of assistive devices. For instance, usage of musculoskeletal modeling driven by electromyography (EMG) signals for designing personalized rehabilitation interventions and human–machine interfaces has been discussed in previous reviews, such as the work by Sartori et al. [10]. Some reviews briefly discuss the benefits of incorporating biomechanical models in predictive simulations for designing assistive devices [9, 11]. Grabke et al. [2] provided valuable insights into the role of musculoskeletal simulation in the design optimization of lower limb assistive devices, including exoskeletons and prostheses. Their work shed light on the significance of musculoskeletal modeling in this context. Our study aims to expand upon their research by incorporating a broader range of recent literature (see Fig. 1). Additionally, we aim to explore various other applications of biomechanical models in the development of assistive devices, beyond just design optimization. In recent years, the availability of efficient numerical methods and open-source software for predictive simulations based on complex models has significantly accelerated the development of assistive devices [11]. Figure 1 shows an exponential increase in the number of papers using biomechanical models in developing assistive devices.

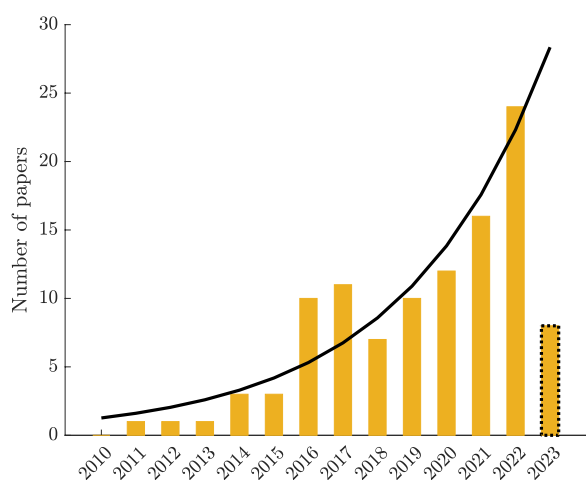


Fig. 1 Number of papers per year focusing on applications of biomechanical models in lower limb exoskeleton development included in our review (see “Biomechanical models in developing assistive devices” section for the search method). We covered only some part of 2023 (until end of June)

However, a comprehensive review specifically targeting the applications of biomechanical models in the development of lower limb exoskeletons is lacking, which is addressed in this article.

The purpose of this paper is twofold: first, to systematically review the existing literature on the applications of biomechanical models in the development of assistive devices; and second, to critically analyze these applications to identify gaps in the current research and propose potential directions for future work. Our review combines elements of both a systematic review, following predefined search strategies and selection criteria, and a critical review, where we synthesize findings to highlight areas that require further investigation [12]. By combining these approaches, this review aims to provide a comprehensive understanding of the field and guide future research efforts.

In the following, we begin by introducing different categories of biomechanical models in “Biomechanical gait models” section. “Biomechanical models in developing assistive devices” section details the specific methodologies used to systematically screen and select relevant literature for this review. Additionally, we discuss the applications of biomechanical modeling in the development of lower limb exoskeletons. Subsequently, in the final section, we will engage in a discussion of our findings and outline potential future directions in the field. By focusing on more recent research (shown in Fig. 1), this review intends to highlight the importance of biomechanical models for the advancement of lower limb exoskeletons and to support future research in this field.

Biomechanical gait models

Biomechanical models of gait encompass a range of models that aim to describe and understand human gait patterns and mechanics (see Fig. 2). The intricate nature of human gait arises from a complex, high-dimensional, and nonlinear interplay between the human body and its environment, posing challenges in the development of an accurate gait model [3]. To address the complexity of gait mechanics and motor control, conceptual models were developed to provide condensed representations of the underlying dynamics [13, 14]. These models offer a macroscopic view of locomotion tasks while capturing targeted key features of biological gaits. The main purpose of conceptual models is to capture the fundamental principles and relationships involved in human locomotion in a more accessible and manageable manner [3]. On the other hand, detailed models, such as musculoskeletal models, provide a more comprehensive representation of the human body and its underlying dynamic and motor control. These models incorporate skeletal segments, joints, muscles, tendons, and their associated properties

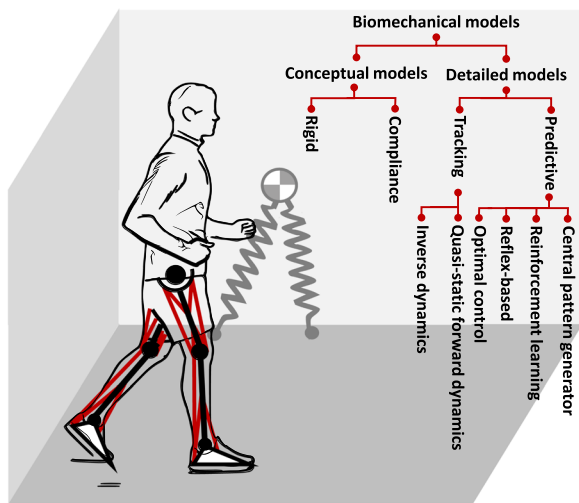


Fig. 2 Overview of various biomechanical models for gait, classified into conceptual and detailed categories along with their subcategories. Conceptual models serve as abstract representations of complex mechanics of gait. Detailed models attempt to integrate the mechanical principles of biological systems with the neural control of these systems, providing a more complete picture of the underlying interactions between the nervous and musculoskeletal systems

and interactions [15]. With a more complex musculoskeletal system, these models enable a more detailed description of biomechanical factors influencing gait patterns and can be used to study various aspects of human locomotion, including muscle coordination, joint loading, and the effects of assistive devices. The list of conceptual and detailed models presented in this review is derived from the template anchor modeling paradigm [3] which is a well accepted categorization for understanding the biomechanics of human movement [16]. This section is intended to provide an introductory overview of the models that are relevant to the development of assistive devices.

Conceptual models

In the context of human gait, a conceptual model offers the advantage of representing the fundamental characteristics of gait behavior in a parsimonious manner. This approach allows researchers to capture the underlying principles and mechanisms governing gait, without becoming entangled in intricate details pertaining to individual joints and muscles. By encoding body motion with respect to a minimal set of variables, a conceptual model effectively mitigates the challenge of high dimensionality, facilitating the study of the general system behavior [3]. Moreover, by presenting an intrinsic hypothesis concerning the high-level control strategy underlying a given task, a conceptual model facilitates a

deeper understanding of the neural and biomechanical mechanisms that drive behavior. This concept known as “*Template & Anchor*” [3] is a methodology that leverages lessons learned from conceptual models to develop more detailed morphological and physiological models to investigate specific involvement of multiple legs, joint torques, muscle recruitment, and neural networks activation. Noteworthy examples include the revelation of the role of leg force feedback in posture control [17, 18], as well as the role of local positive muscle force feedback in governing leg stiffness [19]. Here, we divide conceptual models into two categories, namely compliant and rigid models.

Compliant conceptual models

Compliant conceptual models of gait [20], such as the spring-loaded inverted pendulum (SLIP) model [21], have proven to be valuable tools for understanding and studying the mechanics of gait. An illustrative example involves the utilization of a bipedal spring-mass model [13], which demonstrates how the compliant behavior of the stance leg during running can replicate the stance dynamics observed in walking, highlighting the ability of a shared mechanical system to exhibit distinct motor behaviors through the same mechanical system setup. Extensions of the SLIP model were presented by adding the trunk and damping in the leg [22, 23] to better represent human movement mechanics and motor control with template-based models. In [24], utilizing leg force feedback to adjust hip joint stiffness was introduced to stabilize the upper body around the supporting leg in running. This parsimonious control circuitry in the template models, which was presented as force-modulated compliance (FMCH) model of walking [17], could replicate the virtual pivot point (VPP) concept observed in human walking [25]. In [26], the effect of wobbling masses on impact force during running is investigated. These models also prove beneficial in identifying key characteristics of gait that may undergo modifications in diverse populations, including individuals with neurological or musculoskeletal impairments [27].

Rigid conceptual models

Rigid conceptual models mostly drive from the inverted pendulum model [28] which approximates the center of mass of the body as a point mass located above a pivot point and is subject to gravitational forces. While these models do not correctly represent the stereotypical double-hump ground reaction of human walking, it helps elucidate fundamental principles and relationships. For instance, the inverted pendulum model helps describe the mechanical work required to redirect the velocity of the center of mass during step-to-step transitions and

metabolic determinants of the preferred step width in human walking [14, 29]. Also, this model is utilized to estimate metabolic cost of gait [30]. Notably, the inverted pendulum models have also contributed to understanding important principles governing gait stability. For instance, passive leg dynamics offer stabilization in the sagittal plane during walking, while active control is necessary for lateral stability [31]. These models have also been successfully used to generate walking pattern for bipedal robots [32].

Detailed models

These models encompass a range of approaches, some of which primarily address musculoskeletal dynamics, while others additionally strive to integrate neural control. By doing so, they aim to offer a more comprehensive understanding of the intricate interactions between the nervous and musculoskeletal systems. Also, complex musculoskeletal models provide a detailed framework for exploring how the neuro-musculoskeletal system manifests the principles elucidated by conceptual models [4]. Accurate modeling of the musculoskeletal system is important in comprehending both pathological and healthy gait, as well as investigating the interplay between the musculoskeletal and neural systems [33]. Moreover, these models have potential in personalized clinical decision-making and the design of assistive technologies such as exoskeletons [11]. Simulation approaches using detailed models can be categorized into two main types: tracking simulation and predictive simulation.

Tracking simulation

Tracking simulations refer to a kind of simulation wherein the errors between simulated and experimental data are minimized or constrained. The objective of tracking simulations is to reproduce the observed behavior and to estimate muscle forces, activations, and contributions to joint motion.

- **Inverse dynamics:** Inverse dynamics calculate the generalized forces, such as net forces and torques, responsible for a specific motion. This approach utilizes experimental measurements of subject kinematics and external forces to estimate the acceleration of the body segments within the model by performing double differentiation of joint angles and positions. The estimated acceleration, combined with external forces like ground reaction forces, is then incorporated into the model's equations of motion to solve for the internal joint forces and moments necessary to produce the observed motion. The process entails formulating an optimization problem to decompose the net joint moments into individual muscle forces

at each time instant, commonly referred to as static optimization [34]. Static optimization assumes that the musculoskeletal system is in static equilibrium at the desired pose and simplifies the problem by ignoring the subsequent dynamics of the movement. Therefore, this method assumes stiff/rigid tendons and does not account for activation dynamics.

- **Quasi-static forward dynamics:** To incorporate activation dynamics, a common approach is to utilize dynamic optimization techniques to identify a combination of muscle excitations that best reproduces experimental data [35]. Computed muscle control (CMC) is an alternative approach that involves solving a series of static optimization problems to determine the muscle excitations required to follow a given kinematic trajectory. CMC also incorporates a proportional-derivative (PD) controller to refine muscle excitations in order to reduce tracking errors between experimental and predicted joint angles. CMC has demonstrated successful applications in various musculoskeletal models and movement tasks, including walking, running, and jumping [36–38]. Notably, this method also permits the inclusion of additional inputs, such as EMG and ultrasound data, as control signal for muscles or to estimate model parameters, like for musculotendons as part of the inverse problem [39, 40].

Predictive simulation

Predictive simulations refer to a kind of simulation which do not necessarily require experimental movement data as input.

- **Optimal control:** Predictive simulations often assume that the central nervous system can be centrally controlled to optimize performance by minimizing suitable functions, such as the metabolic cost of transport. Within this framework, predictive simulations can be formulated as optimal control problems [11]. This approach involves solving for muscle controls in an open-loop manner, commonly referred to as trajectory optimization. However, it is important to note that these approaches do not provide explicit descriptions of gait control policies and are thus inadequate for capturing how the neuro-musculoskeletal system handles uncertainties, such as sensorimotor noise and external perturbations [11, 33].
- **Reflex-based:** This approach involves the derivation of control policies that govern the relationship between muscle controls and the state of the musculoskeletal system, thereby encompassing feedback control. These control policies are established based

on the integration of principles originating from legged mechanics [4]. Approaches that aim to solve for gait control policies offer the ability to capture the robustness exhibited by the neuro-musculoskeletal system when confronted with various sources of noise and perturbations [41, 42].

- **Reinforcement learning:** Reinforcement learning (RL) emerges as an alternative approach to generate control strategies for forward dynamics simulations in an automated fashion. RL constitutes a machine learning technique employed to address decision-making problems by aiming to learn an optimal policy. This policy enables an agent to maximize its cumulative reward through interactions with the environment. In the context of learning human locomotion, the RL environment is represented by the musculoskeletal system and the physics-based simulation environment. The reward function employed in RL could address specific objectives such as achieving a target velocity with reduced muscle effort, among others [43]. Moreover, RL methods may incorporate learning from reference or imitation learning to ensure that the acquired optimal policy exhibits natural human-like behavior [44].
- **Central pattern generator:** Central pattern generator (CPG) utilizes oscillatory neural circuits to generate rhythmic and coordinated muscle activations, enabling tasks like walking, running, or other cyclic movements without continuous input from higher brain centers [45]. Also, feedback from somatic senses, such as joint angles and foot-ground contact signals, is then feedback to the neural system, which, in turn, regenerates the neural rhythm pattern based on this information. This theory posits that human locomotion arises from the cooperative interplay between neural rhythm and the dynamic rhythm of the body [46]. In [47] the idea of central pattern generator is combined by muscle synergy hypotheses to generate muscle excitations that can effectively reproduce both walking and running behaviors in a human musculoskeletal model.

