

RESEARCH ARTICLE SUMMARY

PROSTHETICS

Tissue-integrated bionic knee restores versatile legged movement after amputation

Tony Shu*, Daniel Levine, Seong Ho Yeon, Ethan Chun, Christopher C. Shallal, John McCullough, Rickard Bränemark, Matthew J. Carty, Marco Ferrone, Sean Boerhout, Alexander Ko, Corey L. Sullivan, Gloria Zhu, Michael Nawrot, Matthew Carney, Ged Wieschhoff, Gabriel Friedman, Hugh Herr*



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INTRODUCTION: Attempts to restore the body after amputation have been widespread for centuries. Typical approaches have emphasized iterative mechanical improvements, which have resulted from the difficulties and cultural aversions associated with surgical revision. Today, the most advanced, commercially available lower-extremity prostheses are still physically separated from the body and only capable of repetitive walking patterns and preprogrammed movements. By contrast, recent studies show that providing even a modest amount of neuromuscular information to the prosthesis through a minimally invasive bionic interface can unlock essential lower-extremity capabilities, such as terrain adaptation, obstacle avoidance, and biomimetic power generation. The results suggest that further anatomical integration may yield additional legged agility.

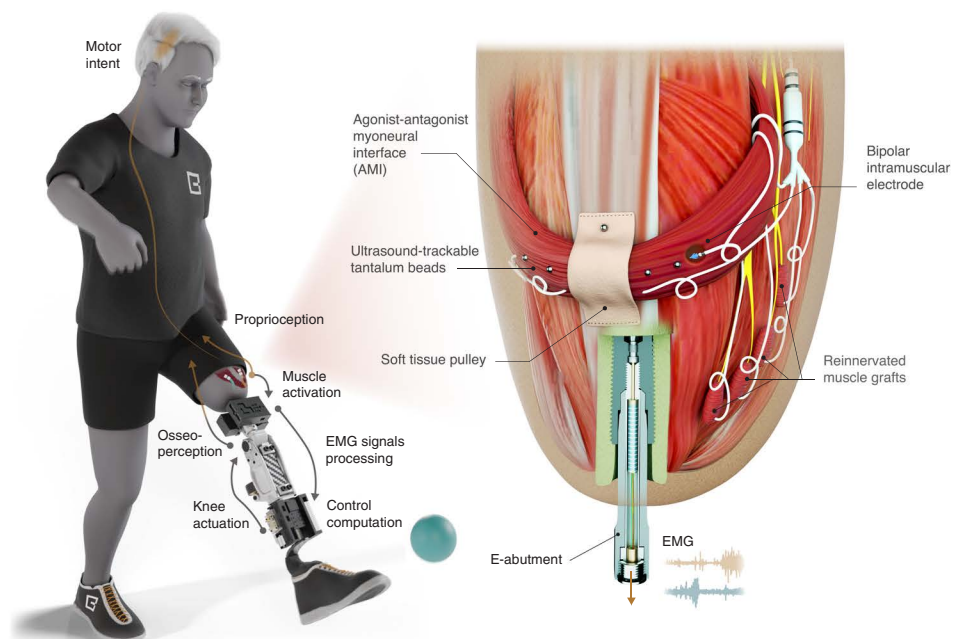
RATIONALE: We hypothesized that engineering residual soft and hard tissues toward a seamless interface between the nervous system and prosthesis would enable versatile lower-extremity behaviors driven by user intent. We developed a vertically integrated bionic amputation platform, the osseointegrated mechanoneural prosthesis, to improve control signal detection and neuromuscular function at the above-knee amputation level. The osseointegrated mechanoneural prosthesis consists of three functional layers that seek to (i) maximize prosthetic knee agility through continuous, user-controlled flexion and extension; (ii) stabilize two-way energy and information exchange between user and prosthesis through a bone-anchored femur implant; and (iii) restore physiological neuromuscular signaling by reconstructing original muscle geometries.

RESULTS: Two human subjects with preexisting conventional transfemoral amputation were surgically enhanced with the osseointegrated mechanoneural prosthesis. We found that they demonstrated significantly improved performance relative to a cohort of subjects with conventional transfemoral amputation when controlling a bionic knee to avoid obstacles while walking. We determined that this advantage may be attributable to their reconstructed residual knee muscles, the improved control-signal quality from the permanently implanted electrodes within their muscles, and the lack of prosthetic socket interference. Our testing also developed a versatile prosthetic knee controller capable of computationally mirroring the user's phantom limb movements when utilized by the osseointegrated mechanoneural prosthesis. Furthermore, we demonstrated that increasing anatomical prosthetic integration in subjects with preexisting amputation can enhance prosthetic embodiment, uncovering a self-perceptive metric to more thoroughly assess the outcomes of amputation design and prosthesis selection.

CONCLUSION: Our results suggest that increased prosthetic integration at the above-knee amputation level can yield improved signaling and joint control in certain physical tasks. We posit that the capabilities demonstrated by the osseointegrated myoneural prosthesis provide evidence that further anatomical integration with the prosthesis, rather than the maintenance of an artificial separation, is required for advancing progress toward physiological function, embodiment, and rehabilitative potential after limb loss. □

*Corresponding author. Email: tonyshu@mit.edu (T.S.); herr@media.mit.edu (H.H.). Cite this article as T. Shu *et al.*, *Science* **389**, eadv3223 (2025). DOI: 10.1126/science.adv3223

Facilitating information and energy exchange through a vertically integrated bionic amputation platform. The osseointegrated mechanoneural prosthesis sustains continuous knee control from motor intent originating in the central nervous system. A stylized posterior-lateral view of the transfemoral residuum reveals an agonist-antagonist myoneural interface created from residual knee extensor and flexor muscles.



PROSTHETICS

Tissue-integrated bionic knee restores versatile legged movement after amputation

Tony Shu^{1,2*}, Daniel Levine^{1,2}, Seong Ho Yeon^{1,2}, Ethan Chun³, Christopher C. Shallah^{2,4}, John McCullough^{2,5}, Rickard Bränemark^{2,6,7}, Matthew J. Carty^{2,8}, Marco Ferrone⁹, Sean Boerhout⁵, Alexander Ko², Corey L. Sullivan⁸, Gloria Zhu³, Michael Nawrot^{2,5}, Matthew Carney^{1,2}, Ged Wieschhoff¹⁰, Gabriel Friedman¹¹, Hugh Herr^{1,2*}

Lower-extremity prostheses have evolved through mechanical redesigns that prioritize improved cyclic locomotion. However, this limited approach to limb restoration has precluded necessary progress toward recovering the versatile acyclic movements that constitute the remainder of human athleticism. We present an osseointegrated mechanoneural prosthesis that incorporates modified hard and soft tissues along with permanently implanted hardware in a neuroembodied design. We developed a biomimetic coupling between neuromuscular signaling and joint movement that exceeds the versatility of established control methods, which depend upon conventional amputation musculature and surface electromyography. Our findings also reveal that superior residual neuromuscular function can enable prosthetic movement speeds surpassing that of intact physiology. Anatomical prosthetic integration may be necessary for meeting, and possibly exceeding, the movement capabilities of an intact limb.

Attempts to restore the body after amputation have been prevalent throughout history (1). Typical approaches are centered around iterative mechanical designs, owing to the difficulties and cultural aversions associated with anatomical modification (2–4). Today, research on lower-extremity prostheses continues to emphasize improvements in device design, mechanical interfacing, and mechatronic control strategies to facilitate basic cyclic gait (5). However, recent studies have demonstrated that essential lower-extremity capabilities, including terrain adaptation, obstacle avoidance, and graded biomimetic power generation, readily emerge after enabling bidirectional information exchange between a user and their prosthesis through a minimally invasive bionic interface (6–8). It is increasingly apparent that further anatomical integration may be necessary to unlock additional legged agility.

Overcoming obstacles to versatile bionic knee control

At the transfemoral (TF) level, machine learning strategies have attempted to use muscle activity estimated through surface electromyography (EMG) to initiate gait transitions (9–11), sitting and standing (12), joint flexion and extension in free space (13), and obstacle avoidance during level-ground walking (14). All use windowed sampling methods that discretize and limit the control input bandwidth from the user. Additionally, only a finite set of joint behavior labels is used for classification. These

structural limitations suggest that such approaches may not generalize to continuously variable tasks, such as dribbling a ball. By contrast, other recent studies have applied surface EMG from residual neuromusculature to proportionally compute an output torque or impedance (15) at the prosthetic knee (16). These direct control strategies more closely resemble physiological neuromuscular function and promise great versatility, having separately demonstrated stair ascent (17, 18), level-ground walking (19, 20), and diverse extension-dependent movements such as sitting, standing, lunging, and squatting with a fixed set of control laws (21).

Direct control strategies that rely on surface EMG signals are susceptible to the noise introduced by skin perspiration and impact artifacts, an effect that is exacerbated by prosthetic sockets (22). However, recent preclinical trials involving subjects with transhumeral (23, 24) and transradial (25) amputation have largely circumvented these issues by using permanently implanted intramuscular electrodes routed through the axial conduit of an experimental bone-anchored—or osseointegrated—implant. In addition to serving as a protected signal conduit, the implant eliminates the need for a prosthetic socket by directly facilitating mechanical attachment to the prosthesis.

Lastly, while high EMG signal-to-noise ratios (SNRs) were sustained throughout the aforementioned studies on osseointegration, the subjects' residual muscles were not arranged in a manner approximating that of normal physiology. This may preclude their ability to generate fast and accurate neuromuscular control signals, because of a lack of proprioceptive feedback from antagonist muscle stretch (4). By contrast, the agonist-antagonist myoneural interface (AMI) is a prosthetic control interface that mechanically couples and instruments residual agonist and antagonist muscles to detect neuromuscular activity. The AMI is hypothesized to induce antagonist stretch upon agonist contraction and produce physiological proprioception and augmented muscle control for the user. Subjects with transtibial amputation having the AMI have demonstrated improved control of virtual and physical prosthetic ankle and subtalar joints using surface EMG compared to persons with amputation without such constructs (3, 6, 8, 26).

We propose a vertically integrated bionic amputation platform, the osseointegrated mechanoneural prosthesis (OMP), intended to improve prosthetic control strategy, control-signal detection, and neuromuscular function (Fig. 1A). The OMP consists of three functional layers that seek to (i) maximize prosthetic knee agility under a direct neuromuscular controller capable of continuously variable flexion and extension; (ii) stabilize bidirectional energy and information exchange between user and prosthesis through a bone-anchored femoral implant; and (iii) restore physiological neuromuscular signaling by reconstructing agonist-antagonist relationships.

Structurally, the OMP creates an AMI pair out of the residual biceps femoris (BF) and rectus femoris (RF) muscles for knee control (Fig. 1B). The AMI constructs are instrumented with permanently implanted intramuscular electrodes that are internally routed through the osseointegrated implant's central conduit (the e-OPRA Implant System, Integrum AB, Mölndal, Sweden) (Fig. 1C). The bionic knee continuously generates torque to physically realize the user's perceived phantom limb movements, based on the muscle activity of their agonist-antagonist constructs. Simultaneously, users are continuously updated on the estimated dynamics of the prosthetic knee by receiving proprioceptive feedback from the AMI and reactive forces from osseoperception. We hypothesized that engineering residual soft and hard tissues toward an integrative interface between the nervous system and external mechatronics would enable versatile lower-extremity behaviors driven by user volition.

Results

We implemented the OMP in subjects with preexisting, unilateral TF amputation (OMP, $n = 2$) (Fig. 1, D and E). Their performance and relative prosthetic embodiment were assessed throughout several functional tasks. OMP subjects were compared with two other cohorts (table S1),

¹Program in Media Arts and Sciences, MIT Media Lab, MIT, Cambridge, MA, USA. ²K. Lisa Yang Center for Bionics, MIT, Cambridge, MA, USA. ³Department of Electrical Engineering & Computer Science, MIT, Cambridge, MA, USA. ⁴Harvard-MIT Program in Health Sciences and Technology, MIT, Cambridge, MA, USA. ⁵Department of Mechanical Engineering, MIT, Cambridge, MA, USA. ⁶Integrum AB, Mölndal, Sweden. ⁷Department of Orthopaedics, Gothenburg University, Gothenburg, Sweden. ⁸Division of Plastic Surgery, Brigham and Women's Hospital, Boston, MA, USA. ⁹Department of Orthopaedic Surgery, Brigham and Women's Hospital, Boston, MA, USA. ¹⁰Department of Radiology, Brigham and Women's Hospital, Boston, MA, USA. ¹¹Department of Neurosurgery, Massachusetts General Hospital, Boston, MA, USA. *Corresponding author. Email: tonyshu@mit.edu (T.S.); hherr@media.mit.edu (H.H.)

