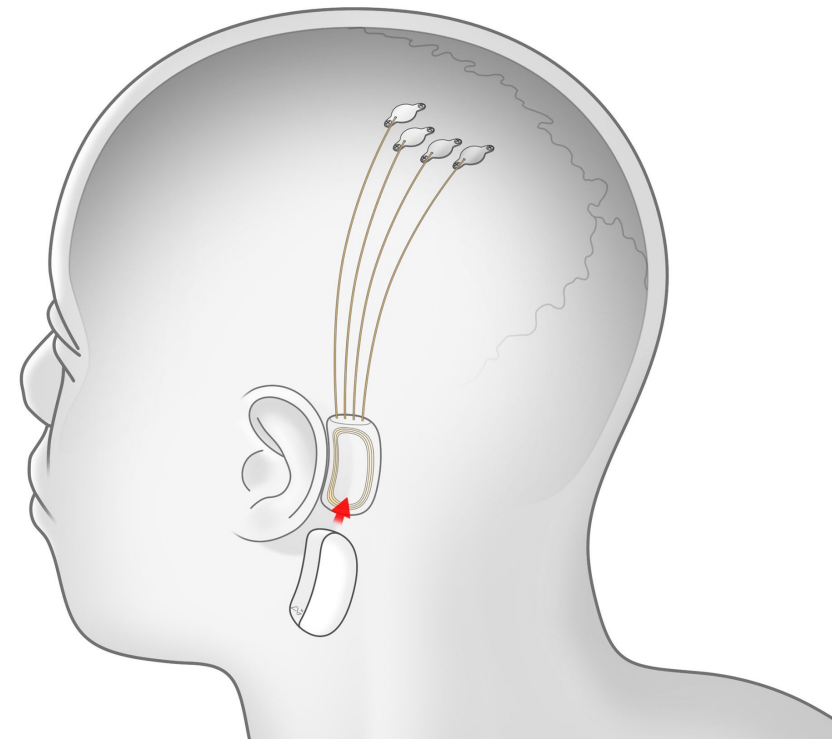


Implantable and wearable human-machine interfaces

Silvestro Micera

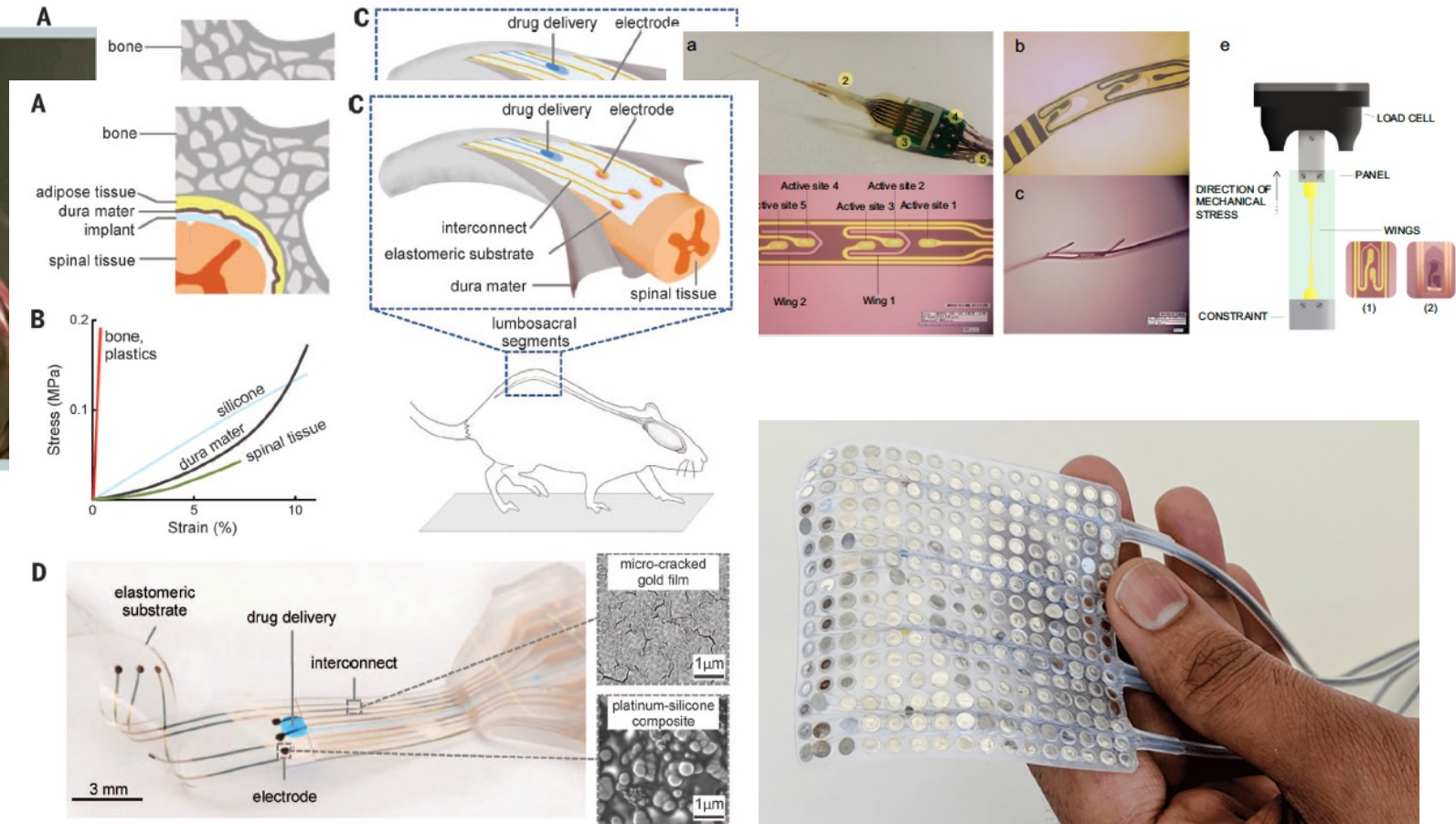
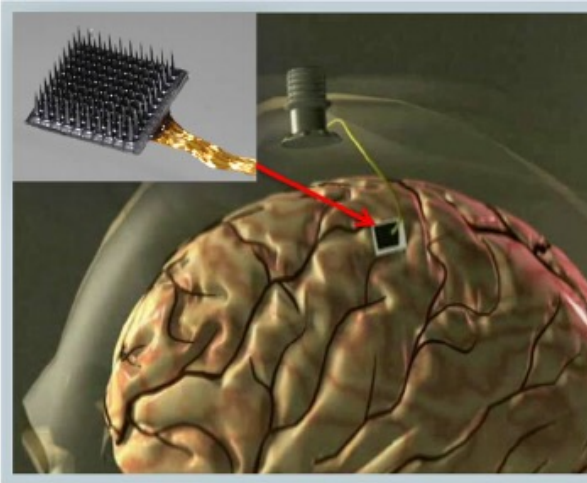


Neural Engineering

- Neural engineering (also known as neuroengineering) is a discipline within biomedical engineering that uses **engineering techniques** to **understand, repair, replace, or enhance neural systems**.
- Neural engineers are uniquely qualified to solve design problems at the interface of living neural tissue and non-living constructs (Hetling, 2008).