Biomechanical models in developing assistive devices

Biomechanical models can play a significant role in the development of assistive devices by providing valuable insights and tools for design, optimization, and evaluation. For the scope of this review, we focused on exoskeletons that work in conjunction with the biological joints, excluding prosthetics and full body exoskeletons that support complete limb function.

Most of the publications were found using the following Google Scholar query: (“*gait model*” OR “*neuromuscular model*” OR “*musculoskeletal model*” OR *SLIP* OR “*inverted pendulum*” OR “*hill-type*”) AND (*ortho* OR *exos* OR “*wearable robot*” OR “*assistive device*” OR “*rehabilitation robot*” OR *assistance*) AND (*gait* OR *locomotion* OR *lower limb*) among the records published since January 2010 up to the end of June 2023. Articles published prior to 2010 were excluded to ensure the review covered recent advancements and current trends in the field. This cutoff was chosen based on the rapid development of modeling techniques in recent years, which has significantly influenced the conceptual and detailed models we discuss (see Fig. 1). First, we screened the references based on their titles, followed by abstracts, and finally, the full-text to determine their relevance to our review’s scope. Subsequently, we thoroughly read and categorized the selected articles into four application areas: (1) Design, (2) Control, (3) Assessment, and (4) Estimation (see Fig. 3).

Design

Given the high costs and time demands involved in human experiments, biomechanical modeling could serve as a valuable tool to design assistive devices and test ideas regarding assistance strategies. Also, during the design process and before prototyping an assistive device, it is crucial to predict the effects it may have on the users due to the close interaction between the human and the device.

In a recent study by Koelewijn et al. [49], virtual participants were used in a musculoskeletal simulation to replicate human gait adaptations and changes in energy expenditure observed during walking with an exoskeleton. This study demonstrated the potential of musculoskeletal simulation in accurately predicting the effects of assistance on gait and energy expenditure. Robertson et al. [50] utilized a predictive model of human neuro-mechanical adaptation to a passive elastic exoskeleton applied at the ankle joint to investigate the effects of exoskeleton stiffness on muscle-tendon mechanics and energetics. Similarly, Bianco et al. [51] conducted a study to examine the effects of ankle exoskeleton assistance on center of mass kinematics through predictive simulation, offering insights for designers aiming to enhance balance stabilization during walking. Another study by Han et al. [44] employed predictive simulation to assess the effects of an ankle exoskeleton on physical human-robot interaction (pHRI). In [52], the effects of different controller on the interaction force between human and exoskeleton are investigated. Predictive simulation is also used to study the performance of an assist-as-needed controller regarding the reductions in

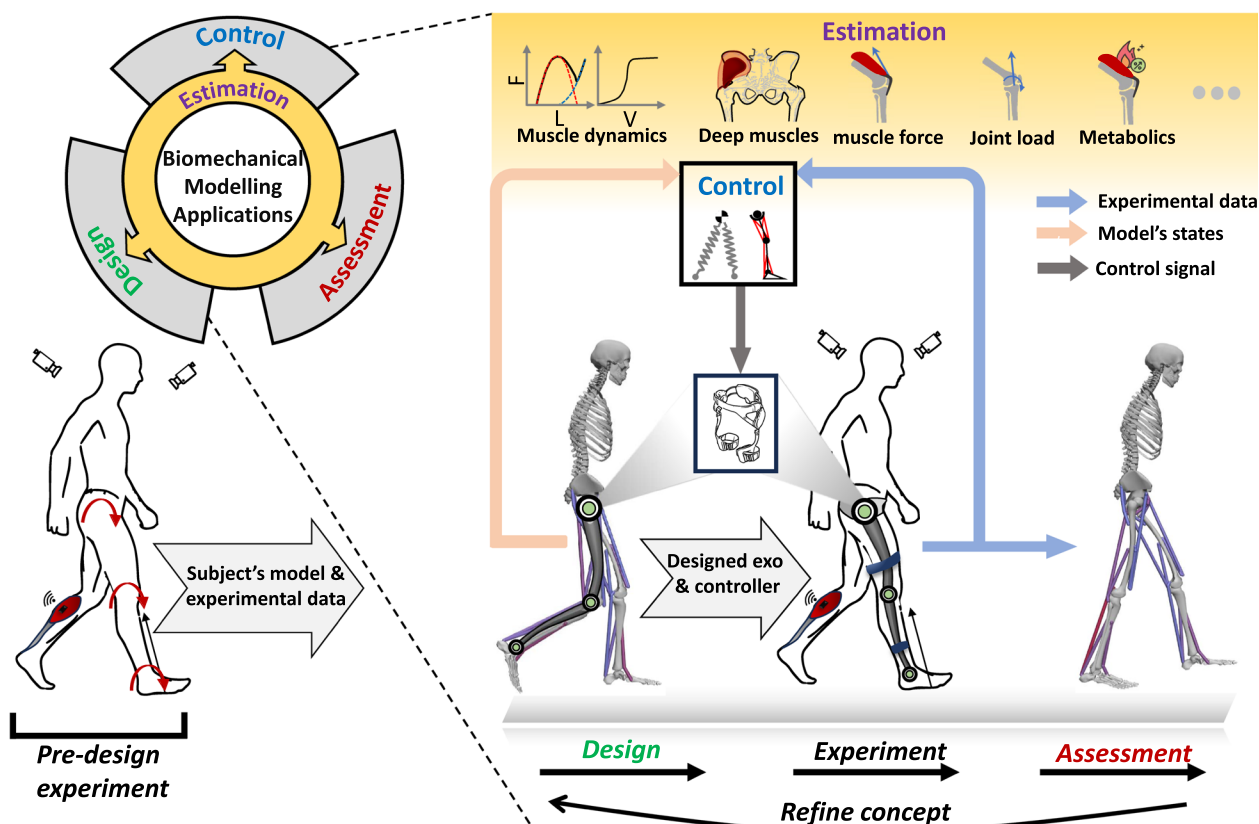


Fig. 3 Applications of biomechanical gait models in the development of lower-limb exoskeletons for design, control, assessment and estimation. Estimated variables (e.g., muscle activation, muscle dynamics, muscle force, joint load, metabolic cost, etc.) can be used in other mentioned applications. By leveraging biomechanical models, these applications contribute to the design and refinement of assistive devices that enhance gait in both impaired and unimpaired individuals. Predesign state refers to experimental data collection for model development and tracking simulation in the design process. We used OpenSim software to generate visualization for the musculoskeletal model [48]

the metabolic cost and muscles' activity [53]. In [54], a simulation study conducted to assess the effectiveness of impedance control applied to a lower limb exoskeleton in assisting disabled people during gait swing phase. In [55] the functionality of a passive load carrying exoskeleton tested in simulation environment. The simulation results show that the exoskeleton can reduce the foot pressure of the users, which validated through experiment. Some studies considered tracking simulation to predict the effects of an exoskeleton on metabolic cost and muscle activities [37, 56–58]. A tracking simulation of an unpowered ankle-foot exoskeleton shows the potential of the device to both reduce muscle forces and powers [59]. The simulation results in [60] demonstrate that a passive knee exoskeleton effectively reduces the exerted force on the extensor knee muscle and calf plantarflexion muscle during gait. These findings have been experimentally validated. Also, a tracking simulation was used in [61] to estimate the effects of a knee exoskeleton on knee contact force. This study shows a trade-off between interaction forces and

physiological torque, which should be considered when developing controllers for the knee exoskeleton.

One of the crucial steps in designing assistive devices is determining which joints to assist, a decision influenced by the specific application and user requirements. For instance, several studies used tracking simulation to study the effects of ideal assistance in different application and on different users. In Dembia et al. [37], an optimization approach was utilized to determine the optimal assistance for an ideal actuator supporting lower limb joints. They found that devices providing assistance for hip flexion, knee flexion, and hip abduction have greater potential regarding metabolic benefits compared to the ankle plantar flexion device during load carrying [37]. In a similar study, Liu et al. [62] developed an ideal actuator that delivered assistance torque proportional to the human joint torque during load carrying. Results of this study show that hip extension assistance has more advantage regarding metabolic reduction, especially on slope, which is in contrast with the results from [37] that shows the advantage of assisting hip flexion in load carrying.

This observation suggests that the optimal assistance could deviate from the biological joint torque. Uchida et al. [38] employed a similar approach as Dembia et al. [37] to investigate the effects of ideal assistance in each joint during running at different speeds. The results of their study suggested that for slow running, assisting more distal joints was advantageous, while for fast running, assisting more proximal joints was beneficial in terms of reducing metabolic costs. In [63] a walking assistance using optimized timed forces at the waist is investigated, inspiring from a conceptual model of human gait. Biomechanical models were also applied to design assistive device for pathological gaits. For example, musculoskeletal modeling of ideal assistance suggested that providing hip support to the elderly during walking could result in significantly greater metabolic benefits compared to ankle support [64]. Lim et al. [65, 66] employed a predictive simulation based on dynamic optimization to examine the potential advantages of hip exoskeletons in assisting gait with ankle pathology.

Moreover, biomechanical simulation can be used to guide exoskeleton structure and arrangement design. For instance, an estimation of muscle forces based on a tracking musculoskeletal simulation is employed to inform the design of cable paths in an exosuit [67]. In [68], a bionic muscle was designed by inspiration from Hill-type muscle model to assist the ankle and knee joints. Tracking simulation also employed in [69] to investigate the advantages of hybrid actuation in designing lower limb exoskeletons to reduce the metabolic cost of walking with heavy loads. Additionally, Rosenberg et al. [70] explored the potential impacts of powered and passive ankle-foot orthoses on muscle demand in children with cerebral palsy and crouched gait using a tracking musculoskeletal simulation. Nguyen et al. [71] utilized a fully predictive simulation based on reflex control to investigate the effects of unilateral and bilateral ankle assistance. Kim et al. [72] developed a mechanism for an exoskeleton specifically designed to assist running gait, leveraging the representation of running gait using a spring-loaded inverted pendulum model. Another design aspect related to the arrangement is single versus multi-joint interaction. For instance, Bianco et al. [73] demonstrated through musculoskeletal simulation that coupling degrees of freedom can yield similar metabolic benefits as independently controlled multi-joint devices. Their findings suggest that coupling degrees of freedom can simplify control while still maintaining metabolic advantages comparable to multi-joint devices. Also, a predictive simulation [74] shows that ankle-knee multi-joint assistance is more effective in reducing the metabolism of human walking on slope compared to the single-joint or other combination of two-joint assistance. In [75] a fully

predictive simulation is used to investigate the impact of single and multi-joint passive exoskeleton assistance on vertical jumping height.

Optimizing design parameters like mechanical elements properties and geometrical parameters of an assistive device allows for searching the best possible design that maximize the desired outcomes. Moreover, optimization enables designers to account for individual variability and user-specific customization of design. One approach is to try different combination of design parameters to find optimal design, which is time-consuming [76]. Another approach to tune design parameters of an assistive device is human-in-the-loop (HIL) optimization, which vary the design parameters systematically during the experiment to find optimal parameters [77]. For instance, in [77], a HIL optimization is used to personalize an ankle-foot prosthetic stiffness in order to reduce metabolic cost of walking. Biomechanical models can also provide such a framework for the designer by considering the assistive device in the simulation of user movements and analyzing biomechanical data to find optimal design parameters that maximize the device's effectiveness. Fang et al. [78] and Khamar et al. [79] proposed a general HIL optimization approach based on the MATLAB-OpenSim interface, which enables the optimization of geometry and material parameters for wearable robots. This framework was validated through the design of a knee exoskeleton for assisting flexion/extension movements [80]. In [81], a tracking musculoskeletal simulation was utilized to optimize the parameters of a serial elastic actuator. Similarly, Aftabi et al. [82] employed a tracking simulation study to investigate the effects of different hip exoskeleton spring stiffness on metabolic cost and fatigue during running gait. Ostrach et al. [83] investigated the effects of different knee exoskeleton stiffness on hopping height using predictive simulation. Guan et al. [84] investigated the effects of optimizing spring stiffness in a passive hip device on muscle activities for patients with spinal cord injury. In order to identify the most effective geometry for assistive devices, Marconi et al. [85] and Liu et al. [86] utilized musculoskeletal simulation to explore the effects of mass and mass distribution of the device. They showed the importance of device mass distribution on muscle activations. Another study employed musculoskeletal simulation to optimize the anchor point position of a cable-driven exosuit to reduce muscle activities [87]. Similarly, Guan et al. [84] investigated the effects of spring attachment point in a passive hip device on muscle activation for patients with spinal cord injury. The study conducted in [88] examined the impact of misalignment between the knee exoskeleton and the user's biological joint on knee muscles through simulation. The findings indicate that such misalignment can lead to an increase

in the force generated by the vastus lateralis muscle. Additionally, biomechanical models facilitate sensitivity analysis on the design and control parameters of assistive devices. By simulating the device's performance under various conditions and manipulating its design or control parameters, designers can identify the parameters with the most significant impact on performance and make informed decisions regarding optimization. For instance, Hegarty et al. [89] conducted a simulation study to quantify the effects of assumptions about mechanical properties (e.g., rotational stiffness, damping, and equilibrium angle) of ankle-foot orthoses (AFOs) on the estimation of lower-limb muscle forces during stance in children with cerebral palsy. Their findings revealed that AFO stiffness had the more substantial effect on muscle force compared to the damping and equilibrium angle.