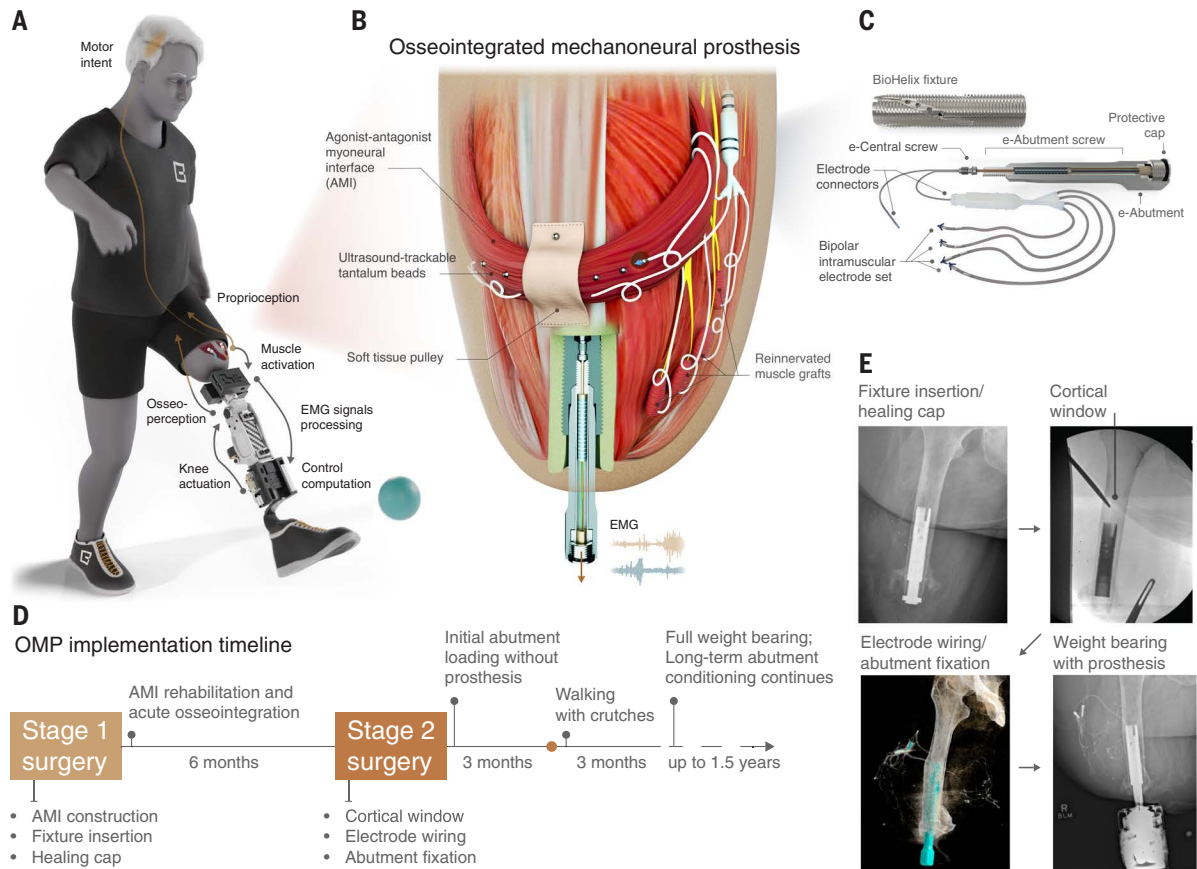


Fig. 1. Facilitating information and energy exchange through a vertically-integrated bionic amputation platform. (A) Process flow diagram demonstrating how the osseointegrated mechanoneural prosthesis sustains continuous knee control from motor intent originating in the central nervous system. Orange traces indicate biological neural pathways; gray traces indicate computational and mechanical pathways. (B) Stylized posterior-lateral view of the osseointegrated mechanoneural prosthesis implemented in the transfemoral residuum, including an agonist-antagonist soft-tissue interface created from residual knee extensor and flexor muscles. (C) Artificial hardware (e-OPRA system, Integrum AB) implanted within the residuum to facilitate information and energy exchange between the user and an external prosthesis. (D) Timeline of the two-stage surgical procedure to implement the osseointegrated mechanoneural prosthesis. (E) Radiologic still images and reconstructions demonstrating the progress of implementing the osseointegrated mechanoneural prosthesis.

one with unilateral TF amputation possessing the AMI without the e-OPRA implant system (AMI, $n = 8$), and the other a control cohort with neither the AMI nor e-OPRA implant system (CTL, $n = 7$). All subjects utilized the bionic knee developed specifically for this study, consisting of a powered knee prosthesis (fig. S1) and a direct neuromuscular controller (fig. S2). Although OMP subjects utilized intramuscular electrodes, both AMI and CTL subjects necessarily utilized thin, flexible electrodes within their prescribed prosthetic sockets for surface EMG acquisition (fig. S3).

Augmenting neuromuscular control through agonist-antagonist coupling and intramuscular sensing

We previously determined that persons with transtibial AMI constructs demonstrate augmented afferent proprioceptive feedback (8), improved bilateral coordination between affected and intact musculature (3), and greater phantom limb proprioception and control (26) compared with those having conventional transtibial amputations. These results suggest a positive correlation between quantity of afferent proprioceptive feedback to the central nervous system (CNS), phantom limb proprioception, and neuromuscular control quality. To extend our characterization to the TF domain, we estimated the secondary muscle spindle firing rate of corresponding residual musculature under voluntary isometric contraction to quantify afferent proprioceptive feedback (Fig. 2A). Simultaneous measurements of muscle activations and fascicle strains from both muscles revealed that estimated net secondary muscle

spindle firing rates are also significantly greater from the TF AMI than from corresponding conventional residual musculature (Fig. 2B). These results indicate the degree of proprioceptive augmentation per subject and suggest that TF AMI constructs may provide more intense phantom knee proprioception and improved neuromuscular control.

Maximizing control of prosthetic knee kinematics through anatomical integration

To characterize the control implications of augmented proprioceptive feedback and improved EMG collection methodology, subjects were assessed on their ability to generate control information in a free-space reaching task without prosthetic interactions. Reference levels of low, medium, and high knee extension were first proprioceptively and visually conveyed to each seated subject through manipulation of the intact contralateral limb. Subjects were then blindfolded and instructed to extend and hold their phantom knee joints at corresponding levels of extension while their muscle activations were recorded (Fig. 3A, i). OMP subjects generated more distinguishable levels of extensor activation, as measured by Jensen-Shannon divergence (JSD), between adjacent low and medium extension levels compared to CTL subjects (Fig. 3A, ii). In this extension range, wherein fine motor control dominates, OMP subjects also generated more information than predicted by the regression model created from AMI and CTL subject data (fig. S4A).

We proceeded to assess subjects' abilities to incorporate visual feedback toward free-space control of the physical bionic knee. Subjects

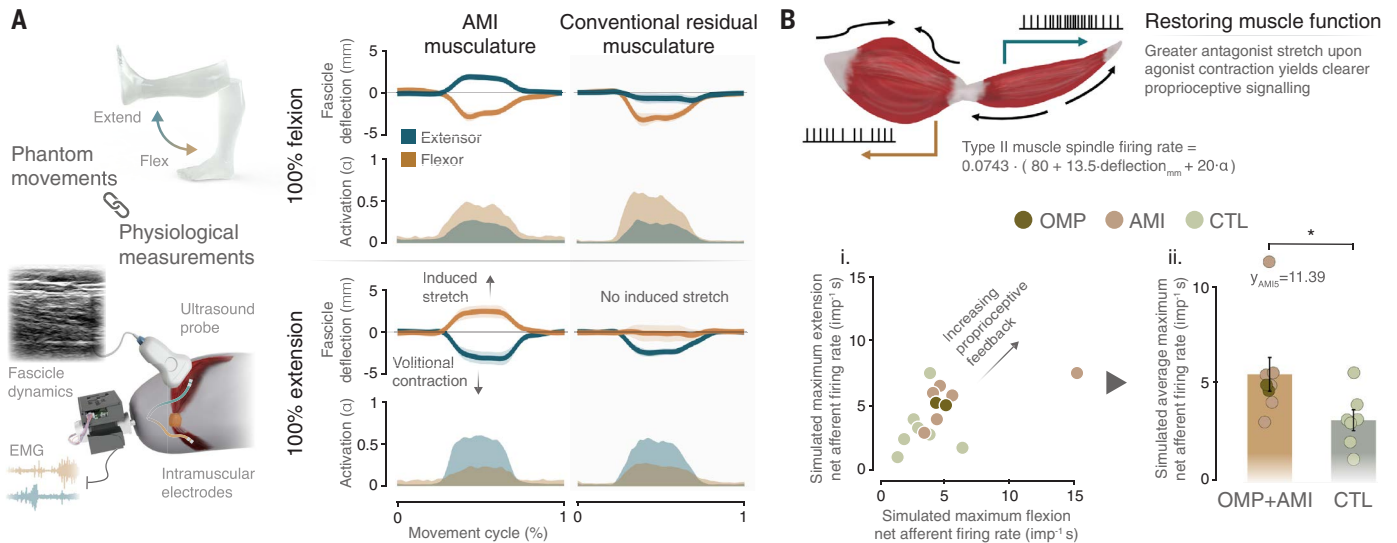


Fig. 2. Agonist-antagonist architecture increases proprioceptive feedback associated with phantom knee movement. (A) Assessment of residual knee muscle function throughout maximum voluntary phantom knee movements. Concurrent muscle fascicle strains and average muscle activations are presented for subjects possessing the agonist-antagonist myoneural interface (AMI) in aggregate ($n = 5$ trials per direction per subject, $n = 2$ OMP subjects, and $n = 8$ AMI subjects aggregated). Corresponding data generated by subjects with conventional amputation are presented adjacently on a gray background ($n = 5$ trials per direction per subject, $n = 7$ CTL subjects). Fascicle deflection shaded regions indicate SEM. (B) Calculation of simulated afferent proprioceptive information generated during maximum voluntary phantom knee movements. Net afferent firing rate is calculated as the signed difference of the Type II muscle spindle firing rate of the antagonist muscle less that of the agonist muscle. Panel (i) shows simulated maximum net firing rates for both flexion and extension per subject ($n = 5$ trials per direction per subject). Panel (ii) shows the simulated average maximum net firing rate from both flexion and extension per subject ($n = 2$ OMP subjects and $n = 8$ AMI-equipped subjects aggregated, $n = 7$ CTL subjects, Wilcoxon rank-sum test, * $P = 0.04$).

were seated with the mechanically isolated bionic knee positioned in the anatomically correct volume of their missing limb (Fig. 3B). Reflective markers placed on the shoe and background provided visual indicators for the three levels of knee extension used previously. For each trial, noise-canceling headphones provided rhythmic instructions to alternately hold the bionic knee at a specific level of extension and relax the joint. OMP subjects were significantly more accurate than CTL subjects when reaching for both low- and medium-extension targets in terms of average absolute angular error of the knee when held at steady state (Fig. 3B). Analogous to the previous trend regarding extensor activation information, OMP subjects may be more accurate than expected compared with AMI and CTL subjects when normalizing against degree of proprioceptive augmentation (fig. S4B).

To determine the limits of dynamic neuromuscular control independent of mechatronic limitations, we developed a rhythmic bandwidth task wherein subjects were instructed to flex and extend their phantom knee joint at full perceived range of motion in tempo with an accelerating click track until desynchronization (movie S2). Corresponding EMG signals from the residual knee muscles were recorded and processed by using our direct neuromuscular knee controller (fig. S2) to drive the kinematic trajectory of a modeled prosthetic knee joint (Fig. 3C, i). Subjects possessing the TF AMI construct demonstrated significantly greater peak control bandwidth with the AMI than with their intact contralateral limb, indicating supraphysiological performance (Fig. 3C, ii). By contrast, the CTL cohort demonstrated no significant difference in bandwidth between both sides. As no significant difference in the control bandwidth of the contralateral limb was observed between both groups, it can be inferred that both share a similar relevant athletic ability. Lastly, relating maximum modeled knee movement speed to degree of proprioceptive augmentation suggests a positive correlation with saturation up to a limit (fig. S4C).

Overall, these results suggest that TF AMI constructs provide increased proprioceptive information, fine motor control, and dynamic control bandwidth over conventional residual TF musculature in

isolation from physical prosthetic interactions and whole-body dynamics. Furthermore, the advantages of intramuscular electrodes over surface electrodes are not only limited to SNR improvements (fig. S5) but may also include practical control advantages, as evidenced by the significant performance improvements OMP subjects demonstrate over CTL subjects that are not also demonstrated by the AMI cohort.

Enabling diverse physical capabilities by coengineering tissues and mechatronics

Having assessed prosthetic control in isolation, we proceeded to investigate tasks involving progressively greater environmental contact dynamics. We reassessed each OMP subject's ability to walk on level ground after recovering from their final operative procedure (Fig. 1D). Kinetics of the bionic knee prosthesis measured during level-ground walking suggest that our controller appropriately compensates for the nonphysiological inertia of the mechatronic system to achieve physiological swing dynamics (Fig. 4A, i). Additionally, both OMP1 and OMP2 could use the bionic knee to match or exceed the preoperative maximum level-ground walking speed achieved with their prescribed variable-damping prosthesis (Fig. 4A, ii).

