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Current Opinion in
Biomedical Engineering

Taking both sides: seeking symbiosis between intelligent prostheses and human motor control during locomotion

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Abstract

Robotic lower limb prostheses aim to replicate the power-generating capability of biological joints during locomotion to empower individuals with lower limb loss. However, recent clinical trials have not demonstrated clear advantages of these devices over traditional passive devices. We believe this is partly because the current designs of robotic prothesis controllers and clinical methods for fitting and training individuals to use them do not ensure good coordination between the prosthesis and user. Accordingly, we advocate for new holistic approaches in which human motor control and intelligent prosthesis control function as one system (defined as human–prosthesis symbiosis). We hope engineers and clinicians will work closely to achieve this symbiosis, thereby improving the functionality and acceptance of robotic prostheses and users' quality of life.

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Current Opinion in Biomedical Engineering 2021, **20:**100314

This review comes from a themed issue on **Novel Biomedical Technologies; Rehabilitation Robotics**

Edited by **Ashish Deshpande**

Received 22 September 2020, revised 5 May 2021, accepted 15 June 2021

Available online xxx

https://doi.org/10.1016/j.cobme.2021.100314

Keywords

Robotic lower limb prostheses, Human–prosthesis symbiosis, Human-in-the-loop optimization, Reinforcement learning, Gait biomechanics, Augmented biofeedback..

Introduction

New technologies for robotic lower limb prostheses are becoming more accessible to individuals with lower limb loss (LLL) [1,2]. These prostheses can mimic the torque-generating capabilities of biological joints to empower those with LLL; yet, even during the most common locomotor task — walking — these advanced prostheses fail to show clear advantages over energetically passive devices for the users [3–7]. For example, it is well known that an appropriate level of ankle push-off power is responsible for energetically efficient walking in humans [8]. For individuals with transtibial LLL wearing passive ankle–foot prostheses, the metabolic cost of transport is considerably high. Theoretically, powered prosthetic ankles can restore the push-off function of the missing ankle and therefore improve the user's energetics and preferred speed during walking. In reality, this benefit has not been consistently shown [5–7,9].

What causes this discrepancy? One plausible explanation is poor human–prosthesis coordination [6]. Human locomotion is a complex, dynamic process that involves the coordination of many joints controlled by one unified controller (the human nervous system). In addition, innate musculoskeletal structures, such as bi-articular muscles, contribute to the coordination of adjacent joints. When individuals with LLL wear a robotic prosthesis (i.e. a human–prosthesis system), the innate mechanism for between-joint coordination is altered, leading to two different controllers: (1) the human nervous system, which operates the intact joints and body segments, and (2) the computerized controller of the robotic prosthetic joints. The restoration of normal gait requires good coordination between these two controllers to merge the mechanics of the biological and prosthetic joints. Unfortunately, with current prosthesis designs and clinical methods, these controllers are largely disconnected functionally. On the one hand, computerized controllers in robotic prostheses do not consider factors such as motor impairment or compensatory motor strategies used by users, and they are not designed to optimize the overall gait performance of human–prosthesis systems. On the other hand, individuals with LLL do not always adapt or learn to use the active power provided by the prosthesis effectively or efficiently.

Hence, to maximize the walking function of individuals who wear advanced robotic lower limb prostheses, we believe the prosthesis controller and the user's motor control system must demonstrate good coordination and coadaptation to function seamlessly as one entity (defined as human–prosthesis symbiosis here). Although human–robot interaction or collaboration has been studied extensively [10,11], the symbiotic relationship between robotic prosthesis legs and their users has not, partly because robotic prosthetic legs have only become available within the last 10 years. Hence, in this article, we reviewed the results and limitations of recent research on the structures of robotic prosthesis controllers, approaches to optimizing the performance of these controllers, and user behaviors when interacting with these controllers during walking; we then proposed the concept of human–prosthesis symbiosis be considered in engineering, biomechanical, and clinical approaches to improve mobility and quality of life among individuals with LLL. Although most of the relevant research that has been conducted has included only individuals with unilateral LLL due to difficulty obtaining sufficient sample sizes, we believe the same symbiosis concept can be applied to those with bilateral LLL, as well as other individuals with neurological deficits (via exoskeletons).