Control

The use of biomechanical models to control assistive devices holds great potential for improving the performance and usability of these devices. By incorporating biomechanical models, assistive devices could offer more natural assistance to users by considering their movement dynamics. Here, we review the uses of biomechanical models in desired trajectories design and in adaptive model-based control (see Fig. 4).

Offline trajectory designing

One of the approaches in designing controller for exoskeletons is to use a predefined assistance profile [90]. A state-of-the-art approach to design assistance profile is to parameterize a general profile and optimize these control parameters in a HIL optimization [91–94]. Biomechanical simulation can be used to simulate the human musculoskeletal system and the exoskeleton in order to tune the control parameters. Ratnakumar et al. [95] utilized a musculoskeletal model with a reflex-based controller [4] in a predictive simulation to optimize a parameterized hip assistance torque profiles. The same approach employed in [74] to optimize control parameters of single-joint or multi-joint assistance during slope walking. Afschrift et al. [96] used the same model to tune control parameters for an assistive device aimed at improving balance. Experimental results of this study show reduced center of mass (CoM) deviations in perturbed walking while using CoM velocity feedback in the controller compared to the same controller without CoM feedback. Lim et al. [65] used dynamic optimization simulation to optimize control parameters to reduce energy expenditures in pathological gait with a hip exoskeleton.

Biomechanical simulation can also be used to identify the optimal assistance pattern or trajectory that aligns with the desired objectives without parameterizing the

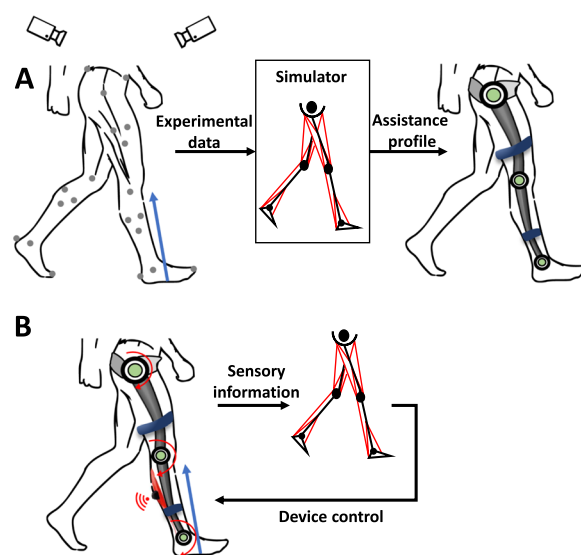


Fig. 4 Using biomechanical models to design a controller for assistive devices. **A** Offline design of the desired trajectory. **B** Adaptive model-based control

profile. Dembia et al. [37], Uchida et al. [38], and Bianco et al. [73] employed detailed neuromuscular models to determine the optimal assistance trajectory for an ideal actuator, aiming to minimize metabolic cost while assuming the gait kinematics and kinetics remain unchanged with assistance. Franks et al. [97] employed the same approach to identify optimal assistance trajectories and conducted experimental tests with three subjects wearing the assistive device. The results of their study demonstrated that an optimized profile for a hip-knee-ankle device can reduce metabolic cost during walking up to 26%, showing the potential of this method. Although this approach achieved notable reductions in metabolic cost, it fell short of the results obtained through HIL optimization using the same device, highlighting the need for further improvement. Another study by Lee et al. [98] investigated the reduction in metabolic cost during running gait with an exosuit by comparing a simulation-optimized actuation profile based on Uchida et al. [38] with a profile derived from scaled-biological hip moment data. The findings revealed a higher reduction in metabolic cost when employing the simulation-optimized actuation profile, emphasizing its effectiveness in designing assistance profiles for assisting running gait. In another approach, instead of optimizing the assistance profile directly, some studies have considered the use of estimated muscle force to design the assistance profile. For instance, Wang et al. [99] developed an assistance force profile for an ankle exosuit based on simulated soleus muscle force. In this approach, a tracking simulation

is utilized to estimate the force exerted by the soleus muscle. Subsequently, leveraging the simulated muscle dynamics, a scaled version of the force primarily generated by soleus muscle contraction is employed as the assistance profile.

Adaptive model-based control

In adaptive model-based control, a model is utilized within the control loop to generate assistance based on sensory feedback from the user. This section categorizes adaptive model-based control methods as follows:

- Reflex-based control: Here, controllers are derived from models of human locomotion that incorporate principles of legged mechanics. One prominent model is the gait model introduced by Geyer et al. [4], which is controlled by muscle reflexes and capable of producing different human gait patterns in a stable manner even in the presence of disturbance. An extended version of this model [100] has been successfully used to control leg prostheses, as demonstrated in Thatte et al. [101]. Researchers have also explored the applicability of this model's controller version in exoskeletons. Wu et al. [102] conducted a preliminary evaluation of this controller on a lower-limb knee and hip robotic gait trainer, showing improvements in gait for subjects with incomplete spinal cord injuries. In Tamburella et al. [103], an ankle exoskeleton is controlled based on the reflexes of the soleus and tibialis anterior muscles to assist individuals with incomplete spinal cord injuries. The same controller is employed in Dzeladini et al. [104] to assist healthy subjects. Shafer et al. [105] designed an ankle exoskeleton controlled by positive force feedback to assist healthy individuals during walking gait, investigating the effects of varying gain and delay in the reflex loop on metabolic cost. The idea of positive force feedback combined with an adaptive fuzzy interface to personalized assistance from an ankle exoskeleton [106]. The reflex model introduced by Geyer et al. [4] was further extended by incorporating a center of mass velocity reflex to the ankle joint, enhancing its ability to replicate human ankle torque responses to perturbations [107]. This extension was later utilized to design a controller for an ankle exoskeleton to improve balance [96]. The concept of assisting balance using reflex-based control was also explored in Yin et al. [108] by incorporating a center of mass position reflex into a virtual neuromuscular controller to improve standing balance.

Another group of reflex controllers is developed based on ground reaction force feedback, referred

to as force modulated compliance (FMC) control [17]. In this approach, a reflex mechanism based on ground reaction force is employed to adjust the stiffness in the assistive device, drawing inspiration from the observed virtual pivot point concept in human gait and conceptual models of human locomotion [18, 25]. Zhao et al. [109] implemented this method on a gait training exoskeleton to provide assistance at the hip joint. Also, in [110], ground reaction force was used to modulate the stiffness in both the hip and knee joints of a gait training exoskeleton. Sharbafi et al. [111] employed FMC to drive a biarticular assistive device mounted in parallel to the hamstring muscle in a predictive simulation study, assisting both the hip and knee during the stance phase. This controller was extended to drive biarticular actuators parallel to both the hamstring and rectus femoris muscles in the design of BATEX (biarticular thigh exosuit) in a tracking simulation study [57]. The FMC controller was also utilized in a tracking simulation to control the assistance level in an assistive device acting on hip abduction [112].

- EMG-based control: In this approach, the EMG signal from the subject is used as the control input to a musculoskeletal model, which then provides real-time estimates of biological joint torques. A portion of these estimated joint torques is utilized to dynamically control the generated torques. Durandau et al. [113] employed this method to assist the knee and ankle joints of patients with post-stroke and incomplete spinal cord injuries using a multifunctional robotic exoskeleton in real time. The study utilized measured EMG signals from eight muscles to compute neural activation for 12 muscle-tendon units in a subject-specific musculoskeletal model, enabling the estimation of knee and ankle joint moments. Fleischer et al. [114] designed and controlled an exoskeleton for knee joint support based on estimated knee torque using EMG signals from six muscles acting on the knee joint and a musculoskeletal model of the knee joint. The same approach was implemented to drive an ankle exoskeleton in Durandau et al. [115], providing assistance to a healthy subject and resulting in reduced muscle activities. A similar experiment was conducted in [116], demonstrating the ability of the proposed framework to provide real-time information about joint work and underlying muscle mechanics. The experiment conducted in [115] was extended to include multiple subjects and tested under various walking conditions and transitions, without the need for redoing the calibration step [117]. The results of this study indicated that the proposed controller enabled individuals to volun-

ily control a robotic exoskeleton across a continuous range of locomotion conditions while reducing muscle activation. In another study, Karavas et al. [118] developed a detailed subject-specific musculoskeletal model of the human knee to best match the user's kinematic and dynamic behavior, enabling the estimation of knee joint moments. The estimated torque in [118] was then used to control the impedance of an exoskeleton. In [119], a musculoskeletal model of the knee joint is used to control a rehabilitation device based on EMG signals. The objective of the study was to develop an adaptive control strategy for knee rehabilitation that can provide assistance or resistance as needed during different phases of therapy. In [120], the authors utilized an EMG-driven musculoskeletal model to estimate the voluntary torque of the ankle joint. This estimated torque was then incorporated into an assist/resist-as-needed controller, resulting in a higher human contribution ratio. Furthermore, [121] demonstrated that utilizing an EMG-driven musculoskeletal model in an assist/resist-as-needed controller enables more natural and human-like human-robot cooperation compared to linear proportional EMG control.

- **Artificial motor primitives-based control:** Motor primitives in the context of locomotion are the fundamental building blocks or elemental patterns of movement that combine to form complex locomotion patterns [122]. In this approach, motor primitives are utilized to generate stimulation signals for a musculoskeletal model [123]. These signals are then transformed into muscle-tendon forces, which are further converted into joint torques. A portion of these computed torques is employed as assistance. The controller in this method is adaptable to the subject's gait patterns, as it relies on the actual kinematics of the users to estimate muscle-tendon length. This approach has been successfully applied to control a hip flexion/extension exoskeleton [123–125].

Assistance assessment

The current experimental methods for investigating the cause-and-effect relationship of assistive devices in human gait still face limitations due to the invasiveness of some measurement techniques and the complex interaction between different systems. The utilization of biomechanical modeling can provide valuable support and a deeper understanding of the effects of assistive devices on human locomotion, ultimately enhancing device design. These models target the simulation of device and user behavior and facilitate the quantitative assessment of device performance with respect to e.g. energy efficiency, injury risk, and comfort. For

example, as high knee contact force during locomotion can lead to increased stress and knee damage, several studies employed musculoskeletal simulations to evaluate the effects of assistance on knee contact force [126]. In [127], a musculoskeletal simulation is used to study how the developed exoskeleton to assist stair climbing affects the knee contact force. Mclain et al. [126] demonstrated that a powered knee exoskeleton has the potential to reduce knee load by minimizing the required muscle work. In a study by Yamamoto et al. [128], musculoskeletal simulation was used to investigate the effect of changing the plantar flexion resistance of an ankle-foot orthosis on knee joint reaction and knee muscle forces. The peak knee joint reaction force in the early stance phase significantly increased in the strong plantar flexion resistance condition compared to no assistance, which may cause various knee problems such as knee pain and knee osteoarthritis.

Musculoskeletal simulation has also been utilized to explore the effects of assistance on muscle-tendon mechanics. In a study by Yap et al. [129], the impact of a knee brace on leg muscle forces was investigated through simulation and a significant difference was found in the muscle forces of the rectus femoris, gastrocnemius, soleus and tibialis anterior in assisted and not assisted conditions. Analyzing the effects of a passive ankle-foot orthosis on healthy gait using a musculoskeletal model shows that the device behaves more similarly to the soleus muscle and induces knee extension accelerations earlier in stance as the soleus typically exhibit [130]. In another study by Choi et al. [131], musculoskeletal simulation was used to analyze the effects of an ankle-foot orthosis with dorsiflexion resistance on Achilles tendon function during walking in healthy subjects. Musculoskeletal modeling also demonstrated that an ankle-foot orthosis can alter gastrocnemius operating length in post-stroke hemiplegic gait [132]. Musculoskeletal simulation was also utilized to analyze the effects of ankle exoskeletons in a hopping task, as demonstrated by Farris et al. [133, 134]. Furthermore, Jackson et al. utilized an EMG-driven musculoskeletal simulation in their study to explore how modifications in exoskeleton assistance influence plantarflexor muscle-tendon mechanics, thereby affecting metabolic cost [135]. In [136] a simulation study is employed to investigate how connecting the legs with a spring improves human running economy, as observed in experimental studies. Results of this study show that most of the savings occurred during stance phase and in muscles actuating more proximal muscles. In another study by Mo et al. [137], musculoskeletal simulation was employed to estimate the effects of an exoskeleton on the metabolic cost of post-stroke gait.

