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Supplementary Materials for

A regenerative peripheral nerve interface allows real-time control of an artificial hand in upper limb amputees

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The PDF file includes:

Other Supplementary Material for this manuscript includes the following:

(available at stm.sciencemag.org/cgi/content/full/12/533/eaay2857/DC1)

Movie S11 (.mp4 format). P3's real-time continuous two DOF thumb using the LUKE arm.
Movie S12 (.mp4 format). P3 and P4's real-time continuous control during functional tasks.

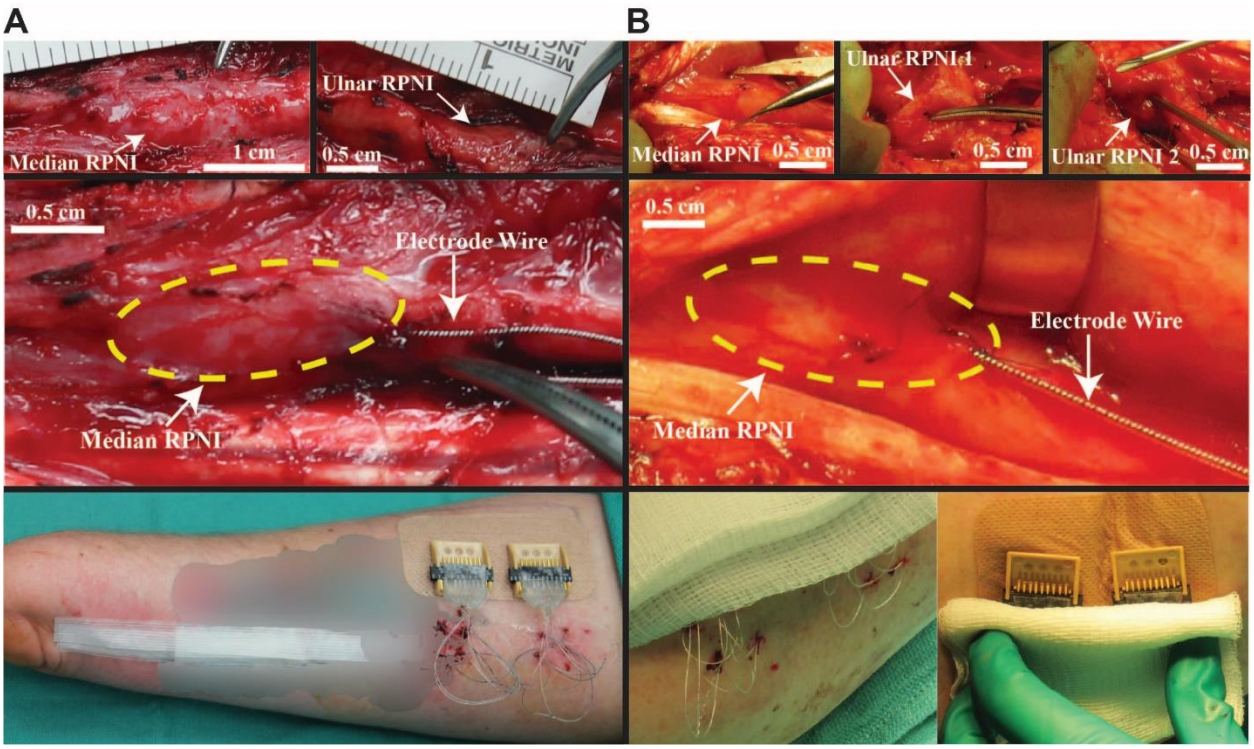

Fig. S1. Electrode implantation for P3 and P4. (**A**) (Top) Surgical photos show the RPNIs three years post-implantation. (Middle) Example of wire insertion into the RPNI muscle graft (dashed line). (Bottom) Final connector setup after all electrodes have been implanted (Partially blurred to protect participant identification). (**B**) (Top) Surgical photos show the median RPNI, ulnar RPNI 1, and ulnar RPNI 2 twelve months post-implantation. (Middle) Example of wire insertion into the RPNI muscle graft (dashed line). (Bottom) Final connector setup after all electrodes have been implanted.

