Tapping into skeletal muscle biomechanics for design and control of lower-limb exoskeletons: a narrative review

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Abstract

Lower-limb exoskeletons and exosuits ("exos") are traditionally designed with a strong focus on mechatronics and actuation, whereas the "human-side" is often disregarded or minimally modelled. Muscle biomechanics principles and skeletal muscle response to robot-delivered loads should be incorporated in design/control of exos. In this narrative review, we summarize the advances in literature with respect to the fusion of muscle biomechanics and lower-limb exoskeletons. We reported methods to measure muscle biomechanics directly and indirectly and summarized the studies that incorporated muscle measures for improved design and control of intuitive lower-limb exos. Finally, we delved into articles that studied how the human-exo interaction influenced muscle biomechanics during locomotion. To support neurorehabilitation and facilitate everyday use of wearable assistive technologies, we believe that future studies should investigate and predict how exoskeleton assistance strategies would structurally remodel skeletal muscle over time. Real-time mapping of the neuromechanical origin and generation of muscle force resulting in joint torques should be combined with musculoskeletal models to address time varying parameters such as adaptation to exos and fatigue. Development of smarter predictive controllers that steer rather than assist biological components could result in a synchronized human-machine system that optimizes the biological and electromechanical performance of the combined system.

Keywords:

musculoskeletal modelling, human locomotion, human-machine interaction, sensor based control

Word count: 5967 *(including in-line references & headings)*

Introduction

Lower-limb exoskeletons and exosuits are worn in parallel with the body to assist, augment, or otherwise affect mobility. Collectively referred to as "exos", exoskeletons and exosuits are often used in gait rehabilitation or as a mobility aid. [1] Exos deliver mechanical assistance to targeted biological joint(s) and thus interact directly with the wearer's musculoskeletal system. To effectively unload or augment the biological joint, knowledge of joint biomechanics is typically incorporated into the design or control of the exo. Generally speaking, the research field has a good comprehension of lower-limb joint-level biomechanics including: dynamic (quasi-)stiffness, [2–6] distribution of work across the joints, [7–9] and how factors such as speed, terrain, and load change the joint dynamics. [10–12] However, skeletal muscles are the actual actuators that generate movement. [13,14] Therefore, there are clear advantages to movement support technology which interacts at the muscle level.

The quantity of published research, which combines muscle/tendon biomechanics with exos is small, but exhibits a slow upwards trends in recent years. Figure 1 illustrates the long-standing and increasing interest in muscle/tendon biomechanics research. The increase in exo research is comparatively more recent, likely due to technological advancements improving the feasibility of exo research. [15] Emerging in 2005, published research combining the fields of exos and muscle/tendon biomechanics has slowly increased, although it still trails behind both of its components.

Understanding of muscle-level biomechanics has improved with time, facilitated by improvements in technology and modelling. Well established techniques, like ultrasound, were able to capture muscle mechanics in intact humans *in vivo* during stationary tasks. [16–18] Improvements in technology allowed capture of muscle mechanics in dynamic situations such as walking. [19–21] Advances in high-density electromyography (HD-EMG) and blind source separation enabled measuring the firing activity of contractile microstructures (*i.e.,* motor units) in human muscles *in vivo*, [22,23] which was critical to understanding how whole-body movement is accomplished via fibre contraction at the microscale. [24] Computational muscle-level models combined with a rise in open-source platforms and models, and an increase in computing power also served to advance our understanding of muscle-level biomechanics at macro- and microscale. Improvements in implementing trajectory optimization for musculoskeletal modelling facilitated faster modelling and simulations, which allowed researchers to more easily simulate and investigate numerous models. [25] In 2015, a modelling toolbox called CEINMS, integrated electromyographic (EMG) driven and EMG-informed algorithms into the musculoskeletal modelling environment of OpenSim. [26] The resulting open-source neuromusculoskeletal modelling platform was able to better simulate, test, and understand how muscle activity controls movement. Researchers have also developed tools to facilitate advanced optimal control (Moco in OpenSim) and customizable control (SCONE) in neuromuscular simulations. [27,28] Furthermore, recent advancements have combined computationally fast musculoskeletal models with reinforcement learning to explore muscle mechanics during real-life tasks. MyoSuite, an open-source framework with reinforcement learning capable musculoskeletal models, enables in silico design of robotic devices and controllers, thereby speeding up the design of personalized exos for in vivo real-world applications. [29,30] With a better understanding of muscle-level biomechanics we gleaned insights into the mechanisms of mobility and biomechanical principles about which exoskeletons can be designed and controlled.

Traditionally, the key players in exo design and control have been mechatronic and actuation aspects, while the human aspects have often been disregarded or minimally incorporated.

Many exoskeletons, both old and new, exclusively use techniques other than muscle-level biomechanics for their controllers and design. A number of review articles discuss the state-of-the-art for non-muscle-level exoskeleton control and design, [1,31–33] so we only briefly summarize them here. Generally, exo design and control focuses on the robotic part of the human-robot system, placing high importance on the output torque of the device *(Figure 2)*. Oftentimes, exos use position or torque tracking to enforce a pre-defined kinematic or kinetic profile, and the human must yield and adapt to the robot's actuation rather than working symbiotically. [34–37] Impedance control considers the interaction between human and robot, resulting in a controller that is responsive to the human while still enforcing predetermined dynamics. [37–40] Volitional controllers, such as proportional myoelectric controllers, further shift the controller focus from the robot to the human component of the human-robot system by using human measures to inform the output. [41–43] However, proportional myoelectric controllers measure the emergent behaviour of the underlying muscle actions and therefore do not fully capture the muscle mechanics. Human-in-the-loop optimization acts to tune the exo parameters to optimize for a chosen output parameter which is often human energy expenditure or muscle activity. [44–46] Although a powerful and state-of-the-art technique, human-in-the-loop optimization can be time intensive and risks falling into local minima traps. Some consideration to muscle properties have also been included in design – most noticeably exos which employ contractile elements mimicking musculoskeletal properties, such as the McKibben pneumatic actuator (commonly referred to as an "artificial muscle"). [41,47] However, McKibben actuators require a compressed air source, thus limiting the locations the exo can be used in. In addition to little incorporation of muscle-level biomechanics in exo design and control, no exo has taken into consideration the short- and long-term response of skeletal muscle to robot-delivered mechanical loads. Inclusion of muscle-level biomechanics may overcome some shortfalls in current exo design and control.

The design and control of exos has been increasingly inspired by muscle-level biomechanics over time. Earlier exoskeletons had heavy and bulky form factors, with a focus on providing enough power to compensate for 100% of biological joint torque-generating capacity. [48,49] Time and experience led to smaller, and less-bulky exos, with a wide variety of actuation methods. The development of light-weight yet strong materials, more compact powerful batteries and motors, and innovative design all contributed to reducing the bulk and weight of exos. Artificial pneumatic muscles which attempted to mimic biological muscle properties and were originally developed for prosthesis use, became a popular actuation method for exos.[41,47,50,51] Linear springs, acting in-line with muscle-tendon units such as the *triceps surae* complex, have also been used in exo design as a form of musculotendon mimicry. [52,53] Straps and cables, a more recent form of exo actuation, are often inspired by biological tendons. [54,55] While these techniques are guided by muscle properties, none of them rely on muscle-level biomechanics, which is the next logical step for exo development.

Inclusion of muscle-level biomechanics in exo design/control has the potential to break through some of the barriers to wide-spread exo success. Despite technological advancements, there is substantial room for improvement in exo design/control, particularly for real world environments. In this narrative review, we will discuss how muscle-level biomechanics has been and could be effectively implemented in exo control and design. We introduce the techniques and hardware used to understand muscle-level biomechanics and then discuss how muscle-level biomechanics can inform design and personalization. Next, we consider control choices and integrating real-time muscle-level biomechanics estimators within robotic control logics. After presenting how muscle-level biomechanics affects the human-machine interaction, we end the review with recommendations and predictions of research within muscle-level biomechanics and lower-limb exos. Throughout the manuscript, we classified techniques as "Direct" if they measured a muscle property through sensors, and "Indirect" if the technique used a musculoskeletal model with or without sensor input to estimate a muscle property.

Measuring muscle biomechanics

Incorporation of muscle biomechanics into exo design, control, or personalization requires a method to measure or estimate muscle biomechanics. The measurement or estimation technique usually needs to provide relevant biomechanical data *in vivo*, real-time (not for evaluation purposes), and during dynamic movement. Furthermore, sensors should be compatible with the physical structure of the exo. In this section, we reviewed muscle measurement methods and sensors to measure or estimate muscle biomechanics that meet the requirements for use with exoskeletons.

Direct measures

While various sensing methods measure parameters that can provide information about muscle-level kinetics and kinematics, the depth and accuracy of measurements are different. We presented the methods in order from the deepest to most superficial measurements.

Sarcomere Microendoscopy

Sarcomere microendoscopy can directly measure the second-harmonic frequencies of light generated in the muscle fibres to visualize muscle sarcomeres and their contractile dynamics. Llewellyn *et al.*[56] showed that second-harmonic generation with 920 nm illumination can effectively visualize sarcomeres in human extensor digitorum muscle *in vivo*. They showed that

visualizing sarcomere contractile dynamics in millisecond scale resolution can overcome cardiac and respiratory motion artifacts which is possible through high-speed data acquisition.
As sarcomere length determines force production capacity in muscles, microendoscopy can reveal muscle biomechanics *in vivo* while being minimally invasive. Sanchez *et al.*[57] developed a wearable microendoscope to visualize sarcomere twitch dynamics in individual motor units of major skeletal muscles including *soleus* and *vastus lateralis*. Although sarcomere microendoscopy is still an invasive method and it has never been used in conjunction with exoskeletons, it is a potential measurement method which can deepen the knowledge of muscle biomechanics to inform design, control, and individualization of lower limb exoskeletons. For instance, because many movement disorders exhibit or originate from disruptions in sarcomere structure and performance, rehabilitative exos could be designed based on how they affect motor unit contractile dynamics and the structure of sarcomeres in short- and long- term. Similarly, different types of exos can take advantage of the evaluation of user adaptation and how adaptation results in desired or undesired remodelling in the muscle, which is advantageous for real-word applications.

Sarcomere microendoscopy demonstrated how joint angle affects sarcomere length and contractile dynamic. Cromie *et al.*[58] measured sarcomere length in *carpi radialis brevis* while wrist was in flexion and extension. The results showed substantial sarcomere length variability in an individual fibre. More studies addressed how joint angle changes sarcomere length and affects muscle force generating capacity in lower limbs. [59,60] As the changes in the sarcomere length at different angles were in the range of 2 to 4 μm for the *soleus* and the measurement precision of the method is ~30 nm, the measurement is therefore suitable for tracking the length of sarcomeres in lowerlimb movement. [60] Additionally, Lichtwark *et al.*[61] showed that fascicle length change can represent sarcomere length change.

Furthermore, sarcomere microendoscopy can equip research in the field of lower limb exos to investigate muscle adaptation. Pincheria *et al.*[62] determined how three weeks of eccentric exercise training changes sarcomeres in *biceps femoris long head*. They estimated sarcomere length and number as well as fascicle length before and after the training. The results showed an increase in the sarcomere length while the sarcomere numbers in series did not change, as well as a heterogeneous change in fascicle length.

Ultrasound imaging

Ultrasonography enables deriving muscle architectural (*e.g.,* volume, pennation angle, physiological cross-sectional area) and functional parameters (*e.g.,* fascicle kinematics), which are critical to understanding muscle biomechanics. As muscles are in series with tendons, other common biological measurements like joint kinematics and kinetics, or EMG cannot provide enough details to measure the separate kinetics and kinematics of muscles and tendons without many assumptions and models. Muscle-tendon biomechanics can provide useful information for individualization, fatigue recognition, real-time and overground joint torque estimation etc., which can enhance control and design in lower-limb exos.

Fukunaga *et al.*[63] used real-time ultrasonography to determine fascicle length and pennation angle of human *vastus lateralis* muscle *in vivo* and non-invasively at rest and during static contraction. Ultrasonography enabled *in vivo* measuring of parameters that can inform muscle level kinetics and kinematics such as physiological cross-sectional area of muscles, [64] investigating differences in longitudinal strain of the Achilles tendon, [65] as well as studying force-velocity behaviour of the *medial gastrocnemius* muscle-tendon unit. [66] Manual tracking of muscle architectures with ultrasonography is subjective and time-consuming, which led to algorithms developed for automated tracking of fascicle length, [67] for which the accuracy and repeatability is assessed, [68] and the source code and standalone version of the semi-automated fascicle tracking algorithm was made open-source. [69]

Recently, studies used muscle ultrasonography during gait to estimate parameters like volitional motion or ability and muscle power, which can be useful for exo control. For instance, Nuckols *et al.*[70] used ultrasound imaging to estimate the onset of *soleus* concentric contraction just before push off, when the *soleus* begins to generate positive power, in real time during various gait conditions. They showed that an exo control strategy based on muscle positive power could adapt to the individuality of contraction timing (e.g., healthy and post stroke patient) and how it changed with changes in gait (e.g., speed and incline). Nuckols *et al.* also compared gait segmentation based on automated ultrasound detection of the *soleus* contraction onset with ground reaction forces and found the error was within 1% of the gait cycle. Other approaches to link human mechanics to exo control strategies include optimization and grid search (i.e. parameter sweeping) which explore and determine appropriate exo control parameters for a specific gait condition. [71] However, both techniques are time-consuming and not necessarily generalizable to differences in gaits and terrains. Direct EMG or matching to kinetics and kinematics of joints are also approaches that try to intuitively adapt to human gait, but their performance is not as good as optimization or grid sweep. One possible reason is that joint kinetics and kinematics and EMG cannot completely determine the dynamic state of muscles that are the real actuators of human gait.