Intelligent prosthesis control and its effects on the human–prosthesis system

Prosthesis control to enable walking

Most of the existing control methods for robotic lower-limb prostheses aim to enable people with LLL to walk with "normative" prosthesis ankle/knee kinematics or kinetics [12–15], which are defined for specific gait phases based on the biomechanics of individuals without LLL. Therefore, the controller must monitor each gait phase. Typically, discrete gait phases (e.g. the double/single stance and swing phases), often used in the field of biomechanics, are defined and estimated via onboard sensors [12,13,16]. This type of controller is called a finite-state machine. The concept of virtual constraints has recently been used to characterize the continuous coordination of kinematics among lower-limb joints within a gait cycle in persons without LLL [14,15]. By monitoring the residual thigh motion (approximate hip angle) in people with transfemoral LLL, for example, the controller can continuously adjust the prosthetic knee and ankle angles during walking based on predefined joint coordination constraints. These controllers directly coordinate with the action of the user's residual limb and yields better adaptability to varied walking speeds and inclination angles than do discrete finite-state machines. They even enable users to walk backwards and kick their leg.

One major challenge is how to predefine the prosthesis control parameters based on the gait biomechanics of persons without LLL. Individuals with LLL demonstrate very different gait patterns from each other and from those without LLL, partly due to weakness in the intact joints [17], decreased proprioception [18], poor socket fit [19], etc. Since it is difficult to directly model these factors in prosthesis control, the control parameters need to be modified for individual users, even when the goal is to merely reproduce "normative" joint kinematics or kinetics to enable walking [1–5,13]. In clinics, the parameters are tuned manually and heuristically by prosthetists when each individual walks with a robotic prosthesis. Recently, our research group developed new machine learning approaches, such as an expert system [20] and model-free reinforcement learning (RL)-based optimal adaptive control [21–23], to reduce this burden on prosthetists. RL-based methods are especially powerful because they are based on well-known theories in adaptive optimal control and can develop prosthesis tuning policies through trial-and-error learning in real time while the user walks with the prosthesis. RL is model-free because it does not require an explicit mathematical model to describe the human motor deficits and human–prosthesis system or prior tuning knowledge from prosthetists. RL has excellent scalability and can tune high-dimensional control spaces. More importantly, RL results in a tuning policy that can adaptively adjust prosthesis control parameters across different timeframes and walking environments (e.g. ramp ascent) [23].

Prosthesis control to optimize walking function

Now that many control methods can enable walking, researchers and engineers are currently focused on modifying the prosthesis control parameters to improve users' gait performance (indicated by gait symmetry [21], balance [24], and energetic expenditure [25]) and perceived preference [25] during walking. These factors are important for improving the walking function of individuals with LLL, that is, their capability to walk at normal speeds with improved endurance, walk with appropriate loading patterns to prevent the development of secondary health issues, and walk safely and confidently in real-world environments.

Unfortunately, robotic prosthesis controllers have not been optimized to maximize users' gait performance or preferences yet. One critical knowledge gap is whether — and if yes, how — robotic prosthesis or exoskeleton controllers influence the user's gait performance, preferences, and even tissue health [26]. Without such knowledge, the use of gait performance measures as prosthesis control optimization goal(s) can be challenging. Only a few related studies have been conducted [24,25,27–30]. One research group developed a novel ankle prosthesis emulator that can precisely simulate various prosthesis joint mechanics with a powerful off-board motor [31]. This emulator enabled the systematic study of the influence of a control parameter (such as push-off work [24,25] or timing [27]) on gait performance measures, including the metabolic cost, balance, preference, and perceived balance of prosthesis users. Our group examined the influence of 12 impedance control parameters of a robotic prosthesis knee during an entire stride on gait temporal and spatial symmetry [28]. Among these studies, only two were conducted in individuals with LLL, with small sample sizes [25,28]. In general, the results of these studies showed that the effects of prosthesis control vary largely across individuals with LLL. Prosthesis control cannot directly explain the changes in gait performance measures; near-normal gait performance cannot be completely achieved by adjusting the prosthesis control alone because gait performance also depends on the movement of the user, with large interindividual variability.