We then investigated each cohort's ability to make use of the myoneural control layer (fig. S2) to perform static sitting and standing movements. This task measured subjects' abilities to generate knee extension torque with reduced requisite whole-body agility by enforcing consistent ground contact with both feet (Fig. 4B). Representative EMG activity and kinetics generated by OMP1 demonstrate consistent and appropriate positive power generation at the prosthetic knee (Fig. 4B, i), and both OMP subjects demonstrated the ability to perform the sit-to-stand task without any handrail assistance by the third and final trial (Fig. 4B, ii). Ground reaction forces (GRF) collected from both OMP subjects suggest that they are able to utilize myoneural control of the prosthetic knee to achieve improved bilateral symmetry compared with use of their prescribed variable-damping prostheses (Fig. 4B, iii). In comparison, AMI subjects demonstrated improvement

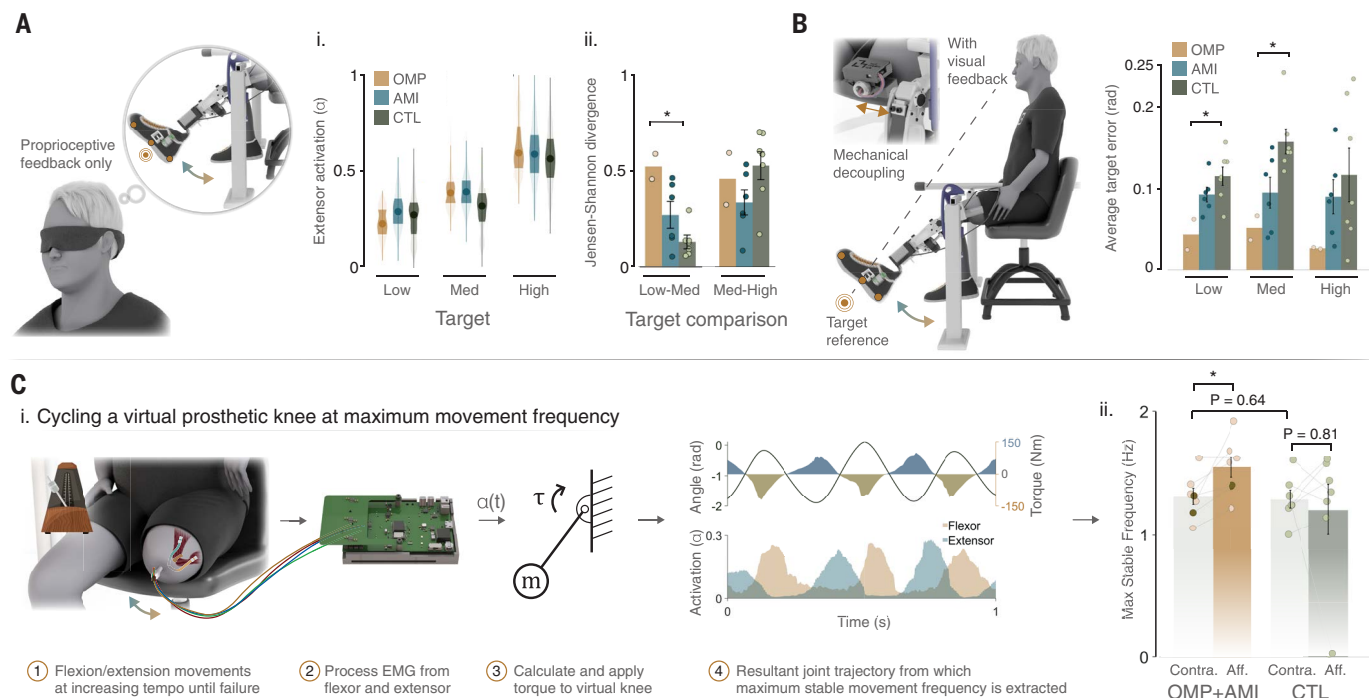


Fig. 3. Prosthetic knee control is maximized through soft and hard tissue augmentations. (A) Panel (i) shows activation of extensor muscles for three levels of steady-state prosthetic knee extension without visual feedback. Activation distributions are calculated per target level per subject and plotted in aggregate by cohort. Panel (ii) shows significance testing performed on the average Jensen-Shannon divergence between adjacent target level activation distributions per subject to determine the information available to distinguish targets ($n = 8$ movements per target level per subject, Kruskal-Wallis with post hoc comparisons and Bonferroni correction, $*P < 0.05$). (B) Evaluation of volitional free-space targeting ability with visual feedback. Panel at right shows target error calculated as the average absolute angular deviation of the bionic knee joint measured at steady-state extension ($n = 8$ movements per target level per subject, Kruskal-Wallis with post hoc comparisons and Bonferroni correction, $*P < 0.05$). (C) Evaluation of maximum full range of motion volitional knee movement bandwidth. Panel (i) shows how time-series EMG collected from cycling the phantom knee is processed into modeled kinematic knee trajectories. In step 3, $\alpha(t)$ = muscle activation; τ = torque at the modeled knee joint; and m = mass of the modeled shank. Panel (ii) shows maximum physical cycling frequencies measured from the contralateral knee and maximum modeled cycling frequencies calculated from the affected knee ($n = 2$ OMP subjects, and $n = 8$ AMI subjects aggregated, $n = 7$ CTL subjects, Wilcoxon rank-sum between two populations, Wilcoxon signed-rank within populations between contralateral and affected sides, $*P < 0.05$, OMP subjects: brown circles, AMI subjects: pink circles, CTL subjects: gray circles). All bars indicate mean and SEM.

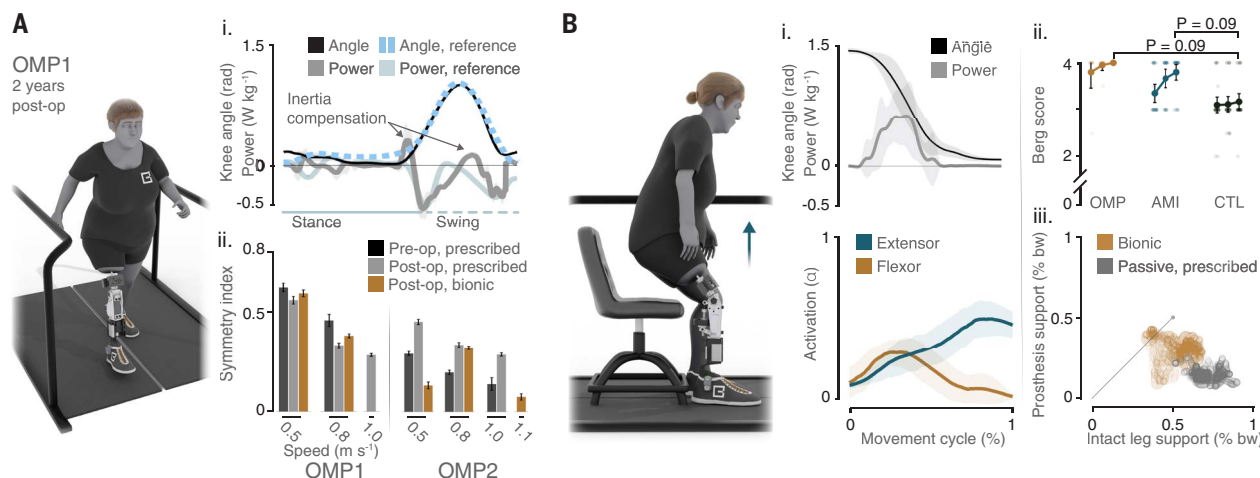


Fig. 4. The OMP facilitates fundamental human movement. (A) Level-ground walking with the bionic knee prosthesis after OMP implementation. Panel (i) shows representative kinetics and kinematics recorded at the bionic knee joint from OMP1 walking at 0.8 ms^{-1} ($n = 10$ steps) along with physiologically intact reference trajectories (51). Panel (ii) shows the bilateral symmetry index (0 being perfect symmetry) and maximum speeds achieved by OMP1 and OMP2 both pre- and postoperatively. (B) Sit-to-stand task performance. Panel (i) shows average muscle activation and resultant bionic knee dynamics for OMP1 during their last experimental trial ($n = 5$ movements). Panel (ii) shows sit-to-stand Berg scores over three successive trials for each cohort with significance testing performed on the last trial between all cohorts ($n = 5$ trials per subject, Kruskal-Wallis test with post hoc comparison and Bonferroni correction). Panel (iii) shows time-normalized traces of bilateral vertical ground reaction forces between legs generated by both OMP subjects during sit-to-stand movements ($n = 5$ movements per subject per condition). The time dimension is reduced to better show balance trends. All shaded regions indicate SEM. All bars indicate mean and SEM.

by the third and final trial to successfully complete the task mostly unassisted (Fig. 4B, ii). By contrast, the CTL cohort demonstrated limited improvement throughout all three trials and continued to rely on handrail assistance. However, none of the comparisons of final trial performance differences between cohorts reached significance. These data suggest the possibility of a causal relationship between the myoneural and mechanical augmentations provided by the OMP and improved functional outcomes in tasks that require physical interaction and direct control of the bionic knee.

We instructed all cohorts in static obstacle drills to assess their abilities to perform free-space knee positioning movements interspersed with discrete ground impact events. Subjects performed two types of obstacle drills with two sizes of obstacles each (Fig. 5A). The over-back obstacle drill required that subjects clear the obstacle with the bionic knee in the forward direction before returning to their starting position. The top-tap obstacle drill required that subjects

make contact with only the top of the obstacle using any part of the prosthetic foot in both forward and return movements. Subjects were instructed to perform as many successful cycles within 30 s as possible for each combination of drill type and obstacle size. OMP subjects significantly outperformed CTL subjects by average successful completion percentage across all four variants of the obstacle drill (Fig. 5C, i), whereas no other significant performance differences were observed between cohorts. Knee muscle activations and kinematic trajectories from representative subjects of each cohort suggest that some socket users may experience impact-induced artifacts in the EMG channels used for knee control that cause illegal contact with the obstacle upon initial weight-bearing (Fig. 5C, ii, and movie S4). These artifacts occurred despite computational methodologies that were deliberately implemented to filter out such artifacts (22). By contrast, evidence of these impact artifacts was not observed in OMP subjects, who performed with almost no flaws throughout all task variants. The outcomes of this