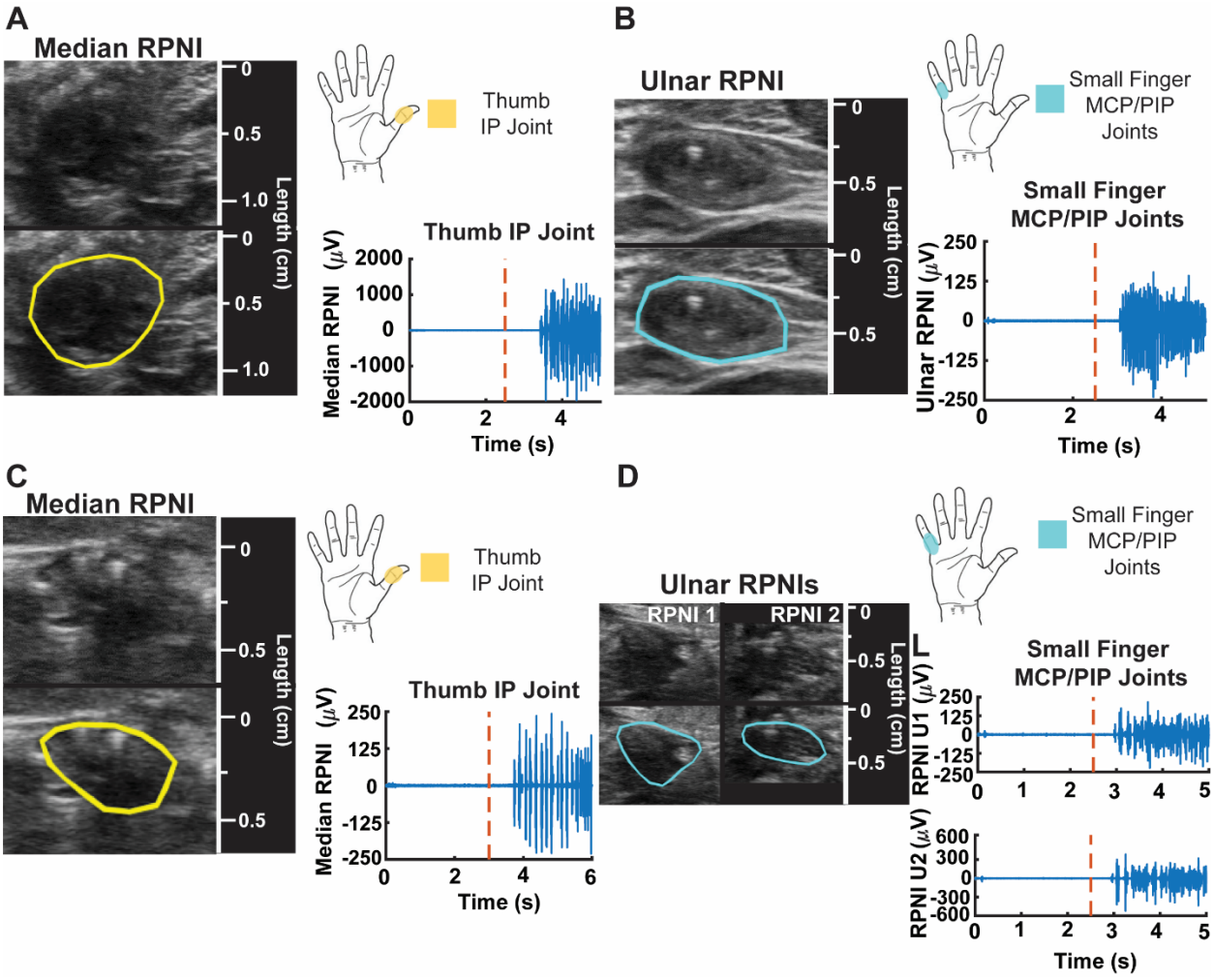

Fig. S2. P3 and P4's RPNI sonograms, motor map, and electrophysiology. (**A**) P3's median RPNI sonogram captured 31 months post-RPNI surgery, and a sample of EMG signals recorded after cued thumb movement (red dashed line). (**B**) P3's ulnar RPNI sonogram captured 31 months post-RPNI surgery and a sample of ulnar RPNI EMG signals (blue) recorded after cued small finger movement (red dashed line). (**C**) P4's median RPNI sonogram captured 16 months post-RPNI surgery and 4 months post-indwelling electrode surgery. EMG signals (blue) were recorded after cued thumb movement (red dashed line) in the median RPNI. (**D**) P4's sonograms of ulnar RPNI 1 and 2 captured 16 months post-RPNI surgery and 4 months post-indwelling electrode surgery. EMG signals (blue) were recorded after cued small finger movement (red dashed line) in the ulnar RPNIs (RPNI U1, RPNI U2), respectively.