Moreover, muscle architecture can be input into data-driven (e.g., using machine learning) or mechanistic (e.g., musculoskeletal modelling) models that can estimate motion intention. Jahnandish *et al.*[72] performed image enhancement and model fitting to extract ultrasound features of *rectus femoris* muscle, namely thickness, angle between aponeuroses, pennation angle, fascicle length, and image echogenicity. The echogenicity, defined as the ability to send and receive an ultrasound wave, was measured by averaging the intensity of all pixels in the region of interest. Then, they estimated knee joint angle and angular velocity during non-weight-bearing knee flexion/extension based on the trained model with an average root mean square error value of 7.45° and 0.262 rad/s, which is close to a similar study which used sEMG. Muscle thickness and image echogenicity showed the highest correlation with both angle and angular velocity. Also, some studies showed that inputs from both s-EMG and ultrasound images (fascicle length and pennation angle) can increase accuracy of ankle joint moment prediction by machine learning[73] models or neural and musculoskeletal[74] models.

While studies used ultrasound B-mode probes to extract fascicle kinematics based on 2D images, Yan *et al.*[75] developed a measurement system to use ultrasound wearable A-mode probes (1D measurement) to estimate the acoustic nonlinearity parameter of skeletal muscles *in vivo*. The acoustic non-linearity parameter changes in tissues due to diseases or residual stress, which suggested that similar changes may occur with contraction in muscles. Yan *et al.* showed high correlation between the acoustic nonlinearity parameter of *biceps brachii* muscle and elbow joint torque, with an average coefficient of determination (R2) of 0.861. Hence, they proposed the acoustic nonlinearity parameter as supplementary information for force control of exoskeletons.

Shear wave tensiometry

An emerging research technique to directly and non-invasively measure superficial tendon and ligament kinetics is shear wave tensiometry. [76] The non-invasive device is placed on the skin, directly over the target tendon or ligament. A vibrational stimulus is delivered to the tendon (via the skin) which propagates through the tendon at a speed dependent on the tendon axial load due to real-time characteristics of the tendon modulating the propagation of the vibration. The shear wave speed can be calculated knowing the distance between two miniature accelerometers placed along the tendon direction and measuring the arrival time of the propagated signal.

Shear wave tensiometry shows promising capabilities for applications in lower limb exos. First, it is applicable to lower limb exos, as the impulses are detectable throughout the gait cycle and can track dynamically varying wave speed. [77] Several studies used shear wave tensiometry to track the dynamics of standing balance and measure gait kinetics in clinical and able-bodied populations, including children, adults, and older adults[78–82]. Second, in more dynamic tasks like running and jumping, Schmitz *et al.*[83] proposed adding redundant accelerometers and using a Kalman filter to mitigate random sensor noise due to the high rate of loading and impact events. Harper *et al.*[84] developed a wearable shear wave tensiometer with dynamic range to track unconstrained locomotion. A later work combined this with inertial measurement units[85] to measure the work and power output of *Triceps Surae* outdoors. Schneebeli *et al.*[86] used intraclass correlation coefficient (ICC3.1) to test the test-retest (ICC3.1 0.87–0.99), inter-section (ICC3.1 0.75–0.93) and intra-session (ICC3.1 0.85–0.96) reliability of shear wave tensiometry, which shows promising use in clinical and research settings.

High Density Electromyography (HD-EMG)

Non-invasive and flexible or woven textile bi-dimensional grids of electrodes can measure muscle high density electromyograms (HD-EMGs). [87] HD-EMG is an interferent electrical signal generated by the superposition of action potentials generated by hundreds of skeletal muscle fibres during contraction. Because skeletal muscle fibres are directly innervated by alpha motor neurons (neural cells residing in the spinal cord), the HD-EMGs carry information about alpha motor neuron activity, which is directly associated to the control of movements. [88] Blind source separation can be used to disentangle the interferent HD-EMG and decode both discharge timings of motor neurons as well as the resulting action potentials travelling along innervated skeletal fibres. HD-EMG holds great potential to explore the neuro-mechanics of movement in individuals wearing exoskeletons. Many studies have addressed HD-EMG in upper limb gesture recognition and exoskeleton controllers, but the literature in lower limb exoskeletons is scarce.

Some studies investigated HD-EMG during locomotion and demonstrated that spatial patterns of electromyograms can reveal how muscles adapt to different locomotion modes. Schlink *et al.*[23] compared different signal processing methods to reduce motion artifacts in HD-EMG during human locomotion and proposed canonical correlation analysis filtering during fast walking and running. Schlink *et al.*[89] also showed that spatial patterns of electromyograms are heterogeneous and differ among lower limb muscles and locomotion speeds, which could be due to preferential recruitment of faster motor units under greater loads. Moreover, they showed that fatigue alters spatial myoelectric patterns in the *medial gastrocnemius* during locomotion, while lower limb biomechanics remains similar, a potential strategy to avoid overuse injuries. [90] Exos can use HD-EMG to recognize fatigue or locomotion mode to tune assistance (e.g., timing and magnitude of torque). Also, HD-EMG can reveal muscle recruitment strategies, impairments, and adaptations of users as valuable information for exoskeleton design.

Force myography (FMG)

FMG refers to a broad category of methods that non-invasively measure muscle biomechanics by quantifying how muscle external geometry changes. FMG usually includes an array of sensors to detect muscle deformation or stiffness due to contraction, and methods that process the collected data to extract the desired parameters. FMG can vary in type of sensors (e.g., force or pressure sensors, strain sensors, bending sensors), sensor arrangement, and data processing method (e.g. signal processing and feature extraction, machine learning techniques), with specific limitations associated with each technique. [37] However, sensor characteristics and device configuration can adversely affect the reliability of FMG signals. For instance, many researchers calibrated the pre-load forces when the device is donned based on the user's oral feedback. [91] Moreover, some methods are based on cross-sectional area increase of the muscles. [92] These methods can be used in some applications like gesture recognition but cannot estimate individual muscle force without making assumptions on the contribution of the individual muscles to the cross-sectional area increase. Also, some techniques are only applicable to static situations as they cannot handle motion artifacts. [93]

Some recent studies developed and used soft and wearable strain sensors to monitor muscle contractions. [92,94] Alvares *et al.*[94] used sensors based on strain-mediated contact in anisotropically resistive structures (SCARS) to measure changes in muscle deformation which correlate with muscle input and knee torque.

Many studies include FMG in hand rehabilitative and assistive exoskeletons to enhance user intention in upper body, [95–99] but FMG in lower limb applications is limited. Jiang *et al.*[100] proposed a wearable gait phase determination system based on FMG. The proposed force myography band could correctly detect more than 99.9% of gait phases over 12965 gait phase segments with an average temporal error of 55.2 ms. With upper limb applications motivating hardware and processing improvements in FMG, there is an increased likelihood of interesting applications for lower limb exos in the future.

Indirect measures

Aside from the direct measurements mentioned above, real-time musculoskeletal models have been used to estimate biomechanical parameters *in vivo*, such as muscle-tendon forces, [101] kinematics, joint torques, [102,103] joint stiffness , [5,6] and compressive loads, [104] which can be used in exoskeleton controls, [105–108] without using invasive measurement sensors.

One research direction is to use optimization to estimate individual muscle forces from the net joint torques (often got from inverse dynamics[109,110]), named static optimization. [111–114] Specifically, researchers developed real-time computing platforms that utilize the static optimization method in estimating muscle forces. [115,116] However, optimization-based muscle force estimation for lower limbs often requires force plates to measure ground reaction forces, which limits this potential in out-of-lab applications. Trajectory optimization can avoid this issue by modelling the ground contacts, however, the objective function is normally movement-type specific and may not reflect an individual person or patient. [25,117] Furthermore, the computation time is long and prevented it from being used in the real-time control of wearable robotic devices.

To solve this problem, muscle force estimation using sEMG driven musculoskeletal (MSK) models have been developed, which requires joint angles and sEMG signals as input. At first, due to computational complexity, studies were focused on only one joint and its corresponding muscles[118,119] and an infinitely stiff tendon model was also used in the muscle models to save in computational time; [120] Later, these types of studies were expanded to multiple joints and muscles as well as incorporating an elastic tendon to cover more complex movements; [102,121] Recently, the open source Calibrated EMG-Informed NeuroMusculoSkeletal Modelling Toolbox (CEINMS) was developed to lower the entry to this field. [26,103] Furthermore, experimental EMG paired with inverse dynamics allowed for the personalization of muscle-tendon models to the user as they represent the inputs/outputs pair. [26] Not only can this method estimate muscle forces, but studies also demonstrated that it could accurately estimate joint torque and extrapolate results for unknown tasks (not used for the muscle-tendon model parameters personalisation), and even other degrees of freedom. [122] Since musculoskeletal models were directly driven by the sEMG signals, calculated muscle forces and joint torques can be prior to the electromechanical delay of actual musculoskeletal systems, which provides a big advantage in exoskeleton control as it gives a windows of opportunity where optimal assistance can be provided to the user. [106,107] By knowing the force of each muscle that wraps over a joint, joint stiffness[5,6,123,124] and compressive loads can be estimated. [104,125–129] As these parameters are more closely relevant to either human-robot interactions or injury risks, they are more suitable to be directly used as control parameters in exoskeletons. Even though the above-mentioned studies have shown very promising results on reproducing joint torques, validating the actual muscle forces in vivo on human subjects poses ethical challenges, making it difficult to directly measure and validate these forces. However, experimental studies conducted on cats have provided valuable insights into the effectiveness of various approaches, such as static optimization, trajectory optimization, and surface electromyography (sEMG). [130–133] The similarities in muscle structures and types between humans and cats support the belief that these methods can be reliable in interpreting human movements as well. While there may be some species-specific differences, the fundamental principles underlying muscle mechanics and control are expected to be comparable. In general, indirect measurement methods provide very useful muscle biometric information using very simple sensor setups, compared to direct methods, which has advantages in real-life applications.

Muscle and tendon biomechanics for exoskeleton design or personalization

A main objective of exos is to interact with the human wearing them. Thus, this interaction will influence the design and control of the exo. For a long time, the human neuromusculoskeletal system was ignored in the conception of exoskeletons resulting in devices that were powerful but bulky and with little to no benefit for the user. [49] To overcome this challenge, exoskeleton emulators for iterative design were established; the most established of which is the human-in-the-loop technique. [46] Although emulators can result in the creation of optimal design and control,[52] they require a large amount of human data (3600 recorded conditions in the cited study).

Direct measurements

Direct measurements of muscle biomechanics can provide useful information to inspire novel designs or to help tune exoskeletons. Ultrasound imaging can reveal the effects of exo stiffness on force production in muscles and tendons. Farris *et al.*[134] evaluated the effect of parallel elastic assistance of ankle exoskeleton in hopping on *soleus* muscle-tendon-unit mechanics using *in vivo* ultrasound imaging. They showed that parallel assistance to *soleus* muscle reduces muscle force, but average positive fascicle power does not significantly change. This can help with tuning the stiffness of lower limb exos to optimize metabolic cost. Takahashi *et al.*[135] investigated foot-ankle interplay during walking by adding stiffness to the foot through shoes and insoles. They used ultrasound imaging to show that a stiffer foot results in decreased shortening velocity and increased force output in *soleus* muscle. The results suggested added foot/shoe stiffness as a potential design parameter to improve locomotion economy in tasks where muscles should generate more muscle force (e.g., walking with load carriage) or operate with less economy (e.g., fast walking speeds close to the walk-to-run transition). Also, Nuckols *et al.*[136] showed how exoskeleton stiffness alters *soleus* muscle contractile dynamics and affects metabolic rate during walking. They used ultrasound imaging to show that exoskeletons with higher rotational stiffness increase fascicle length and velocity and decrease fascicle force. However, the change in contractile dynamics results in a bowl-shape metabolic cost. Hence, measuring contractile behaviour can help to design or tune exos to steer more economical force production in the muscles. Moreover, Beck *et al.*[137]

showed how artificially fast balance-correcting exoskeleton torque can improve balance by 9% and how it affects fascicle mechanics.

Moreover, direct measurements can help exo personalisation through design and evaluation of assistance profile. Nuckols *et al.*[138] demonstrated that ultrasound imaging can measure muscle dynamics to develop exosuit assistance profiles that are tailored to the individual and adaptive to dynamic walking tasks. Also, Schmitz *et al.*[139] used shear wave tensiometer to directly measure force in the Achilles tendon during walking assisted with ankle exosuit while carrying load. They performed a pilot experiment in an unconstrained outdoor environment to evaluate nine different exosuit assistance profiles based on reduction in the peak force in Achilles tendon. The most efficient exosuit assistance profile could reduce metabolic cost by 9.6%.

Indirect measurements

Human-exoskeleton simulation can acquire the same benefits of emulators without requiring a high volume of human data. As previously presented, there is a wealth of literature on neuromusculoskeletal modelling based on cadaveric studies or human experiments. Nevertheless, one of the main and active challenges is the simulation of how human and mechanical devices interact. One of the main axes of simulation-research is based on predictive simulation using optimal control, which can reproduce the interaction between the human-exoskeleton system and the environment. Optimal control can also predict the effect of exos on humans or human biomechanical variables in unknown conditions. Fournier *et al.* began with a biomechanical simulation of healthy and spinal cord injury kinematics at varied walking speeds,[140] then added a simulated exoskeleton to the human neuromusculoskeletal system, which allowed them to predict ground reaction forces. Predictive simulation and optimal control can also be used to predict the effect of exos with different mechanical properties, for example Sreenivasa *et al.*[141] looked into the optimal stiffness of an ankle-foot orthosis for reducing muscle effort in children with gait abnormality and Febrer-Nafría *et al.*[142] optimized parameters such as angle shape for the kinematic assistance delivered through an active knee exoskeleton to a spinal cord injury (SCI) patient. In both cases, after testing their simulation with pre-recorded human data, they created an optimization routine that tracked real kinematics or torque parameters and/or tried to minimize power, muscle activation or jerk.