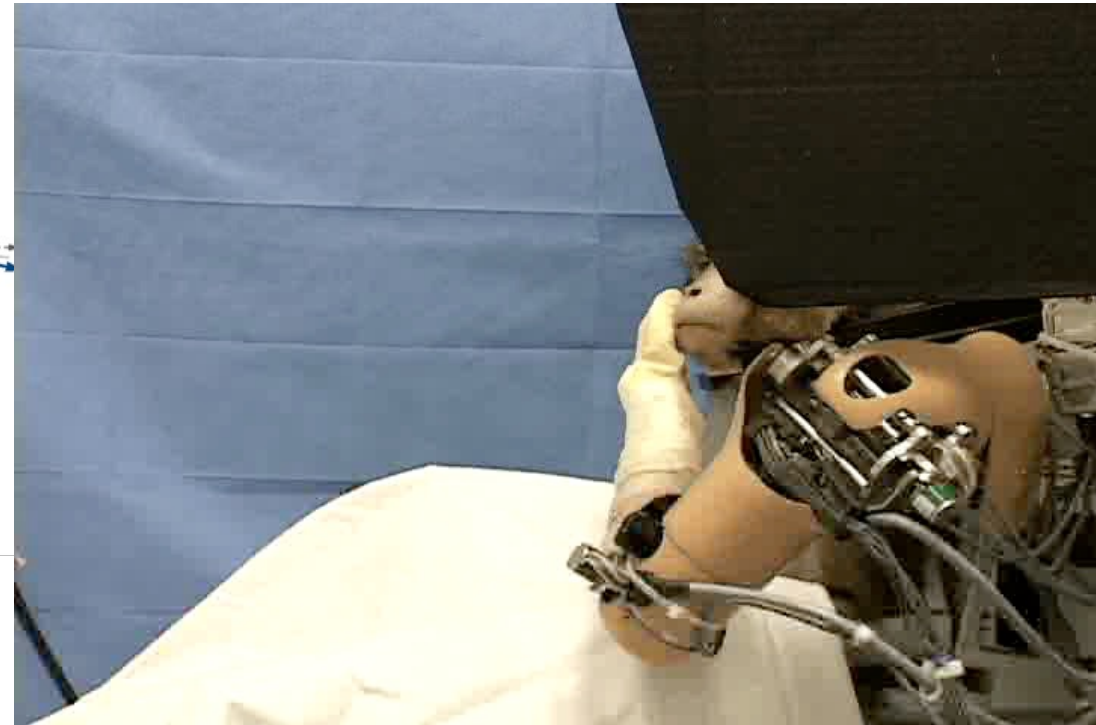
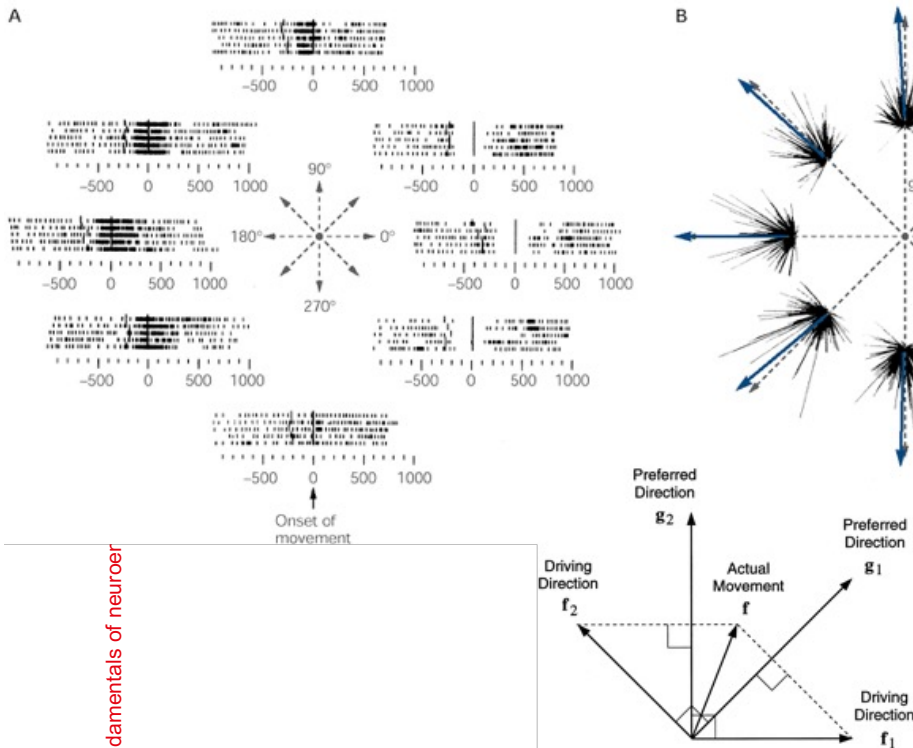
■