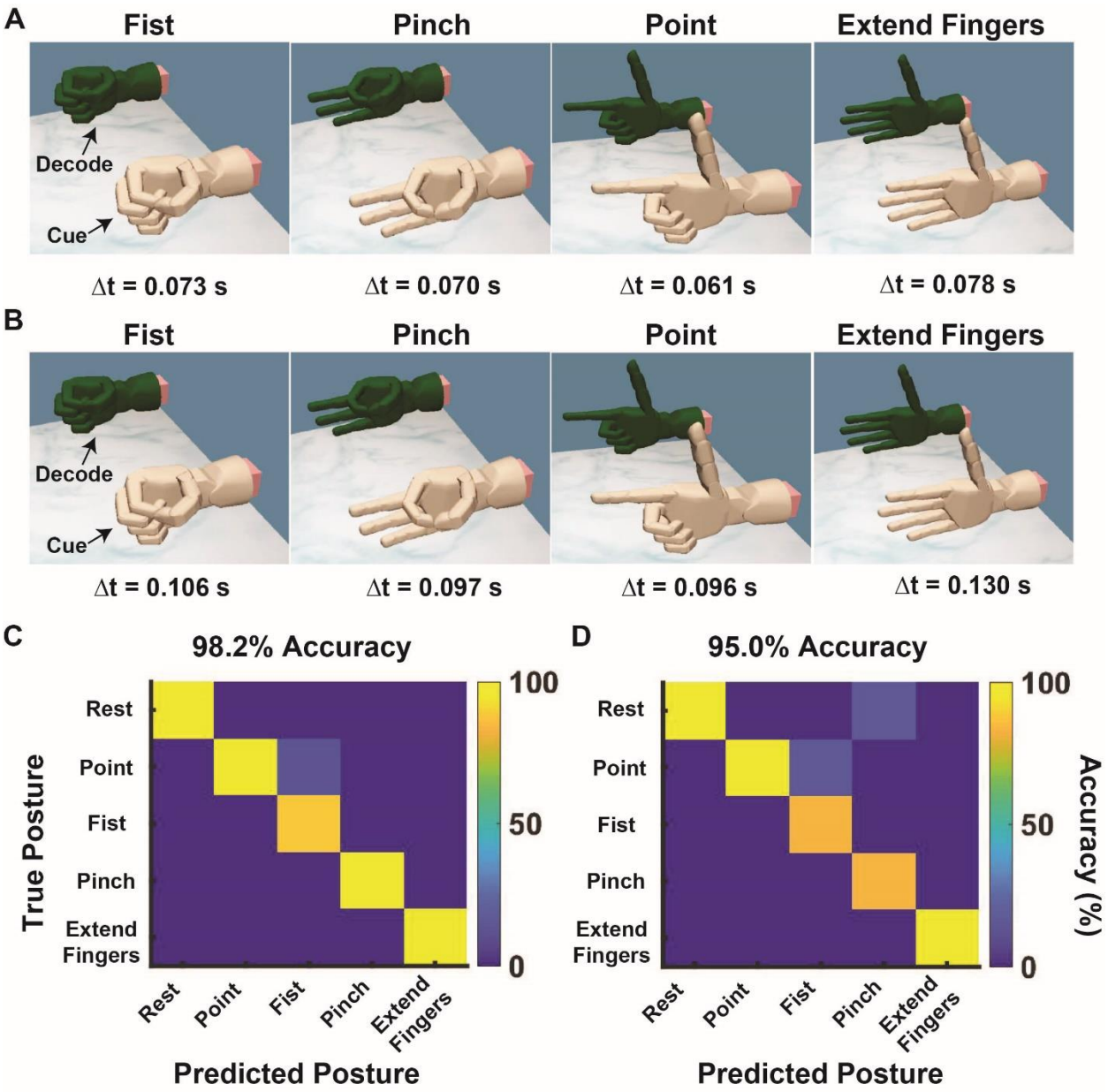

Fig. S3. Real-time classification of grasping hand postures. (**A**), (**B**) P3 and P4's discrete control of fist, pinch, point, and extended fingers during a posture mirroring task. The fastest recorded motion selection times are shown for each posture. (**C**), (**D**) Offline confusion matrix of the postures used in (A) and (B), respectively. The y-axis represents the true posture, while the x-axis represents the predicted posture. The color map indicates the accuracy (%) of the classifier's prediction.