To optimize robotic prosthesis controllers to maximize users' walking function, many technical challenges must be solved. This requires the prosthesis controller to (1) treat the human and robotic prosthesis as one entity, which is difficult to model; (2) monitor the human–prosthesis system state (e.g. gait performance measures) beyond the gait phases and residual limb motion only; and (3) adapt to the physical conditions of individual users (e.g. height, weight, hip strength), which also vary within users over time. One idea is to develop a personalized musculoskeletal model and use computer simulations to optimize the wearable robot control parameters [32]. Another novel and promising solution is to optimize the wearable device control heretically with human-in-the-loop based on (1) search-based methods [33–36] or (2) model-free, reinforcement learning-based optimal adaptive control [21,22]. With this method, the responses of the human–robot system (e.g. the gait performance measures) to control settings can be directly assessed during walking. The search-based optimization methods iteratively search for an extremum on the system response surface to determine the optimal control parameters, while RL-based optimal adaptive controllers learn and approximate robot control policies by determining minimized/maximized cumulative costs/rewards, which can directly reflect gait measurements. Search-based optimization has been successfully applied to robotic exoskeletons to minimize the metabolic cost of transport; however, it has been only successfully demonstrated in able-bodied, healthy individuals [34,35], not in people who have motor deficits. RL-based optimal adaptive control has been used to personalize robotic prosthesis/exoskeleton control; however, the optimization goal is mainly to produce desired device joint kinematics [21,37,38] rather than desired walking function parameters in human users. Given the novelty and promising yet preliminary results, we believe more research and development on such human-in-the-loop methods are needed to make them clinically viable for robotic prosthesis personalization and intrauser adaptation and maximize walking function in individuals with LLL.

Influence of human control and adaptation on the human–prosthesis system

There is increasing evidence that individuals' motor control significantly influences the function of robotic prostheses during gait. When tuning a robotic knee controller to achieve desired knee kinematics (in terms of both magnitude and timing), we found that the prosthesis controller cannot precisely regulate the timing of the knee profile due to the significant influence of human actions on gait event timing [21]. We also found that users do not always make effective use of the active torque provided by the robotic prostheses [6]. We observed that when walking with a manually tuned ankle–foot prosthesis, some people did not move their residual shank and amputated limb to the appropriate position when the active propulsive torque was provided, thereby directing the prosthesis-side limb more vertically (upward) rather than anteriorly (forward) [6]. Such human motor behaviors reduce the efficiency of energy transfer from the robotic prosthesis in walking, even at the local joint level. Interestingly, a very similar phenomenon has been also observed with wearable ankle exoskeletons [39].

These results underscore the importance of training users to adjust their motor patterns and effectively use the power provided by wearable robots for improved locomotion. Human movement control is even more critical when the goal is to improve gait performance. Many engineers have focused on optimizing the prosthesis control side. However, the prosthesis is only a subsystem and affects gait performance to a limited extent at the system level; the behaviors of the user, the other subsystem, influence and even dominate some gait performance measures. Nevertheless, little attention has been paid to optimize gait biomechanics when people walk with robotic prostheses. For example, when a powered prosthesis is fit in clinics, individuals with LLL practice walking on different terrains while a prosthetist manually tunes the prosthesis control parameters. It takes only a couple of hours, and this process is insufficient to guarantee human–prosthesis symbiosis regarding gait performance [6]. In research settings, users are given time (ranging from 20 min to three weeks) to practice walking with a new device in a laboratory or at home. However, there are currently no standards for how to properly instruct them to use the new device or determine when acclimation is complete [40]. The assumption that users can automatically adapt to and coordinate with robotic prostheses by only practicing walking (without instructions) may be questionable. This is because the abnormal gait patterns of individuals with LLL may be partly derived from a lack of knowledge on how robotic prostheses function and the transfer of a maladaptive motor pattern that they learned when using their passive devices [41]. Instead, device-specific training is necessary for users to learn the appropriate gait patterns to best use the power produced by modern prostheses and achieve optimal gait performance.