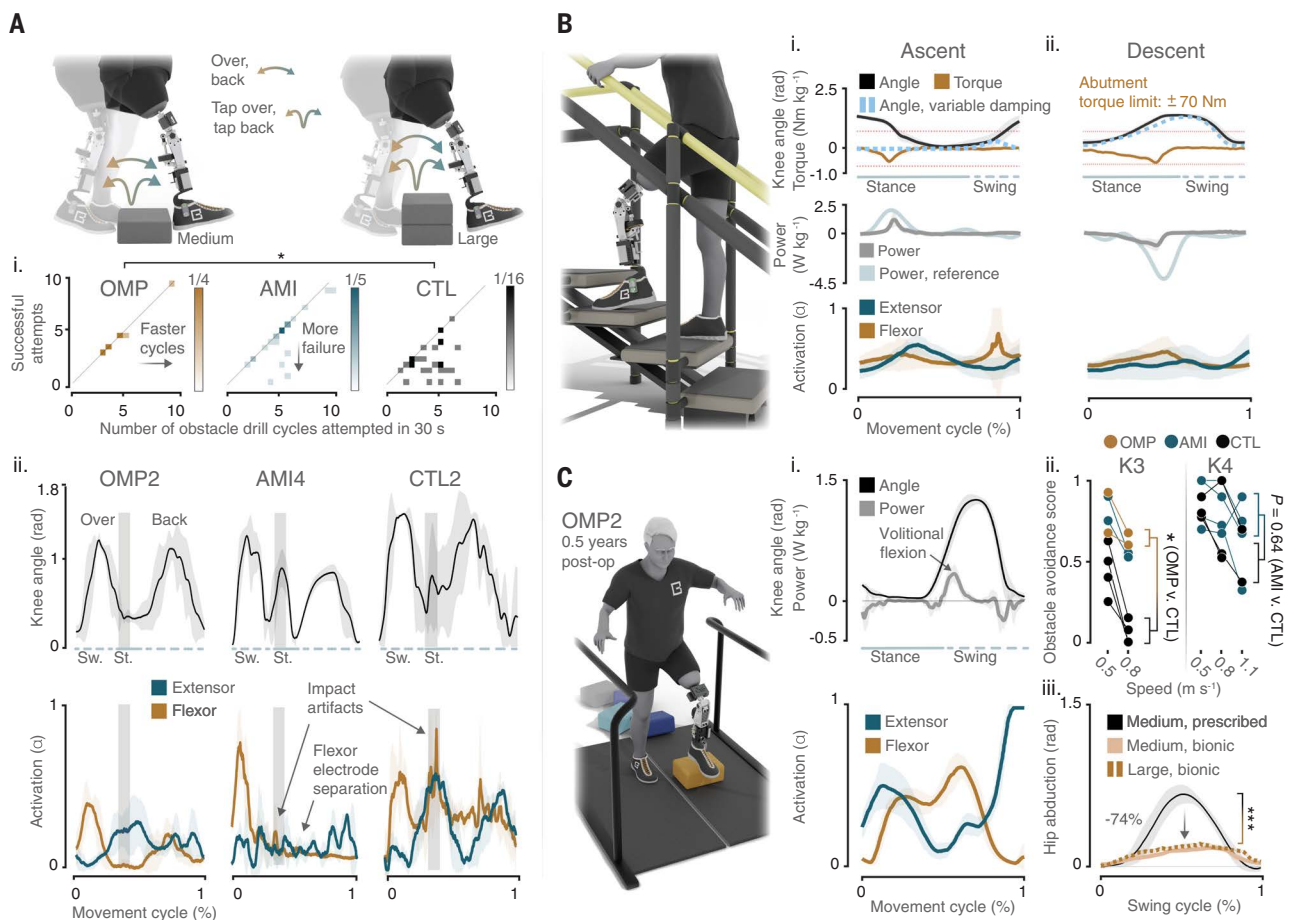


Fig. 5. Physical realization of phantom joint movements produces versatile behaviors. (A) Static obstacle drill performance. Panel (i) shows distributions of obstacle avoidance performances for each cohort with all four task variants plotted together. Color shade represents local distribution height. Significance testing between cohorts performed with subjects' average successful completion percentage ($n = 4$ task variants averaged per subject, Kruskal-Wallis test with post hoc comparison and Bonferroni correction, $*P = 0.023$). Panel (ii) shows representative muscle activations and bionic knee kinematics for the over-back task with large obstacles ($n \geq 4$ sequential movement cycles per subject). Gray rectangles indicate periods of ground impact. (B) OMP performance during stair ascent and descent. Panel (i) shows kinematics, kinetics, and muscle activity for OMP subjects during step-over-step stair ascent with the bionic knee. Panel (ii) shows the same for step-over-step stair descent ($n = 10$ gait cycles per condition per subject). Variable-damping knee ascent kinematic recorded from OMP2 during step-by-step gait ($n = 4$ gait cycles). Variable-damping knee descent kinematics (50) and physiologically intact reference power trajectories (51) are provided for reference. Horizontal red lines designate abutment torque limits. (C) Bionic knee control over incoming obstacles. Panel (i) shows representative muscle activations and bionic knee dynamics for OMP2 ($n = 8$ sequential obstacle avoidance movements). Panel (ii) compares obstacle performance score at the fastest tested speed by cohort ($n = 10$ obstacles to calculate score, Kruskal-Wallis test with post hoc comparison and Bonferroni correction, $*P = 0.048$; table S2). Subjects at K3 and K4 activity levels graphed separately. Panel (iii) compares OMP subjects' peak hip abduction when using their prescribed variable-damping prosthesis and bionic knee to overcome obstacles ($n = 10$ movements per subject per condition, Wilcoxon signed-rank, $***P < 0.001$). All shaded regions indicate SEM. All bars indicate mean and SEM.

experiment suggest that osseointegration is an effective solution to maintaining EMG signal integrity during high-impact events through elimination of prosthetic socket interference.

All cohorts were tasked with ascending and descending stairs to determine their abilities to exert continuous neuromuscular control throughout whole-body postural changes, alternating stance and swing transitions, and positive power generation and damping phases. OMP subjects gained the ability to ascend stairs with a step-over-step gait with handrail assistance when using the bionic knee instead of being limited to a step-by-step gait typical of variable-damping knees (Fig. 5B, i). They achieved step-over-step gait kinematics with handrail assistance during both ascent and descent despite being limited to 70 N·m of absolute torque at the knee joint to prevent damage to both the residual femur and e-OPRA abutment itself (27). Rates of stair ascent and descent were calculated for all cohorts (fig. S6). Some CTL subjects were observed to necessarily revert to a stiff-legged gait to ascend, and some AMI subjects demonstrated difficulty maintaining knee flexion at terminal swing during stair ascent despite their relative ease with knee flexion during the initial swing phase (movie S5).

Lastly, subjects were challenged with avoiding foam block obstacles regularly placed in the path of the bionic limb while walking on a treadmill at various speeds (movie S3). This task was designed to evaluate each subject's ability to effectively utilize the bionic knee in a cognitively and physically demanding situation (table S2). Among subjects rated at the K3 activity level, only the OMP cohort demonstrated a significantly greater ability to avoid obstacles compared with CTL subjects when comparing best trial score at their fastest tested walking speed of 0.8 ms⁻¹ (Fig. 5C, ii). Among K4 subjects, no significant differences in best trial score were found between AMI and CTL subjects at their fastest tested walking speed of 1.1 ms⁻¹. Representative muscle activations and resultant knee kinematics recorded from OMP2 reveal consistent, sustained flexor activations when clearing obstacles (Fig. 5C, i), eliminating the pathological hip abduction otherwise required to circumduct obstacles when using variable damping knee prostheses (Fig. 3E, iii) (28).

The results of this section suggest that OMP subjects, but not necessarily AMI subjects, may have advantages over CTL subjects when controlling the bionic knee toward certain functional objectives. These advantages cannot be solely explained by augmented neuromusculature

alone but may be partially attributable to the mechanical interfacing and intramuscular sensing capabilities provided by the e-OPRA implant system.

Enhancing prosthetic embodiment by promoting agency and ownership

To determine subjective outcomes of bionic knee interactions beyond performance-based metrics, we administered a questionnaire (table S3) after each of the previous experiments (free-space knee extension, static obstacle drills, level-ground obstacle avoidance, and stair ascent and descent) to quantify relative changes to perceived prosthetic embodiment. To account for individual subjectivity, changes in embodiment were assessed relative to each subject's own scores regarding embodiment of their prescribed prosthesis before exposure to the bionic knee. OMP subjects demonstrated positive and significantly greater average embodiment changes relative to CTL subjects after the stair ascent and descent task (Fig. 6B, i). Regarding changes to subcategories of embodiment averaged over all tasks, OMP subjects demonstrated positive and significantly greater average changes relative to CTL subjects in ownership and agency (Fig. 6B, ii). Furthermore, OMP subjects demonstrated positive and significantly greater average changes relative to even AMI subjects in agency.

Discussion

This work investigated anatomical prosthetic integration as a means to increase agility and embodiment at the TF level. OMP subjects demonstrated significantly improved performance relative to the CTL cohort when controlling the bionic knee to avoid obstacles. This advantage may be attributable not only to enhanced agonist-antagonist neuromuscular physiology but also to greater control-signal integrity as a function of permanently implanted intramuscular electrodes and the lack of prosthetic socket interference. Our testing also validated a direct neuromuscular knee controller capable of remarkable task versatility when utilized in the OMP, highlighting the potential of biomimetic control schemes that computationally mirror the user's neuromuscular architecture. In addition, we demonstrated that increasing anatomical prosthetic integration in subjects with preexisting amputation can enhance prosthetic embodiment, uncovering a self-perceptive metric to more thoroughly assess the outcomes of amputation design

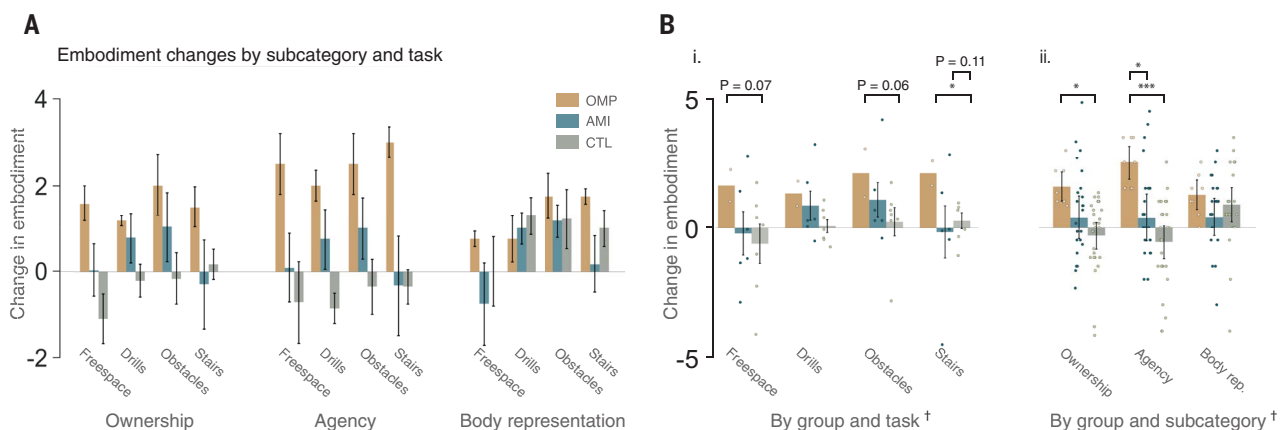


Fig. 6. The OMP sustains outsized improvements in embodiment and bionic performance. (A) Overall embodiment questionnaire results reported by subject, task, and subcategory of embodiment. Changes in embodiment are relative to baseline values established by use of each subject's prescribed prosthesis. (B) Aggregated changes in embodiment. Dagger indicates a statistically significant interaction in a parsimonious linear mixed effects model (group, group:subcategory, and group:task fixed effects; individual subject random intercept. $P = 0.02$). Panel (i) shows embodiment questionnaire results reported by subject and task averaged over all embodiment subcategories. Statistical significance between groups for each task type was determined through separate, preplanned, and complementary analyses (multiple comparisons with Bonferroni correction within task type, $*P < 0.05$). Panel (ii) shows embodiment questionnaire results reported by cohort group and embodiment subcategory across tasks. Statistical significance between groups for each embodiment subcategory type was determined through separate, preplanned, and complementary analyses (multiple comparisons with Bonferroni correction within task type, $*P < 0.05$, $***P < 0.001$).

and prosthesis selection. Together, these results suggest that anatomical prosthetic integration and the physical realization of phantom joint dynamics should not be excluded in the pursuit of further lower-extremity restoration.

Our experiments sought to attribute disparities in performance to differences in neuromuscular structure, control-signal acquisition, and mechanical prosthetic attachment by applying multiple comparisons between cohorts (fig. S7A). Without additional context, OMP subjects would not be expected to perform better than other cohorts because of their age, body mass index, and time since original TF amputation interpreted as an indicator of muscle atrophy. In OMP subjects, all three factors exceed those of almost all other subjects (fig. S7B and table S1). Thus, any significant advantages demonstrated by the OMP cohort were achieved despite their inherent disadvantages.

Regarding agonist-antagonist coupling in the TF case, subjects with the AMI (whether OMP or AMI cohort proper) demonstrated significantly greater maximum cycling frequency when using their residual musculature to control a modeled knee than when cycling corresponding intact muscles to move their physiological joint (Fig. 2D, ii). As no such advantage was observed in the CTL cohort under the same conditions, and no modeled knee features are obviously biased toward either comparison group, it is difficult to attribute this performance disparity to a particular parameter tuning. The CTL cohort did not perform significantly worse when cycling their residual musculature compared with cycling their intact joint, despite their limited ability to generate activity in proprioceptive afferents upon antagonist stretch. Conversely, those with the AMI performed significantly better in the same bilateral self-comparison while inducing no more than physiological afferent stretch (29). Thus, we hypothesize that (i) the rhythmic control of amputated musculature can exceed that of its counterpart in an intact limb; (ii) the ability of amputated musculature to achieve supraphysiological movement speeds is related to both reduced distal inertia and sufficiently restored proprioceptive feedback; and (iii) supraphysiological movements of amputated musculature can be realized as physical prosthetic joint kinematics.

The results of the free-space reaching tasks suggest that intramuscular electrodes sensing AMI musculature possess control advantages over other tested sensor-musculature combinations. When relying on only proprioceptive feedback, OMP subjects generated significantly more information to discriminate between low and medium phantom knee extension levels compared with CTL subjects (Fig. 2C, ii). This implies that OMP subjects were better able to generate graded control signals at low levels of activation using advantages agnostic to any downstream prosthetic interactions. In contrast, the CTL cohort's minimal JSD between low and medium levels of phantom knee extension qualitatively suggests that they are unable to distinguish finer levels of knee position. With additional visual feedback of prosthetic knee position, OMP subjects congruently demonstrated significant improvements in position control accuracy over CTL subjects at low and medium knee extension levels (Fig. 2C, i). Notably, AMI subjects equipped with only surface electrodes did not demonstrate significant advantages over CTL subjects in terms of information generation or joint position accuracy. These comparisons imply that the increased signal-to-noise ratio provided by intramuscular electrodes, along with the absence of prosthetic socket interference, may contribute meaningfully toward improved prosthetic knee control tasks.