Central and peripheral interfaces



Motor Neuroprosthetics

Brain decoding



Motor Neuroprosthetics

Brain decoding

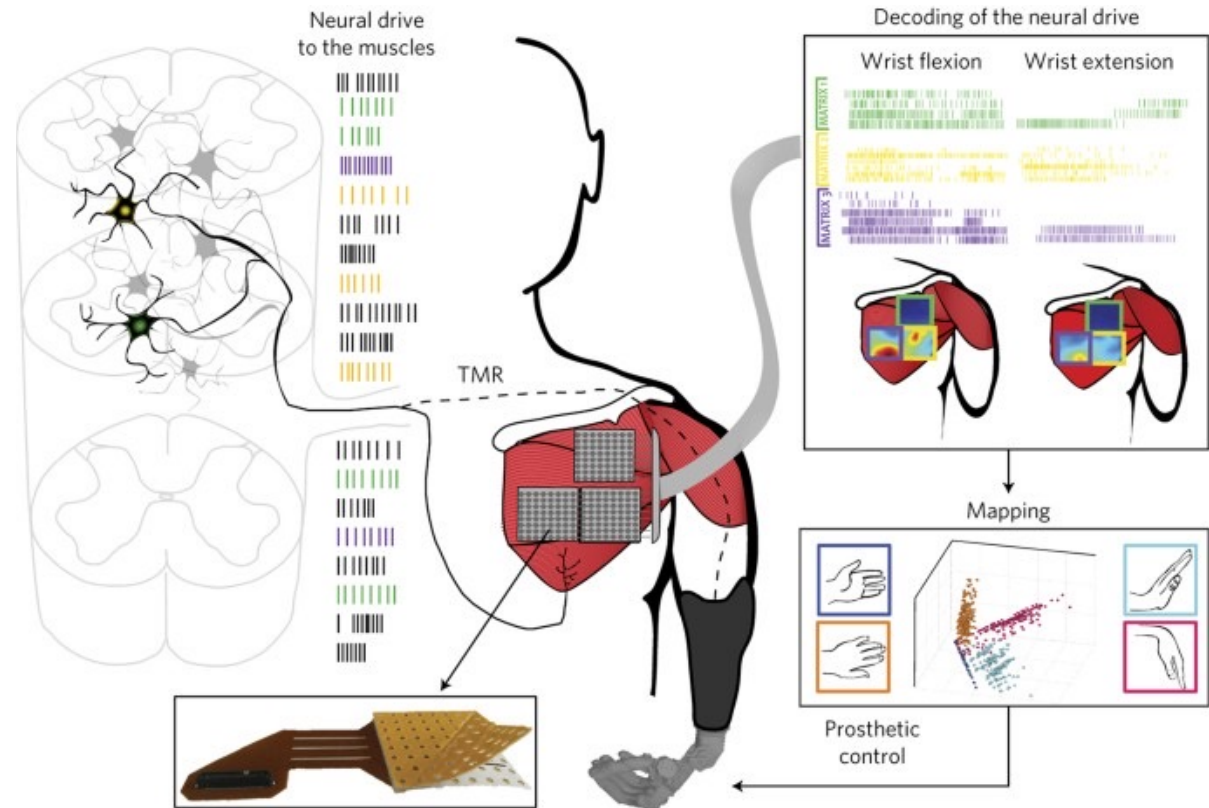
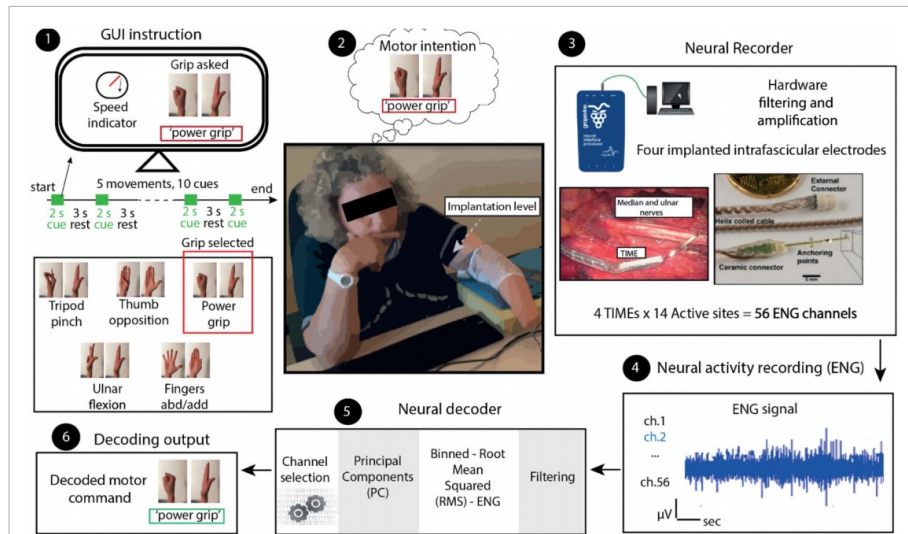
BrainGate Pilot Clinical Trial
3D + Grasp Control of a Robotic Arm
Participant S3
Trial Day 1959 / 12 April 2011
Hochberg *et al.*, 2012



Caution: Investigational Device. Limited by Federal Law to Investigational Use.