Simulation can also be used to create a set of requirements for exos. Afschrift *et al.* investigated a capability gap (torque that a weakened muscle can produce against the torque task requirement computed using inverse dynamics), which allowed identification of the minimum level of assistance required for people with muscle weakness (reduction of maximal force capability in the muscle) to realise certain tasks. [143] This is an effective technique to determine the minimum power of the actuator in the exo for people with muscle weakness. Following the same philosophy, a study simulated ideal actuators to find the best single degree of freedom (DOF) or multi-DOF joint to actuate to minimize metabolic cost during running. [144] Results showed that at low running speeds (2 m/s) all joints provided the same metabolic reduction but at higher speeds, the hip could create better metabolic savings. For multi-DOF, a combination of hip, knee and ankle offered the highest metabolic reduction. Another interesting simulation study[145] showed how coupled joint assistance (using the same actuator/assistance on multiple DOF) had the same or similar effect on metabolic savings as multi-actuator assistance and provide better metabolic reduction than assisting only one DOF. This provided important guidelines in exoskeleton design to save on hardware components i.e., going from one actuator per DOF to one actuator crossing multiple joints thus providing cheaper devices.

There remains three main issues and challenges that delay the broad adoption of these simulation tools. The first one, which is common to not only neuromusculoskeletal modelling simulation but simulators in general, is the gap between simulation and reality which limits the transferability of simulation results to the real system. The issue of transferability was observed in a study[146] where results obtained in simulation promised a higher metabolic reduction (69%) than what was obtained in the real system (25.9%). Using simplified musculoskeletal models (3 DOF 9 muscles model[146]) can contribute to poor transferability. The second challenge is the idealization of exo components and structures. For instance, exoskeletons are usually modelled as a simplified mechanical structure that is rigidly connected to the human skeletal system, with the force produced by the actuator ideally transmitted directly to the skeletal system without loss due to friction, soft tissue connection, and shear forces. [146,147] An interesting study[148] tried to tackle part of this problem by implementing a spring and damper contact model between the human and the skeletal system, which resulted in accurately reproduced kinematics of the real exoskeleton system. Nevertheless, their model needed to be calibrated with multiple experimental recordings of the real human and exoskeleton. The third shortcoming is the current inability to simulate the change (or learning) of the neural system due to the exos assistance. The lack of modelled learning limits the ability to effectively design assistance for neurorehabilitation of patients such as stroke survivors. An interesting solution would be to replace optimization for simulating the neural command by a machine learning algorithm wherein a neural network trained on the simulation could adapt to the different assistances. [149]

Muscle biomechanics for exoskeleton control

Muscle biomechanics can provide useful information to estimate valuable control signals for different applications including fatigue, volitional ability, and joint torque. Understanding generation of joint torques is a useful for exoskeleton control. Direct or indirect measurement of joint torque can allow creation of a symbiotic system between the human and exo by providing assistance proportional to the force produced by the user (Figure 3). Although joint torque can be estimated through inverse dynamics, estimation through muscle biomechanics may be more suitable for exoskeletons applications, particularly applications in uncontrolled (non-laboratory) environments.

Direct measurements

Despite attempts and innovations to directly measure muscle biomechanics during gait or other lower-limb movements to estimate useful control signals for muscle in the loop controllers (e.g., estimating joint torque or fatigue), we could find only one study that actually used a direct measurement of muscle biomechanics to estimate a parameter for the control parameter. Sheng *et al.*[150] used real-time ultrasound-based muscle fatigue assessment to robustly control their hybrid (functional electrical stimulation and electrical motor) knee exoskeleton to switch between its modes and avoid extensive stimulation of the fatigued muscle.

Neuromusculoskeletal modelling

One indirect way of accessing joint torque is by using a neuromusculoskeletal model fed by EMG. Using neuromusculoskeletal modelling in combination with an exoskeleton is a recent technique, which was primarily delayed by the limitation of achieving real-time computation of the complex model (multi-DOF and multi-musculotendon unit). [109,122] Fleischer and Hommel[151] were the first to present the possibility of using a real-time neuromusculoskeletal model for the control of an unilateral knee exoskeleton. Durandau *et al.*[105] further developed the methods to apply it to a lower-limb exoskeleton for the knee and ankle and tested it on patients (SCI and stroke). The results showed the possibility of using this kind of system for rehabilitation purposes, where muscle effort is reduced while also reducing neural control variability. Furthermore, the same system is used for a bilateral ankle exoskeleton during diverse walking conditions[106] showing the possibility to reduce the muscular effort in variable walking speed and showing better adaptability than the current state-of-the-art speed adaptative controller[52,152] although the metabolic reduction is less. Finally, neuromusculoskeletal models offer the possibility to compute biomechanical variables other than joint torque, such as stiffness, which can also benefit robotic control. Yao *et al.*[153] combined real-time muscle stiffness computation (*tibialis anterior*) and joint torque to control a non-ambulatory ankle exoskeleton. The joint torque estimation is used as an input command to the torque controller and the muscle stiffness is used to modulate the stiffness coefficient of the admittance controller used for the torque controller. Nevertheless, this method relies on EMG sensors which are subject to noise and muscle crosstalk as well as interference from electromechanical devices (i.e. an exoskeleton).

Neural control models can be used to drive musculoskeletal models for exoskeletons, which reduces reliance on EMG sensors. Ruiz *et al.*[154–156] explored the possibility of using a motor primitive-based neural control model for controlling leg exoskeletons together with musculoskeletal models. They conducted experiments to evaluate the performance of the neuromusculoskeletal model-based controller. A full-leg exoskeleton that had motors at the ankle, knee and hip was used as the hardware platform. Participants were asked to perform a locomotion track involving ground-level walking, ascending stairs, and descending stairs and several transitions between these tasks. They showed that the assistance significantly decrease time to perform tasks. Dzeladini *et al.*[157] showed that a reflex-based neuromuscular controller (NMC) for an ankle orthosis can reduce the net metabolic cost compared to the transparent mode without disturbing the walking dynamics at slow and normal speeds. Later, they extended the neuromuscular control framework into a hip and knee robotic exoskeleton and tested it on SCI patients. [158,159] Their results showed that NMC enabled SCI subjects to walk at several speeds, including near healthy speeds, in a healthy-like manner. Shafer *et al.*[160] implemented a simple reflex-based neuromuscular controller for an ankle exoskeleton to study the effects of the reflex control parameters, such as the reflex gains and reflex time delay on users. They found that the reflex-based assistance could systematically reduce users' biological ankle moment, however, it didn't reduce their overall metabolic cost. Until now, most studies have looked at the immediate effect on the neuromusculoskeletal system, but long-term effects have not yet been investigated. The direct effect of assistance on the neural system has also been overlooked.

Changes to Muscle Biomechanics when using Lower-Limb Exoskeletons

In this section, we summarized the changes to muscle biomechanics as a result of using exoskeleton assisted movement. Studies investigated these changes during actuation of lower-limb joints during either walking, seated knee flexion/extension, hopping, squatting, or sit-to-stand tasks. The influence on plantar flexion and dorsiflexion is commonly studied when using ankle exoskeletons, and are summarized in Table 1, whereas the following sections address actuation of either the knee or hip joints. We also briefly discuss the studies that used commercial lower limb exoskeletons or robotic gait trainers such as Lokomat and Lopes.

Active actuation of knee or hip joint

Many studies showed that knee exoskeletons can reduce activity of associated muscles. Some studies that actuated the knee joint provided additional passive supports at either ankle or hip. [161–168] The results showed reductions in *soleus*, [163] *rectus femoris*, *tibialis anterior*, *gastrocnemius lateralis*, and *semitendinosus*[162] during gait, and during swing phase, the *biceps* *femoris*, [161] *tibialis anterior*, and *semitendinosus*[162] when walking with powered as compared to minimal impedance mode. In minimal impedance mode, also called “free” or “transparent” mode, the exo attempts to be transparent to the user and minimally impact walking biomechanics either by providing no torque or actively controlling for minimal interaction torque. Active knee assistance with passive hip support reduced muscle activity of hip and knee extensors. [166] This general decrease in EMG activity was further associated with a decreasing trend over the time with assisted walking due to adaptation. [166]

Studies also evaluated knee exoskeletons in other tasks such as squatting[167] or knee flexion-extension. [165,168] A knee exoskeleton also reduced knee extensor muscle activity when using a controller that is capable of injecting the minimal amount of energy needed to support oscillations of the knee. [165]

Passive springs placed anteriorly on the hip stored and released energy thereby reducing plantar flexor activity during walking. [169] Actuated hip exoskeletons increased muscle activity of *tibialis anterior, rectus femoris, and gastrocnemius medialis* in the minimal impedance mode, whereas that of the *semitendinosus* reduced. [164] However, providing assistance reduced the muscle activity of the *tibialis anterior*, *rectus femoris*, and *gastrocnemius medialis* but increased activity of the *semitendinosus.* [164]

Actuation across multiple joints, and use of Robotic Gait Trainers, and commercial exoskeletons

An exoskeleton with active knee and ankle actuation reduced muscle activity for both healthy and participants with stroke in the knee flexors and extensors, and ankle plantar and dorsiflexors. [105] Increased assistance reduced the variability of muscle activity in this study. Lower limb exoskeletons with hip and knee actuation and passive ankle support reduced muscle activity of the *vastus medialis*, *gastrocnemius medialis*,[170,171] *tibialis anterior*, *rectus femoris*, *soleus*[170] when compared to walking with a minimal impedance mode. Activity of *semitendinosus* and *biceps femoris* increased when walking slowly with the exoskeleton. [170] Furthermore, muscle synergy patterns were shown to be altered when wearing such exoskeletons [172]. Otálora and colleagues[173] showed that actuation of the hip, knee, and ankle joints reduced activity in the knee flexors and extensors, and *tibialis anterior*.

Gait training devices such as the LOPES and Lokomat provide different degrees of actuation of the lower limb and, unlike exoskeletons, can also provide body weight support. Walking in the LOPES in zero-impedance mode showed a decrease in muscle activity of the muscles involved in push off whereas an increase in activity of muscles that contribute to acceleration and deceleration of the swing leg. [174,175] The activation timing was rather unchanged. [174] The virtual pivot point model implemented in LOPES II through admittance control also showed decreased muscle activity in *rectus femoris, hamstring, medial gastrocnemius,* and *gluteus maximus* muscles. [175] Literature about how the Lokomat impacted post training muscle activity has been inconclusive. The Lokomat imposes able-bodied joint trajectories through impedance control, with varying levels of exo guidance force. At higher levels of guidance force the joint trajectories are more rigid and it is increasingly difficult for the muscles of the user to influence or affect the trajectory of the Lokomat. The results depended on guidance level, [176,177] speed, [176,178] or body weight support. [177,179] Walking on the Lokomat increased the activity of *biceps femoris* in healthy participants, [176,177,179] *vastus lateralis* [176,179] *erector spinae*, *tibialis anterior*, [179] *tibialis anterior* and *rectus femoris*. [177] However, another study identified a general lowering of muscle activity compared to treadmill walking in participants with stroke as well as healthy walkers. [180] For participants with SCI, Lokomat training reduced *vastus lateralis* and *rectus femoris* activity during stance phase, and increased *gastrocnemius medialis* during swing phase. [181] The Lokomat was also used to differentially assist either side during gait, and showed an inverse relation to muscle activity on the other side. [178] The activity in the trunk muscles during training with the Lokomat was similar to quiescent supine lying. [182] Using a robotic trainer that only assisted the hip increased activity of knee flexors. [183]

Commercially available exoskeletons have been rigorously studied in literature. [182,184–194] For instance, studies reported reduction in *rectus femoris*, [186,187] *gluteus medius*, *medial hamstring*, *tibialis anterior*, *soleus*, [187] *gluteus maximus*, *rectus femoris*, *vastus lateralis*, and *gastrocnemius* and an increase in *biceps femoris*[186] when walking with the Ekso GT, which assists the user in a predefined trajectory. However, the change in muscle activity depended on gait phase, whether the user had voluntary control in the exoskeleton, and the speed of reference walking without exoskeleton. [186] Voluntary control increased burst duration compared to fast walking. [186]

The Ekso has often used to train participants with neurological impairments. [182,184–186,188–193] Participants with multiple sclerosis showed a new muscle synergy when walking with the exoskeleton. [193] Incomplete SCI participants showed non-reciprocal firing patterns and reduced muscle activations especially that of the *rectus femoris*[190] and *tibialis anterior.* [186] A reduced variability in muscle activity was seen when walking with the exoskeleton. [190] Alamro[182] observed an increase in trunk EMG when walking with Ekso-assisted compared to the Lokomat for SCI participants. Trunk EMG activation remained similar between Ekso overground and treadmill walking.

Stroke participants were studied at all three phases; acute, sub-acute, and chronic with the Ekso. [184,185,188,189,191,192] Participants with acute stroke showed reduction in *soleus* and *rectus femoris* activity on affected side during stance phase with the exoskeleton. [184] *Vastus Lateralis* and *rectus femoris* showed the largest dissimilarity in activation with the exoskeleton on the affected side. [184] Using the Ekso for training in sub-acute stroke improved bilateral symmetry of *tibialis anterior* and decreased co-contractions of the proximal muscles, suggesting improvement in proximal muscle activity. [189] Activation timing for the *semitendinosus* was improved in the paretic leg after training. [191] The Ekso trained group also showed more physiological motor control in the semitendinosus and *rectus femoris.* [191] Chronic stroke participants who trained with the Ekso showed reduced affected side *rectus femoris* activity during swing phase, [188] increase in *rectus femoris*, reduction in affected *biceps femoris*, increase in unaffected *biceps femoris*, reduced *soleus* and *tibialis anterior* activity was seen. [185] The synergy modules necessary to reconstruct lower limb muscle activities were more similar to healthy walking post Ekso training. [192]

This section overviewed the impact on muscles as a result of assistance provided by exos. In sum, we see a reduction in muscle activity across joints, and tasks, as well as changes to muscle synergies. This understanding must be accounted for when designing novel controllers that interact with the muscle directly.