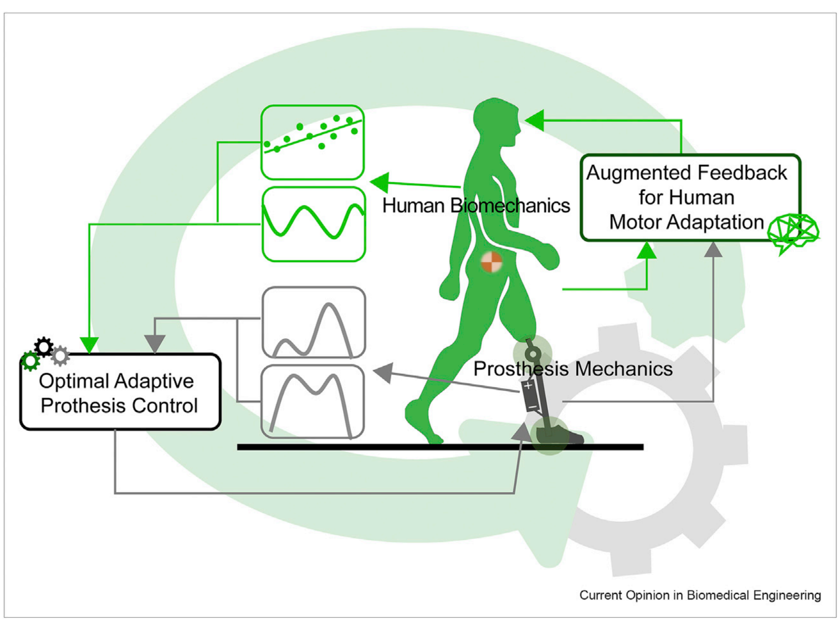
There are several engineering methods that can be used to facilitate training and movement learning to help people with LLL coordinate with the action of robotic prostheses. One approach is to use augmented biofeedback [17,41–43] to cue the user to make certain modifications (e.g. residual limb position, gait timing, loading) based on the action of prosthesis to achieve human–prosthesis coordination. This type of training can be even carried out in the real world due to recent advancements in wearable sensors and augmented reality [44]. In addition, providing feedback of the prosthesis' action (proprioception) via surgical techniques and neural interfaces [18] or haptic devices [45] may enhance the user's awareness of the machine's states and lead to coordinated body movements.

Future directions for human–prosthesis symbiosis

In our opinion, to maximize the benefits of modern robotic prostheses for individuals with LLL, it is necessary for both the user and robotic controller to function together (Figure 1). For prosthesis intelligent control, the controllers need to adapt to individual user impairments and motor behaviors, sense the overall system states, and optimize human–prosthesis gait performance measures. For human movement control, it is essential to communicate the prosthesis system states to the user and for him or her to learn to move appropriately to maximize the energy transferred from the robotic device. This requires (1) research and innovations on the optimal adaptive control of robotic prostheses and user training strategies for effective coordination with robotic devices and (2) collaborations among researchers in biomedical engineering, biomechanics, and rehabilitation clinics so that the behaviors of both systems are appropriately considered.

One challenge in implementing this concept is identifying a paradigm that can promote human–prosthesis coadaptation. Specifically, should the intelligent machine and human motor control systems adapt concurrently or alternately? We must first understand the learning rates of and interactions between the two systems. Another challenge is determining which common objective(s) for human–prosthesis systems yield the highest level of symbiosis. Many challenges in formulating and resolving this multiobjective optimization problem for human–prosthesis systems remain. Furthermore, merging human motor control with computerized prosthesis control, as discussed in this article, is one way to enable symbiosis; however, it cannot fully address situations in which immediate adaptation is required, such as obstacle avoidance [46], and tasks that are not preprogrammable, such as playing tennis. For these situations, the users should dominate the prosthesis operations. This requires direct efferent neural control of the robotic prosthesis joint [18,47,48], which is a future research direction related to human–prosthesis symbiosis. Finally, our proposed framework can be extended to other assistive devices including exoskeletons for people with neuromotor deficits. These topics related to physical human–robot interactions

Figure 1



Human–prosthesis symbiosis requires seamless coordination and coadaptation between prosthesis control and human mov gait control.

should be explored in parallel to achieve human–robot symbiosis for everyone who may benefit.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

Acknowledgements

The authors thank Yue Wen, Stephanie Huang, Ming Liu, I-Chieh Lee, and Bretta Fylstra, Aaron Fleming, and Ruofan Wu for shaping our opinion through their research and discussion. We thank NIH (EB024570) and NSF (1563454/1563921, 1808752/1808898, 1954587, 1926998) for sponsoring our research on this topic.

References

Papers of particular interest, published within the period of review, have been highlighted as:

* of special interest

1. OSSUR, The power knee, The Power Knee ed. https://www.ossur.com/en-us/prosthetics/knees/power-knee.

2. Ottobock, Empower (Previous BiOM), Empower Ankle ed. https://www.ottobockus.com/prosthetics/lower-limb-prosthetics/solution-overview/empower-ankle/.

3. Brandt A, Wen Y, Liu M, Stallings J, Huang HH: **Interactions between transfemoral amputees and a powered knee prosthesis during load carriage**. *Sci Rep* Nov 03 2017, **7**:14480. https://doi.org/10.1038/s41598-017-14834-7.