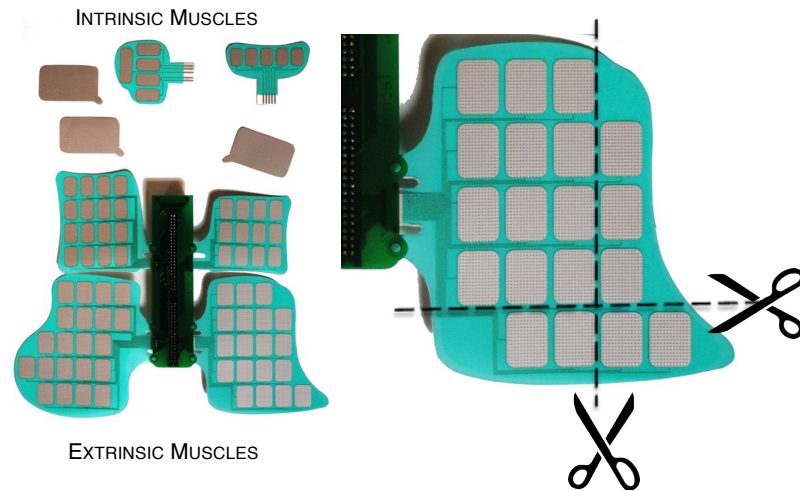
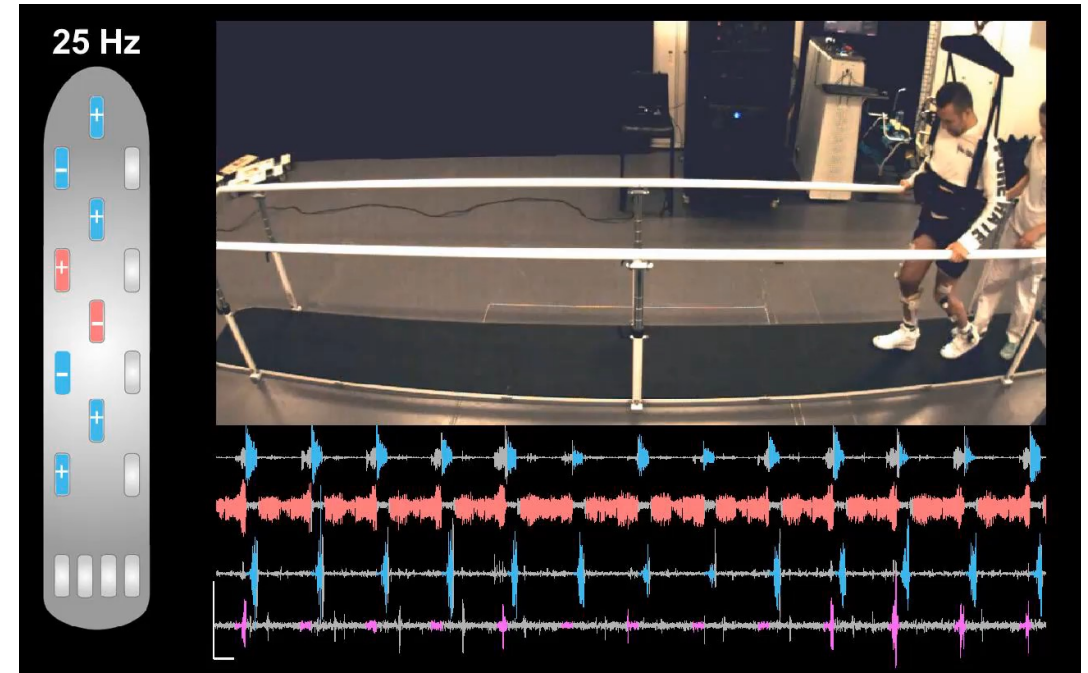
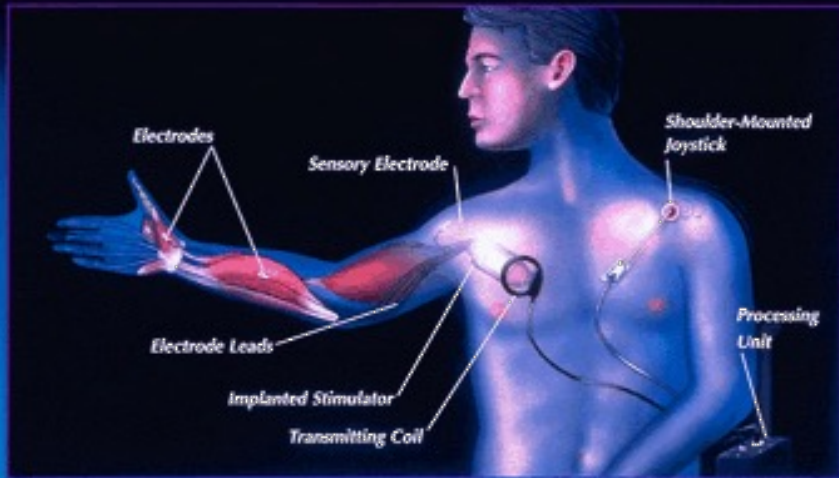
Motor Neuroprosthetics