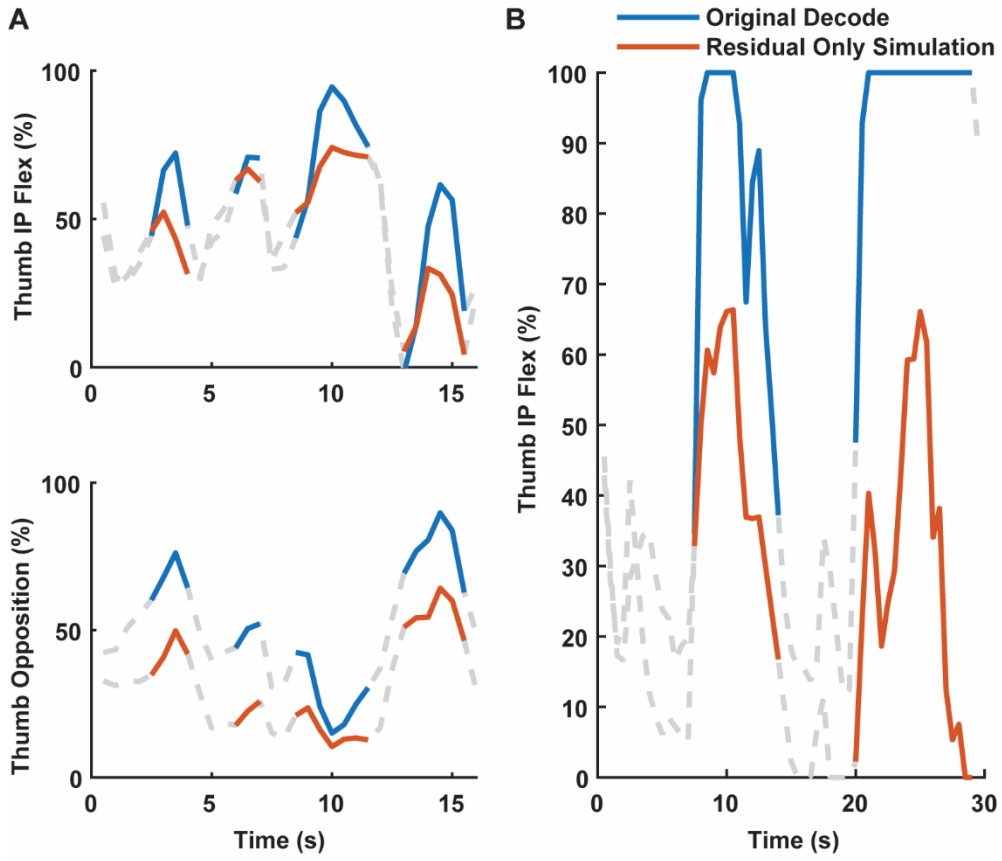

Fig. S4. Original and simulated decodes during functional tasks. (**A**) P3's decoded 2 degree of freedom thumb during the box and blocks task. Solid lines represent periods of active thumb movement on the LUKE arm. The solid blue lines represent original real-time predictions using RPNI and residual extensor muscle EMG. The solid orange lines represent simulated predictions using only residual muscle EMG. (**B**) P4's decoded and simulated thumb flexion during the SHAP abstract object tasks. Solid lines represent periods of active thumb movement on the i-limb.

Table S1. Details of a subset of muscles missing in each participant and their function.

Participant	Level of Amputation	Missing Muscles	Nerve	Function
P1*	Proximal transradial	Flexor Digitorum Superficialis	Median	Flex digits 2-5 at MCP/PIP joints
		Flexor Digitorum Profundus	Median and Ulnar	Median half: Flex digits 2-3 at DIP joint, Ulnar half: Flex digits 4-5 at DIP joint
		Flexor Pollicis Longus	Median	Flex digit 1 at IP joint
P2**	Shoulder disarticulation	Biceps Brachii	Musculocutaneous	Flex elbow joint, supinates the forearm
		Triceps Brachii	Radial and axillary	Extends forearm, adducts arm
		Brachialis	Musculocutaneous and radial	Flex elbow joint
		Coracobrachialis	Musculocutaneous	Adducts humerus, flex the arm at glenohumeral joint
P3, P4	Wrist disarticulation	Abductor Pollicis Brevis	Median	Abduct digit 1– assists to oppose and extend digit 1
		Flexor Pollicis Brevis	Median and Ulnar	Flex digit 1 at MCP/CMC joints – assists to oppose digit 1
		Opponens Pollicis	Median	Flex digit 1 at CMC joint – assists to oppose digit 1
		Lumbricals 1 and 2	Median	Simultaneously flex digit 2 and 3 at MCP joint and extend 2 or 3 at PIP joint
		Flexor Digiti Minimi Brevis	Ulnar	Flex digit 5 at MCP joint
		Opponens Digiti Minimi	Ulnar	Oppose digit 5 – flex/rotate 5th metacarpal
		Lumbicals 3 and 4	Ulnar	Simultaneously flex digit 4 or 5 at MCP joint and extend digit 4 or 5 at PIP joint