Estimation

Biomechanical models could also be employed for estimating variables that are challenging to measure directly or are inherently unmeasurable in the context of assistive devices. These models offer valuable insights into various factors such as muscle forces, joint loads, joint moments, contact forces, and metabolic costs. This information can be utilized in the design, control or evaluation process of assistive devices. For instance, muscle models are employed to translate muscle activation into muscle force and joint torques [99, 117, 138, 139]. By incorporating EMG data, neuromusculoskeletal models have demonstrated robustness in estimating knee joint moments over an extended period in a multi-day experiment [140]. In another study [141], a combination of neuromusculoskeletal models with EMG signals and data-driven predictions of ground reaction forces and center of pressure was utilized to enhance joint torque estimation. Musculoskeletal simulations have been employed in [142] to compute muscle force and state estimates. These predictions can approximate the human cost function for optimization. For example, by estimating the metabolic cost using a musculoskeletal model, control parameters of a hip exoskeleton were optimized in the HIL optimization experiment [143]. Further applications of musculoskeletal modeling, e.g., in investigating joint loading, were summarized in a systematic review by Holder et al. [144].

Discussion and future perspectives

Biomechanical gait models, ranging from conceptual models to more detailed models, hold significant potential in the advancement of assistive devices like lower limb exoskeletons. The utilization of biomechanical models enables researchers and engineers to gain deeper insights into the dynamics and control architecture of human movement, as well as the intricate interactions among muscles, bones, and tendons generating locomotion. This knowledge serves as a valuable foundation for designing novel or improved assistive devices that are safe, effective, and comfortable for users [103, 108].

Our review showed that biomechanical models have various applications in the design and development of exoskeletons: (1) Exo Design: Biomechanical models could guide exoskeleton design by identifying optimal joints for assistance, informing structural arrangements, optimizing mechanical properties and geometries, and allowing pre-prototyping evaluation through predictive capabilities. (2) Control: Biomechanical models could help to find the best assistance profiles for different applications and users using tracking or predictive simulations. They could optimize control parameters for specific control rules, and facilitating effective human-machine interaction through the incorporation

of biomechanical models within the human-device loop [145]. (3) Assessment: Neuromuscular models derived from biomechanical modeling can be leveraged to evaluate the effects of assistive devices and establish cause-and-effect relationships between the device and the user. These models provide valuable information regarding the device's effectiveness, efficiency, and potential areas that may require improvement. (4) State Estimation: Biomechanical models serve as a platform for estimating unmeasurable or hard-to-measure variables.

In the following, we discuss relevant areas which appear little researched yet as well as future perspectives on using biomechanical models in the exoskeleton field.

Validation

Simulation models are simplifications of real-world systems and behaviors. The validation of a simulation model provides a high level of confidence in its suitability for a specific intended purpose [146]. This encompasses both qualitative and quantitative behavior. Validation ensures the reliability and accuracy of the simulation-based predictions. A few studies that have validated simulation results have demonstrated the significant potential of designing assistive devices and controllers using biomechanical models. For instance, a simulation-optimized assistance profile for assisting the hip joint during running yielded greater metabolic benefits compared to a generic assistance profile [98]. Similarly, the application of a simulation-optimized assistance profile on a hip-knee-ankle exoskeleton during walking resulted in a reduction in metabolic cost [97]. These validation studies highlight the potential of biomechanical simulation in predicting the response to assistance, as demonstrated in the use of an ankle-foot orthosis in a healthy subject [147]. Although some experimental studies have not directly compared their results with simulation studies, they have demonstrated satisfactory agreement. For example, an experimental study investigating multi-joint assistance revealed that assisting the hip, knee, and ankle simultaneously could lead to the largest metabolic reductions, while the combination of hip-ankle, knee-ankle, and hip-knee assistance resulted in progressively lesser metabolic benefits [148]. These experimental findings align with the results obtained from simulation studies [73]. Integrating a musculoskeletal model within the control loop has also shown promising results, including reduced muscle activity and the ability to adapt to various conditions [117].

While the optimization and control of assistive devices using musculoskeletal models hold theoretical promise, there is a lack of rigorous experimental validation for the design and control of assistive devices. For instance, the advantages of assisting hip abduction in load-carrying

tasks shown in simulations [37, 112], have never been validated with human experiments, as seen in Fig. 5. This figure indicates a discrepancy between the number of studies focusing solely on simulation versus those incorporating experimental validation. A significant proportion of studies on devices assisting proximal joints (e.g., hip) rely solely on simulation (blue curve). Studies that solely consider experiments often involve the integration of biomechanical models within the control loop. The number of experimental studies is dominant in more distal joints, such as the ankle joint. This observation might be attributed to the relative ease of using biological signals like EMG for more distal joints compared to proximal joints [117, 149].

To improve gait assistance with the help of musculoskeletal modeling, further validation research is required. The required validation studies depend on the type of assistive device, the target user population, and the intended use case. Nevertheless, functionality validation by comparing the experimental outcomes with the simulation predictions (e.g. using emulators [93]) is advantageous. Also, comparing the simulation results with existing experimental results from existing state-of-the-art devices can be considered while validating simulation-based designed assistive device or controllers. For instance, in [150], the simulation result of finding optimal assistance patterns is validated based on the existing

state-of-the-art human-in-the-loop optimization results [91]. Further, performing sensitivity analysis on the simulation model and parameters enhances result reliability and design validity. The use of different simulation tools and models of varying complexity also increases confidence in the consistency of the design.

Improving models

Improving the fidelity of models is vital for the development of more practical assistive devices. Between the conceptual and detailed neuro-musculoskeletal models, the second group is utilized more for the design and control of assistive devices. These models consist of two main components: the musculoskeletal design and the neural control. The inclusion of personalization in the musculoskeletal modeling could enhance the model functionality in assistance enhancement and facilitate understanding of inter-subject variations in gait patterns [151]. Strategies such as extracting bony geometries and joint centers from magnetic resonance imaging scans [152], personalizing musculotendon parameters based on electromyography (EMG) or ultrasound data [39, 40], and customizing the location of muscle attachments [153] could improve a model's accuracy. Another approach is to involve more biomechanical details of the body in the models. For instance, modeling the foot as a two-segment instead of a single-segment system has a negligible effect on knee torque estimation in inverse simulations while significantly impacting knee torque in predictive simulations [11]. The inclusion of more accurate dynamical models of the muscles can also improve the accuracy of simulation results [154]. Furthermore, integrating the viscoelastic behavior of soft biological tissue into digital human models holds promise for improving the design of wearable assistive devices, thereby increasing their efficiency and efficacy [155].

The next level which could make the neuromuscular models closer to the biological body is the inclusion of neural control. One common approach to modeling neural control and resolving the muscle redundancy problem is to optimize a performance criterion that represents the high-level goal of the motor task. Personalizing this optimization criterion can lead to improved simulation results. A potential solution for personalizing the optimization objective involves determining a weighted cost function from a family of possible cost functions, representing an inverse optimal control problem that can be addressed using a bilevel optimization approach [156]. In this approach, the lower level involves optimizing the targeted movement by minimizing the cost function subject to the dynamic equations of the musculoskeletal model. The upper level adjusts the weights for each cost function to

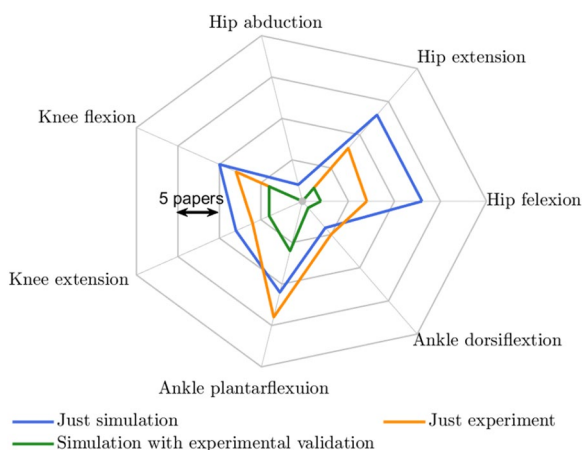


Fig. 5 The number of reviewed papers that designed exoskeletons and/or controllers based on biomechanical models. Just simulation means the designed exoskeletons and controllers are tested in simulation without experimental validation. The green curve shows papers that designed an exoskeleton and/or controller in simulation and validated it in an experiment. The orange curve shows papers that used biomechanical models in a control loop without testing it in a simulation environment. The total curve shows the total number of papers which considered designing a controller based on biomechanical models for a specific degree of freedom. Each level in this graph represents five papers

minimize the discrepancy between the lower-level solution and experimental data [156–159]. Optimization-based neural control offers mathematical solutions that optimize performance according to predefined criteria without providing acceptable insights into the underlying neural control. However, when studying neurological disorders affecting gait performance, it is imperative to investigate the neural control structures involved in generating muscle activations [11]. Despite considerable efforts to uncover the underlying neural circuits and pathways associated with movement control [4, 41, 160], the complexity of developed control models still falls short of that observed in human motor control. In this context, translating findings from conceptual models into neural control [18, 161, 162], exploring novel ideas about neural control through perturbation studies [42, 107, 163], or developing mathematical models based on clinical definitions of neurological symptoms [11, 164] can improve simulation models' prediction ability. Moreover, based on a simulation study, it is proposed that the integration of optimization and reflex excitation leads to improved predictions of experimentally optimized assistive torque profiles using human-in-the-loop optimization [150]. Additionally, considering uncertainty during gait simulation can make the models more realistic. For instance, the co-contraction of antagonistic muscle pairs, often observed in human movement and deemed inefficient in deterministic simulations, appears to minimize effort in systems with uncertainty [165].

When considering simulations of human movement augmented by assistive devices, incorporating a more precise model of the device can substantially enhance the predictive capabilities of the models. Research by Nguyen et al. [166] demonstrates that the electrical dynamics of the motor could critically influence simulation outcomes. Additionally, incorporating the dynamics of physical interactions, such as the viscoelastic properties of soft biological tissues, into biomechanical gait models is essential for accurately predicting exoskeleton performance. Neglecting these interaction dynamics can significantly degrade exoskeleton efficacy estimates and interpretations, as demonstrated by Yandell et al. [167]. Therefore, future research should prioritize integrating these dynamics into biomechanical models to minimize the sim-to-real gap and improve the design and control of assistive devices [155, 167]. Calibrating contact models can lead to a more accurate estimation of interaction forces between humans and exoskeletons, which is essential for assessing user comfort and the effectiveness of the interaction [168]. Additionally, it is worth noting that perfect alignment between the exoskeleton model and human joint axes is assumed in exoskeleton simulations.

However, in practical exoskeleton usage, misalignment between human and exoskeleton joints is often observed, resulting in unrealistic simulation outcomes [169].

In summary, further research on modeling to be used for movement assistance applications could be done in different directions: (1) More detailed modeling: involvement of more intricate musculoskeletal simulations, (2) neural control: exploring new models to approach human neural control, (3) personalization: adaptation of the model parameters based on individual bodies and motor control, (4) cost function identification: exploring new approaches (e.g., multi-objective optimization or inverse optimal control) to identify biological cost function to optimize the models, (5) Stochastic modeling: Including uncertainty and noise in the models, (6) template modeling exploration: Extension of conceptual models and their combination with detailed models. These different research lines could help improve understanding of human motor control, realize more realistic predictions of human-exo interaction, and yield more synergistic cooperation of man and machine.

Model-based design and control of assistive devices for pathological gait

One of the primary motivations behind developing exoskeletons was to assist impaired individuals and enhance their mobility, aiming to improve their quality of life [170]. A systematic study assessing the use of exoskeletons in individuals with multiple sclerosis demonstrated that exoskeletons could preserve gait speed, significantly enhance functional mobility, and mitigate perceived fatigue [170]. Similarly, powered lower limb exoskeletons have been investigated as a novel form of robotic therapy to target motor impairments in individuals with cerebral palsy and enhance their gait training [171]. Despite the growing body of evidence supporting the effectiveness of model-based designed assistive devices and controllers, our review shows a prevalent focus on studies involving healthy subjects, as shown in Fig. 6. This figure shows that using biomechanical models to inform design of lower limb exoskeletons for pathological gait have received less attention compared to the whole category of lower limb exoskeletons to assist pathological gait (the user groups identified through scanning two review paper on lower limb exoskeletons [172, 173]). Simulation studies have demonstrated promising results in modeling pathological gait [27, 33, 174]. Investigations on the modeling of pathological gaits and model-based design and control of assistive devices could highly enhance the quality of assisting patient locomotion.