Discussion and future predictions

Exos have been designed with the goal of enhancing human movement. However, current technologies have shown only modest results in healthy individuals and limited clinical impact. A central element hampering progress is that exos do not interact directly with underlying skeletal muscles, but instead deliver external mechanical loads that directly influence the biological skeletal system. As such, current systems do not consider how biological muscles, tendons, joints, react to mechanically delivered torques. In this context, research in exos has overlooked the effect of robotic assistance, especially at extreme ends of the spatiotemporal scale (e.g., cell growth over months or years). [88,195] This is a critical aspect of human-exo physical interaction as skeletal muscles will remodel new structural properties if exposed long enough to exo-delivered torques. The current inability to predict how exo assistance strategies would remodel skeletal muscle structurally hampers progress in longitudinal neurorehabilitation and in day-to-day adoption of wearable assistive technologies.

In the future we envision research advances aimed at 'closing-the-loop' between exos and human skeletal muscle biology. [88] In this context, we envision that future exos should be capable of delivering coordinated mechanical torques to alter, in a controlled way, skeletal muscle form and function over time scales ranging from seconds (e.g., a movement cycle) to months (e.g., the recovery stage following a neuromuscular injury) and beyond (e.g., across ageing stages).

We envision this will require developments in three key directions: (1) recording both neural and mechanical function underlying muscle contraction (e.g., motor neuron discharges and innervated skeletal fibre force) in the intact moving human *in vivo*, (2) fusing recorded neuro-mechanical data with numerical models to predict skeletal muscle adaptation in response to exos-delivered torques over time and (3) developing predictive controllers to steer skeletal muscle form and function with enough certainty to induce a targeted, positive change in the future. This will open to a new class of muscle-centred exos that directly respond to biological cues to maintain integrity of skeletal muscles over the lifespan.

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Figures

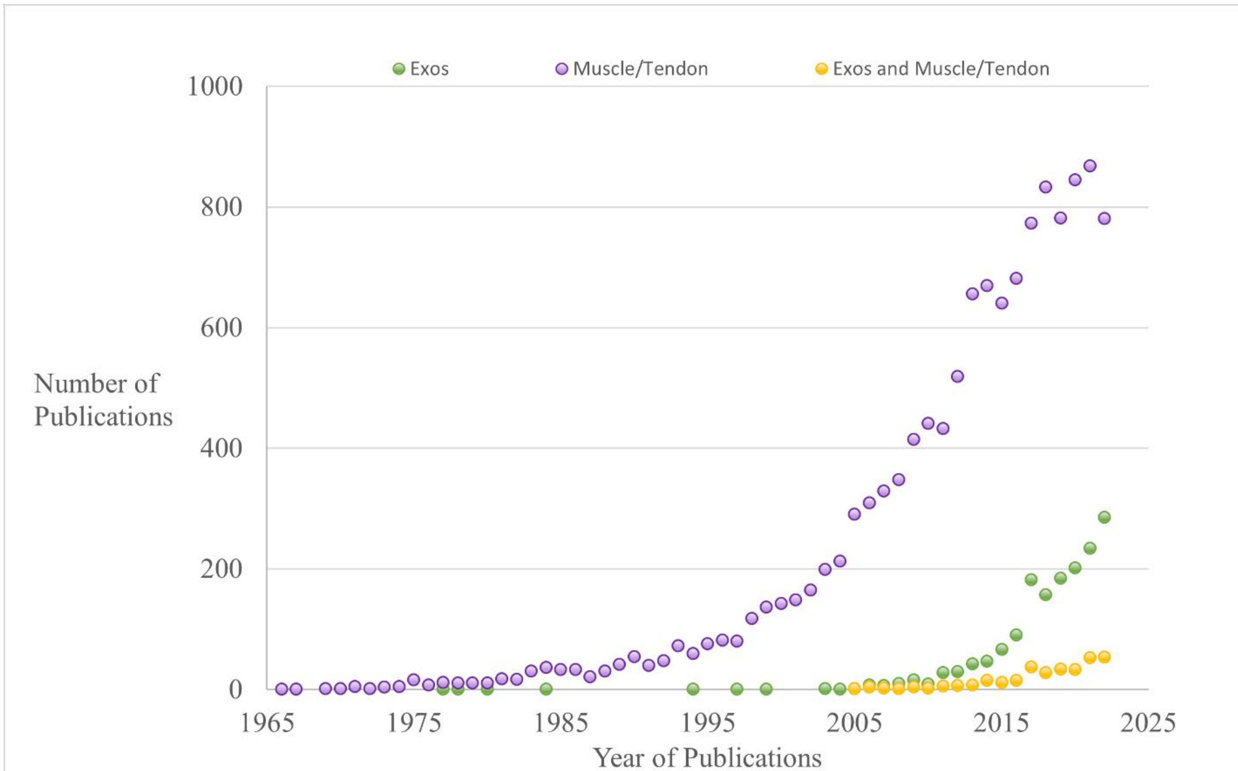

Figure 1. The number of studies published over time on exos, muscle/tendon biomechanics, and both exos & muscle-tendon biomechanics from 1965 to 2022. The data were found through the PubMed database (https://pubmed.ncbi.nlm.nih.gov). All data searches were in English and for lower limb extremities (KEYWORD: gait OR walking OR (lower AND (limb OR extremities))) in human (KEYWORD: human OR participant OR patient). Specific data searches were: A) exos (KEYWORD: (exoskelet* OR exosuit)), B) Muscle/tendon biomechanics (KEYWORD: (muscle mechanics) OR ((muscle OR tendon) AND (biomechanics))), and C) muscle/tendon biomechanics and exos (KEYWORD: (muscle mechanics) OR ((muscle OR tendon) AND (biomechanics)) AND (exoskelet* OR exosuit)).

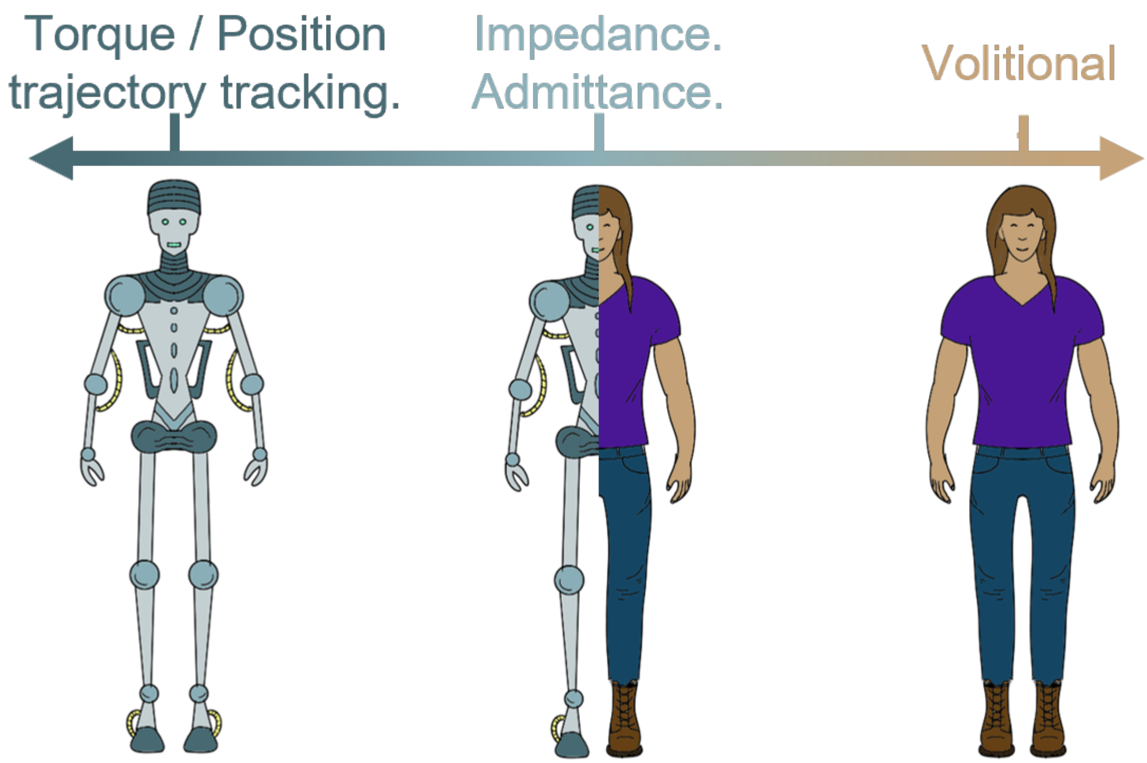

Figure 2. Visual representation of the "focus" of high level exo controllers in terms of the robot-human system. Controllers on the left of the scale prioritize the robot part of the system, while the controllers to the right of the scale focus on the human part.

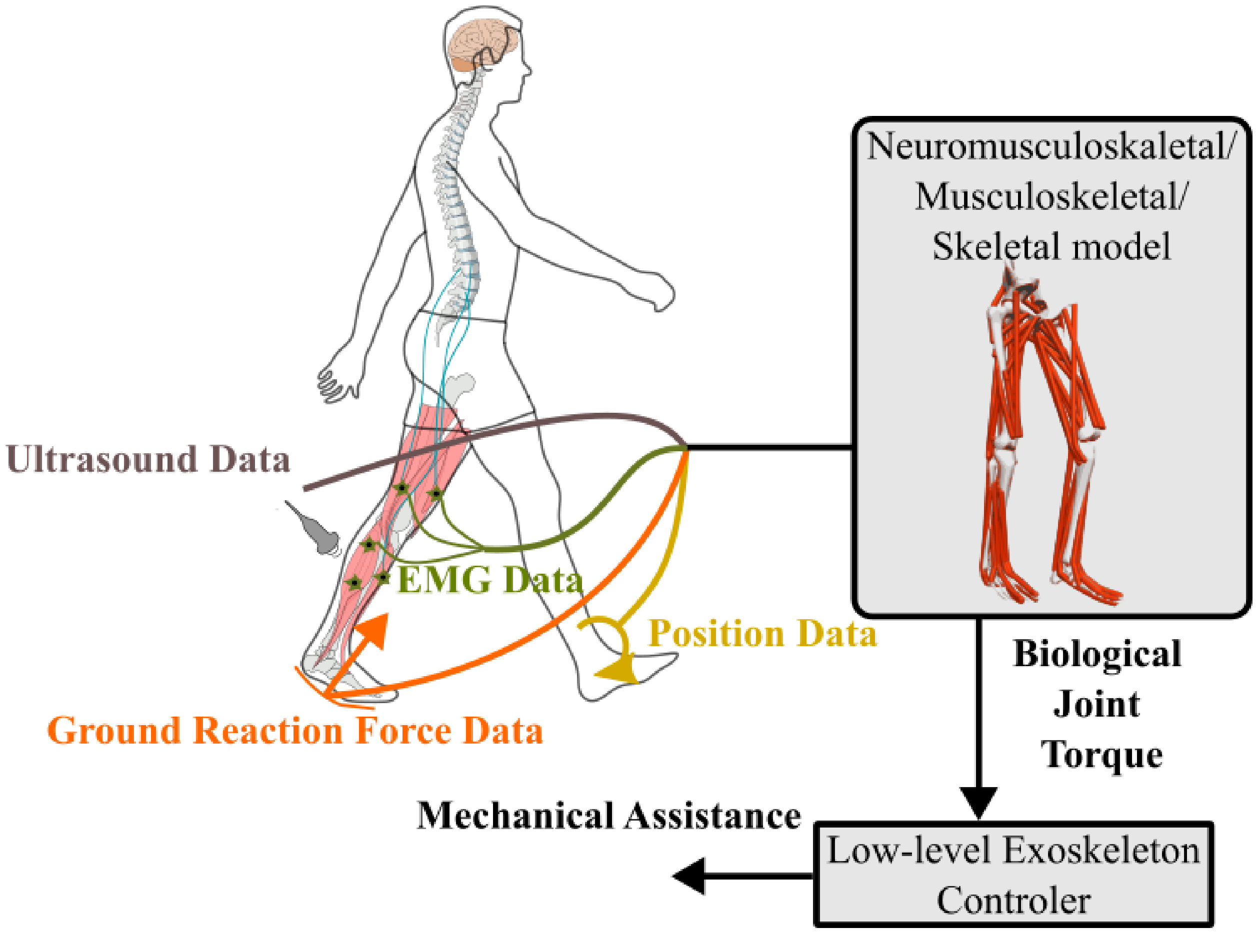

Figure 3. A general exoskeleton controller using a biomechanical model.

Tables

Table 1: Summary of changes to muscle-tendon biomechanics when participants wore an ankle exoskeleton.