The cyclic sit-to-stand, static obstacle drill, stair ascent and descent, and obstacle avoidance tasks represent an increasing level of requisite whole-body coordination and dynamic interaction between each subject and the environment. Not only did OMP subjects start from the highest performance baseline in the first trial, they were able to complete the sit-to-stand task wholly unassisted by the third and final trial (Fig. 3B, ii). AMI subjects achieved lower initial performance but qualitatively demonstrated rapid improvement to near-perfect performance by the third trial. By contrast, CTL subjects qualitatively demonstrated

limited improvement over the course of testing, with most still requiring handrail assistance by the end. Comparative traces of the OMP cohort's bilateral vertical ground reaction forces (GRF) for each leg over the third trial (Fig. 2B, iii), along with representative muscle activation and knee torque trajectories (Fig. 2B, i), suggest that OMP subjects achieved this performance by appropriately coordinating positive power generation at the bionic knee rather than trivially relying on their intact side for full support. Although differences in performance between cohorts did not reach significance, the data suggest that OMP subjects are able to appropriately generate assistive knee torque toward coordinated whole-body movements.

In the static obstacle drill, OMP subjects demonstrated significantly higher average success rates across all four experimental conditions compared with CTL subjects, while no other significant performance differences were observed between cohorts (Fig. 3C, i). Contributing factors for the OMP cohort's improved performance can be induced through representative knee kinematics and muscle activation trajectories during the large obstacle over-back drill (Fig. 3C, ii). At the moment of ground impact after clearing the obstacle in the forward direction, AMI4 and CTL2 subjects demonstrated recurring, nonphysiological activation signal artifacts in the flexor EMG channel that caused unintended knee flexion and failure of the drill cycle by illegal obstacle contact. Additionally, AMI4 reported difficulties flexing the prosthetic knee upon the return portion of the movement cycle (Fig. 3C, ii), which we hypothesize to be due to posture-dependent socket loading leading to separation of the flexor electrode from the skin. By contrast, OMP2's knee kinematics and muscle activation trajectories remained qualitatively smoother and artifact-free throughout the movement cycles. Insignificant differences in score between AMI and CTL cohorts in this experiment suggest that the effect of improved neuromuscular function from agonist-antagonist coupling is not sufficient to produce detectable improvements in hybrid swing and stance task performance with the population sizes studied. Rather, as demonstrated by the OMP cohort's near-perfect scores, it may also be necessary to maintain the integrity of the electrode-muscle interface, achieved in this case through elimination of socket interference.

The obstacle avoidance experiment assessed each subject's ability to utilize the bionic knee toward achieving whole-body coordination in a highly dynamic environment. The OMP cohort's obstacle avoidance performance while walking at 0.8 m/s was significantly better than that of K3 CTL subjects (Fig. 3E, ii). The K3 AMI cohort did not perform significantly better than the K3 CTL cohort. Recalling the OMP subjects' athletic disadvantages related to their general physiology (fig. S7B and table S1), their significant performance improvement over K3 CTL subjects can be attributed to the extent of their bionic integration in a similar manner as in previous analyses. However, these advantages appear insufficient to enable OMP subjects to match the performance of most K4 subjects, who are capable of high-impact activities (Fig. 3E, ii). Indeed, the fastest tested treadmill walking speed for K4 subjects in the obstacle avoidance experiment exceeds the maximum walking speed of either OMP subject without obstacles (Fig. 3A). We conclude that although OMP subjects demonstrated unparalleled within-class performance owing to their high degree of anatomical integration, there are still reasonable limitations of the platform's ability to compensate for general athletic ability.

Despite gaining the ability to ascend step-over-step, OMP subjects still required the use of handrails to complement use of the bionic knee for positive power production during stair ascent and damping during stair descent. This necessity is due to the current design of the e-OPRA abutment that limits it to no more than 70 N·m in bending, and by mechanical transmission, that permits no more than 70 N·m of torque to be sustained at the bionic knee. This bending limit is shared by the clinical TF OPRA system (27), optimistically suggesting that any advantages of the OMP platform over the clinical TF OPRA system may be considered potential benefits for an individual who is

already opting for osseointegration. Although TF socket users are not mechanically limited in the same manner with respect to maximum bending limits, some AMI and CTL subjects experienced separate issues related to unintentional knee extension upon hip flexion when attempting to ascend stairs (movie S3). Multiple AMI and CTL subjects were unable to control the degree of their extensor and flexor activations to maintain the knee in a flexed position to take the next step despite repeated attempts. This surprising outcome highlights three potential limitations related to controller design, mechanical prosthesis attachment interface, and even surgical design. First, the controller assumes only two muscle-specific channels of EMG information to inform impedance at the knee despite potential nonredundant information contributable by other residual muscles. Second, some TF socket-users may necessarily cocontract muscles within their residuum to support the weight of the prosthesis during hip flexion, thereby coupling muscle activity required for socket stability with that assumed to be solely dedicated to joint control. Similarly, postural changes may affect surface EMG acquisition within the socket by altering the internal pressure gradient and nonlinearly shifting the impedance of the electrodes. Third, the bionic knee has no ability to provide mechanical feedback to the soft tissues of the residuum as in an intact knee, reducing the accuracy of proprioceptive sensation. During stair ascent, physiologically intact subjects demonstrate knee extensor activation and hip flexor activation at terminal swing before single stance of the subsequent step (30). Both extensor and flexor muscles receive constant dynamic feedback on the shank's state through rotation of the knee joint, and relevant muscles are informed to maintain knee flexion. By contrast, subjects with TF amputation may retain this natural tendency to activate their extensors at terminal swing, but for some, the degree of activation may be difficult to control with interference from the socket and without dynamic feedback from the shank. This would explain the uncontrollable knee extension observed in some subjects during ascent. In this investigation, the BF and RF muscles were selected for AMI construction given their large size, matched agonist to antagonist sizes, superficial nature, and line of action. These characteristics led to an ease of surgical construction and a balance of agonist-antagonist muscle dynamics. It is possible that the direct neuromuscular knee controller may benefit from the use of a plurality of knee AMI constructs to more closely reflect the redundancy of intact anatomy and to provide greater knee control information. Multiple AMI pairs may provide a range of neuromuscular characteristics resulting from the use of both biarticular and monoarticular neuromechanical functionalities.

Although the OMP cohort's improved ownership and agency are reasonably attributable to their high degree of anatomical integration, osseoperception, and task performance, no significant differences in body representation were observed between any cohorts (Fig. 4B, ii). Assuming that the three subcategories of embodiment are appropriately defined (31, 32), and considering that the bionic knee prosthesis appeared the same to all subjects, this result may not be surprising. We hypothesize that further improvements to all subcategories of embodiment, but especially body representation, may require providing additional feedback to the subject through cutaneous or proprioceptive modalities. It remains to be determined whether the acute changes in embodiment measured are consistent with long-term use of a bionic device or if prosthetic embodiment is dependent on a shifting baseline that is observable by exposing subjects to devices that are better or worse than their current device regardless of their current device's objective capabilities.

Our results demonstrated that an increase in invasiveness at the transfemoral level can yield outsized improvements in outcomes pertaining to successful rehabilitation after transfemoral amputation. The individual and combined surgical interventional factors assessed may inform the commercial development of bionic knee prostheses. We posit that the capabilities demonstrated by the osseointegrated myoneural prosthesis provide evidence that further anatomical integration with

the prosthesis, rather than the maintenance of an artificial separation, is required for advancing progress toward physiological function, embodiment, and rehabilitative potential after limb loss.

Materials and methods

Experimental design

This study was undertaken in conjunction with registered clinical trial NCT03720171 which seeks to evaluate the feasibility of achieving direct control over a neuromechanical prosthetic system using the e-OPRA implant system (Integrum AB) in subjects with unilateral transfemoral amputation (Fig. 1C). We additionally utilized and extended results related to registered clinical trial NCT03913273 pertaining to the agonist-antagonist myoneural interface (AMI), which is a prosthetic control interface that reconstructs the neuromuscular tissues of the residual limb to recreate agonist-antagonist muscle dynamics and preserve afferent proprioceptive signaling. Specifically, this study investigates outcomes pertaining to the OMP platform that combines the e-OPRA implant system with the AMI and a directly controllable prosthetic joint within a single individual with amputation. The study follows a prospective, non-randomized design wherein sex is not considered. A total of 15 subjects were recruited into three investigational cohorts (table S1), and the effects of independent variables were assessed through multiple comparisons between these cohorts. We recruited a total of 2 subjects with the OMP platform (OMP cohort), 6 subjects with the AMI (AMI cohort), and 8 subjects with conventional transfemoral amputations (CTL cohort), including targeted muscle reinnervation and targeted sensory reinnervation procedures. We hypothesized that OMP subjects, through combined enhancements provided by the AMI and e-OPRA implant system, would demonstrate greater rehabilitation potential through increased prosthetic control and embodiment compared to subjects without such enhancements. To test this hypothesis, we: (i) developed a bionic knee prosthesis and direct knee controller capable of continuous control of joint impedance during both stance and swing phases; (ii) evaluated the influence of each potential enhancement through progressive experiments ranging from isolated neuromuscular assessments to full-body gait dynamics with the bionic knee prosthesis; and (iii) indicated clinical relevance by comparing performance and embodiment outcomes relative to subjects' prescribed variable damping knee prostheses.

All experiments were conducted in a controlled lab or hospital environment under researcher supervision. Experiments were designed to minimize the influence of training effects. Only a brief period of acclimatization to each new task was afforded to each subject before data collection. The bionic knee device was unpowered between periods of active experimentation and during breaks provided for subject comfort. For each subject, primary data collection involving interactions with the bionic knee prosthesis typically occurred over a period of 3 experimental days, and no experiment spanned multiple days. It is estimated that each subject was exposed to a total of 90 min of active control over the bionic knee prosthesis during the course of experimental data collection.

Considering the novelty of the OMP platform compared to socket-based suspensions, both OMP subjects were necessarily involved in the process of adapting the bionic knee prosthesis and EMG system for their needs before experimental data collection. The totality of their involvement consisted of approximately 10 lab visits each to perform mechanical adjustments, ensure proper mounting of electronics and routing of wires, and ensure that signals provided to the direct neuromuscular controller were conditioned similarly to those processed from our previous work involving socket-based suspensions (7, 8, 33). During these visits, OMP subjects were exposed to primitive forms of active knee control, e.g., proportional impedance control in free space based on muscle activations, but they were not exposed to the final structure and gains of the direct neuromuscular controller before experimentation. Further, OMP subjects were not exposed to the

conditions of the experiments performed for data collection beyond out-of-context, isolated movements, e.g., standing from a seated position and walking across the room with crutches.

Subject recruitment

A total of 15 subjects with relevant biometrics were recruited for this study (table S1). Two subjects with preexisting conventional transfemoral amputation were first pre-screened by medical staff at Mass General Brigham Hospital (Boston, Massachusetts) to confirm eligibility to receive the OMP platform under Mass General Brigham IRB protocol #2017P000685. Once consented, these 2 subjects received the OMP platform and consented to human subjects testing at MIT (Cambridge, Massachusetts) under MIT IRB protocol #1703900740. A total of 6 subjects with the unilateral transfemoral AMI were recruited under MIT IRB protocol #1702832726. A total of 8 subjects with conventional unilateral transfemoral amputation were recruited under MIT IRB protocol #1702832726. Cohort sizes were based upon our previous relevant study designs (3, 8) and further constrained by funding, subject availability, and federal limitations on investigational device exemptions. Subjects and researchers were not blinded to the testing conditions. All subjects were proficient in the use of prescribed passive knee prostheses and assessed to be capable of ambulation with variable cadence (K-levels 3 and 4). Exclusion criteria consisted of conditions detrimental to neuromuscular health beyond amputation, including coronary artery disease, diabetes mellitus, chronic obstructive pulmonary disease, extensive microvascular compromise, pregnancy, diseases specifically affecting neuromuscular control, and active smoker. All subjects provided written informed consent prior to testing. The study protocol can be made available upon reasonable request to the corresponding author. The period of recruitment and data collection occurred from 2017 to 2024. All data were collected at the MIT Media Lab (Cambridge, Massachusetts) and Mass General Brigham Hospital (Boston, Massachusetts).

Osseointegrated myoneural prosthesis surgical procedure

The implementation of the OMP consists of two major surgical stages to accommodate the process of osseointegration followed by recovery and rehabilitation procedures after each (Fig. 2D). Stage 1 introduces the BioHelix fixture to the residual femur to begin the process of osseointegration and implementing soft tissue modifications (Fig. 1C). Stage 2 includes routing of permanent intramuscular electrodes through the newly introduced external e-abutment. Specifically, a revisional TF AMI was constructed in each of the two OMP subjects with preexisting transfemoral amputation to improve phantom limb proprioception for subsequent high-fidelity control of a prosthetic knee joint. The rectus femoris was selected to serve as the primary extensor controller and the biceps femoris was selected to serve as the primary flexor controller. Additionally, a fascicular split was performed on the sciatic nerve with distal ends introduced to autologous muscle grafts. This latter procedure was performed to promote peripheral nerve regeneration, attempt prophylactic prevention of symptomatic neuromas, and provide muscular targets for the potential application of feedback through functional electrical stimulation (FES). With respect to hard tissues, the distal end of the residual femur was transected approximately 1 cm and reamed to the appropriate diameter. The e-OPRA BioHelix fixture (Integrum AB) was subsequently introduced into the medullary cavity.