MCP – metacarpophalangeal joint, PIP – proximal interphalangeal joint, DIP – distal interphalangeal joint, IP – interphalangeal joint, CMC – Carpometacarpal joint

*P1 is also missing all the muscles missing in P3 and P4.

**P2 is also missing all the muscles missing in P1, P3, and P4.

Table S2. Quantitative analysis of ultrasound videos for P1.

Participant	Finger movement		Pixel mean intensity change (%)	Pixel standard deviation change (%)	Compared against surrounding tissue Mean intensity p – value, Standard deviation p – value
P1	Thumb MCP/IP flexion	Surrounding Tissue	1.20	0.28	N/A
		Median RPNI 1	8.34	10.80	p < .001, .001
		Median RPNI 2	2.33	0.61	p < .001, = .005
		Median RPNI 3	5.91	0.81	p = .03, < .001
		Median RPNI 4	1.45	0.20	p = .74, .02
		Surrounding Tissue	1.23	0.52	N/A
		Ulnar RPNI 1	6.08	11.6	p = .47, < .001
		Surrounding Tissue	0.33	0.11	N/A
		Ulnar RPNI 2	1.11	0.16	p < .001, .001
	Index finger PIP/DIP flexion	Surrounding Tissue	0.18	0.25	N/A
		Median RPNI 1	4.49	6.74	p < .001, .002
		Median RPNI 2	0.60	3.07	p = .52, < .001
		Median RPNI 3	7.90	11.8	p = .005, < .001
		Median RPNI 4	0.16	4.63	p = .18, .01
		Surrounding Tissue	0.28	0.09	N/A
		Ulnar RPNI 1	3.02	3.22	p = .06, .01
		Surrounding Tissue	0.08	0.62	N/A
		Ulnar RPNI 2	4.59	7.28	p < .001, .001

CMC – Carpometacarpal joint, MCP – metacarpophalangeal joint, PIP – proximal interphalangeal joint, DIP – distal interphalangeal joint, IP – interphalangeal joint

Table S2. Quantitative analysis of ultrasound videos for P1. (continued)

Participant	Finger movement		Pixel mean intensity change (%)	Pixel standard deviation change (%)	Compared against surrounding tissue Mean intensity p – value, Standard deviation p – value
P1	Small finger PIP/DIP flexion	Surrounding Tissue	0.02	0.24	N/A
		Median RPNI 1	2.01	1.02	p = .008, .48
		Median RPNI 2	1.41	2.20	p = .005, < .001
		Median RPNI 3	0.64	0.19	p = .009, .005
		Median RPNI 4	0.57	2.03	p = .50, .01
		Surrounding Tissue	0.86	0.33	N/A
		Ulnar RPNI 1	12.8	11.2	p < .001, .001
		Surrounding Tissue	0.67	0.16	N/A
		Ulnar RPNI 2	1.24	2.37	p < .001, .001

CMC – Carpometacarpal joint, MCP – metacarpophalangeal joint, PIP – proximal interphalangeal joint, DIP – distal interphalangeal joint, IP – interphalangeal joint

Table S3. Calculated movement selection times for several postures between P3 and P4.