Actuation Type	Task	Muscle/Tendon(s)	Condition varied	Changes to muscle biomechanics
Passive	Hopping	Plantar flexors	Ankle joint stiffness	Decreased activity, force, and force rate[134,196,197] Operating at less optimal fibre length and increased fibre velocity[134,198] Increased fascicle excursion, and overall no change in averaged positive fascicle power[134]
Active	Walking	*soleus*	Ankle joint Stiffness	Reduced muscle force, increased fascicle length and velocity [136]
		Plantar flexors	Inclination of walking surface	Increase in inclination results in lower reductions in muscle activity[199]
		Plantar flexors	Exoskeleton work	Increasing work reduced activity, and increased muscle synergy weights[200]
		soleus	Exoskeleton torque	Increasing torque reduced activity, and increased muscle synergy activations[200]
		Plantar flexors	Adaptation to walking with exoskeleton	Decreased activity[201]
		soleus	Controller type	Gait timing controllers are better than myoelectric controller proportional to *soleus* activity[202] myoelectric controller proportional to *gastrocnemius medialis* reduces *soleus* activity[203]
		-	Speed, step length, and walking incline	Increased apparent efficacy with increasing speed or step length[204] and drops when the surface incline increases[199]
	Walking with load	*Achilles* tendon	With and without exo, carrying additional load	Increase in tendon force with increase in load carried, but reduced with exo assistance[139]
	Walking in participants with chronic stroke	Bilateral *latissimus dorsi, erector spinae, external oblique,* hip flexors and extensors, knee flexors and extensors, plantar flexors and dorsiflexors.	With and without exo	Improved similarity of synergies in either side[205]

References

1. Young AJ, Ferris DP. State of the art and future directions for lower limb robotic exoskeletons. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. 2017;25(2):171-182. doi:10.1109/TNSRE.2016.2521160
2. MacLean MK, Ferris DP. Effects of simulated reduced gravity and walking speed on ankle, knee, and hip quasi-stiffness in overground walking. *PLoS One*. 2022;17(8):e0271927. doi:10.1371/journal.pone.0271927
3. Shamaei K, Sawicki GS, Dollar AM. Estimation of Quasi-Stiffness and Propulsive Work of the Human Ankle in the Stance Phase of Walking. Awad HA, ed. *PLoS One*. 2013;8(3):e59935. doi:10.1371/journal.pone.0059935
4. Rouse EJ, Gregg RD, Hargrove LJ, Sensinger JW. The difference between stiffness and quasi-stiffness in the context of biomechanical modeling. *IEEE Trans Biomed Eng*. 2013;60(2):562-568. doi:10.1109/TBME.2012.2230261
5. Cop CP, Cavallo G, van 't Veld RC, et al. Unifying system identification and biomechanical formulations for the estimation of muscle, tendon and joint stiffness during human movement. *Progress in Biomedical Engineering*. 2021;3(3):033002. doi:10.1088/2516-1091/ac12c4
6. Cop CP, Schouten AC, Koopman B, Sartori M. Electromyography-driven model-based estimation of ankle torque and stiffness during dynamic joint rotations in perturbed and unperturbed conditions. *J Biomech*. 2022;145:111383. doi:10.1016/j.jbiomech.2022.111383

7. Farris DJ, Sawicki GS. The mechanics and energetics of human walking and running: a joint level perspective. *J R Soc Interface*. 2012;9(66):110-118. doi:10.1098/RSIF.2011.0182

8. Zelik KE, Takahashi KZ, Sawicki GS. Six degree-of-freedom analysis of hip, knee, ankle and foot provides updated understanding of biomechanical work during human walking. *Journal of Experimental Biology*. 2015;218(6):876-886. doi:10.1242/jeb.115451

9. Montgomery JR, Grabowski AM. The contributions of ankle, knee and hip joint work to individual leg work change during uphill and downhill walking over a range of speeds. *R Soc Open Sci*. 2018;5(8). doi:10.1098/RSOS.180550

10. Kirtley C, Whittle MW, Jefferson RJ. Influence of walking speed on gait parameters. *J Biomed Eng*. 1985;7(4):282-288. doi:10.1016/0141-5425(85)90055-X

11. Voloshina AS, Kuo AD, Daley MA, Ferris DP. Biomechanics and energetics of walking on uneven terrain. *J Exp Biol*. 2013;216(Pt 21):3963-3970. doi:10.1242/jeb.081711

12. Schache AG, Brown NAT, Pandy MG. Modulation of work and power by the human lower-limb joints with increasing steady-state locomotion speed. *J Exp Biol*. 2015;218(Pt 15):2472-2481. doi:10.1242/jeb.119156

13. Zajac FE. Muscle coordination of movement: A perspective. *J Biomech*. 1993;26(SUPPL. 1):109-124. doi:10.1016/0021-9290(93)90083-Q

14. Alcazar J, Csapo R, Ara I, Alegre LM. On the shape of the force-velocity relationship in skeletal muscles: The linear, the hyperbolic, and the double-hyperbolic. *Front Physiol*. 2019;10:769. doi:10.3389/fphys.2019.00769

15. Sawicki GS, Beck ON, Kang I, Young AJ. The exoskeleton expansion: Improving walking and running economy. *J Neuroeng Rehabil*. 2020;17(1):1-9. doi:10.1186/S12984-020-00663-9/TABLES/1

16. Peetrons P. Ultrasound of muscles. *Eur Radiol*. 2002;12(1):35-43. doi:10.1007/S00330-001-1164-6/METRICS

17. Pillen S, van Alfen N. Skeletal muscle ultrasound. *Neurol Res*. 2013;33(10):1016-1024. doi:10.1179/1743132811Y.0000000010

18. Walker FO, Cartwright MS, Wiesler ER, Caress J. Ultrasound of nerve and muscle. *Clinical Neurophysiology*. 2004;115(3):495-507. doi:10.1016/J.CLINPH.2003.10.022

19. Hodson-Tole EF, Lai AKM. Ultrasound-derived changes in thickness of human ankle plantar flexor muscles during walking and running are not homogeneous along the muscle mid-belly region. *Scientific Reports 2019 9:1*. 2019;9(1):1-11. doi:10.1038/s41598-019-51510-4

20. Fukunaga T, Kubo K, Kawakami Y, Fukashiro S, Kanehisa H, Maganaris CN. In vivo behaviour of human muscle tendon during walking. *Proc R Soc Lond B Biol Sci*. 2001;268(1464):229-233. doi:10.1098/RSPB.2000.1361

21. Lai A, Lichtwark GA, Schache AG, Lin YC, Brown NAT, Pandy MG. In vivo behavior of the human soleus muscle with increasing walking and running speeds. *J Appl Physiol*. 2015;118(10):1266-1275. doi:10.1152/JAPPLPHYSIOL.00128.2015/ASSET/IMAGES/LARGE/ZDG9991514290006.JPEG

22. Dai C, Hu X. Independent component analysis based algorithms for high-density electromyogram decomposition: Systematic evaluation through simulation. *Comput Biol Med*. 2019;109:171-181. doi:10.1016/J.COMPBIOMED.2019.04.033

23. Schlink BR, Nordin AD, Ferris DP. Comparison of Signal Processing Methods for Reducing Motion Artifacts in High-Density Electromyography During Human Locomotion. *IEEE Open J Eng Med Biol*. 2020;1:156-165. doi:10.1109/OJEMB.2020.2999782

24. Sartori M, Yavuz UŞ, Farina D. In Vivo Neuromechanics: Decoding Causal Motor Neuron Behavior with Resulting Musculoskeletal Function. *Sci Rep*. 2017;7(1):13465. doi:10.1038/s41598-017-13766-6

25. De Groote F, Falisse A. Perspective on musculoskeletal modelling and predictive simulations of human movement to assess the neuromechanics of gait. *Proceedings of the Royal Society B: Biological Sciences*. 2021;288(1946):20202432. doi:10.1098/rspb.2020.2432

26. Pizzolato C, Lloyd DG, Sartori M, et al. CEINMS: A toolbox to investigate the influence of different neural control solutions on the prediction of muscle excitation and joint moments during dynamic motor tasks. *J Biomech*. 2015;48(14):3929-3936. doi:10.1016/j.jbiomech.2015.09.021

27. Dembia CL, Bianco NA, Falisse A, Hicks JL, Delp SL. OpenSim Moco: Musculoskeletal optimal control. *PLoS Comput Biol*. 2020;16(12):e1008493. doi:10.1371/journal.pcbi.1008493

28. Geijtenbeek T. SCONE: Open Source Software for Predictive Simulation of Biological Motion. *J Open Source Softw*. 2019;4(38):1421. doi:10.21105/joss.01421

29. Caggiano V, Wang H, Durandau G, Sartori M, Kumar V. MyoSuite -- A contact-rich simulation suite for musculoskeletal motor control. May 2022. https://arxiv.org/abs/2205.13600v1. Accessed August 8, 2023.

30. Wang H, Caggiano V, Durandau G, Sartori M, Kumar V. MyoSim: Fast and physiologically realistic MuJoCo models for musculoskeletal and exoskeletal studies. *Proc IEEE Int Conf Robot Autom*. 2022:8104-8111. doi:10.1109/ICRA46639.2022.9811684

31. Anam K, Al-Jumaily AA. Active Exoskeleton Control Systems: State of the Art. *Procedia Eng*. 2012;41:988-994. doi:10.1016/J.PROENG.2012.07.273

32. Chen G, Chan CK, Guo Z, Yu H. A Review of Lower Extremity Assistive Robotic Exoskeletons in Rehabilitation Therapy. *Critical Reviews™ in Biomedical Engineering*. 2013;41(4-5):343-363. doi:10.1615/CRITREVBIOMEDENG.2014010453

33. Ma Y, Wu X, Yi J, Wang C, Chen C. A Review On Human-Exoskeleton Coordination Towards Lower Limb Robotic Exoskeleton Systems. *International Journal of Robotics and Automation*. 2019;34(4). doi:10.2316/J.2019.206-0193

34. Kwa HK, Noorden JH, Missel M, Craig T, Pratt JE, Neuhaus PD. Development of the IHMC mobility assist exoskeleton. *Proc IEEE Int Conf Robot Autom*. 2009:2556-2562. doi:10.1109/ROBOT.2009.5152394

35. Zhang J, Cheah CC, Collins SH. Experimental comparison of torque control methods on an ankle exoskeleton during human walking. *Proc IEEE Int Conf Robot Autom*. 2015;2015-June(June):5584-5589. doi:10.1109/ICRA.2015.7139980

36. Witte KA, Zhang J, Jackson RW, Collins SH. Design of two lightweight, high-bandwidth torque-controlled ankle exoskeletons. *Proc IEEE Int Conf Robot Autom*. 2015;2015-June(June):1223-1228. doi:10.1109/ICRA.2015.7139347

37. Anam K, Al-Jumaily AA. Active Exoskeleton Control Systems: State of the Art. *Procedia Eng*. 2012;41:988-994. doi:10.1016/J.PROENG.2012.07.273

38. Aguirre-Ollinger G, Colgate JE, Peshkin MA, Goswami A. Active-impedance control of a lower-limb assistive exoskeleton. *2007 IEEE 10th International Conference on Rehabilitation Robotics, ICORR'07*. 2007:188-195. doi:10.1109/ICORR.2007.4428426

39. Veneman JF, Kruidhof R, Hekman EEG, Ekkelenkamp R, Van Asseldonk EHF, Van Der Kooij H. Design and evaluation of the LOPES exoskeleton robot for interactive gait rehabilitation. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. 2007;15(3):379-386. doi:10.1109/TNSRE.2007.903919

40. Maggioni S, Reinert N, Lünenburger L, Melendez-Calderon A. An adaptive and hybrid end-point/joint impedance controller for lower limb exoskeletons. *Frontiers Robotics AI*. 2018;5(OCT):379651. doi:10.3389/FROBT.2018.00104/BIBTEX

41. Ferris DP, Lewis CL. Robotic lower limb exoskeletons using proportional myoelectric control. In: *Proceedings of the 31st Annual International Conference of the IEEE Engineering in Medicine and Biology Society: Engineering the Future of Biomedicine, EMBC 2009*. Vol 2009. IEEE Computer Society; 2009:2119-2124. doi:10.1109/IEMBS.2009.5333984

42. Koller JR, Jacobs DA, Ferris DP, Remy CD. Learning to walk with an adaptive gain proportional myoelectric controller for a robotic ankle exoskeleton. *J Neuroeng Rehabil*. 2015;12(1):1-14. doi:10.1186/S12984-015-0086-5/FIGURES/8

43. Hybart RL, Ferris DP. Neuromechanical Adaptation to Walking with Electromechanical Ankle Exoskeletons Under Proportional Myoelectric Control. *IEEE Open J Eng Med Biol*. 2023:1-11. doi:10.1109/OJEMB.2023.3288469

44. Xu L, Liu X, Chen Y, et al. Reducing the muscle activity of walking using a portable hip exoskeleton based on human-in-the-loop optimization. *Front Bioeng Biotechnol*. 2023;11:1006326. doi:10.3389/FBIOE.2023.1006326/BIBTEX

45. Diaz MA, Voss M, Dillen A, et al. Human-in-the-Loop Optimization of Wearable Robotic Devices to Improve Human-Robot Interaction: A Systematic Review. *IEEE Trans Cybern*. 2022. doi:10.1109/TCYB.2022.3224895

46. Zhang J, Fiers P, Witte KA, et al. Human-in-the-loop optimization of exoskeleton assistance during walking. *Science (1979)*. 2017;356(6344):1280-1284. doi:10.1126/science.aal5054

47. Klute GK, Czerniecki JM, Hannaford B. McKibben artificial muscles: Pneumatic actuators with biomechanical intelligence. *IEEE/ASME International Conference on Advanced Intelligent Mechatronics, AIM*. 1999:221-226. doi:10.1109/AIM.1999.803170

48. Dollar AM, Herr H. Lower extremity exoskeletons and active orthoses: Challenges and state-of-the-art. *IEEE Transactions on Robotics*. 2008;24(1):144-158. doi:10.1109/TRO.2008.915453

49. Zoss AB, Kazerooni H, Chu A. Biomechanical design of the Berkeley lower extremity exoskeleton (BLEEX). *IEEE/ASME Transactions on Mechatronics*. 2006;11(2):128-138. doi:10.1109/TMECH.2006.871087

50. Wehner M, Quinlivan B, Aubin PM, et al. A lightweight soft exosuit for gait assistance. *Proc IEEE Int Conf Robot Autom*. 2013:3362-3369. doi:10.1109/ICRA.2013.6631046