After a recovery period, the second stage was performed to mate a titanium abutment to the osseointegrated BioHelix fixture. At this time, intramuscular electrodes were implanted into the revisional transfemoral AMI muscle constructs and autologous muscle grafts with leads routed through a femoral cortical window to the abutment. A total of 16 electrodes in eight bipolar pairs were implanted into the residuum with redundancy on the two muscles of the transfemoral AMI construct (Fig. 1B). Myoelectric activity generated by the interface

is conducted through implanted intramuscular electrodes to a distal, externally-accessible port in the e-abutment (Fig. 1B). Autologous muscle grafts are reinnervated with mixed nerves and instrumented with intramuscular electrodes to access additional myoelectric information. The e-abutment's external surface provides a mechanical attachment point for a prosthetic knee.

Clinical data were collected in the preoperative, intraoperative, and perioperative periods, and included patient demographics, surgical time, x-rays, fluoroscopy movies, input/output, and pain control regimen and changes to such. Mean subject age was 60.10 ± 0.87 years at the time of the first stage and 60.97 ± 0.18 years at the second stage. Mean operative time was 482.50 ± 61.52 min for the first stage and 773.00 ± 65.05 min for the second stage. Intravenous fluid requirements, estimated blood loss, and urine output were all within safe margins during all procedures. Average length of post-operative stay was 3.50 ± 0.71 days for the first stage and 5.00 ± 0.00 days for the second stage. No complications or adverse events were noted in the postoperative period that were attributable to the e-OPRA system, and no infections were reported at all (34).

Bionic knee prosthesis

A single degree-of-freedom (DOF) mechatronic knee platform based on the initial series-elastic design of Carney *et al.* (35) was developed and used for all subsequent experiments in this study (fig. S1). The range of motion of the knee was limited by hardware and software to between 0° and 90° of flexion. On-board computation and sensors were selected to achieve continuous control of knee torque. A software interface enabled receipt of (EMG data streams from custom EMG processing hardware previously designed by our group (33). Force sensitive resistors were fixed to the sole of the foot cosmesis at toe, midsole, and heel positions to determine ground contact. System identification of the open loop torque bandwidth in the unloaded condition resulted in a mechatronic control bandwidth of 4.5 Hz. Inversion of the transfer function with an additional low-pass filter centered at 20 Hz yielded a realizable feedforward term. The feedforward term was used to tune the closed loop torque controller outlined in fig. S2, yielding a closed loop torque control bandwidth of approximately 10 Hz to encompass the full dynamic range of human knee movement. The same controller was applied to the system in the loaded condition to favor simplicity of implementation over theoretical gains in mechatronic bandwidth with the use of a separately tuned feedforward term for the stiffer equivalent system.

EMG processing and muscle activation

For subjects with prosthetic sockets, surface EMG was acquired using the techniques and thin electrodes developed by Yeon *et al.* (33). For OMP subjects, distal leads of the intramuscular electrodes were directly routed from the abutment to the same EMG processing hardware. For all subjects, EMG was processed to mitigate motion artifacts using the cumulative histogram filtering technique described by Yeon and Herr (22). EMG was collected from the palpated flexor and extensor muscles in CTL subjects, from the palpated biceps femoris and rectus femoris muscles in AMI subjects, and from the fixed, corresponding bipolar pairs of known insertion point in OMP subjects. For AMI and CTL subjects, raw EMG signals were collected at a sampling rate of 2 kHz and band-passed with a finite impulse response (FIR) filter (stop-band: 0 to 60 Hz, >350 Hz; pass-band: 70 to 350 Hz; stop-band attenuation: 85 dB; order: 198). OMP subjects demonstrated unique noise harmonics within the pass-band at 180 Hz and 300 Hz that were selectively isolated using corresponding notches (fig. S3) (stop-band attenuation: 45 dB; order: 300). Scalar values of processed EMG were extracted by calculating the root-mean-square (RMS) of the rectified EMG (100-ms window size).

To obtain an instantaneous value of activation $[\alpha(t)]$ for each muscle utilized for control, its processed EMG signal was first normalized to

produce an excitation signal $[\mu(t)]$. Specifically, normalization was performed by dividing each processed EMG reading by the peak processed EMG amplitude associated with maximum voluntary contraction (MVC) of that muscle to yield a scalar excitation value between 0 and 1. Subjects' MVCs and peak processed EMG values associated with each muscle were calibrated at the beginning of every experiment. Resultant peak processed EMG values were either utilized as divisors directly or first adjusted according to the specific experimental protocol. Resultant instantaneous excitation signals were subsequently transformed using the nonlinear scaling curve identified by Manal & Buchanan (36) to yield instantaneous activation signals. The superlinear slope of the scaling curve increases the sensitivity of the activation signal at the low end of muscle activation, a quality the researchers empirically determined from previous experience to be conducive for perceived prosthesis responsiveness. To better facilitate computation, the nonlinear scaling curve was approximated by a quintic function in this study (fig. S3).

Unified neuromuscular knee controller

The desired torque at the bionic knee joint is determined from the summation of contributions from an impedance-based finite state machine (FSM) and a continuous, myoneural impedance in conjunction with the current dynamical state of the joint:

$$\tau_{\text{des}} = \tau_{\text{des,FSM}} + \tau_{\text{des,neural}} + \tau_{\text{des,gravity}}$$

The basic structure of this summation is shown in fig. S2. The FSM alternates between two primary states, stance and swing, depending on detection of ground contact by any of the force-sensitive resistors at the bottom of the cosmesis. Its primary role is to guarantee safety under all operating conditions, execute cyclic gait patterns without interrupting continuous myoneural control, and inform myoneural control by adjusting gains to amplify or mitigate the contribution of muscle activation control signals. Within both FSM states are several unmodulated impedance-based components that individually contribute to the instantaneous, intrinsically desired torque at any time their activation conditions are satisfied:

$$\tau_{\text{des,FSM}} = \sum_{i=0}^n [K_{\text{FSM},i} \cdot (\theta_{\text{des,FSM},i}) + B_{\text{FSM},i} \cdot \dot{\theta}]$$

Rather than separately codifying a specific gait modality such as stair ascent or descent, components are designed to heuristically assist with generalized flexion and extension movements. For example, one component exists to provide variable damping whenever the prosthesis is in stance and flexing, and it will activate during both stair descent, sitting, and other less common movements without explicit classification of terrain. Another component activates during swing once cyclic stance and swing cycles are detected. This component provides flexion torque during the stance to swing transition to compensate for the reflected inertia of the shank through the variable gear train (movie S6), and it is active during both stair ascent and level-ground walking. It remains inactive during acyclic swing and stance patterns to allow impedance contributions from myoneural control to dominate.

In parallel, several myoneural impedance modulation components that are informed by device state and flexor and extensor activations contribute to the final torque output at the joint. The components may be active in any combination at any time, precluding any mutually exclusive activation conditions. Like the impedance-based FSM, the myoneural control structure does not contain features that explicitly classify terrain. Impedance control parameters consisting of stiffness, damping, and angular joint setpoint are a function of the flexor and extensor muscle activations and the dynamical state of the device. These define an instantaneous desired torque:

$$\tau_{\text{des,neural}} = K_{\text{neural}}(\alpha, \bar{\theta}) \cdot [\theta_{\text{des,neural}}(\alpha, \bar{\theta}) - \theta] + B_{\text{neural}}(\alpha, \bar{\theta}) \cdot \dot{\theta}$$

Parameters vary smoothly over the domain of the involved continuous variables through the use of logistic, distributive, and affine functions that are repurposed for their ability to shape the impedance parameters. Parameters shift discretely based on the categorical variables. Graphical representations of these functions used to determine stiffness, damping, and setpoint for myoneural impedance can be seen in fig. S2. As a concrete example, angular setpoint in degrees is typically calculated as a continuous logistic function of the current difference in muscle activations that is discretely modulated by the previous history of muscle activations:

$$\theta_{\text{des,neural}} = \theta_{\text{min}} + \theta_{\delta}(\alpha, \bar{\theta})$$

To compute this, a θ_{lock} is first acquired and stored as the instantaneous knee angle whenever the difference in muscle activations, $\Delta\alpha = \alpha_{\text{BF}} - \alpha_{\text{RF}}$, changes sign. θ_{lock} is then bound to the range $[0.02 \cdot (\theta_{\text{max}} - \theta_{\text{min}}), 0.98 \cdot (\theta_{\text{max}} - \theta_{\text{min}})]$ before being converted into an intermediate value α_{lock} using:

$$\alpha_{\text{lock}} = \frac{\ln\left(\frac{\theta_{\text{max}} - \theta_{\text{min}}}{\theta_{\text{lock}}} - 1\right)}{-10}$$

Bounding the range of θ_{lock} avoids undefined values and tail regions of diminishing slope in the equation for α_{lock} . Subsequently, θ_{δ} is an additive deviation from θ_{min} defined as:

$$\theta_{\delta} = \frac{\theta_{\text{max}} - \theta_{\text{min}}}{1 + e^{-10(\alpha_{\text{lock}} + \Delta\alpha)}}$$

It can be seen that the expression for α_{lock} is an inverse logistic function with bound range that determines an equivalent value in terms of muscle activation for θ_{lock} . It sets a baseline value to which $\Delta\alpha$ is added in the calculation of θ_{δ} , which is a logistic function that is scaled by the range of motion and determines knee setpoint. Unlike the ankle joint's neutral position which is bound by ligaments that hold the low-mass foot approximately perpendicular to the shank at rest (3, 8), the knee has no neutral position and may rest at any angle according to the relative influence of gravity. The calculation of $\theta_{\text{des,neural}}$ presented here allows a subject to utilize a floating neutral position set whenever muscle activity initiates that is adaptable to multiple task contexts. The use of a bound logistic function to smoothly vary θ_{δ} promotes predictable motion within the finite range of motion. Finally, the resetting nature of θ_{lock} whenever the sign of $\Delta\alpha$ changes provides the user the ability to hold an arbitrary knee angle with high stiffness through the use of even perceived co-contraction despite the influence of noisy EMG signals observed at higher levels of activation (37).

Myoneural stiffness and damping are generally defined using a linear combination of logistic and affine functions that are modulated by α_{BF} and α_{RF} . The gains and baseline values applied in these functions vary widely depending on dynamical state and historical context. For example, in certain contexts, such as knee flexion during stance, the ability to generate flexion torque is disabled as both muscle activations are applied toward generating knee extension torque only. The majority of stiffness and damping functions take the form of:

$$K_{\text{neural}} = K_{\text{min}} + \left(\frac{K_{\text{base}} \cdot L}{1 + D e^{g(\theta)}} - K_{\text{min}} \right) \cdot f(\alpha) + C(K_{\text{base}} - K_{\text{min}}) \cdot h(\alpha)$$

and

$$B_{\text{neural}} = B_{\text{base}} \left(1 + \frac{L}{1 + D e^{g(\theta)}} \right) \cdot g(\alpha) + C$$

where L , D , and C are all constants that tune the scale of the individual features and vary by context. Logistic and affine components allow for smooth increases of sensitivity, or “boosting,” of individual impedance parameters as a function of knee angle during critical portions of different movements.

The controller requires only a few parameters to be tuned from subject to subject. Beyond accounting for MVC to compute α_{BF} and α_{RF} , unitless K_{base} and B_{base} scalars are tuned to compensate for individual variations from subject to subject according to:

$$K_{base} = 1.4 \cdot mass_{kg} \cdot (\theta_{max,deg} - \theta_{min,deg})$$

and

$$B_{base} = 0.1 \cdot K_{base}$$

The scaling for K_{base} ensures sufficient torque generation for the most demanding tasks of stair ascent and descent when muscles are activated near their maximum value. The scaling for B_{base} ensures stable behavior of the joint across operating conditions during stance and swing. For OMP subjects, both values were scaled as usual, but peak torque was clamped to an absolute value of 70 N·m due to abutment loading limits as defined in the associated MIT IRB protocol. A detailed pseudocode implementation of the controller loop running at a fixed 1-kHz rate is provided in an online repository (38).