4. Hafner BJ, Askew RL: **Physical performance and self-report outcomes associated with use of passive, adaptive, and active prosthetic knees in persons with unilateral, transfemoral amputation: randomized crossover trial**. *J Rehabil Res Dev* 2015, **52**:677–700. https://doi.org/10.1682/JRRD.2014.09.0210.

5. * Gardiner ES, Kelly BM, Wensman J, Gates DH: **A controlled clinical trial of a clinically-tuned powered ankle prosthesis in people with transtibial amputation**. *Clin Rehabil* Mar 2018, **32**: 319–329. https://doi.org/10.1177/0269215517723054.

This randomized controlled clinical trial included people with transtibial limb loss using a robotic ankle-foot prosthesis. Compared to non-powered prostheses, the robotic prosthesis did not significantly improve the energetics or preferred speed of the users.

6. * Fylstra B, Lee I, Huang S, Brandt A, Lewek M, Huang H. *Human-Prosthesis Coordination: A Pilot Study Exploring Timing and Limb Position During Powered Propulsion*, vol. 80. Bristol, Avon: Clin Biomech; 2020:105171. https://doi.org/10.1016/j.clinbiomech.2020.105171.

Although the powered ankle prosthesis that is commercially available was designed to provide positive mechanical work around the ankle joint during walking, the amount of net ankle work varied across people with LLL. Less ankle work was coupled with an earlier push-off timing and a more vertical residual shank, indicating suboptimal human-prosthesis coordination.

7. Ferris AE, Aldridge JM, Rabago CA, Wilken JM: **Evaluation of a powered ankle-foot prosthetic system during walking**. *Arch Phys Med Rehabil* Nov 2012, **93**:1911–1918. https://doi.org/10.1016/j.apmr.2012.06.009.

8. Huang TW, Shorter KA, Adamczyk PG, Kuo AD: **Mechanical and energetic consequences of reduced ankle plantar-flexion in human walking**. *J Exp Biol* Nov 2015, **218**:3541–3550. https://doi.org/10.1242/jeb.113910.

9. Ingraham KA, Choi H, Gardiner ES, Remy CD, Gates DH: **Choosing appropriate prosthetic ankle work to reduce the metabolic cost of individuals with transtibial amputation**. *Sci Rep* Oct 17 2018, **8** (in English).

10. Losey DP, McDonald CG, Battaglia E, O'Malley MK: **A review of intent detection, arbitration, and communication aspects of shared control for physical human–robot interaction**. *Appl Mech Rev* 2018, **70**.

11. Vicentini F: **Collaborative robotics: a survey**. *J Mech Des* 2021, **143**, 040802.

12. Au S, Berniker M, Herr H: **Powered ankle-foot prosthesis to assist level-ground and stair-descent gaits**. *Neural Netw* May 2008, **21**:654–666.

13. Sup F, Bohara A, Goldfarb M: **Design and control of a powered transfemoral prosthesis**. *Int J Robot Res* 2008, **27**:263–273.

14. Zhao H, Horn J, Reher J, Paredes V, Ames AD: **First steps toward translating robotic walking to prostheses: a nonlinear optimization based control approach**. *Auton Robots* 2017, **41**: 725–742.

15. * Quintero D, Villarreal DJ, Lambert DJ, Kapp S, Gregg RD: **Continuous-phase control of a powered knee-ankle prosthesis: amputee experiments across speeds and inclines**. *IEEE Trans Robot* Jun 2018, **34**:686–701. https://doi.org/10.1109/TRO.2018.2794536.

This study developed a novel prosthesis controller based on the virtual constraints of joint kinematics coordination during walking. The controller operates continuously and can assist walking at different speeds and inclines.

16. Gabert L, Hood S, Tran M, Cempini M, Lenzi T: **A compact, lightweight robotic ankle-foot prosthesis: Featuring a powered polycentric design**. *IEEE Robot Autom Mag* 2020, **27**: 87–102.

17. Brandt A, Huang HH: **Effects of extended stance time on a powered knee prosthesis and gait symmetry on the lateral control of balance during walking in individuals with unilateral amputation**. *J Neuroeng Rehabil* Nov 29 2019, **16**:151. https://doi.org/10.1186/s12984-019-0625-6.

18. * Clites TR, *et al.*: **Proprioception from a neurally controlled lower-extremity prosthesis**. *Sci Transl Med* May 30 2018, **10**. https://doi.org/10.1126/scitranslmed.aap8373.