Peripheral decoding

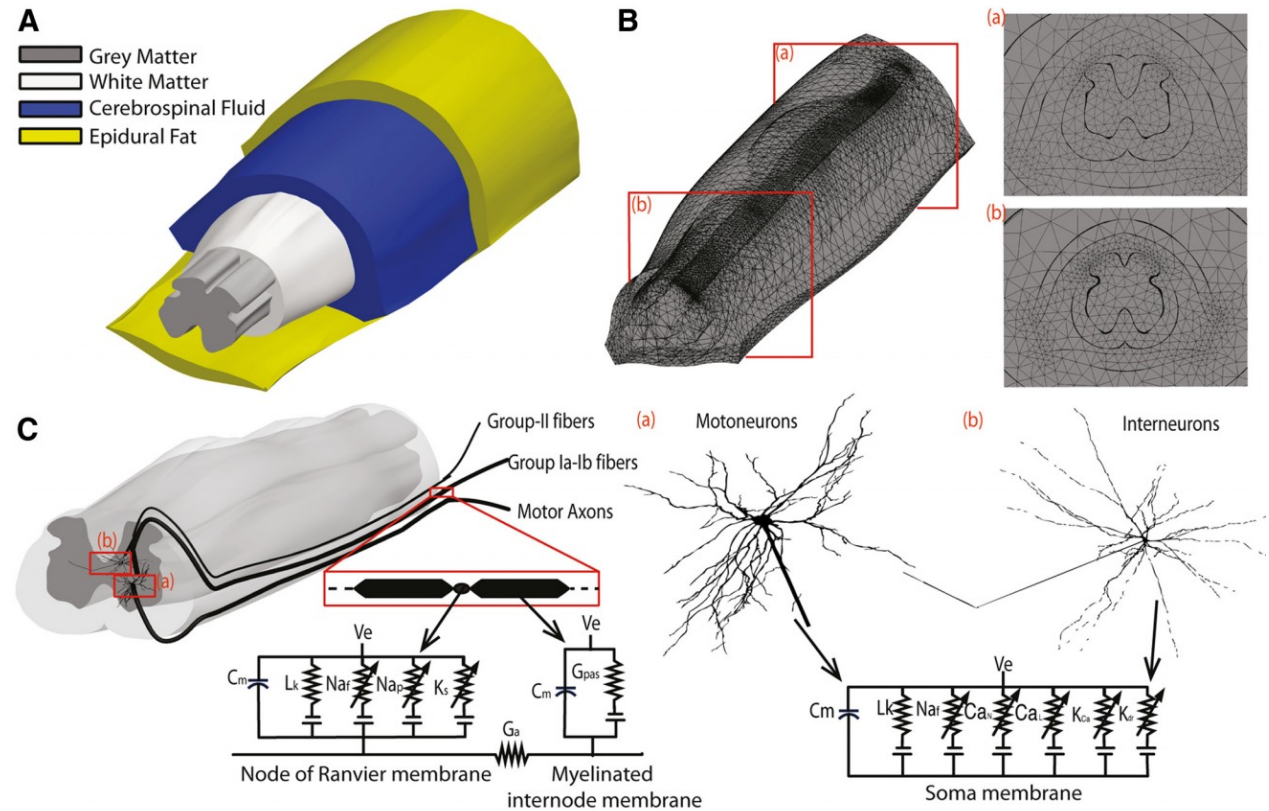
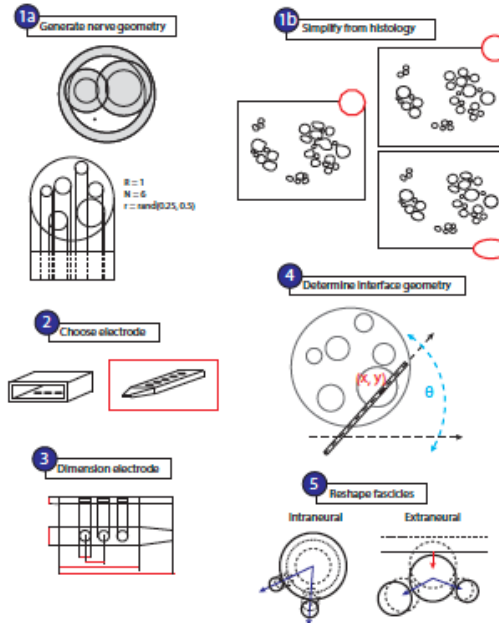


Electrical stimulation (actuation)