Moreover, studies that do consider model-based design for pathological gait sometimes rely on validation through testing on healthy subjects [175]. However,

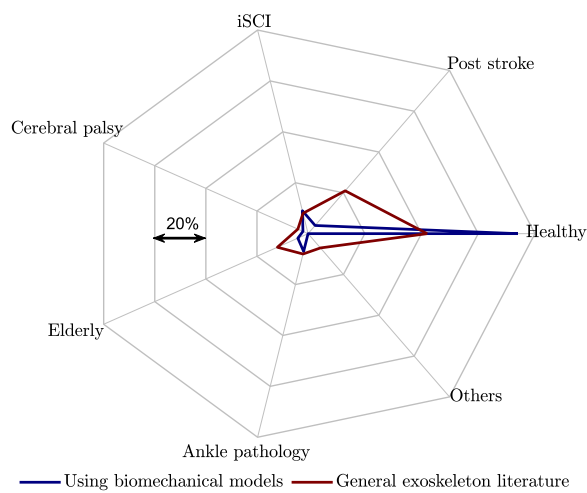


Fig. 6 Distribution of user groups in lower limb exoskeleton research: biomechanical model-based design reviewed in this article (blue) vs. general exoskeleton literature review from [172, 173] (red). “Others” include multiple sclerosis, poliomyelitis, spinocerebellar degeneration patients and research papers that are not specifically categorized under the aforementioned user groups

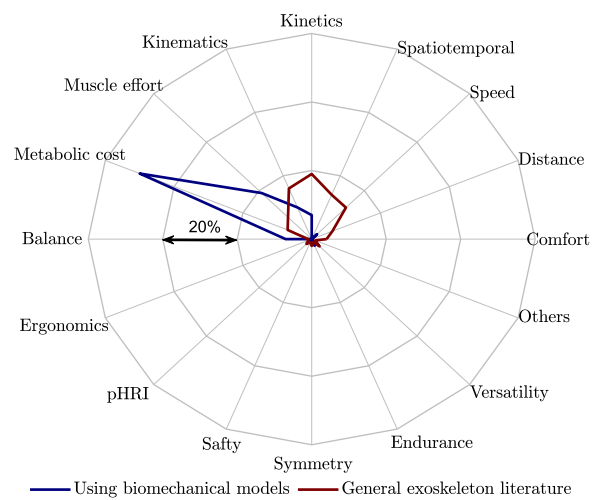


Fig. 7 Distribution of design criteria in lower limb exoskeleton research. Biomechanical model-based design reviewed in this article (blue) vs. general exoskeleton literature review from [172, 173] (red). “Others” include cognitive effort, dependability and coordination

experimental findings indicate that improving gait in healthy individuals using designed devices or controllers does not guarantee the same effectiveness in assisting pathological gait. For instance, increasing ankle push-off work with a powered prosthesis has been shown to reduce metabolic rate in non-amputees [176], but this does not necessarily translate to metabolic rate reduction in transtibial amputees [177].

Design objectives of assistive devices

Lower-limb assistive devices serve the purpose of providing support, compensating for impairments, or assisting individuals in various tasks and activities. This study indicates that a majority (69%) of the papers that utilize biomechanical models to design and control lower-limb assistive devices prioritize the objective of reducing metabolic cost and muscle effort. However, a comprehensive review study on the performance indicators of lower limb exoskeletons indicates a predominant focus on improving kinetics, kinematics, spatiotemporal parameters, and speed as the design objectives for general lower-limb exoskeletons, with only 16% of papers considering the reduction of metabolic cost and muscle effort as a primary goal [173]. One possible explanation for this observation is that most model-based designs and controllers are developed and tested on healthy users (refer to “[Model-based design and control of assistive devices for pathological gait](#)” section). For this particular user group, the prioritization of reducing metabolic cost and muscle effort may be more relevant. However, different design objectives

may take precedence when addressing pathological gait. Predictive simulation holds promise in uncovering the physiological factors contributing to altered gait, thereby aiding in the design of assistive devices for target groups with movement difficulties. Moreover, it allows for the investigation of the effects of assistive devices on gait improvement beyond the scope of reducing metabolic cost and muscle effort, thus incorporates other important design objectives [44, 174, 178].

To improve user acceptance of assistive systems, considering subjective criteria is required, which received less attention in exoskeleton studies (see Fig. 7). In [179], user demands are considered in lower limb prosthetic design to improve user acceptance, which is transferable to the exoskeletons and can be considered in simulation studies. The parallel development of biomechanical models and the consideration of individual differences in body perception and psychological states can provide valuable insights into the interactions between the human body and robotic devices. This can lead to an improved realization of the seamless integration of the assistive device into the human body schema.

Open-source data, model and software

Open-source data, models, and software have emerged as valuable tools for accelerating the development of assistive devices, facilitating the design process, and fostering collaborative efforts. An exemplary illustration of such open-source software is OpenSim, a freely available software enabling users to construct musculoskeletal models and conduct dynamic simulations encompassing a diverse range of movements [180]. By leveraging

open-source models, researchers can circumvent the time-consuming and costly process of developing models from scratch. Furthermore, the presence of extensive online communities facilitates collaboration, knowledge sharing, and troubleshooting. In addition to enhancing collaboration and reducing costs, the utilization of open-source data, models, and software contributes to transparency and reproducibility within research endeavors.

The availability of open-source models and software packages has witnessed significant growth in recent years, exhibiting great potential for advancing the design and control of assistive devices [48, 181–184]. However, the scarcity of accessible datasets for developing and testing exoskeletons poses a challenge for researchers and developers seeking to create and enhance exoskeleton designs. This limitation hinders researchers' ability to reproduce and build upon previous work. Notably, specific universities and research institutions have initiated the generation and sharing of their datasets, thereby making significant contributions to the progress of exoskeleton technology [185]. Additionally, some of these institutions are openly sharing their computer-aided design (CAD) and hardware specifications, facilitating experiment replication and fostering improvements in exoskeleton models through simulation [186].

Another promising approach is to use biomechanical models to generate datasets. For example, musculoskeletal models can produce synthetic data for data-driven methods, particularly in wearable technology. This synthetic data provides a valuable resource for training machine learning algorithms, allowing them to learn patterns and relationships within human movement without the need for extensive real-world data collection [187]. Additionally, musculoskeletal simulations can create highly controlled and varied scenarios—such as specific joint movements—that are challenging to replicate in real-life experiments.

Role of assistive devices in the biomechanical models development

This paper highlights the immense potential of biomechanical models, ranging from conceptual models to detailed models, in advancing the development of exoskeletons. However, the utilization of assistive devices such as exoskeletons to enhance the predictive capabilities and accuracy of biomechanical models has received limited attention thus far. To improve biomechanical models, it is crucial to gain a deeper understanding of the characteristics and behavior of the human body. Perturbation study can serve as a valuable tool in this regard. Exoskeletons can be employed as perturbation devices to reshape human locomotion and investigate the resulting responses. For instance, in [188], a robotic exoskeleton was employed to

shift people's energetically optimal step frequency to frequencies higher and lower than normally preferred, with the aim of exploring whether individuals could optimize their energetic costs in real-time. Also, the same device is used in [189] to study how humans initiate energy optimization and converge on their optimal gaits. Findings indicate that, following a perturbation from their preferred gait, most participants tend to exploit their original gait, which is suboptimal now, rather than exploring the new energetic landscape. However, once providing them with the experience of lower-cost gaits, the nervous system can learn to predict this new optimal gait and rapidly return to it if perturbed away. In the works of Ahn et al. [190] and Baye et al. [191], exoskeletons were used to apply periodic mechanical perturbations during walking. These studies can advance our understanding of the control architecture governing human locomotion by exploring how participants adapt themselves to this perturbation. Furthermore, exoskeletons have been employed to identify subject-specific muscle parameters within a model, as demonstrated in [192, 193].

Using exoskeletons as perturbation tools, researchers can gain valuable insights into the characteristics and behavior of the human body, refine biomechanical models, and ultimately drive the development of exoskeleton technology.

Author contributions

V.F. conceptualization, methodology, writing—original draft, writing - review & editing, visualization. A.S. writing—review & editing, supervision, funding acquisition. S.S. writing—review & editing, supervision. O.V.S. writing—review & editing, supervision, funding acquisition. M.A.S. writing—review & editing, supervision, funding acquisition.

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Declarations

Ethics approval and consent to participate

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Consent for publication

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References

1. Siviy C, Baker LM, Quinlivan BT, Porciuncula F, Swaminathan K, Awad LN, Walsh CJ. Opportunities and challenges in the development of exoskeletons for locomotor assistance. *Nat Biomed Eng.* 2022;7:1–17.
2. Grabke EP, Masani K, Andrysek J. Lower limb assistive device design optimization using musculoskeletal modeling: a review. *J Med Devices.* 2019;13(4): 040801.
3. Full RJ, Koditschek DE. Templates and anchors: neuromechanical hypotheses of legged locomotion on land. *J Exp Biol.* 1999;202(23):3325–32.
4. Geyer H, Herr H. A muscle-reflex model that encodes principles of legged mechanics produces human walking dynamics and muscle activities. *IEEE Trans Neural Syst Rehabil Eng.* 2010;18:263–73.
5. Baud R, Manzoori AR, Ijspeert A, Bouri M. Review of control strategies for lower-limb exoskeletons to assist gait. *J NeuroEng Rehabil.* 2021;18(1):1–34.
6. Sylvester AD, Lautzenheiser SG, Kramer PA. A review of musculoskeletal modelling of human locomotion. *Interface Focus.* 2021;11(5):20200060.
7. Smith SH, Coppack RJ, van den Bogert AJ, Bennett AN, Bull AM. Review of musculoskeletal modelling in a clinical setting: current use in rehabilitation design, surgical decision making and healthcare interventions. *Clin Biomech.* 2021;83: 105292.
8. Luis I, Afschrift M, De Groot F, Gutierrez-Farewik EM. Evaluation of musculoskeletal models, scaling methods, and performance criteria for estimating muscle excitations and fiber lengths across walking speeds. *Front Bioeng Biotechnol.* 2022;10:1002731.
9. Febrer-Nafria M, Nasr A, Ezati M, Brown P, Font-Llagunes JM, McPhee J. Predictive multibody dynamic simulation of human neuromusculoskeletal systems: a review. *Multibody Syst Dyn.* 2022;58:1–41.
10. Sartori M, Llyod DG, Farina D. Neural data-driven musculoskeletal modeling for personalized neurorehabilitation technologies. *IEEE Trans Biomed Eng.* 2016;63(5):879–93.
11. De Groot F, Falisse A. Perspective on musculoskeletal modelling and predictive simulations of human movement to assess the neuromechanics of gait. *Proc R Soc B.* 2021;288(1946):20202432.
12. Grant MJ, Booth A. A typology of reviews: an analysis of 14 review types and associated methodologies. *Health Inf Libr J.* 2009;26(2):91–108.
13. Geyer H, Seyfarth A, Blickhan R. Compliant leg behaviour explains basic dynamics of walking and running. *Proc R Soc B Biol Sci.* 2006;273(1603):2861–7.
14. Donelan JM, Kram R, Kuo AD. Mechanical work for step-to-step transitions is a major determinant of the metabolic cost of human walking. *J Exp Biol.* 2002;205(23):3717–27.
15. Rajagopal A, Dembia CL, DeMers MS, Delp DD, Hicks JL, Delp SL. Full-body musculoskeletal model for muscle-driven simulation of human gait. *IEEE Trans Biomed Eng.* 2016;63(10):2068–79.
16. Sharbafi MA, Seyfarth A. Bioinspired legged locomotion: models, concepts, control and applications. Butterworth-Heinemann; 2017.
17. Sharbafi MA, Seyfarth A. Fmch: a new model for human-like postural control in walking. In: 2015 IEEE/RSJ international conference on intelligent robots and systems (IROS). IEEE; 2015. p. 5742–7.
18. Firouzi V, Bahrami F, Sharbafi MA. Human balance control in 3d running based on virtual pivot point concept. *J Exp Biol.* 2022;225(4):jeb243080.
19. Geyer H, Seyfarth A, Blickhan R. Positive force feedback in bouncing gaits? *Proc R Soc Lond Ser B Biol Sci.* 2003;270(1529):2173–83.
20. Seipel J, Kvalheim M, Revzen S, Sharbafi MA, Seyfarth A. Conceptual models of legged locomotion. In: Bioinspired legged locomotion. Elsevier; 2017. p. 55–131.
21. Blickhan R. The spring-mass model for running and hopping. *J Biomech.* 1989;22(11–12):1217–27.
22. Poulakakis I, Grizzle JW. The spring loaded inverted pendulum as the hybrid zero dynamics of an asymmetric hopper. *IEEE Trans Autom Control.* 2009;54(8):1779–93.
23. Saranlı U, Arslan Ö, Ankaralı MM, Morgül Ö. Approximate analytic solutions to non-symmetric stance trajectories of the passive spring-loaded inverted pendulum with damping. *Nonlinear Dyn.* 2010;62:729–42.
24. Sharbafi MA, Seyfarth A. Stable running by leg force-modulated hip stiffness. In: 5th IEEE RAS/EMBS international conference on biomedical robotics and biomechatronics. IEEE; 2014. p. 204–10.
25. Maus H-M, Lipfert S, Gross M, Rummel J, Seyfarth A. Upright human gait did not provide a major mechanical challenge for our ancestors. *Nat Commun.* 2010;1(1):70.
26. Liu W, Nigg BM. A mechanical model to determine the influence of masses and mass distribution on the impact force during running. *J Biomech.* 2000;33(2):219–24.
27. Sharbafi MA, Zadavec M, Matjačić Z, Seyfarth A. A 3d template model for healthy and impaired walking. In: 2018 IEEE/RSJ international conference on intelligent robots and systems (IROS). IEEE; 2018. p. 1218–25.
28. Winter DA. Human balance and posture control during standing and walking. *Gait Posture.* 1995;3(4):193–214.
29. Maxwell Donelan J, Kram R, Arthur D K. Mechanical and metabolic determinants of the preferred step width in human walking. *Proc R Soc Lond Ser B Biol Sci.* 2001;268(1480):1985–92.
30. Faraji S, Wu AR, Ijspeert AJ. A simple model of mechanical effects to estimate metabolic cost of human walking. *Sci Rep.* 2018;8(1):10998.
31. Bauby CE, Kuo AD. Active control of lateral balance in human walking. *J Biomech.* 2000;33(11):1433–40.
32. Kajita S, Kanehiro F, Kaneko K, Yokoi K, Hirukawa H. The 3d linear inverted pendulum mode: a simple modeling for a biped walking pattern generation. In: Proceedings 2001 IEEE/RSJ international conference on intelligent robots and systems. Expanding the societal role of robotics in the next millennium (Cat. No. 01CH37180), vol. 1. IEEE; 2001. p. 239–46.
33. Falisse A, Serrancolí G, Dembia CL, Gillis J, Jonkers I, Groote FD. Rapid predictive simulations with complex musculoskeletal models suggest that diverse healthy and pathological human gaits can emerge from similar control strategies. *J R Soc Interface.* 2019;16:8.
34. Heintz S, Gutierrez-Farewik EM. Static optimization of muscle forces during gait in comparison to EMG-to-force processing approach. *Gait Posture.* 2007;26(2):279–88.
35. Kaplan ML, Heegaard JH. Predictive algorithms for neuromuscular control of human locomotion. *J Biomech.* 2001;34(8):1077–83.
36. Thelen DG, Anderson FC, Delp SL. Generating dynamic simulations of movement using computed muscle control. *J Biomech.* 2003;36(3):321–8.
37. Dembia CL, Silder A, Uchida TK, Hicks JL, Delp SL. Simulating ideal assistive devices to reduce the metabolic cost of walking with heavy loads. *PLoS ONE.* 2017;12:7.
38. Uchida TK, Seth A, Pouya S, Dembia CL, Hicks JL, Delp SL. Simulating ideal assistive devices to reduce the metabolic cost of running. *PLoS ONE.* 2016;11:9.
39. Delabastita T, Afschrift M, Vanwaseele B, De Groot F. Ultrasound-based optimal parameter estimation improves assessment of calf muscle-tendon interaction during walking. *Ann Biomed Eng.* 2020;48:722–33.
40. Falisse A, Van Rossom S, Jonkers I, De Groot F. Emg-driven optimal estimation of subject-specific hill model muscle-tendon parameters of the knee joint actuators. *IEEE Trans Biomed Eng.* 2016;64(9):2253–62.
41. Song S, Geyer H. A neural circuitry that emphasizes spinal feedback generates diverse behaviours of human locomotion. *J Physiol.* 2015;593(16):3493–511.
42. Song S, Geyer H. Evaluation of a neuromechanical walking control model using disturbance experiments. *Front Comput Neurosci.* 2017;11:15.
43. Song S, Kidziński Ł, Peng XB, Ong C, Hicks J, Levine S, Atkeson CG, Delp SL. Deep reinforcement learning for modeling human locomotion control in neuromechanical simulation. *J Neuroeng Rehabil.* 2021;18(1):1–17.
44. Han JI, Lee J-H, Choi HS, Kim J-H, Choi J. Policy design for an ankle-foot orthosis using simulated physical human-robot interaction via deep reinforcement learning. *IEEE Trans Neural Syst Rehabil Eng.* 2022;30:2186–97.
45. Ijspeert AJ. Central pattern generators for locomotion control in animals and robots: a review. *Neural Netw.* 2008;21(4):642–53.
46. Hase K, Miyashita K, Ok S, Arakawa Y. Human gait simulation with a neuromusculoskeletal model and evolutionary computation. *J Vis Comput Animat.* 2003;14(2):73–92.
47. Aoi S, Ohashi T, Bamba R, Fujiki S, Tamura D, Funato T, Senda K, Ivanenko Y, Tsuchiya K. Neuromusculoskeletal model that walks and runs across