Evaluation of neuromuscular function

To obtain a measure of peripheral neuromuscular function, movies of the residual agonist and antagonist muscles responsible for knee flexion and extension were collected via ultrasound (US) probe (MicrUs Pro L-40N, Teledyne S.r.l, Milan) as each subject volitionally moved their phantom limb at preset levels of perceived effort. Muscles were selected for optimal signal quality and separation, and selection was performed by palpation and consultation of surgical charts when available. For each muscle, 10 trials at each of 25, 50, 75, and 100% levels of effort were recorded when acting as the agonist and antagonist. Each trial sequentially consisted of 2 s of rest, 2 s of sustained effort, and 2 s of rest. Ultrasound measurements from both agonist and antagonist muscles were processed to quantify fascicle strain using UltraTrack fascicle measurement software (39, 40). Simultaneous EMG was recorded from each muscle using surface electrodes or implanted intramuscular electrodes (OMP only) as patients contracted each muscle at preset levels of perceived effort using the custom EMG sensor system (33). In this investigation, secondary spindle firing rates were not measured directly, but rather were estimated using the following equation with inputs of measured fascicle strain and muscle activation at each level of perceived effort:

$$\text{Type II muscle spindle firing rate} = 0.0743 \cdot (80 + 13.5 \cdot \text{deflection}_{mm} + 20 \cdot \alpha)$$

Specifically, the scalar constant $K = 0.0743$ was determined using Formento *et al.*'s proposed methodology to adapt the rodent model to human muscles (41):

$$\text{Type II muscle spindle firing rate}_{max} = K \cdot (80 + 13.5 \cdot \text{deflection}_{mm,max} + 20 \cdot \alpha_{\text{deflection}_{mm,max}})$$

where the “max” subscript indicates the maximum corresponding value expected to be observed from a muscle during typical physical activities like walking and passive joint movement, and $\alpha_{\text{deflection}_{mm,max}}$ indicates the activation of the muscle at the time of maximum deflection during such a typical activity. To find the value of K for the human knee muscles used in this study, we first set the maximum Type II muscle spindle firing rate to 30 impulses (imp)/s to represent the typical maximum value observed in humans (41). Next, the calculation of maximum deflection expected within the typical operating range of human muscle was determined using

$$\text{deflection}_{mm,max} = \delta \cdot \bar{l}_0$$

where δ is the normalized stretch factor and $\bar{l}_0$ is the average fascicle resting length. To solve the equation for the rectus femoris muscle, an average resting fascicle length of 80 mm was used based on the

reported physiological range in literature (39). A normalized stretch factor of 0.3 was used based upon maximum expected fascicle lengthening of the rectus femoris during both walking and passive knee flexion within the range of motion (42, 43). Finally, the constant K was calculated by setting $\alpha_{\text{deflection}_{mm,max}}$ to 0, corresponding to the value observed at terminal swing while walking and during passive knee flexion (42, 43). Hence, the equation anticipates a typical maximum firing rate of 30 imp/s at 24 mm of stretch with minimal EMG activation for the rectus femoris. For the biceps femoris, an average resting fascicle length of 80 mm was also used based on the reported physiological range in literature (39). Without more detailed literature support, the values of δ and $\alpha_{\text{deflection}_{mm,max}}$ determined for the rectus femoris were also assumed to describe the biceps femoris as it is the corresponding biarticular muscle that acts as a direct antagonist in the physiological knee. This calculation yielded a single scaling factor of 0.0743 applicable to both biceps femoris and rectus femoris muscles. Importantly, the structure of the Type II firing rate equation admits the alpha-gamma motoneuron linkage for static fibers that accounts for the increased afferent feedback induced by homonymous muscle activation (44). This consideration increases the complexity of the analysis, especially compared to a simpler treatment that would qualitatively relate the magnitude of fascicle length deflection to the quantity of proprioceptive information generated. However, the approach utilized provides the utility of quantifying afferent feedback in units of impulses per second using techniques established from neurophysiology. This yields a metric that can be directly measured in follow-up studies on similar subject populations to assess modeling accuracy without the need for intermediate derivations.

Average muscle fascicle strain and muscle activation trajectories for the first five knee extension and flexion cycles at 100% effort without recording artifacts were used to calculate the net secondary muscle spindle firing rates. Values for strain and activation were averaged from a 1-s duration in the middle of each trial when muscles were held isometrically at the desired effort level. Net secondary muscle spindle firing rates were calculated as the difference between the antagonistic afferents (from lengthened fibers) less the agonistic afferents (from shortened fibers) of each muscle pair.

For OMP subjects, the SNRs of knee extension and flexion signals at MVC were calculated as:

$$SNR_{dB} = 10 \log_{10} \frac{EMG_{Max,Movement}^2}{EMG_{Max,Rest}^2}$$

where $EMG_{Max,Rest}$ is the quiescent processed EMG noise floor when the subject is fully relaxed. Signal power ratio was calculated as the ratio of the signal power of intramuscular electrode readings over the signal power of surface electrode readings of the same muscle and movement according to:

$$\text{Signal power ratio} = \frac{EMG_{Implanted,Movement_i}^2 - EMG_{Implanted,Rest}^2}{EMG_{Surface,Movement_i}^2 - EMG_{Surface,Rest}^2}$$

where i designates a specific MVC movement. After verifying normality and sphericity of the sampled data, a Student's paired t test was used to determine significant differences in signal power between intramuscular and surface electrodes when measuring the same rectus femoris contraction movements.

For OMP subjects, electrode impedances were tested once after surgical installation and again for each subject's final experimental session in the lab (fig. S5A). For each electrode, monopolar impedance was assessed with a 1-kHz carrier signal. The initial assessment of OMP1's electrodes was delayed to 40 weeks after the second stage surgery due to COVID-19 restrictions. Testing revealed nonfunctional open circuits on electrodes 15 and 16. These were subsequently omitted from experimental usage without loss of ability due to strategic

placement of redundant electrodes. OMP1's final impedance test occurred 192 weeks after their second stage surgery and indicated minimal impedance drift, matching expectations established in previous implementations of the e-OPRA system hardware (24). The initial assessment of OMP2's electrodes at 16 weeks after the second stage surgery confirmed nominal function of all electrodes. OMP2's final impedance test occurred 28 weeks after their second stage surgery and indicated minimal impedance drift.

Free-space reaching performance

Two free-space control tasks were performed to characterize each subject's ability to control a prosthetic knee. The first task evaluated the ability of each subject to generate information usable for prosthesis control while receiving only proprioceptive feedback, and the second evaluated the ability of each subject to accurately position a knee joint with both visual and proprioceptive feedback. In both tasks, subjects were seated on an elevated stool with their residuum exposed. The bionic knee was mounted on an isolated stand in front of the subject's residuum to approximately occupy the volume of the physiological knee. There was no direct mechanical attachment between residuum and bionic knee in order to prevent the user from receiving afferent mechanical feedback to assist with the task. Three target knee positions (low, medium, and high extension) were indicated by alignment of three reflective markers placed on the medial aspect of the prosthesis' shoe with a separate reflective marker placed on a stand on the ground in front of the shank's swing radius. Subjects were instructed to use their fixed visual perspective from their seated position to align the shoe markers with the stand's marker (movie S7). The quantifiable knee joint target angles on the prosthesis were recorded by backdriving the joint to the target positions and confirming alignment through subjects' verbal feedback. EMG information was recorded using intramuscular electrodes for the OMP subjects and wet surface electrodes for AMI and CTL subjects. Before experimental data collection, activation scalings for both the extensor and flexor muscles were initially calibrated by MVC and then refined by allowing the subject to practice reaching for the medium knee extension target only. Subjects indicated whether they wanted more or less sensitivity to achieve the movement, corresponding to reducing and increasing the scaling denominator, respectively. After a 5-min tuning and training session, subjects began the experiment.

In the first reaching task, subjects were blindfolded with the bionic knee's motor disabled to characterize each subject's ability to generate useful information for bionic knee control using proprioceptive feedback only. For each individual reaching trial within the task, a click track at 80 beats per minute (BPM) played through noise-canceling headphones provided verbal instructions to rest for three beats, reach with their phantom knee for three beats, and rest for three beats for a total of eight repetitions. Subjects were instructed on the specific knee extension target at the beginning of each trial, and two trials were performed for each knee extension target presented in a pseudorandom order. EMG trajectories were recorded and processed into muscle activations as they were during the evaluation of neuromuscular function. Performance during this reaching task without visual feedback was determined by calculating the JSD between each subject's average extensor activation distributions between all low and medium extensions and then again between all medium and high knee extensions during the middle second of each repetition wherein muscle activations were assumed to be held constant. The JSD provides a scalar value corresponding to the amount of usable information between two given distributions (45).

Statistically significant information differences at the population level between low and medium and also between medium and high knee extension targets was determined using the non-parametric Kruskal-Wallis test over three groups. For any significant differences between populations, a post-hoc multiple comparison with

Tukey-Kramer correction was performed to determine pairwise significant differences of JSD. *P* values less than or equal to 0.15 are visually indicated in corresponding figures.

In the second reaching task, subjects were allowed to receive visual feedback from the actively controlled bionic knee prosthesis. As in the first task, subjects followed movement instructions from the pre-recorded click track. Subjects were instructed on the specific knee extension target at the beginning of each trial, and two trials were performed for each knee extension target presented in a pseudorandom order. EMG trajectories were recorded and processed into muscle activations as they were during the evaluation of neuromuscular function, and kinematics were recorded from the joint encoder on-board the bionic knee prosthesis.

Performance during this free-space reaching task with visual feedback was determined by calculating the bionic knee's average absolute angular divergence from the target knee angle when held at extension. Specifically, kinematics during the 1-s period centered within the verbal command to "Reach, 2, 3" in the audio track were extracted from each repetition for analysis (audio S1). The calculated absolute angular errors were averaged per target, per subject. The non-parametric Kruskal-Wallis test was used to determine any significant differences between performances of populations reaching for each of the three targets. For any significant differences between populations per target, a post-hoc multiple comparison with Tukey-Kramer correction was performed to determine pairwise significant differences with a threshold value of $P = 0.025$. *P* values ≤ 0.15 are visually indicated in corresponding figures.

Rhythmic bandwidth task

Subjects were assessed on their ability to quickly flex and extend their residual knee muscles at full perceived range of motion. Similar rhythmic bandwidth tests have previously been utilized as a means to measure neuromuscular function and agility in the face of increasing task difficulty (3, 46). Subjects were instructed to flex and extend their phantom knee joint at full perceived range of motion while EMG data from both flexor and extensor muscles and US movies of the extensor muscle were simultaneously recorded to confirm cyclic movements of the appropriate musculature (movie S2). A click track with tempo accelerating from 90 to 200 BPM over the course of 1 min was provided as an audio cue indicating when to move the phantom joint in the opposing direction. Subjects performed cyclic movements until failing to maintain pace with the click track for at least 10 s, at which point the task was stopped. Subjects also cycled the unaffected, contralateral knee in tempo with the click track until failure in a similar manner. Intact knee angle was measured using a digital goniometer (Biometrics Ltd., Newport, UK).

To simulate direct myoneural control of a prosthetic joint and estimate phantom joint kinematics, recorded EMG data were post-processed into muscle activations and used to generate torque about a forward dynamics model of a knee joint and shank. These were represented as a point mass rotating around a pivot with fixed radius under the influence of gravity ($m = 3$ kg, $l = 0.3$ m). The same myoneural impedance modulation components used to calculate torque applied to the bionic knee during swing were used to determine the torque applied to the virtual knee joint. Resultant time domain knee kinematics for both virtual and contralateral knees were analyzed in the frequency domain to extract the maximum stable frequency of movement before the trajectory became acyclic due to the subject's inability to match the demanded movement speed. The frequency at which movements become acyclic was conservatively estimated using the peak frequency value in the power spectrum observed in the 5 s immediately preceding a clear loss of coherence with the accelerating metronome track. The power spectrum was obtained from the corresponding window of data by applying the discrete Fourier transform, squaring the magnitude of the output, and then normalizing it by

sampling frequency. The peak frequency within the result is referred to as the control bandwidth for human joint motion within this manuscript, defined also as the maximum stable frequency of movement for phantom and physiological joints.

Specifically, the maximum stable frequency of movement is a threshold associated with the following statements:

1. Below the maximum stable frequency of movement, phantom and physiological joints obey Fitts' Law, also widely known as the speed-accuracy tradeoff (47).

2. Movements that obey Fitts' Law can be considered to be controlled despite variance in observed ranges of motion.

3. Above the maximum stable frequency of movement, movements lose phase coherence between intended trajectory and output trajectory, analogous to a shift toward 180° of relative phase in studies on bilateral coordination (3, 46).

4. Movements without phase coherence do not obey Fitts' Law and cannot be considered to be controlled.

5. The sinusoidal frequency at which phase coherence is assumed to be lost describes the minimum-jerk trajectories of human movement sufficiently for the analyses presented in the manuscript, despite non-linearities.

Significance testing for differences in control bandwidth between populations was performed by comparing their maximum cycling frequencies with the non-parametric Kruskal-Wallis test. For any significant differences between populations, a post-hoc multiple comparison with Tukey-Kramer correction was performed to determine pairwise significant differences with a threshold value of $P = 0.025$. Significance testing for differences in control bandwidth within a population was performed by comparing maximum cycling frequencies between intact and affected sides with the Wilcoxon signed-rank test with a threshold value of $P = 0.05$. P values ≤ 0.15 are visually indicated, and P values > 0.15 are selectively indicated in corresponding figures.