51. Zhang JF, Yang CJ, Chen Y, Zhang Y, Dong YM. Modeling and control of a curved pneumatic muscle actuator for wearable elbow exoskeleton. *Mechatronics*. 2008;18(8):448-457. doi:10.1016/J.MECHATRONICS.2008.02.006

52. Slade P, Kochenderfer MJ, Delp SL, Collins SH. Personalizing exoskeleton assistance while walking in the real world. *Nature*. 2022;610(7931):277-282. doi:10.1038/s41586-022-05191-1

53. Etenzi E, Borzuola R, Grabowski AM. Passive-elastic knee-ankle exoskeleton reduces the metabolic cost of walking. *J Neuroeng Rehabil*. 2020;17(1):1-15. doi:10.1186/S12984-020-00719-W/FIGURES/7

54. Asbeck AT, De Rossi SMM, Holt KG, Walsh CJ. A biologically inspired soft exosuit for walking assistance. *Int J Rob Res*. 2015;34(6):744-762. doi:10.1177/0278364914562476

55. Chen L, Chen C, Wang Z, Ye X, Liu Y, Wu X. A Novel Lightweight Wearable Soft Exosuit for Reducing the Metabolic Rate and Muscle Fatigue. *Biosensors 2021, Vol 11, Page 215*. 2021;11(7):215. doi:10.3390/BIOS11070215

56. Llewellyn ME, Barretto RPJ, Delp SL, Schnitzer MJ. Minimally invasive high-speed imaging of sarcomere contractile dynamics in mice and humans. *Nature*. 2008;454(7205):784-788. doi:10.1038/nature07104

57. Sanchez GN, Sinha S, Liske H, et al. In Vivo Imaging of Human Sarcomere Twitch Dynamics in Individual Motor Units. *Neuron*. 2015;88(6):1109-1120. doi:10.1016/j.neuron.2015.11.022

58. Cromie MJ, Sanchez GN, Schnitzer MJ, Delp SL. Sarcomere lengths in human extensor carpi radialis brevis measured by microendoscopy. *Muscle Nerve*. 2013;48(2):286-292. doi:10.1002/mus.23760

59. Chen X, Sanchez GN, Schnitzer MJ, Delp SL. Changes in sarcomere lengths of the human vastus lateralis muscle with knee flexion measured using in vivo microendoscopy. *J Biomech*. 2016;49(13):2989-2994. doi:10.1016/j.jbiomech.2016.07.013

60. Chen X, Delp SL. Human soleus sarcomere lengths measured using in vivo microendoscopy at two ankle flexion angles. *J Biomech*. 2016;49(16):4164-4167. doi:10.1016/j.jbiomech.2016.11.010

61. Lichtwark GA, Farris DJ, Chen X, Hodges PW, Delp SL. Microendoscopy reveals positive correlation in multiscale length changes and variable sarcomere lengths across different regions of human muscle. *J Appl Physiol*. 2018;125(6):1812-1820. doi:10.1152/japplphysiol.00480.2018

62. Pincheira PA, Boswell MA, Franchi M V., Delp SL, Lichtwark GA. Biceps femoris long head sarcomere and fascicle length adaptations after 3 weeks of eccentric exercise training. *J Sport Health Sci*. 2022;11(1):43-49. doi:10.1016/j.jshs.2021.09.002

63. Fukunaga T, Ichinose Y, Ito M, Kawakami Y, Fukashiro S. Determination of fascicle length and pennation in a contracting human muscle in vivo. *J Appl Physiol*. 1997;82(1):354-358. doi:10.1152/jappl.1997.82.1.354

64. Barber L, Barrett R, Lichtwark G. Validation of a freehand 3D ultrasound system for morphological measures of the medial gastrocnemius muscle. *J Biomech*. 2009;42(9):1313-1319. doi:10.1016/j.jbiomech.2009.03.005

65. Farris DJ, Trewartha G, McGuigan MP, Lichtwark GA. Differential strain patterns of the human Achilles tendon determined in vivo with freehand three-dimensional ultrasound imaging. *J Exp Biol*. 2013;216(Pt 4):594-600. doi:10.1242/jeb.077131

66. Farris DJ, Sawicki GS. Human medial gastrocnemius force–velocity behavior shifts with locomotion speed and gait. *Proceedings of the National Academy of Sciences*. 2012;109(3):977-982. doi:10.1073/pnas.1107972109

67. Cronin NJ, Carty CP, Barrett RS, Lichtwark G. Automatic tracking of medial gastrocnemius fascicle length during human locomotion. *J Appl Physiol*. 2011;111(5):1491-1496. doi:10.1152/japplphysiol.00530.2011

68. Gillett JG, Barrett RS, Lichtwark GA. Reliability and accuracy of an automated tracking algorithm to measure controlled passive and active muscle fascicle length changes from ultrasound. *Comput Methods Biomech Biomed Engin*. 2013;16(6):678-687. doi:10.1080/10255842.2011.633516

69. Farris DJ, Lichtwark GA. UltraTrack: Software for semi-automated tracking of muscle fascicles in sequences of B-mode ultrasound images. *Comput Methods Programs Biomed*. 2016;128:111-118. doi:10.1016/j.cmpb.2016.02.016

70. Nuckols RW, Swaminathan K, Lee S, Awad L, Walsh CJ, Howe RD. Automated detection of soleus concentric contraction in variable gait conditions for improved exosuit control. In: *2020 IEEE International Conference on Robotics and Automation (ICRA)*. IEEE; 2020:4855-4862. doi:10.1109/ICRA40945.2020.9197428

71. Kim M, Ding Y, Malcolm P, et al. Human-in-the-loop Bayesian optimization of wearable device parameters. *PLoS One*. 2017;12(9):e0184054. doi:10.1371/JOURNAL.PONE.0184054

72. Jahanandish MH, Fey NP, Hoyt K. Lower Limb Motion Estimation Using Ultrasound Imaging: A Framework for Assistive Device Control. *IEEE J Biomed Health Inform*. 2019;23(6):2505-2514. doi:10.1109/JBHI.2019.2891997

73. Zhang Q, Clark WH, Franz JR, Sharma N. Personalized fusion of ultrasound and electromyography-derived neuromuscular features increases prediction accuracy of ankle

moment during plantarflexion. *Biomed Signal Process Control*. 2022;71:103100. doi:10.1016/j.bspc.2021.103100

74. Zhang Q, Kim K, Sharma N. Prediction of Ankle Dorsiflexion Moment by Combined Ultrasound Sonography and Electromyography. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. 2020;28(1):318-327. doi:10.1109/TNSRE.2019.2953588

75. Yan J, Yang X, Zeng J, Liu H. Acoustic Nonlinearity Parameter Estimation for Exoskeleton Control. *IEEE Trans Med Robot Bionics*. 2021;3(4):1002-1010. doi:10.1109/TMRB.2021.3121570

76. Martin JA, Brandon SCE, Keuler EM, et al. Gauging force by tapping tendons. *Nat Commun*. 2018;9(1). doi:10.1038/s41467-018-03797-6

77. Martin JA, Brandon SCE, Keuler EM, et al. Gauging force by tapping tendons. *Nat Commun*. 2018;9(1):1592. doi:10.1038/s41467-018-03797-6

78. Acuña SA, Ebrahimi A, Pomeroy RL, Martin JA, Thelen DG. Achilles tendon shear wave speed tracks the dynamic modulation of standing balance. *Physiol Rep*. 2019;7(23). doi:10.14814/phy2.14298

79. Ebrahimi A, Martin JA, Schmitz DG, Thelen DG. Shear Wave Tensiometry Reveals an Age-Related Deficit in Triceps Surae Work at Slow and Fast Walking Speeds. *Front Sports Act Living*. 2020;2. doi:10.3389/fspor.2020.00069

80. Ebrahimi A, Loegering IF, Martin JA, Pomeroy RL, Roth JD, Thelen DG. Achilles tendon loading is lower in older adults than young adults across a broad range of walking speeds. *Exp Gerontol*. 2020;137:110966. doi:10.1016/j.exger.2020.110966

81. Ebrahimi A, Kuchler RL, Pomeroy RL, Loegering IF, Martin JA, Thelen DG. Normative Achilles and patellar tendon shear wave speeds and loading patterns during walking in

typically developing children. *Gait Posture*. 2021;88:185-191. doi:10.1016/j.gaitpost.2021.05.023

82. Ebrahimi A, Schwartz MH, Martin JA, Novacheck TF, Thelen DG. Atypical triceps surae force and work patterns underlying gait in children with cerebral palsy. *Journal of Orthopaedic Research*. 2022;40(12):2763-2770. doi:10.1002/jor.25307

83. Schmitz DG, Thelen DG, Cone SG. A Kalman Filter Approach for Estimating Tendon Wave Speed from Skin-Mounted Accelerometers. *Sensors*. 2022;22(6):2283. doi:10.3390/s22062283

84. Harper SE, Roembke RA, Zunker JD, Thelen DG, Adamczyk PG. Wearable Tendon Kinetics. *Sensors*. 2020;20(17):4805. doi:10.3390/s20174805

85. Harper SE, Schmitz DG, Adamczyk PG, Thelen DG. Fusion of Wearable Kinetic and Kinematic Sensors to Estimate Triceps Surae Work during Outdoor Locomotion on Slopes. *Sensors*. 2022;22(4):1589. doi:10.3390/s22041589

86. Schneebeli A, Falla D, Cescon C, Barbero M. Measurement of Achilles tendon loading using shear wave tensiometry: A reliability study. *Musculoskelet Sci Pract*. 2022;62:102665. doi:10.1016/j.msksp.2022.102665

87. 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. *Journal of Electromyography and Kinesiology*. 2022;67:102701. doi:10.1016/j.jelekin.2022.102701

88. Sartori M, Sawicki G. Closing the loop between wearable technology and human biology: A new paradigm for steering neuromuscular form and function. *Progress in Biomedical Engineering*. 2021;3(2). doi:10.1088/2516-1091/abe3e0

89. Schlink BR, Nordin AD, Ferris DP. Human myoelectric spatial patterns differ among lower limb muscles and locomotion speeds. *Physiol Rep*. 2020;8(23). doi:10.14814/phy2.14652

90. Schlink BR, Nordin AD, Brooks CN, Ferris DP. Fatigue induces altered spatial myoelectric activation patterns in the medial gastrocnemius during locomotion. *J Neurophysiol*. 2021;125(5):2013-2023. doi:10.1152/jn.00602.2020

91. Xiao ZG, Menon C. A Review of Force Myography Research and Development. *Sensors*. 2019;19(20):4557. doi:10.3390/s19204557

92. Zahid M, Zych A, Dussoni S, et al. Wearable and self-healable textile-based strain sensors to monitor human muscular activities. *Compos B Eng*. 2021;220:108969. doi:10.1016/j.compositesb.2021.108969

93. Islam MRU, Bai S. Payload estimation using forcemyography sensors for control of upper-body exoskeleton in load carrying assistance. *Modeling, Identification and Control: A Norwegian Research Bulletin*. 2019;40(4):189-198. doi:10.4173/mic.2019.4.1

94. Alvarez JT, Gerez LF, Araromi OA, et al. Towards Soft Wearable Strain Sensors for Muscle Activity Monitoring. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. 2022;30:2198-2206. doi:10.1109/TNSRE.2022.3196501

95. Dwivedi A, Gerez L, Hasan W, Yang CH, Liarokapis M. A Soft Exoglove Equipped With a Wearable Muscle-Machine Interface Based on Forcemyography and Electromyography. *IEEE Robot Autom Lett*. 2019;4(4):3240-3246. doi:10.1109/LRA.2019.2925302

96. Julio Fajardo, Antonio Ribas Neto, Willian Silva, Matheus Gomes, Eric Fujiwara, Eric Rohmer. A Wearable Robotic Glove based on Optical FMG Driven Controller. In: *2019 IEEE 4th International Conference on AdvancedRobotics and Mechatronics (ICARM)*. ; 2019:81-86.