Participant	Posture	Movement Selection Time (s), Mean ± SD (n = 5 trials)	Overall Mean Across Postures, Mean ± SD (s)
P3	Thumb MCP Joint	0.124 ± 0.00110	0.172 ± 0.105
	Thumb IP Joint	0.306 ± 0.0251	
	Small Finger	0.275 ± 0.0476	
	Hand Adduction	0.346 ± 0.0596	
	Fist	0.106 ± 0.0292	
	Pinch	0.0942 ± 0.0263	
	Point	0.0862 ± 0.0215	
	Extend Fingers	0.0985 ± 0.0163	
	Rest	0.108 ± 0.00167	
P4	Ring Finger	0.285 ± 0.186	0.234 ± 0.0894
	Thumb IP Joint	0.120 ± 0.0554	
	Small Finger	0.359 ± 0.219	
	Hand Abduction	0.365 ± 0.178	
	Fist	0.236 ± 0.151	
	Pinch	0.229 ± 0.113	
	Point	0.193 ± 0.0906	
	Extend Fingers	0.192 ± 0.0562	
	Rest	0.124 ± 0.018	

Table S4. Summary of observed RPNI grafts and the electrode type used to record EMG.

Participant	RPNI name	Nerve	Electrode type
P1	Median RPNI 1	Median	Fine wire
	Median RPNI 2	Median	none
	Median RPNI 3	Median	none
	Median RPNI 4	Median	none
	Ulnar RPNI 1	Ulnar	Fine wire
	Ulnar RPNI 2	Ulnar	Fine wire
P2	RPNI 1	Unknown	none
	RPNI 2	Unknown	none
P3	Median RPNI	Median	Intramuscular
	Ulnar RPNI	Ulnar	Intramuscular
P4	Median RPNI	Median	Intramuscular
	Ulnar RPNI 1	Ulnar	Intramuscular
	Ulnar RPNI 2	Ulnar	Intramuscular

Movie S1. Ultrasound video capturing P1's median RPNIs.

Ultrasound video capturing P1's median RPNIs during volitional thumb flexion, index finger flexion, and small finger flexion.

Movie S2. Ultrasound video capturing P1's ulnar RPNIs.

Ultrasound video capturing P1's ulnar RPNIs during volitional thumb flexion, index finger flexion, and small finger flexion.

Movie S3. Ultrasound video capturing two RPNIs from P2.

Ultrasound video capturing two of P2's RPNIs during volitional thumb flexion, index finger flexion, and middle, ring, small finger flexion.

Movie S4. P3's real-time discrete control of finger postures.

P3's real-time discrete control of a virtual and physical prosthesis (DEKA LUKE arm) using a classifier algorithm. The classifier predicted between thumb MCP joint, thumb IP joint, small finger, adduction, and rest using only RPNI signals.

Movie S5. P4's real-time discrete control of finger postures.

P4's real-time discrete control of a virtual and physical prosthesis (DEKA LUKE arm) using a classifier algorithm. The classifier predicted between ring finger, thumb IP joint, small finger, abduction, and rest using only RPNI signals.

Movie S6. P3 and P4's real-time discrete control of grasping postures.

P3 and P4's real-time discrete control of a virtual using a classifier algorithm. The classifier predicted between fist, pinch, point, and extend fingers using RPNI and residual muscle signals.

Movie S7. P3's real-time continuous one DOF control up to 300 days.

P3's real-time continuous control of the one degree of freedom thumb IP joint using a regression-based algorithm. The video demonstrates motor performance over time without recalibration of the algorithm, from day 0 up to day 300.

Movie S8. P4's real-time continuous one DOF control up to 97 days.

P4's real-time continuous control of the one degree of freedom thumb IP joint using a regression-based algorithm. The video demonstrates motor performance over time without recalibration of the algorithm, from day 0 up to day 97.

Movie S9. P3 and P4's real-time continuous two DOF thumb control.

P3 and P4's real-time continuous control of the two degree of freedom thumb MCP/CMC/IP joints.

Movie S10. P4's real-time continuous two DOF thumb control using surface EMG.

P4's real-time continuous control of the two degree of freedom thumb MCP/CMC/IP joints using surface EMG.

Movie S11. P3's real-time continuous two DOF thumb using the LUKE arm.

P3's control of the two degree freedom thumb using the physical prosthesis (DEKA LUKE arm). Similar to the virtual target task, P3 had to hit a wand in various positions. Additionally, P3 was asked to mirror movements of an intact thumb with his prosthetic thumb.

Movie S12. P3 and P4's real-time continuous control during functional tasks.

In the first segment, P3 uses a three degree of freedom continuous controller (two degree of freedom thumb + index) to control a physical prosthesis (DEKA LUKE arm). P3 then performs a self-paced box and blocks task. In the second segment, P4 uses a physical prosthesis (Össur i-limb Quantum) to sequentially complete three SHAP abstract object tasks. A two degree of freedom continuous controller provided P4 the ability to control key pinch and power grip to complete the task.