Level-ground walking and obstacle avoidance

Subjects were instructed to perform level-ground walking on a split belt treadmill set to fixed speeds. Subjects used both their prescribed devices and the bionic knee with direct myoneural control disabled. These test conditions were designed to acclimate subjects to walking on a powered prosthetic knee. Subjects rated at a K3 activity level by their certified prosthetists were asked to walk at 0.5 and 0.8 m/s, representing their greatest common speed without excessive difficulty. Subjects rated at a K4 activity level by their certified prosthetists were additionally asked to walk at 1.1 m/s, representing their greatest common speed without excessive difficulty. Once acclimated and able to walk without handrail support, subjects walked for at least 1 min at each speed with each device while ground reaction forces and on-board prosthesis data were recorded. OMP subjects performed level-ground walking both pre- and post-operatively with their prescribed prosthetic knees, and post-operatively with the bionic knee. OMP subjects were additionally tasked with walking as fast as possible beyond 0.8 m/s in all test conditions, if capable. For all testing on the moving treadmill, subjects were actively belayed from a chest harness for safety. Gait symmetry for OMP subjects was determined by a symmetry index adapted from Karamanidis *et al.* (48) and defined as:

Symmetry index =

$$2 \cdot \frac{\text{supportTime}_{\text{unaffected, single}} - \text{supportTime}_{\text{affected, single}}}{\text{supportTime}_{\text{unaffected, single}} + \text{supportTime}_{\text{affected, single}}}$$

A symmetry index of 0 indicates perfect single support symmetry. Negative indices indicate favoring of the affected side and positive indices indicate favoring of the unaffected side.

After acclimation to level-ground walking, subjects were provided efferent myoneural control of the bionic knee. The task required that

subjects avoid 10 foam blocks placed on the treadmill before their affected side at an interval of one per 5 s. This task was designed to evaluate each subject's ability to efferently control the bionic knee within a cognitively and physically demanding context, representing the holistic capabilities of each individual and their specific augmentative interventions when navigating difficult terrain. Performance was scored per block with the overall trial score being the mean of all per block scores (table S2). This point structure incentivizes safer maneuvers to overcome the block, such as those a subject may choose to perform using a prescribed passive prosthesis, instead of more agile movements in the case they are not confident in their ability to control the knee. Obstacle avoidance performance was assessed based on the best of three trial runs at each speed, an approach that heuristically compensates for the opposing influences of fatigue and training effects which may affect individuals at different rates. Subjects were made aware of the scoring rubric and experimental structure to incentivize safe experimentation with different obstacle avoidance strategies from trial to trial. As a note, the rubric suggests performance with a prescribed, variable damping knee prosthesis may score up to 0.5 points per block, and scores above 0.5 points are only possible with efferent joint control, either direct or indirect (28).

Muscle activation scalings were adjusted to each subject's preference over the course of a 3-min practice session to achieve controlled flexion and extension of the knee. Once adjusted, subjects were provided a practice trial involving walking on the treadmill at 0.5 m/s for 10 s before 10 foam blocks of 10-cm height were placed onto the affected leg's treadmill belt every 5 s. Subjects performed three trials of the obstacle avoidance task at each of their level-ground walking speeds with the bionic knee. OMP subjects additionally performed the obstacle avoidance task at each previously tested speed using their prescribed device. OMP subjects were further instructed to avoid a large 20-cm obstacle placed in their path while using the bionic knee to traverse the level-ground walkway at their preferred walking speed. The treadmill was not used because the large obstacle consisted of two stacked concrete blocks. Two trials were performed by each OMP subject. Subjects were allowed to rest between all trials to minimize the effects of fatigue.

Significance testing for differences in obstacle performance between cohorts was performed by comparing the best trial score, equivalent to the obstacle performance score, of K3 and K4 subjects separately and at their max speeds with the non-parametric Kruskal-Wallis test. For any significant differences between populations, a post-hoc multiple comparison with Tukey-Kramer correction was performed to determine pairwise significant differences with a threshold value of $P = 0.05$. The Wilcoxon signed-rank test with a threshold value of $P = 0.05$ was performed to determine significant differences between the average peak hip abduction angles of OMP subjects when using their prescribed prosthetic knee or the bionic knee to overcome obstacles. Medium and large obstacle traversals by the bionic knee were combined for analysis due to their similar trajectories. P values ≤ 0.15 are visually indicated, and P values > 0.15 are selectively indicated in corresponding figures.

Sit-to-stand task

A seated sit-to-stand task was performed to determine each subject's ability to produce useful positive power with the bionic knee while the foot maintained constant ground contact. A series of three trials consisting of five sit to stand movements each was recorded per subject with sufficient rest provided between trials. To tune the flexor and extensor activation scaling denominators, confirm understanding of the task, and allow for practice of the required movements, a 3-min training session was provided before the first trial run wherein the subject provided feedback on more or less sensitivity while performing sit to stand movements with the bionic knee. The expert experimenter performed a binary search to converge upon satisfactory flexor and

extensor activation scaling denominators as indicated through verbal confirmation.

Performance was scored for each movement using the sitting to standing segment of the Berg Balance Scale (49), and point deductions were made for failed attempts and attempts that required handrail support (movie S8). Average performance per trial was calculated by taking the mean of the Berg scores from all five movements. Significance testing for differences in coordination of bilateral power production between populations was performed by comparing the ultimate score of each population in the third trial and proceeding with the non-parametric Kruskal-Wallis test. For any significant differences between populations, a post-hoc multiple comparison with Tukey-Kramer correction was performed to determine pairwise significant differences with a threshold value of $P = 0.025$. P values ≤ 0.15 are visually indicated.

OMP subjects performed additional instances of the sit-to-stand task with their prescribed prosthetic knee both pre- and post-operatively. During these instances, ground reaction forces under each foot were recorded using a split belt treadmill (Bertec Corporation, Columbus, Ohio, USA).

Static obstacle drills

Static obstacle drills were performed in a fixed standing posture to characterize each subject's ability to achieve hybrid free-space positioning movements with intermittent discrete ground contact events using the bionic knee. Two types of drills were performed with two types of obstacles in a 2×2 factorial design. The first type of drill, so called the over-back drill, required that the subject start from a standing position behind a fixed obstacle and overcome the obstacle with the bionic knee without non-physiological hip abduction. After touching the ground on the other side of the obstacle with the prosthetic foot, the subject was required to return the foot over the obstacle to the original starting position without non-physiological hip abduction. Half of a point was awarded for each movement over or back from the obstacle without block contact and without non-physiological hip abduction. The second type of drill, so called the top-tap drill, required that the subject stand behind the fixed obstacle, touch the top of the obstacle with any part of the prosthetic foot, and then touch the ground on the opposite side of the obstacle with any part of the prosthetic foot. The backward movement involved performing this sequence in reverse. Any contact with the obstacle other than on the top resulted in failure of the movement. Half of a point was awarded for each movement over or back from the obstacle with a successful top tap. A medium obstacle corresponding to a cinder block with 10-cm height and a large obstacle corresponding to two stacked cinder blocks with a combined height of 20 cm were used in all drills.

For each of the four combinations of trial conditions, subjects were provided 30 s to complete as many successful obstacle drills as possible. To tune the flexor and extensor activation scaling denominators, confirm understanding of the drills, and allow for practice of the required movements, a 3-min training session was provided before each subject's first trial run wherein the subject provided feedback on more or less sensitivity per channel while performing any desired movements with the bionic knee. Trials were administered in order of over-back with medium obstacle, top-tap with medium obstacle, over-back with large obstacle, and top-tap with large obstacle with sufficient rest provided between trials.

Significance testing for differences in static agility between populations was performed by aggregating scores from all four trials into an averaged success percentage per subject and proceeding with the non-parametric Kruskal-Wallis test. For any significant differences between populations, a post-hoc multiple comparison with Tukey-Kramer correction was performed to determine pairwise significant differences with a threshold value of $P = 0.025$. P values ≤ 0.15 are visually indicated.

Stair ascent and descent

A stair ascent and descent task was performed to determine each subject's ability to produce maximal positive power and damping with the bionic knee while balancing the body throughout alternating stance and swing cycles. Subjects were instructed to ascend and descend a staircase consisting of four steps with a standardized height between steps of 20 cm. Each trial consisted of three full ascent and descent traversals over the flight of stairs. Three trials were performed by each subject at a self-selected speed with sufficient rest provided between trials. To tune the flexor and extensor activation scaling denominators, confirm understanding of the task, and allow for practice of the required movements, muscle activation scalings were adjusted by the examiner according to subject feedback during repeated attempts to take the first ascending step while leading with the bionic knee. This adjustment was performed over 3 min to provide enough familiarity with the task while avoiding major effects of training and fatigue. Subjects were allowed to use the provided handrails as necessary.

For each trial, the average rates of stair ascent and descent were separately calculated in units of steps per second. Trials were terminated early if subjects failed to complete any ascent or descent traversal within 30 s. Significance testing for differences in generating maximal power and damping between populations was performed by comparing the ultimate rate of ascent and descent of each population in the third trial and proceeding with the non-parametric Kruskal-Wallis test. For any significant differences between populations, a post-hoc multiple comparison with Tukey-Kramer correction was performed to determine pairwise significant differences with a threshold value of $P = 0.025$. P values ≤ 0.15 are visually indicated, and P values > 0.15 are selectively indicated in corresponding figures.

OMP subjects were both prescribed the C-Leg 4 variable damping prosthesis (Ottobock SE & Co, Duderstadt, Germany) for use in their daily lives. As a spontaneous experimental addendum, OMP2 was additionally instructed to ascend the staircase with their prescribed device using their typical step-by-step gait while a goniometer on the prosthetic knee recorded joint kinematics. A data collection error prevented prescribed prosthetic knee kinematics during descent from being recorded. Descent kinematics for the C-Leg are instead reproduced from literature for Fig. 5B, ii (50).

Embodiment questionnaires

A prosthetic embodiment questionnaire was administered to each subject before any exposure to the bionic knee to determine a baseline response toward their prescribed knee prosthesis. After each of four of the experimental tasks above (free-space reaching, obstacle drills, obstacle avoidance, stair ascent and descent), subjects were asked to repeat the questionnaire with respect to their perceived embodiment of the effertently controlled bionic knee. Subjects were not administered the questionnaire after the sit to stand task due to redundant coverage of positive power production during the stair ascent task. Differences for each task with respect to each subject's baseline response were recorded and used in subsequent analyses. The questionnaire consisted of 10 questions adapted from the work of Bekrater-Bodmann (31). Questions were subdivided to assess each subcategory of embodiment (ownership, body representation, agency) as defined by Segil *et al.* (32) (table S3).

A linear mixed effects model was fit to explain deviations from baseline embodiment when using the bionic knee. This model was determined to be parsimonious relative to a basket of other candidates after a thorough search based upon Akaike's information criterion. Fixed effects were assumed for group (OMP, AMI, or CTL), group and task interactions, and group and embodiment subcategory interactions. Random effects for subjects were modeled to represent individual-specific deviations from the global intercept:

$$\Delta_{score_i} = \beta_0 + \beta_1 \cdot group_i + \beta_2 \cdot (group_j \times task_k) + \beta_3 (group_j \times subcategory_l) + u_{subject_m} + \epsilon_i$$

Post-hoc comparisons with Bonferroni-correction identified significant interaction effects for group and task interactions ($P = 0.02$) and group and embodiment subcategory interactions ($P = 0.0002$). Main group effects approached significance ($P = 0.12$). P values ≤ 0.15 are visually indicated in corresponding figures.

Correlation between performance and proprioceptive feedback

Affine models were used to explain the relationship between free-space reaching accuracy and information generation relative to proprioceptive feedback. Parameters for each were optimized to minimize the residual squared error. These were of the form:

$$y = b + m \cdot x$$

A growth model with saturation was used to explain the relationship between rhythmic control bandwidth relative to proprioceptive feedback. Parameters were optimized to minimize the residual squared error. A model with saturation was chosen to describe the physical bandwidth limitations of any real system. This model was of the form:

$$y = \frac{y_{\max} \cdot x}{x_{\text{mid}} + x}$$

where $y_{\max}$ is the maximum value y can achieve with increasing x , and x_{mid} is the value of x at which $y = \frac{y_{\max}}{2}$.

For all fitted affine models, Pearson's correlation coefficient and slopes are reported with 95% confidence intervals. Two-tailed P values are calculated for both Pearson's correlation coefficient and slope using the t-distribution. For the fitted growth model with saturation, $y_{\max}$ and x_{mid} are reported with 95% confidence intervals. Two-tailed P values are calculated for both $y_{\max}$ and x_{mid} using the t-distribution. All P values are reported.

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SUPPLEMENTARY MATERIALS

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 Supplementary Text; Figs. S1 to S7; Tables S1 to S3; References (52,53);
 Movies S1 to S8; Audio S1

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