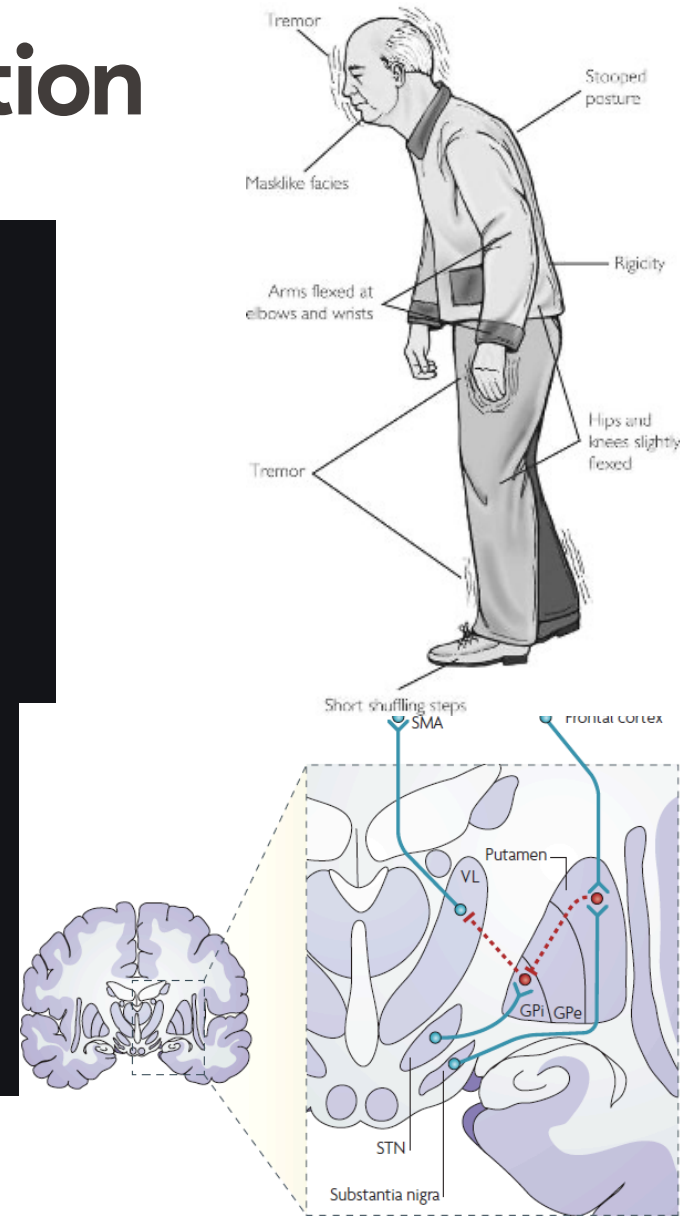
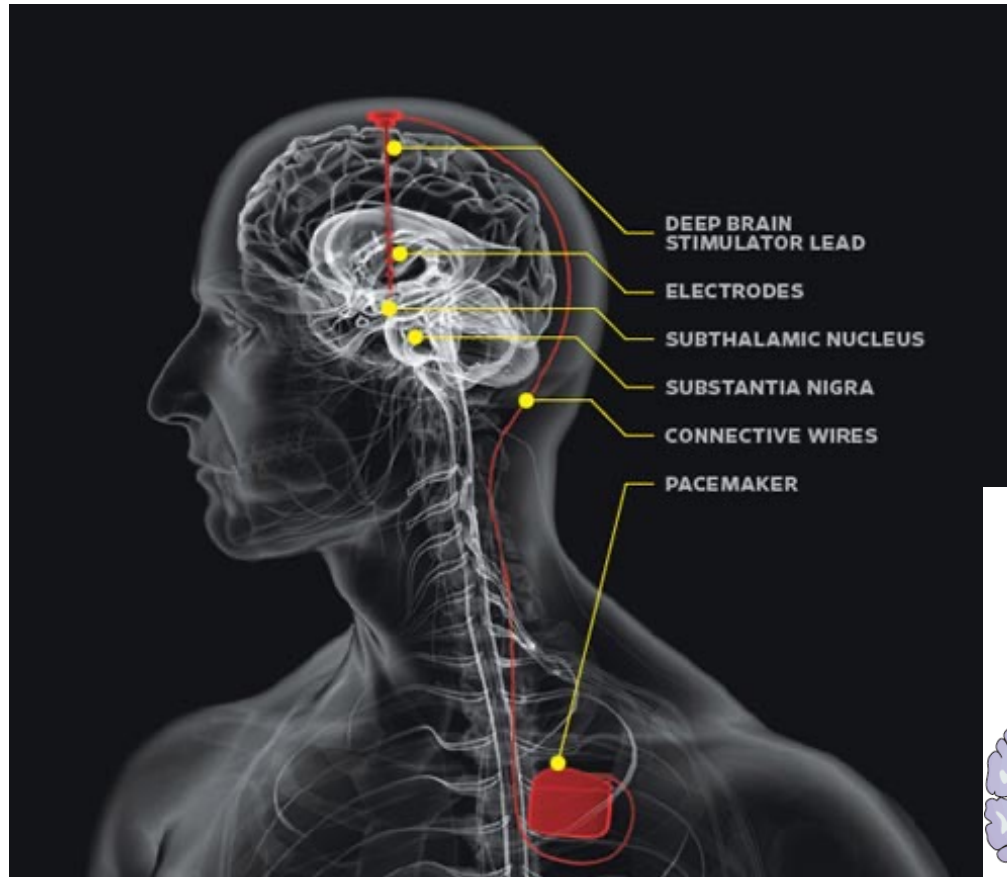
The Freehand System by NeuroControl Corporation