a speed range with a few motor control parameter changes based on the muscle synergy hypothesis. *Sci Rep.* 2019;9:12.

48. Seth A, Hicks JL, Uchida TK, Habib A, Dembia CL, Dunne JJ, Ong CF, DeMers MS, Rajagopal A, Millard M, et al. Opensim: simulating musculoskeletal dynamics and neuromuscular control to study human and animal movement. *PLoS Comput Biol.* 2018;14(7): e1006223.
49. Koelwijn AD, Selinger JC. Predictive simulations to replicate human gait adaptations and energetics with exoskeletons. *IEEE Trans Neural Syst Rehabil Eng.* 2022;30:1931–40.
50. Robertson BD, Farris DJ, Sawicki GS. More is not always better: modeling the effects of elastic exoskeleton compliance on underlying ankle muscle-tendon dynamics. *Bioinspir Biomimetics.* 2014;9(4): 046018.
51. Bianco NA, Collins SH, Liu K, Delp SL. Simulating the effect of ankle plantarflexion and inversion-eversion exoskeleton torques on center of mass kinematics during walking. *bioRxiv; 2022.* 2022–11.
52. Hosseini-Zahraei S, Tali MS, Saberi MH, Kardan I, Akbarzadeh A. A simple opensim-simulink interface for cascaded zero-force control of human-robot interaction in a hip exoskeleton robot. In: 2022 10th RSI international conference on robotics and mechatronics (ICRoM). IEEE; 2022. p. 55–60.
53. Naghavi N, Akbarzadeh A, Khaniki O, Kardan I, Moradi A. Assist-as-needed control of a hip exoskeleton, using central pattern generators in a stride management strategy. *J Intell Robot Syst.* 2023;107(4):53.
54. Mosconi D, Siqueira AA. Simulation of impedance control applied to lower limb exoskeletons: assessment of its effectiveness in assisting disabled people during gait swing phase. In: 43rd annual international conference of the IEEE engineering in medicine & biology society (EMBC). IEEE. 2021; 2021. p. 4694–9.
55. Zhou Z, Chen W, Fu H, Fang X, Xiong C. Design and experimental evaluation of a non-anthropomorphic passive load-carrying exoskeleton. In: 2021 6th IEEE international conference on advanced robotics and mechatronics (ICARM). IEEE; 2021. p. 251–6.
56. Crabtree CA, Higginson JS. Modeling neuromuscular effects of ankle foot orthoses (AFOS) in computer simulations of gait. *Gait Posture.* 2009;29(1):65–70.
57. Firouzi V, Davoodi A, Bahrami F, Sharbafi MA. From a biological template model to gait assistance with an exosuit. *Bioinspir Biomimetics.* 2021;16(6): 066024.
58. Wu Y, Zhu A, Shen H, Shen Z, Zhang X, Cao G. Biomechanical simulation analysis of human lower limbs assisted by exoskeleton. In: 2019 16th International Conference on Ubiquitous Robots (UR). IEEE; 2019. p. 765–70.
59. Liu L, Wei W, Zheng K, Diao Y, Wang Z, Li G, Zhao G. Design of an unpowered ankle-foot exoskeleton used for walking assistance. In: 43rd annual international conference of the IEEE engineering in medicine & biology society (EMBC). IEEE. 2021; 2021. p. 4501–4.
60. Pu S, Luo Z, Shang J, Bai X. Design of a passive knee exoskeleton reducing the load of walking. In: International conference on autonomous unmanned systems. Springer; 2021. p. 687–95.
61. Zhang L, Liu Y, Wang R, Smith C, Gutierrez-Farewik EM. Modeling and simulation of a human knee exoskeleton's assistive strategies and interaction. *Front Neurorobot.* 2021;15: 620928.
62. Liu Y, Liu Y, Song Q, Zhao M, Liu Y, Ren W. Effects of joint assistance on the muscle metabolism and strength in different states based on simulation. *IEEE Access.* 2020;8:218 874-218 897.
63. Antonellis P, Mohammadzadeh Gonabadi A, Myers SA, Pipinos II, Malcolm P. Metabolically efficient walking assistance using optimized timed forces at the waist. *Sci Robot.* 2022;7(64):eabh1925.
64. Cseke B, Uchida T, Doumit M. Simulating ideal assistive strategies to reduce the metabolic cost of walking in the elderly. *IEEE Trans Biomed Eng.* 2022;69:2797–805.
65. Lim B, Hyung S, Kim K, Lee J, Jang J, Shim Y. Simulating gait assistance of a hip exoskeleton: feasibility studies for ankle muscle weaknesses. In: 2016 IEEE/RSJ international conference on intelligent robots and systems (IROS). IEEE; 2016. p. 5664–9.
66. Lim B, Hyoung S, Lee J, Seo K, Jang J, Shim Y. Simulating gait assistance of a hip exoskeleton: case studies for ankle pathologies. In: IEEE international conference on robotics and automation (ICRA). IEEE. 2017; 2017. p. 1022–7.
67. Yan L, Ren L, Wei G. A biologically inspired lower limb cable driven exoskeleton. In: Intelligent robotics and applications: 15th international conference, ICIRA 2022, Harbin, China, August 1–3, 2022, proceedings, Part IV. Springer; 2022. p. 647–55.
68. Zhou X, Liu G, Yang L, Han B. Design and research of lower limb exoskeleton based on a hill-type muscle model for assisting people to walk. In: 2020 6th international conference on control, automation and robotics (ICCAR). IEEE; 2020. p. 558–62.
69. Meng Q, Kong B, Zeng Q, Fei C, Yu H. Concept design of hybrid-actuated lower limb exoskeleton to reduce the metabolic cost of walking with heavy loads. *PLoS ONE.* 2023;18(5): e0282800.
70. Rosenberg M, Steele KM. Simulated impacts of ankle foot orthoses on muscle demand and recruitment in typically-developing children and children with cerebral palsy and crouch gait. *PLoS ONE.* 2017;12(7): e0180219.
71. Nguyen VQ, Umberger BR, Sup FC. Predictive simulation of human walking augmented by a powered ankle exoskeleton. In: 2019 IEEE 16th international conference on rehabilitation robotics (ICORR). IEEE; 2019. p. 53–8.
72. Kim Y, Kwon C, Moon H, Kim K, Cho J, Kong K. Optimization of semi-active pneumatic actuators for an exoskeleton robot for running. In: 2018 15th international conference on ubiquitous robots (UR). IEEE; 2018. p. 119–24.
73. Bianco NA, Franks PW, Hicks JL, Delp SL. Coupled exoskeleton assistance simplifies control and maintains metabolic benefits: a simulation study. *PLoS ONE.* 2022;17:1.
74. Li X, Chen J, Wang W, Zhang F, Han H, Zhang J. Using predictive simulation methods to design suitable assistance modes for human walking on slopes. In: 2020 3rd international conference on control and robots (ICCR). IEEE; 2020. p. 169–75.
75. Ostraich B, Riemer R. Design of a multi-joint passive exoskeleton for vertical jumping using optimal control. *IEEE Trans Neural Syst Rehabil Eng.* 2022;30:2815–23.
76. Barazesh H, Sharbafi MA. A biarticular passive exosuit to support balance control can reduce metabolic cost of walking. *Bioinspir Biomimetics.* 2020;15(3): 036009.
77. Wen T-C, Jacobson M, Zhou X, Chung H-J, Kim M. The personalization of stiffness for an ankle-foot prosthesis emulator using human-in-the-loop optimization. In: 2020 IEEE/RSJ international conference on intelligent robots and systems (IROS). IEEE; 2020. p. 3431–6.
78. Fang J, Yuan Y. Human-in-the-loop optimization of wearable robots to reduce the human metabolic energy cost in physical movements. *Robot Auton Syst.* 2020;127: 103495.
79. Khamar M, Edrisi M, Zahiri M. Human-exoskeleton control simulation, kinetic and kinematic modeling and parameters extraction. *MethodsX.* 2019;6:1838–46.
80. Khamar M, Edrisi M. Designing a backstepping sliding mode controller for an assistant human knee exoskeleton based on nonlinear disturbance observer. *Mechatronics.* 2018;54:121–32.
81. Safavi S, Ghafari AS, Meghdari A. Design of an optimum torque actuator for augmenting lower extremity exoskeletons in biomechanical framework. In: 2011 IEEE international conference on robotics and biomimetics. IEEE; 2011. p. 1979–83.
82. Aftabi H, Nasiri R, Ahmadabadi MN. Simulation-based biomechanical assessment of unpowered exoskeletons for running. *Sci Rep.* 2021;11(1):1–12.
83. Ostraich B, Riemer R. Simulation of a passive knee exoskeleton for vertical jump using optimal control. *IEEE Trans Neural Syst Rehabil Eng.* 2020;28(12):2859–68.
84. Guan X, Ji L, Wang R, Huang W. Optimization of an unpowered energy-stored exoskeleton for patients with spinal cord injury. In: 38th annual international conference of the IEEE engineering in medicine and biology society (EMBC). IEEE. 2016;2016. p. 5030–3.
85. Marconi G, Gopalai AA, Chauhan S. Effects of powered ankle-foot orthoses mass distribution on lower limb muscle forces-a simulation study. *Med Biol Eng Comput.* 2023;61(5):1167–82.
86. Liu Y-X, Zhang L, Wang R, Smith C, Gutierrez-Farewik EM. Weight distribution of a knee exoskeleton influences muscle activities during movements. *IEEE Access.* 2021;9:91 614-91 624.
87. Bermejo-García J, Romero F, Rodríguez-Jorge D, Alonso Sánchez FJ. Computer simulation of a cable driven exosuit: Dynamic optimization of anchor points positions through lower limbs muscle activities. Available at SSRN 4354312.