This study reported a novel surgical technique that can restore proprioception in the prosthetic ankle in transtibial amputees when they use electromyographic signals recorded from the residual muscles to operate the prosthesis.

19. Safari R: **Lower limb prosthetic interfaces: clinical and technological advancement and potential future direction**. *Prosthet Orthot Int* 2020, **44**:384–401.

20. Huang H, Crouch DL, Liu M, Sawicki GS, Wang D: **A cyber expert system for Auto-tuning powered prosthesis impedance control parameters**. *Ann Biomed Eng* 2016, **44**: 1613–1624. https://doi.org/10.1007/s10439-015-1464-7.

21. * Wen Y, Si J, Brandt A, Gao X, Huang HH: **Online reinforcement learning control for the personalization of a robotic knee prosthesis**. *IEEE Trans Cybern* Jun 2020, **50**:2346–2356. https://doi.org/10.1109/TCYB.2019.2890974.

An actor-critic reinforcement learning control system was developed to tune 12 control parameters for a robotic prosthesis knee in order to produce desired knee kinematics during walking. The control does not rely on dynamic models of human-prosthesis systems and can tune 12 prosthesis control parameters with the human-in-the-loop.

22. Wen Y, Si J, Gao X, Huang S, Huang H: **A new powered lower limb prosthesis control framework based on adaptive dynamic programming**. In *English*, vol. 28. IEEE T Neur Net Lear; Sep 2017:2215–2220.

23. Li M, Wen Y, Gao X, Si J, Huang H: **Toward expedited impedance tuning of a robotic prosthesis for personalized gait assistance by reinforcement learning control**. *IEEE Trans Robot* 2021:1–10. https://doi.org/10.1109/TRO.2021.3078317. In press.

24. Kim M, Collins SH: **Once-per-step control of ankle-foot prosthesis push-off work reduces effort associated with balance during walking**. *J Neuroeng Rehabil* May 1 2015, **12**:43. https://doi.org/10.1186/s12984-015-0027-3.

25. Quesada RE, Caputo JM, Collins SH: **Increasing ankle push-off work with a powered prosthesis does not necessarily reduce**

metabolic rate for transtibial amputees. *J Biomech* Oct 3 2016, **49**:3452–3459. https://doi.org/10.1016/j.jbiomech.2016.09.015.

26. Sartori M, Sawicki GS: **Closing the loop between wearable technology and human biology: a new paradigm for steering neuromuscular form and function**. *Prog Biomed Eng* 2021, **3**, 023001.

27. Malcolm P, Quesada RE, Caputo JM, Collins SH: **The influence of push-off timing in a robotic ankle-foot prosthesis on the energetics and mechanics of walking**. *J Neuroeng Rehabil* Feb 22 2015, **12**:21. https://doi.org/10.1186/s12984-015-0014-8.

28. Wen Y, Li M, Si J, Huang H: **Wearer-prosthesis interaction for symmetrical gait: a study enabled by reinforcement learning prosthesis control**. *IEEE Trans Neural Syst Rehabil Eng* Apr 2020, **28**:904–913. https://doi.org/10.1109/TNSRE.2020.2979033.

29. Zhang F, Liu M, Huang H: **Effects of locomotion mode recognition errors on volitional control of powered above-knee prostheses**. *IEEE Trans Neural Syst Rehabil Eng* Jan 2015, **23**: 64–72. https://doi.org/10.1109/TNSRE.2014.2327230.

30. * Bryan GM, Franks PW, Klein SC, Peuchen RJ, Collins SH: **A hip–knee–ankle exoskeleton emulator for studying gait assistance**. *Int J Robot Res* 2020, 0278364920961452.

This paper presents a hip–knee–ankle exoskeleton emulator that can apply high torques and powers and test various control strategies for different locomotion tasks, including running on inclines. This emulator will be used to identify new assistive strategies for human walking.

31. Caputo JM, Collins SH: **A universal ankle-foot prosthesis emulator for human locomotion experiments**. *J Biomech Eng* Mar 2014, **136**, 035002. https://doi.org/10.1115/1.4026225.

32. Akbas T, Sulzer J: **Musculoskeletal simulation framework for impairment-based exoskeletal assistance post-stroke**. In *2019 IEEE 16th International Conference on Rehabilitation Robotics (ICORR)*. IEEE; 2019:1185–1190.