97. Islam MRU, Bai S. Effective Multi-Mode Grasping Assistance Control of a Soft Hand Exoskeleton Using Force Myography. *Front Robot AI*. 2020;7. doi:10.3389/frobt.2020.567491

98. Ribas Neto A, Fajardo J, da Silva WHA, et al. Design of Tendon-Actuated Robotic Glove Integrated with Optical Fiber Force Myography Sensor. *Automation*. 2021;2(3):187-201. doi:10.3390/automation2030012

99. Song X, van de Ven SS, Chen S, et al. Proposal of a Wearable Multimodal Sensing-Based Serious Games Approach for Hand Movement Training After Stroke. *Front Physiol*. 2022;13. doi:10.3389/fphys.2022.811950

100. Jiang X, Chu K, Khoshnam M, Menon C. A Wearable Gait Phase Detection System Based on Force Myography Techniques. *Sensors*. 2018;18(4):1279. doi:10.3390/s18041279

101. Sartori M, Yavuz US, Farina D. In Vivo Neuromechanics: Decoding Causal Motor Neuron Behavior with Resulting Musculoskeletal Function. *Sci Rep*. 2017;7:13465. doi:10.1038/s41598-017-13766-6

102. Sartori M, Reggiani M, Farina D, Lloyd DG. EMG-Driven Forward-Dynamic Estimation of Muscle Force and Joint Moment about Multiple Degrees of Freedom in the Human Lower Extremity. Gribble PL, ed. *PLoS One*. 2012;7(12):e52618. doi:10.1371/journal.pone.0052618

103. Sartori M, Farina D, Lloyd DG. Hybrid neuromusculoskeletal modeling to best track joint moments using a balance between muscle excitations derived from electromyograms and optimization. *J Biomech*. 2014;47(15):3613-3621. doi:10.1016/j.jbiomech.2014.10.009

104. Moya-Esteban A, van der Kooij H, Sartori M. Robust estimation of lumbar joint forces in symmetric and asymmetric lifting tasks via large-scale electromyography-driven

musculoskeletal models. *J Biomech*. 2022;144:111307. doi:10.1016/j.jbiomech.2022.111307

105. Durandau G, Farina D, Asín-Prieto G, et al. Voluntary control of wearable robotic exoskeletons by patients with paresis via neuromechanical modeling. *J Neuroeng Rehabil*. 2019;16(1):91. doi:10.1186/s12984-019-0559-z

106. Durandau G, Rampeltshammer WF, Kooij H van der, Sartori M. Neuromechanical Model-Based Adaptive Control of Bilateral Ankle Exoskeletons: Biological Joint Torque and Electromyogram Reduction Across Walking Conditions. *IEEE Transactions on Robotics*. 2022;38(3):1380-1394. doi:10.1109/TRO.2022.3170239

107. Lotti N, Xiloyannis M, Durandau G, et al. Adaptive Model-Based Myoelectric Control for a Soft Wearable Arm Exosuit: A New Generation of Wearable Robot Control. *IEEE Robot Autom Mag*. 2020;27(1):43-53. doi:10.1109/MRA.2019.2955669

108. Shah C, Fleming A, Nalam V, Liu M, Huang HH. Design of EMG-driven Musculoskeletal Model for Volitional Control of a Robotic Ankle Prosthesis. *IEEE International Conference on Intelligent Robots and Systems*. 2022;2022-October:12261-12266. doi:10.1109/IROS47612.2022.9981305

109. Pizzolato C, Reggiani M, Saxby DJ, Ceseracciu E, Modenese L, Lloyd DG. Biofeedback for Gait Retraining Based on Real-Time Estimation of Tibiofemoral Joint Contact Forces. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. 2017;25(9):1612-1621. doi:10.1109/TNSRE.2017.2683488

110. Delp SL, Anderson FC, Arnold AS, et al. OpenSim: Open-Source Software to Create and Analyze Dynamic Simulations of Movement. *IEEE Trans Biomed Eng*. 2007;54(11):1940-1950. doi:10.1109/TBME.2007.901024

111. Crowninshield RD, Brand RA. A physiologically based criterion of muscle force prediction in locomotion. *J Biomech*. 1981;14(11):793-801. doi:10.1016/0021-9290(81)90035-X

112. Happee R. Inverse dynamic optimization including muscular dynamics, a new simulation method applied to goal directed movements. *J Biomech*. 1994;27(7):953-960. doi:10.1016/0021-9290(94)90267-4

113. Tsirakos D, Baltzopoulos V, Bartlett R. Inverse Optimization: Functional and Physiological Considerations Related to the Force-Sharing Problem. *Crit Rev Biomed Eng*. 1997;25(4-5):371-407. doi:10.1615/CritRevBiomedEng.v25.i4-5.20

114. Erdemir A, McLean S, Herzog W, van den Bogert AJ. Model-based estimation of muscle forces exerted during movements. *Clinical Biomechanics*. 2007;22(2):131-154. doi:10.1016/j.clinbiomech.2006.09.005

115. van den Bogert AJ, Geijtenbeek T, Even-Zohar O, Steenbrink F, Hardin EC. A real-time system for biomechanical analysis of human movement and muscle function. *Med Biol Eng Comput*. 2013;51(10):1069-1077. doi:10.1007/s11517-013-1076-z

116. Stanev D, Filip K, Bitzas D, et al. Real-Time Musculoskeletal Kinematics and Dynamics Analysis Using Marker- and IMU-Based Solutions in Rehabilitation. *Sensors*. 2021;21(5):1804. doi:10.3390/s21051804

117. Ackermann M, van den Bogert AJ. Optimality principles for model-based prediction of human gait. *J Biomech*. 2010;43(6):1055-1060. doi:10.1016/j.jbiomech.2009.12.012

118. Lloyd DG, Besier TF. An EMG-driven musculoskeletal model to estimate muscle forces and knee joint moments in vivo. *J Biomech*. 2003;36(6):765-776. doi:10.1016/S0021-9290(03)00010-1

119. Buchanan TS, Lloyd DG, Manal K, Besier TF. Neuromusculoskeletal Modeling: Estimation of Muscle Forces and Joint Moments and Movements from Measurements of Neural Command. *J Appl Biomech*. 2004;20(4):367-395. doi:10.1123/jab.20.4.367

120. Sartori M, Lloyd DG, Reggiani M, Pagello E. Fast operation of anatomical and stiff tendon neuromuscular models in EMG-driven modeling. In: *2010 IEEE International Conference on Robotics and Automation*. IEEE; 2010:2228-2234. doi:10.1109/ROBOT.2010.5509932

121. Sartori M, Reggiani M, Lloyd D. An EMG-driven Musculoskeletal Model of the Human Lower Limb for the Estimation of Muscle Forces and Moments at the Hip, Knee and Ankle Joints in vivo. In: *Simulation and Programming for Autonomous Robots (SIMPAR)*. ; 2010:137-146. https://simtk.org/home/nmblmodels/. Accessed October 24, 2022.

122. Durandau G, Farina D, Sartori M. Robust Real-Time Musculoskeletal Modeling Driven by Electromyograms. *IEEE Trans Biomed Eng*. 2018;65(3):556-564. doi:10.1109/TBME.2017.2704085

123. Sartori M, Maculan M, Pizzolato C, Reggiani M, Farina D. Modeling and simulating the neuromuscular mechanisms regulating ankle and knee joint stiffness during human locomotion. *J Neurophysiol*. 2015;114(4):2509-2527. doi:10.1152/jn.00989.2014

124. Cop CP, Durandau G, Esteban AM, van 't Veld RC, Schouten AC, Sartori M. Model-Based Estimation of Ankle Joint Stiffness During Dynamic Tasks: a Validation-Based Approach. In: *2019 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*. IEEE; 2019:4104-4107. doi:10.1109/EMBC.2019.8857391

125. van Dieën JH, Kingma I. Total trunk muscle force and spinal compression are lower in asymmetric moments as compared to pure extension moments. *J Biomech*. 1999;32(7):681-687. doi:10.1016/S0021-9290(99)00044-5

126. Bazrgari B, Shirazi-Adl A, Arjmand N. Analysis of squat and stoop dynamic liftings: muscle forces and internal spinal loads. *European Spine Journal*. 2007;16(5):687-699. doi:10.1007/s00586-006-0240-7

127. Kim HK, Zhang Y. Estimation of lumbar spinal loading and trunk muscle forces during asymmetric lifting tasks: application of whole-body musculoskeletal modelling in OpenSim. *Ergonomics*. 2017;60(4):563-576. doi:10.1080/00140139.2016.1191679

128. Stanev D, Moustakas K. Stiffness modulation of redundant musculoskeletal systems. *J Biomech*. 2019;85:101-107. doi:10.1016/j.jbiomech.2019.01.017

129. von Arx M, Liechti M, Connolly L, Bangerter C, Meier ML, Schmid S. From Stoop to Squat: A Comprehensive Analysis of Lumbar Loading Among Different Lifting Styles. *Front Bioeng Biotechnol*. 2021;9. doi:10.3389/fbioe.2021.769117

130. Prilutsky BI, Herzog W, Allinger TL. Forces of individual cat ankle extensor muscles during locomotion predicted using static optimization. *J Biomech*. 1997;30(10):1025-1033. doi:10.1016/S0021-9290(97)00068-7

131. Karabulut D, Dogru SC, Lin YC, Pandy MG, Herzog W, Arslan YZ. Direct Validation of Model-Predicted Muscle Forces in the Cat Hindlimb During Locomotion. *J Biomech Eng*. 2020;142(5). doi:10.1115/1.4045660

132. Kaya M, Leonard T, Herzog W. Coordination of medial gastrocnemius and soleus forces during cat locomotion. *Journal of Experimental Biology*. 2003;206(20):3645-3655. doi:10.1242/jeb.00544

133. Herzog W, Leonard TR, Guimaraes ACS. Forces in gastrocnemius, soleus, and plantaris tendons of the freely moving cat. *J Biomech*. 1993;26(8):945-953. doi:10.1016/0021-9290(93)90056-K

134. Farris DJ, Robertson BD, Sawicki GS. Elastic ankle exoskeletons reduce soleus muscle force but not work in human hopping. *J Appl Physiol*. 2013;115(5):579-585. doi:10.1152/japplphysiol.00253.2013

135. Takahashi KZ, Gross MT, van Werkhoven H, Piazza SJ, Sawicki GS. Adding Stiffness to the Foot Modulates Soleus Force-Velocity Behaviour during Human Walking. *Sci Rep*. 2016;6(1):29870. doi:10.1038/srep29870

136. Nuckols RW, Dick TJM, Beck ON, Sawicki GS. Ultrasound imaging links soleus muscle neuromechanics and energetics during human walking with elastic ankle exoskeletons. *Sci Rep*. 2020;10(1):3604. doi:10.1038/s41598-020-60360-4

137. Beck ON, Shepherd MK, Rastogi R, Martino G, Ting LH, Sawicki GS. Exoskeletons need to react faster than physiological responses to improve standing balance. *Sci Robot*. 2023;8(75). doi:10.1126/scirobotics.adf1080

138. Nuckols RW, Lee S, Swaminathan K, Orzel D, Howe RD, Walsh CJ. Individualization of exosuit assistance based on measured muscle dynamics during versatile walking. *Sci Robot*. 2021;6(60). doi:10.1126/scirobotics.abj1362

139. Schmitz DG, Nuckols RW, Lee S, et al. Modulation of Achilles tendon force with load carriage and exosuit assistance. *Sci Robot*. 2022;7(71):eabq1514. doi:10.1126/scirobotics.abq1514

140. Fournier BN, Lemaire ED, Smith AJJ, Doumit M. Modeling and Simulation of a Lower Extremity Powered Exoskeleton. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. 2018;26(8):1596-1603. doi:10.1109/TNSRE.2018.2854605

141. Sreenivasa M, Millard M, Felis M, Mombaur K, Wolf SI. Optimal Control Based Stiffness Identification of an Ankle-Foot Orthosis Using a Predictive Walking Model. *Front Comput Neurosci*. 2017;11. doi:10.3389/fncom.2017.00023

142. Febrer-Nafría M, Fregly BJ, Font-Llagunes JM. Evaluation of Optimal Control Approaches for Predicting Active Knee-Ankle-Foot-Orthosis Motion for Individuals With Spinal Cord Injury. *Front Neurorobot*. 2022;15. doi:10.3389/fnbot.2021.748148

143. Afschrift M, De Groote F, De Schutter J, Jonkers I. The effect of muscle weakness on the capability gap during gross motor function: a simulation study supporting design criteria for exoskeletons of the lower limb. *Biomed Eng Online*. 2014;13(1):111. doi:10.1186/1475-925X-13-111

144. Uchida TK, Seth A, Pouya S, Dembia CL, Hicks JL, Delp SL. Simulating Ideal Assistive Devices to Reduce the Metabolic Cost of Running. Sandbakk Ø, ed. *PLoS One*. 2016;11(9):e0163417. doi:10.1371/journal.pone.0163417

145. Bianco NA, Franks PW, Hicks JL, Delp SL. Coupled exoskeleton assistance simplifies control and maintains metabolic benefits: A simulation study. Yakovenko S, ed. *PLoS One*. 2022;17(1):e0261318. doi:10.1371/journal.pone.0261318

146. 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: *2020 8th IEEE RAS/EMBS International Conference for Biomedical Robotics and Biomechatronics (BioRob)*. IEEE; 2020:700-707. doi:10.1109/BioRob49111.2020.9224345

147. Nguyen VQ, LaPre AK, Price MA, Umberger BR, Sup FC. Inclusion of actuator dynamics in simulations of assisted human movement. *Int J Numer Method Biomed Eng*. 2020;36(5):e3334. doi:10.1002/CNM.3334

148. Serrancoli G, Falisse A, Dembia C, et al. Subject-Exoskeleton Contact Model Calibration Leads to Accurate Interaction Force Predictions. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. 2019;27(8):1597-1605. doi:10.1109/TNSRE.2019.2924536
149. 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; 2022:8104-8111. doi:10.1109/ICRA46639.2022.9811684
150. Sheng Z, Iyer A, Sun Z, Kim K, Sharma N. A Hybrid Knee Exoskeleton Using Real-Time Ultrasound-Based Muscle Fatigue Assessment. *IEEE/ASME Transactions on Mechatronics*. 2022;27(4):1854-1862. doi:10.1109/TMECH.2022.3171086
151. Fleischer C, Hommel Gü. A Human--Exoskeleton Interface Utilizing Electromyography. *IEEE Transactions on Robotics*. 2008;24(4):872-882. doi:10.1109/TRO.2008.926860
152. Kim J, Lee G, Heimgartner R, et al. Reducing the metabolic rate of walking and running with a versatile, portable exosuit. *Science (1979)*. 2019;365(6454):668-672. doi:10.1126/science.aav7536
153. Yao S, Zhuang Y, Li Z, Song R. Adaptive Admittance Control for an Ankle Exoskeleton Using an EMG-Driven Musculoskeletal Model. *Front Neurorobot*. 2018;12. doi:10.3389/fnbot.2018.00016
154. Ruiz Garate V, Parri A, Yan T, et al. 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. doi:10.1109/MRA.2015.2510778

155. Garate VR, Parri A, Yan T, et al. Motor primitive-based control for lower-limb exoskeletons. In: *2016 6th IEEE International Conference on Biomedical Robotics and Biomechatronics (BioRob)*. Vol 2016-July. IEEE; 2016:655-661. doi:10.1109/BIOROB.2016.7523700