88. MajidiRad A, Yihun Y, Desai J, Hakansson NA. Simulation of exoskeleton alignment and its effect on the knee extensor and flexor muscles. In: 41st annual international conference of the IEEE engineering in medicine and biology society (EMBC). IEEE. 2019;2019. p. 4093–6.
89. Hegarty AK, Petrella AJ, Kurz MJ, Silverman AK. Evaluating the effects of ankle-foot orthosis mechanical property assumptions on gait simulation muscle force results. *J Biomech Eng*. 2017;139(3): 031009.
90. Asbeck AT, De Rossi SM, Holt KG, Walsh CJ. A biologically inspired soft exosuit for walking assistance. *Int Robot Res*. 2015;34(6):744–62.
91. Zhang J, Fiers P, Witte KA, Jackson RW, Poggensee KL, Atkeson CG, Collins SH. Human-in-the-loop optimization of exoskeleton assistance during walking. *Science*. 2017;356(6344):1280–4.
92. Ding Y, Kim M, Kuindersma S, Walsh CJ. Human-in-the-loop optimization of hip assistance with a soft exosuit during walking; 2018. <http://robotics.sciencemag.org/>
93. Bryan GM, Franks PW, Song S, Reyes R, O'Donovan MP, Gregorczyk KN, Collins SH. Optimized hip-knee-ankle exoskeleton assistance reduces the metabolic cost of walking with worn loads. *J Neuroeng Rehabil*. 2021;18(1):1–13.
94. Song S, Collins SH. Optimizing exoskeleton assistance for faster self-selected walking. *IEEE Trans Neural Syst Rehabil Eng*. 2021;29:786–95.
95. Ratnakumar N, Zhou X. Optimized torque assistance during walking with an idealized hip exoskeleton. In: International design engineering technical conferences and computers and information in engineering conference, vol. 85376. American Society of Mechanical Engineers; 2021. V002T02A009.
96. Afschrift M, Van Asseldonk E, Van Mierlo M, Bayon C, Keemink A, Van Der Kooij H, De Groot F. Assisting walking balance using a bio-inspired exoskeleton controller. *bioRxiv*; 2022. 2022–10.
97. Franks PW, Bianco NA, Bryan GM, Hicks JL, Delp SL, Collins SH. Testing simulated assistance strategies on a hip-knee-ankle exoskeleton: a case study. In: 8th IEEE RAS/EMBS international conference for biomedical robotics and biomechanics (BioRob). IEEE. 2020;2020. p. 700–7.
98. Lee G, Kim J, Panizzolo F, Zhou Y, Baker L, Galiana I, Malcolm P, Walsh C. Reducing the metabolic cost of running with a tethered soft exosuit. *Sci Robot*. 2017;2(6):eaan6708.
99. Wang Z, Chen C, Yang F, Liu Y, Li G, Wu X. Real-time gait phase estimation based on neural network and assistance strategy based on simulated muscle dynamics for an ankle exosuit. *IEEE Trans Med Robot Bionics*. 2023;5:100–9.
100. Song S, Desai R, Geyer H. Integration of an adaptive swing control into a neuromuscular human walking model. In: 35th annual international conference of the IEEE engineering in medicine and biology society (EMBC). IEEE. 2013; 2013. p. 4915–8.
101. Thatte N, Geyer H. Toward balance recovery with leg prostheses using neuromuscular model control. *IEEE Trans Biomed Eng*. 2015;63(5):904–13.
102. Wu AR, Dzeladini F, Brug TJ, Tamburella F, Tagliamonte NL, Asseldonk EHV, Kooij HVD, Ijspeert AJ. An adaptive neuromuscular controller for assistive lower-limb exoskeletons: a preliminary study on subjects with spinal cord injury. *Front Neurobot*. 2017;11:6.
103. Tamburella F, Tagliamonte N, Pisotta I, Masciullo M, Arquilla M, Van Asseldonk E, van Der Kooij H, Wu A, Dzeladini F, Ijspeert A, et al. Neuromuscular controller embedded in a powered ankle exoskeleton: effects on gait, clinical features and subjective perspective of incomplete spinal cord injured subjects. *IEEE Trans Neural Syst Rehabil Eng*. 2020;28(5):1157–67.
104. Dzeladini F, Wu AR, Renjewski D, Arami A, Burdet E, Van Asseldonk E, Van Der Kooij H, Ijspeert AJ. Effects of a neuromuscular controller on a powered ankle exoskeleton during human walking. In: 2016 6th IEEE international conference on biomedical robotics and biomechanics (BioRob). IEEE; 2016. p. 617–22.
105. Shafer BA, Philius SA, Nuckols RW, McCall J, Young AJ, Sawicki GS. Neuromechanics and energetics of walking with an ankle exoskeleton using neuromuscular-model based control: a parameter study. *Front Bioeng Biotechnol*. 2021;9:4.
106. Yin K, Xiang K, Pang M, Chen J, Anderson P, Yang L. Personalised control of robotic ankle exoskeleton through experience-based adaptive fuzzy inference. *IEEE Access*. 2019;7:72 221–72 233.
107. Keemink A, Brug T, Van Asseldonk E, Wu A, Van Der Kooij H. Whole body center of mass feedback in a reflex-based neuromuscular model predicts ankle strategy during perturbed walking. *IEEE Trans Neural Syst Rehabil Eng*. 2021;29:2521–9.
108. Yin K, Jin Y, Du H, Xue Y, Li P, Ma Z. Virtual neuromuscular control for robotic ankle exoskeleton standing balance. *Machines*. 2022;10(7):572.
109. Zhao G, Sharbafi MA, Vlutters M, Van Asseldonk E, Seyfarth A. Bio-inspired balance control assistance can reduce metabolic energy consumption in human walking. *IEEE Trans Neural Syst Rehabil Eng*. 2019;27(9):1760–9.
110. Zhao G, Sharbafi M, Vlutters M, Van Asseldonk E, Seyfarth A. Template model inspired leg force feedback based control can assist human walking. In: 2017 international conference on rehabilitation robotics (ICORR). IEEE; 2017. p. 473–8.
111. Sharbafi MA, Barazesh H, Iranikah M, Seyfarth A. Leg force control through biarticular muscles for human walking assistance. *Front Neurobot*. 2018;12:39.
112. Firouzi V, Mohseni O, Sharbafi MA. Model-based control for gait assistance in the frontal plane. In: 9th IEEE RAS/EMBS international conference for biomedical robotics and biomechanics (BioRob). IEEE. 2022; 2022. p. 1–8.
113. Durandau G, Farina D, Asín-Prieto G, Dimbwadyo-Terrer I, Lerma-Lara S, Pons JL, Moreno JC, Sartori M. Voluntary control of wearable robotic exoskeletons by patients with paresis via neuromechanical modeling. *J Neuroeng Rehabil*. 2019;16:1–18.
114. Fleischer C, Hommel G. A human-exoskeleton interface utilizing electromyography. *IEEE Trans Robot*. 2008;24(4):872–82.
115. Durandau G, Rampeltshammer WF, Van Der Kooij H, Sartori M. Myoelectric model-based control of a bi-lateral robotic ankle exoskeleton during even ground locomotion. In: 8th IEEE RAS/EMBS international conference for biomedical robotics and biomechanics (BioRob). IEEE. 2020; 2020. p. 822–6.
116. Durandau G, Rampeltshammer W, Van Der Kooij H, Sartori M. Toward muscle-driven control of wearable robots: A real-time framework for the estimation of neuromuscular states during human-exoskeleton locomotion tasks. In: 2018 7th IEEE international conference on biomedical robotics and biomechanics (BioRob). IEEE; 2018. p. 683–8.
117. Durandau G, Rampeltshammer WF, van der Kooij H, Sartori M. Neuro-mechanical model-based adaptive control of bilateral ankle exoskeletons: biological joint torque and electromyogram reduction across walking conditions. *IEEE Trans Robot*. 2022;38:1380–94.
118. Karavas N, Ajoudani A, Tsagarakis N, Saglia J, Bicchì A, Caldwell D. Tele-impedance based assistive control for a compliant knee exoskeleton. *Robot Auton Syst*. 2015;73:78–90.
119. Hassani W, Mohammed S, Rifai H, Amirat Y. Powered orthosis for lower limb movements assistance and rehabilitation. *Control Eng Pract*. 2014;26:245–53.
120. Yang R, Shen Z, Lyu Y, Zhuang Y, Li L, Song R. Voluntary assist-as-needed controller for an ankle power-assist rehabilitation robot. *IEEE Trans Biomed Eng*. 2022;70:1795–803.
121. Ao D, Song R, Gao J. Movement performance of human-robot cooperation control based on EMG-driven hill-type and proportional models for an ankle power-assist exoskeleton robot. *IEEE Trans Neural Syst Rehabil Eng*. 2016;25(8):1125–34.
122. Giszter SF. Motor primitives-new data and future questions. *Curr Opin Neurobiol*. 2015;33:156–65.
123. Lalouaux H, Sanz-Morère C B, Livolsi C, Pergolini A, Crea S, Vitiello N, Ronsse R. Experimental assessment of a control strategy for locomotion assistance relying on simplified motor primitives. In: 2022 IEEE/RSJ international conference on intelligent robots and systems (IROS). IEEE, 2022; p. 12254–60.
124. Garate VR, Parri A, Yan T, Muniñ M, Lova RM, Vitiello N, Ronsse R. Walking assistance using artificial primitives: a novel bioinspired framework using motor primitives for locomotion assistance through a wearable cooperative exoskeleton. *IEEE Robot Autom Mag*. 2016;23(1):83–95.
125. Ruiz Garate V, Parri A, Yan T, Muniñ M, Molino Lova R, Vitiello N, Ronsse R. Experimental validation of motor primitive-based control for leg exoskeletons during continuous multi-locomotion tasks. *Front Neurobot*. 2017;11:15.
126. McLain BJ, Lee D, Mulrine SC, Young AJ. Effect of assistance using a bilateral robotic knee exoskeleton on tibiofemoral force using a neuromuscular model. *Ann Biomed Eng*. 2022;50(6):716–27.