33. Felt W, Selinger JC, Donelan JM, Remy CD: **"Body-in-the-loop": optimizing device parameters using measures of instantaneous energetic cost**. *PLoS One* 2015, **10**, e0135342. https://doi.org/10.1371/journal.pone.0135342.

34. Zhang J, *et al.*: **Human-in-the-loop optimization of exoskeleton assistance during walking**. *Science* Jun 23 2017, **356**: 1280–1284. https://doi.org/10.1126/science.aal5054.

35. * Kim J, *et al.*: **Reducing the metabolic rate of walking and running with a versatile, portable exosuit**. *Science* Aug 16 2019, **365**:668–672. https://doi.org/10.1126/science.aav7536.

This study presented a human-in-the-loop optimization algorithm to optimize the 2 control parameters of a hip exosuit in order to improve the energetic economy of healthy individuals during walking.

36. 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* Nov 4 2015, **12**:97. https://doi.org/10.1186/s12984-015-0086-5.

37. Peng Z, *et al.*: **Data-driven reinforcement learning for walking assistance control of a lower limb exoskeleton with hemiplegic patients**. In *2020 IEEE International Conference on Robotics and Automation (ICRA)*. IEEE; 2020:9065–9071.

38. Tu X, Li M, Liu M, Si J: **A data-driven reinforcement learning solution framework for optimal and adaptive personalization of a hip exoskeleton**. *IEEE Int Conf Robot Autom (ICRA)* 2021 [In press]. Preprint link: https://arxiv.org/abs/2011.06116,2021.

39. McCain EM, *et al.*: **Mechanics and energetics of post-stroke walking aided by a powered ankle exoskeleton with speed-adaptive myoelectric control**. *J Neuroeng Rehabil* May 15 2019, **16**:57. https://doi.org/10.1186/s12984-019-0523-y.

40. Wanamaker AB, Andridge RR, Chaudhari AM: **When to biomechanically examine a lower-limb amputee: a systematic review of accommodation times**. *Prosthet Orthot Int* Oct 2017, **41**:431–445. https://doi.org/10.1177/0309364616682385.

41. Brandt A, Riddick W, Stallrich J, Lewek M, Huang HH: **Effects of extended powered knee prosthesis stance time via visual feedback on gait symmetry of individuals with unilateral amputation: a preliminary study**. *J Neuroeng Rehabil* Sep 11 2019, **16**:112. https://doi.org/10.1186/s12984-019-0583-z.

42. Browne MG, Franz JR: **Ankle power biofeedback attenuates the distal-to-proximal redistribution in older adults**. *Gait Posture* Jun 2019, **71**:44–49. https://doi.org/10.1016/j.gaitpost.2019.04.011.

43. Liu J, Kim HB, Wolf SL, Kesar TM: **Comparison of the immediate effects of audio, visual, or audiovisual gait biofeedback on propulsive force generation in able-bodied and post-stroke individuals**. *Appl Psychophysiol Biofeedback* Sep 2020, **45**:211–220. https://doi.org/10.1007/s10484-020-09464-1.

44. Karatsidis A, *et al.*: **Validation of wearable visual feedback for retraining foot progression angle using inertial sensors and an augmented reality headset**. *J Neuroeng Rehabil* Aug 15 2018, **15**:78. https://doi.org/10.1186/s12984-018-0419-2.

45. Plauche A, Villarreal D, Gregg RD: **A haptic feedback system for phase-based sensory restoration in above-knee prosthetic leg users**. *IEEE Trans Haptics* Jul-Sep 2016, **9**:421–426. https://doi.org/10.1109/TOH.2016.2580507.

46. Mendez J, Hood S, Gunnel A, Lenzi T: **Powered knee and ankle prosthesis with indirect volitional swing control enables level-ground walking and crossing over obstacles**. *Sci Robot* 2020, **5**.

47. Huang S, Wensman JP, Ferris DP: **Locomotor adaptation by transtibial amputees walking with an experimental powered prosthesis under continuous myoelectric control**. *IEEE Trans Neural Syst Rehabil Eng* May 2016, **24**:573–581. https://doi.org/10.1109/TNSRE.2015.2441061.

48. Fleming A, Huang S, Buxton E, Hodges F, Huang HH: **Direct continuous electromyographic control of a powered prosthetic ankle for improved postural control after guided physical training: a case study**. *Wearable Technol* 2021, **2**.