156. Ruiz Garate V, Parri A, Yan T, et al. Experimental Validation of Motor Primitive-Based Control for Leg Exoskeletons during Continuous Multi-Locomotion Tasks. *Front Neurorobot*. 2017;11(MAR):15. doi:10.3389/fnbot.2017.00015

157. Dzeladini F, Wu AR, Renjewski D, et al. Effects of a neuromuscular controller on a powered ankle exoskeleton during human walking. In: *2016 6th IEEE International Conference on Biomedical Robotics and Biomechatronics (BioRob)*. Vol 2016-July. IEEE; 2016:617-622. doi:10.1109/BIOROB.2016.7523694

158. Wu AR, Dzeladini F, Brug TJH, et al. An Adaptive Neuromuscular Controller for Assistive Lower-Limb Exoskeletons: A Preliminary Study on Subjects with Spinal Cord Injury. *Front Neurorobot*. 2017;11(JUN):30. doi:10.3389/fnbot.2017.00030

159. Wu AR. Human biomechanics perspective on robotics for gait assistance: challenges and potential solutions. *Proceedings of the Royal Society B: Biological Sciences*. 2021;288(1956):20211197. doi:10.1098/rspb.2021.1197

160. 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;9:210. doi:10.3389/fbioe.2021.615358

161. Knaepen K, Beyl P, Duerinck S, Hagman F, Lefeber D, Meeusen R. Human–Robot Interaction: Kinematics and Muscle Activity Inside a Powered Compliant Knee

Exoskeleton. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. 2014;22(6):1128-1137. doi:10.1109/TNSRE.2014.2324153

162. Thangavel P, Vidhya S, Li J, Chew E, Bezerianos A, Yu H. Biomechanical effects of robot assisted walking on knee joint kinematics and muscle activation pattern. In: *2017 International Conference on Rehabilitation Robotics (ICORR)*. IEEE; 2017:252-257. doi:10.1109/ICORR.2017.8009255

163. Malcolm P, Galle S, Derave W, De Clercq D. Bi-articular Knee-Ankle-Foot Exoskeleton Produces Higher Metabolic Cost Reduction than Weight-Matched Mono-articular Exoskeleton. *Front Neurosci*. 2018;12(March):1-14. doi:10.3389/fnins.2018.00069

164. Grazi L, Crea S, Parri A, Molino Lova R, Micera S, Vitiello N. Gastrocnemius Myoelectric Control of a Robotic Hip Exoskeleton Can Reduce the User’s Lower-Limb Muscle Activities at Push Off. *Front Neurosci*. 2018;12(FEB):1-11. doi:10.3389/fnins.2018.00071

165. Tagliamonte NL, Valentini S, Sudano A, et al. Switching Assistance for Exoskeletons During Cyclic Motions. *Front Neurorobot*. 2019;13(June). doi:10.3389/fnbot.2019.00041

166. Haufe FL, Kober AM, Wolf P, Riener R, Xiloyannis M. Learning to walk with a wearable robot in 880 simple steps: a pilot study on motor adaptation. *J Neuroeng Rehabil*. 2021;18(1):157. doi:10.1186/s12984-021-00946-9

167. Wang Z, Wu X, Zhang Y, et al. A Semi-active Exoskeleton Based on EMGs Reduces Muscle Fatigue When Squatting. *Front Neurorobot*. 2021;15(April):1-12. doi:10.3389/fnbot.2021.625479

168. Soma Y, Mutsuzaki H, Yoshioka T, et al. Single-joint Hybrid Assistive Limb in Knee Rehabilitation after ACL Reconstruction: An Open-label Feasibility and Safety Trial. *Prog Rehabil Med*. 2022;7(0):20220036. doi:10.2490/prm.20220036

169. Haufe FL, Wolf P, Riener R, Grimmer M. Biomechanical effects of passive hip springs during walking. *J Biomech*. 2020;98:109432. doi:10.1016/j.jbiomech.2019.109432

170. Sylos-Labini F, La Scaleia V, d'Avella A, et al. EMG patterns during assisted walking in the exoskeleton. *Front Hum Neurosci*. 2014;8(JUNE):1-12. doi:10.3389/fnhum.2014.00423

171. Sado F, Yap HJ, Ghazilla RAR, Ahmad N. Exoskeleton robot control for synchronous walking assistance in repetitive manual handling works based on dual unscented Kalman filter. Huang J, ed. *PLoS One*. 2018;13(7):e0200193. doi:10.1371/journal.pone.0200193

172. Li Z, Liu H, Yin Z, Chen K. Muscle Synergy Alteration of Human During Walking With Lower Limb Exoskeleton. *Front Neurosci*. 2019;12(January):1-9. doi:10.3389/fnins.2018.01050

173. Otálora S, Ballen-Moreno F, Arciniegas-Mayag L, Cifuentes CA, Múnera M. Biomechanical Effects of Adding an Ankle Soft Actuation in a Unilateral Exoskeleton. *Biosensors (Basel)*. 2022;12(10):873. doi:10.3390/bios12100873

174. van Asseldonk EHF, Veneman JF, Ekkelenkamp R, Buurke JH, van der Helm FCT, van der Kooij H. The Effects on Kinematics and Muscle Activity of Walking in a Robotic Gait Trainer During Zero-Force Control. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. 2008;16(4):360-370. doi:10.1109/TNSRE.2008.925074

175. 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; 2017:473-478. doi:10.1109/ICORR.2017.8009293

176. Moreno JC, Barroso F, Farina D, et al. Effects of robotic guidance on the coordination of locomotion. *J Neuroeng Rehabil*. 2013;10(1):79. doi:10.1186/1743-0003-10-79

177. Lin J, Hu G, Ran J, Chen L, Zhang X, Zhang Y. Effects of bodyweight support and guidance force on muscle activation during Locomat walking in people with stroke: a cross-sectional study. *J Neuroeng Rehabil*. 2020;17(1):5. doi:10.1186/s12984-020-0641-6

178. Weiland S, Smit IH, Reinders-Messelink H, van der Woude LH V., van Kammen K, den Otter R. The effect of asymmetric movement support on muscle activity during Lokomat guided gait in able-bodied individuals. Grabowski A, ed. *PLoS One*. 2018;13(6):e0198473. doi:10.1371/journal.pone.0198473

179. Van Kammen K, Boonstra A, Reinders-Messelink H, den Otter R. The Combined Effects of Body Weight Support and Gait Speed on Gait Related Muscle Activity: A Comparison between Walking in the Lokomat Exoskeleton and Regular Treadmill Walking. Haddad JM, ed. *PLoS One*. 2014;9(9):e107323. doi:10.1371/journal.pone.0107323

180. van Kammen K, Boonstra AM, van der Woude LH V., Reinders-Messelink HA, den Otter R. Differences in muscle activity and temporal step parameters between Lokomat guided walking and treadmill walking in post-stroke hemiparetic patients and healthy walkers. *J Neuroeng Rehabil*. 2017;14(1):32. doi:10.1186/s12984-017-0244-z

181. Hornby TG, Kinnaird CR, Holleran CL, Rafferty MR, Rodriguez KS, Cain JB. Kinematic, Muscular, and Metabolic Responses During Exoskeletal-, Elliptical-, or Therapist-Assisted Stepping in People With Incomplete Spinal Cord Injury. *Phys Ther*. 2012;92(10):1278-1291. doi:10.2522/ptj.20110310

182. Alamro RA, Chisholm AE, Williams AMM, Carpenter MG, Lam T. Overground walking with a robotic exoskeleton elicits trunk muscle activity in people with high-thoracic motor-

complete spinal cord injury. *J Neuroeng Rehabil*. 2018;15(1):109. doi:10.1186/s12984-018-0453-0

183. Son C, Lee A, Lee J, et al. The effect of pelvic movements of a gait training system for stroke patients: a single blind, randomized, parallel study. *J Neuroeng Rehabil*. 2021;18(1):185. doi:10.1186/s12984-021-00964-7

184. Androwis GJ, Pilkar R, Ramanujam A, Nolan KJ. Electromyography Assessment During Gait in a Robotic Exoskeleton for Acute Stroke. *Front Neurol*. 2018;9(AUG):1-12. doi:10.3389/fneur.2018.00630

185. Calabrò RS, Naro A, Russo M, et al. Shaping neuroplasticity by using powered exoskeletons in patients with stroke: a randomized clinical trial. *J Neuroeng Rehabil*. 2018;15(1):35. doi:10.1186/s12984-018-0377-8

186. Ramanujam A, Cirnigliaro CM, Garbarini E, Asselin P, Pilkar R, Forrest GF. Neuromechanical adaptations during a robotic powered exoskeleton assisted walking session. *J Spinal Cord Med*. 2018;41(5):518-528. doi:10.1080/10790268.2017.1314900

187. Swank C, Wang-Price S, Gao F, Almutairi S. Walking With a Robotic Exoskeleton Does Not Mimic Natural Gait: A Within-Subjects Study. *JMIR Rehabil Assist Technol*. 2019;6(1):e11023. doi:10.2196/11023

188. Swank C, Almutairi S, Wang-Price S, Gao F. Immediate kinematic and muscle activity changes after a single robotic exoskeleton walking session post-stroke. *Top Stroke Rehabil*. 2020;27(7):503-515. doi:10.1080/10749357.2020.1728954

189. Infarinato F, Romano P, Goffredo M, et al. Functional Gait Recovery after a Combination of Conventional Therapy and Overground Robot-Assisted Gait Training Is Not Associated

with Significant Changes in Muscle Activation Pattern: An EMG Preliminary Study on Subjects Subacute Post Stroke. *Brain Sci*. 2021;11(4):448. doi:10.3390/brainsci11040448

190. Almutairi S, Swank C, Wang-Price S, Gao F, Medley A. Walking with and without a robotic exoskeleton in people with incomplete spinal cord injury compared to a typical gait pattern. *NeuroRehabilitation*. 2021;49(4):585-596. doi:10.3233/NRE-210187

191. Longatelli V, Pedrocchi A, Guanziroli E, Molteni F, Gandolla M. Robotic Exoskeleton Gait Training in Stroke: An Electromyography-Based Evaluation. *Front Neurorobot*. 2021;15(November):1-13. doi:10.3389/fnbot.2021.733738

192. Zhu F, Kern M, Fowkes E, et al. Effects of an exoskeleton-assisted gait training on post-stroke lower-limb muscle coordination. *J Neural Eng*. 2021;18(4):046039. doi:10.1088/1741-2552/abf0d5

193. Afzal T, Zhu F, Tseng SC, et al. Evaluation of Muscle Synergy During Exoskeleton-Assisted Walking in Persons With Multiple Sclerosis. *IEEE Trans Biomed Eng*. 2022;69(10):3265-3274. doi:10.1109/TBME.2022.3166705

194. Tan CK, Kadone H, Watanabe H, et al. Differences in Muscle Synergy Symmetry Between Subacute Post-stroke Patients With Bioelectrically-Controlled Exoskeleton Gait Training and Conventional Gait Training. *Front Bioeng Biotechnol*. 2020;8(July):1-19. doi:10.3389/fbioe.2020.00770

195. Sartori M, Llyod DG, Farina D. Neural data-driven musculoskeletal modeling for personalized neurorehabilitation technologies. *IEEE Trans Biomed Eng*. 2016;63(5):879-893. doi:10.1109/TBME.2016.2538296

196. Ferris DP, Bohra ZA, Lukos JR, Kinnaird CR. Neuromechanical adaptation to hopping with an elastic ankle-foot orthosis. *J Appl Physiol*. 2006;100(1):163-170. doi:10.1152/japplphysiol.00821.2005

197. Farris DJ, Sawicki GS. Linking the mechanics and energetics of hopping with elastic ankle exoskeletons. *J Appl Physiol*. 2012;113(12):1862-1872. doi:10.1152/japplphysiol.00802.2012

198. Farris DJ, Hicks JL, Delp SL, Sawicki GS. Musculoskeletal modelling deconstructs the paradoxical effects of elastic ankle exoskeletons on plantar-flexor mechanics & energetics during hopping. *Journal of Experimental Biology*. 2014;217(22):4018-4028. doi:10.1242/jeb.107656

199. Sawicki GS, Ferris DP. Mechanics and energetics of incline walking with robotic ankle exoskeletons. *Journal of Experimental Biology*. 2009;212(1):32-41. doi:10.1242/jeb.017277

200. Steele KM, Jackson RW, Shuman BR, Collins SH. Muscle recruitment and coordination with an ankle exoskeleton. *J Biomech*. 2017;59:50-58. doi:10.1016/j.jbiomech.2017.05.010

201. Galle S, Malcolm P, Derave W, De Clercq D. Adaptation to walking with an exoskeleton that assists ankle extension. *Gait Posture*. 2013;38(3):495-499. doi:10.1016/j.gaitpost.2013.01.029

202. Koller JR, Remy CD, Ferris DP. Biomechanics and energetics of walking in powered ankle exoskeletons using myoelectric control versus mechanically intrinsic control. *J Neuroeng Rehabil*. 2018;15(1):42. doi:10.1186/s12984-018-0379-6

203. Kinnaird CR, Ferris DP. Medial Gastrocnemius Myoelectric Control of a Robotic Ankle Exoskeleton. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. 2009;17(1):31-37. doi:10.1109/TNSRE.2008.2008285

204. Sawicki GS, Ferris DP. Powered ankle exoskeletons reveal the metabolic cost of plantar flexor mechanical work during walking with longer steps at constant step frequency. *Journal of Experimental Biology*. 2009;212(1):21-31. doi:10.1242/jeb.017269

205. Rinaldi L, Yeung LF, Lam PCH, Pang MYC, Tong RKY, Cheung VCK. Adapting to the Mechanical Properties and Active Force of an Exoskeleton by Altering Muscle Synergies in Chronic Stroke Survivors. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. 2020;28(10):2203-2213. doi:10.1109/TNSRE.2020.3017128