127. Böhme M, Köhler H-P, Thiel R, Jäkel J, Zentner J, Witt M. Preliminary biomechanical evaluation of a novel exoskeleton robotic system to assist stair climbing. *Appl Sci*. 2022;12(17):8835.
128. Yamamoto M, Shimatani K, Hasegawa M, Murata T, Kurita Y. Estimation of knee joint reaction force based on the plantar flexion resistance of an ankle-foot orthosis during gait. *J Phys Ther Sci*. 2018;30(8):966–70.
129. Yap YT, Gouwanda D, Gopalai AA, Chong YZ. Musculoskeletal gait simulation to investigate biomechanical effect of knee brace. *J Biomech Eng*. 2023;145(2): 024502.
130. Arch ES, Stanhope SJ, Higginson JS. Passive-dynamic ankle-foot orthosis replicates soleus but not gastrocnemius muscle function during stance in gait: insights for orthosis prescription. *Prosthet Orthot Int*. 2016;40(5):606–16.
131. Choi H, Peters KM, MacConnell MB, Ly KK, Eckert ES, Steele KM. Impact of ankle foot orthosis stiffness on Achilles tendon and gastrocnemius function during unimpaired gait. *J Biomech*. 2017;64:145–52.
132. Choi H, Bjornson K, Fatone S, Steele KM. Using musculoskeletal modeling to evaluate the effect of ankle foot orthosis tuning on muscletendon dynamics: a case study. *Disabil Rehabil Assist Technol*. 2016;11(7):613–8.
133. Farris DJ, Sawicki GS. Linking the mechanics and energetics of hopping with elastic ankle exoskeletons. *J Appl Physiol*. 2012;113(12):1862–72.
134. Farris DJ, Hicks JL, Delp SL, Sawicki GS. Musculoskeletal modelling deconstructs the paradoxical effects of elastic ankle exoskeletons on plantar-flexor mechanics and energetics during hopping. *J Exp Biol*. 2014;217(22):4018–28.
135. Jackson RW, Dembia CL, Delp SL, Collins SH. Muscle-tendon mechanics explain unexpected effects of exoskeleton assistance on metabolic rate during walking. *J Exp Biol*. 2017;220(11):2082–95.
136. Stingel JP, Hicks JL, Uhlrich SD, Delp SL. How connecting the legs with a spring improves human running economy. *bioRxiv*; 2023. 2023–04.
137. Mo F, Zhang Q, Zhang H, Long J, Wang Y, Chen G, Ye J. A simulation-based framework with a proprioceptive musculoskeletal model for evaluating the rehabilitation exoskeleton system. *Comput Methods Progr Biomed*. 2021;208: 106270.
138. Ai Q, Ding B, Liu Q, Meng W. A subject-specific EMG-driven musculoskeletal model for applications in lower-limb rehabilitation robotics. *Int J Humanoid Robot*. 2016;13(03):1650005.
139. Simonetti D, Koopman B, Sartori M. Automated estimation of ankle muscle EMG envelopes and resulting plantar-dorsi flexion torque from 64 garment-embedded electrodes uniformly distributed around the human leg. *J Electromyogr Kinesiol*. 2022;67: 102701.
140. Schulte RV, Zondag M, Buurke JH, Prinsen EC. Multi-day EMG-based knee joint torque estimation using hybrid neuromusculoskeletal modelling and convolutional neural networks. *Front Robot AI*. 2022;9: 869476.
141. Lam SK, Vujaklija I. Joint torque prediction via hybrid neuromusculoskeletal modelling during gait using statistical ground reaction estimates: an exploratory study. *Sensors*. 2021;21(19):6597.
142. Markowitz J, Herr H. Human leg model predicts muscle forces, states, and energetics during walking. *PLoS Comput Biol*. 2016;12(5): e1004912.
143. Gordon DF, McGreavy C, Christou A, Vijayakumar S. Human-in-the-loop optimization of exoskeleton assistance via online simulation of metabolic cost. *IEEE Trans Robot*. 2022;38:1410–29.
144. Holder J, Trinler U, Meurer A, Stief F. A systematic review of the associations between inverse dynamics and musculoskeletal modeling to investigate joint loading in a clinical environment. *Front Bioeng Biotechnol*. 2020;8: 603907.
145. Tagliamonte N, Wu A, Pisotta I, Tamburella F, Masciullo M, Arquilla M, van Asseldonk E, van der Kooij H, Dzeladini F, Ijspeert A, et al. Benefits and potential of a neuromuscular controller for exoskeleton-assisted walking. In: *Wearable robotics: challenges and trends: proceedings of the 5th international symposium on wearable robotics, WeRob2020, and of WearRAcon Europe 2020, October 13–16, 2020*. Springer; 2022. p. 281–5.
146. Sargent RG. Verification and validation of simulation models. In: *Proceedings of the 2010 winter simulation conference*. IEEE; 2010. p. 166–83.
147. Febrer-Nafria M, Buurke T, D'Hondt L, De Waele L, Van Campenhout A, Desloovere K, De Grootte F. Musculoskeletal simulations capture the experimentally observed response to ankle-foot-orthosis use in a healthy subject. *Gait Posture*. 2022;97:534–5.
148. Franks PW, Bryan GM, Martin RM, Reyes R, Lakmazaheri AC, Collins SH. Comparing optimized exoskeleton assistance of the hip, knee, and ankle in single and multi-joint configurations. *Wearable Technologies*. 2021;2:e16.
149. Rabe KG, Lenzi T, Fey NP. Performance of sonomyographic and electromyographic sensing for continuous estimation of joint torque during ambulation on multiple terrains. *IEEE Trans Neural Syst Rehabil Eng*. 2021;29:2635–44.
150. Rayati M, Nasiri R, Ahmadabadi MN. Improving muscle force distribution model using reflex excitation: towards a model-based exoskeleton torque optimization approach. *IEEE Trans Neural Syst Rehabil Eng*. 2022;31:720–8.
151. Arones MM, Shourijeh MS, Patten C, Fregly BJ. Musculoskeletal model personalization affects metabolic cost estimates for walking. *Front Bioeng Biotechnol*. 2020;8: 588925.
152. da Luz SB, Modenese L, Sancisi N, Mills PM, Kennedy B, Beck BR, Lloyd DG. Feasibility of using MRIS to create subject-specific parallel-mechanism joint models. *J Biomech*. 2017;53:45–55.
153. Pellikaan P, van der Krogt M, Carbone V, Fluit R, Vigneron L, Van Deun J, Verdonshot N, Koopman HF. Evaluation of a morphing based method to estimate muscle attachment sites of the lower extremity. *J Biomech*. 2014;47(5):1144–50.
154. Nuckols RW, Dick TJ, Beck ON, Sawicki GS. Ultrasound imaging links soleus muscle neuromechanics and energetics during human walking with elastic ankle exoskeletons. *Sci Rep*. 2020;10(1):1–15.
155. Scherb D, Wartzack S, Miehling J. Modelling the interaction between wearable assistive devices and digital human models—a systematic review. *Front Bioeng Biotechnol*. 2023;10:1044275.
156. Nguyen VQ, Johnson RT, Sup FC, Umberger BR. Bilevel optimization for cost function determination in dynamic simulation of human gait. *IEEE Trans Neural Syst Rehabil Eng*. 2019;27(7):1426–35.
157. Weng J, Hashemi E, Arami A. Adaptive reference inverse optimal control for natural walking with musculoskeletal models. *IEEE Trans Neural Syst Rehabil Eng*. 2022;30:1567–75.
158. Tomasi M, Artoni A. Identification of motor control objectives in human locomotion via multi-objective inverse optimal control. *J Comput Nonlinear Dyn*. 2023;18:1–23.
159. Veerkamp K, Waterval N, Geijtenbeek T, Carty C, Lloyd D, Harlaar J, van der Krogt M. Evaluating cost function criteria in predicting healthy gait. *J Biomech*. 2021;123: 110530.
160. Dzeladini F, Van Den Kieboom J, Ijspeert A. The contribution of a central pattern generator in a reflex-based neuromuscular model. *Front Human Neurosci*. 2014;8:371.
161. Davoodi A, Mohseni O, Seyfarth A, Sharbafi MA. From template to anchors: transfer of virtual pendulum posture control balance template to adaptive neuromuscular gait model increases walking stability. *R Soc Open Sci*. 2019;6(3): 181911.
162. Firouzi V, Seyfarth A, Sharbafi MA. Tip model: a combination of unstable subsystems for lateral balance in walking. In: *2019 IEEE/RSJ international conference on intelligent robots and systems (IROS)*. IEEE; 2019. p. 476–82.
163. Schumacher C, Berry A, Lemus D, Rode C, Seyfarth A, Vallery H. Biarticular muscles are most responsive to upper-body pitch perturbations in human standing. *Sci Rep*. 2019;9(1):14492.
164. Scholl P, Firouzi V, Karimi MT, Seyfarth A, Sharbafi MA. Virtual pivot point model predicts instability in parkinsonian gaits. In: *2023 IEEE international conference on systems, man, and cybernetics (SMC)*. IEEE; 2023. p. 5261–6.
165. Koelewijn AD, Van Den Bogert AJ. Antagonistic co-contraction can minimize muscular effort in systems with uncertainty. *PeerJ*. 2022;10: e13085.
166. Nguyen VQ, LaPre AK, Price MA, Umberger BR, Sup FC IV. Inclusion of actuator dynamics in simulations of assisted human movement. *Int J Numer Methods Biomed Eng*. 2020;36(5): e3334.
167. Yandell MB, Quinlivan BT, Popov D, Walsh C, Zelik KE. Physical interface dynamics alter how robotic exosuits augment human movement: implications for optimizing wearable assistive devices. *J Neuroeng Rehabil*. 2017;14:1–11.

168. Serrancoli G, Falisse A, Dembia C, Vantilt J, Tanghe K, Lefeber D, Jonkers I, De Schutter J, De Groot F. Subject-exoskeleton contact model calibration leads to accurate interaction force predictions. *IEEE Trans Neural Syst Rehabil Eng.* 2019;27(8):1597–605.
169. Chander DS, Böhme M, Andersen MS, Rasmussen J, Cavatorta MP. Simulating the dynamics of a human-exoskeleton system using kinematic data with misalignment between the human and exoskeleton joints. In: *Computer methods, imaging and visualization in biomechanics and biomedical engineering II: selected Papers from the 17th international symposium CMBBE and 5th conference on imaging and visualization, September 7–9, 2021.* Springer; 2022. p. 65–73.
170. Dijkers MP, Akers KG, Dieffenbach S, Galen SS. Systematic reviews of clinical benefits of exoskeleton use for gait and mobility in neurologic disorders: a tertiary study. *Arch Phys Med Rehabil.* 2021;102(2):300–13.
171. Bunge LR, Davidson AJ, Helmore BR, Mavrandonis AD, Page TD, Schuster-Bayly TR, Kumar S. Effectiveness of powered exoskeleton use on gait in individuals with cerebral palsy: a systematic review. *PLoS ONE.* 2021;16(5): e0252193.
172. Pamungkas DS, Caesarendra W, Soebakti H, Analia R, Susanto S. Overview: types of lower limb exoskeletons. *Electronics.* 2019;8(11):1283.
173. Pinto-Fernandez D, Torricelli D, del Carmen Sanchez-Villamanan M, Aller F, Mombaur K, Conti R, Vitiello N, Moreno JC, Pons JL. Performance evaluation of lower limb exoskeletons: a systematic review. *IEEE Trans Neural Syst Rehabil Eng.* 2020;28(7):1573–83.
174. Song S, Geyer H. Predictive neuromechanical simulations indicate why walking performance declines with ageing. *J Physiol.* 2018;596(7):1199–210.
175. Yao S, Zhuang Y, Li Z, Song R. Adaptive admittance control for an ankle exoskeleton using an EMG-driven musculoskeletal model. *Front Neuro-robot.* 2018;12:16.
176. Caputo JM, Collins SH. Prosthetic ankle push-off work reduces metabolic rate but not collision work in non-amputee walking. *Sci Rep.* 2014;4(1):7213.
177. Quesada RE, Caputo JM, Collins SH. Increasing ankle push-off work with a powered prosthesis does not necessarily reduce metabolic rate for transtibial amputees. *J Biomech.* 2016;49(14):3452–9.
178. Di Russo A, Stanev D, Armand S, Ijspeert A. Sensory modulation of gait characteristics in human locomotion: a neuromusculoskeletal modeling study. *PLoS Comput Biol.* 2021;17(5): e1008594.
179. Beckerle P, Christ O, Schürmann T, Vogt J, von Stryk O, Rinderknecht S. A human-machine-centered design method for (powered) lower limb prosthetics. *Robot Auton Syst.* 2017;95:1–12.
180. Delp SL, Anderson FC, Arnold AS, Loan P, Habib A, John CT, Guendelman E, Thelen DG. Opensim: open-source software to create and analyze dynamic simulations of movement. *IEEE Trans Biomed Eng.* 2007;54(11):1940–50.
181. Wang H, Caggiano V, Durandau G, Sartori M, Kumar V. Myosim: Fast and physiologically realistic mujoco models for musculoskeletal and exoskeletal studies. In: *2022 international conference on robotics and automation (ICRA).* IEEE; 2022. p. 8104–11.
182. Geijtenbeek T. Scone: open source software for predictive simulation of biological motion. *J Open Source Softw.* 2019;4(38):1421.
183. Werling K, Raitor M, Stingel J, Hicks J L, Collins S, Delp S, Liu CK. Rapid bilevel optimization to concurrently solve musculoskeletal scaling, marker registration, and inverse kinematic problems for human motion reconstruction. *bioRxiv;* 2022. 2022–08.
184. Dembia CL, Bianco NA, Falisse A, Hicks JL, Delp SL. Opensim moco: musculoskeletal optimal control. *PLoS Comput Biol.* 2020;16(12): e1008493.
185. Rosenberg MC, Banjanin BS, Burden SA, Steele KM. Predicting walking response to ankle exoskeletons using data-driven models. *J R Soc Interface.* 2020;17(171):20200487.
186. Bryan GM, Franks PW, Klein SC, Peuchen RJ, Collins SH. A hip-knee-ankle exoskeleton emulator for studying gait assistance. *Int J Robot Res.* 2021;40(4–5):722–46.
187. Park H, Cho J, Park J, Na Y, Kim J. Sim-to-real transfer learning approach for tracking multi-DOF ankle motions using soft strain sensors. *IEEE Robot Autom Lett.* 2020;5(2):3525–32.
188. Selinger JC, O'Connor SM, Wong JD, Donelan JM. Humans can continuously optimize energetic cost during walking. *Curr Biol.* 2015;25(18):2452–6.
189. Selinger JC, Wong JD, Simha SN, Donelan JM. How humans initiate energy optimization and converge on their optimal gaits. *J Exp Biol.* 2019;222(19):jeb198234.
190. Ahn J, Hogan N. Walking is not like reaching: evidence from periodic mechanical perturbations. *PLoS ONE.* 2012;7(3): e31767.
191. Baye-Wallace L, Thalman CM, Lee H. Entrainment during human locomotion using a lightweight soft robotic hip exosuit (sr-hexo). *IEEE Robot Autom Lett.* 2022;7(3):6131–8.
192. Lian P, Ma Y, Zheng L, Xiao Y, Wu X. A three-step hill neuromusculoskeletal model parameter identification method based on exoskeleton robot. *J Intell Robot Syst.* 2022;104(3):44.
193. Jayaneththi VR, Vilorio J, Wiedemann LG, Jarrett C, McDaid AJ. Robotic assessment of neuromuscular characteristics using musculoskeletal models: a pilot study. *Comput Biol Med.* 2017;86:82–9.

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