Computational models

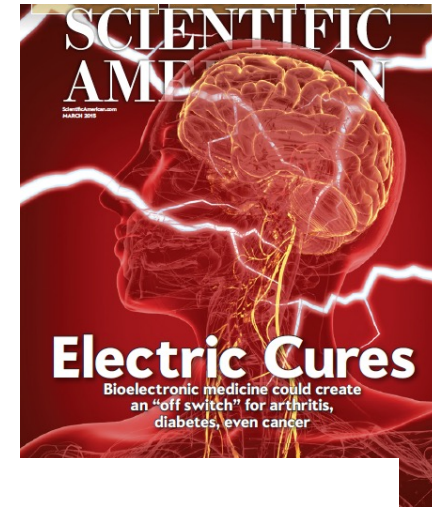
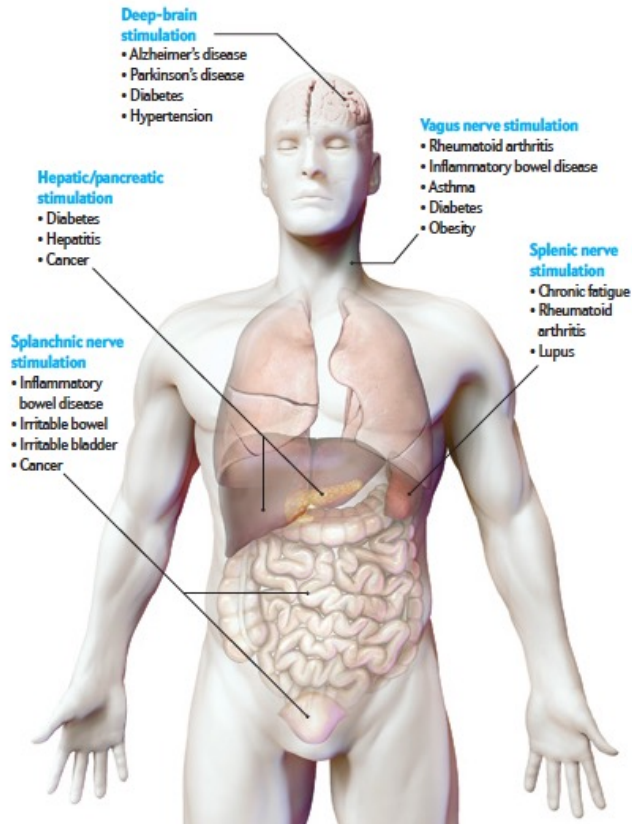


Deep Brain Stimulation



- GPi: internal globus pallidus
- GPe: external globus pallidus
- STN: subthalamic nucleus
- SMA: supplementary motor area
- SNr: substantia nigra
- VL: ventrolateral nucleus of the thalamus

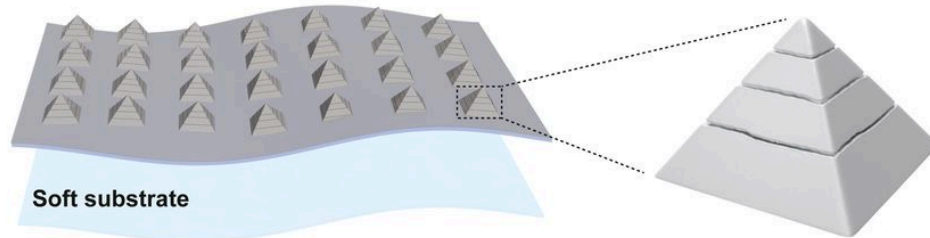
Bioelectronic Medicine



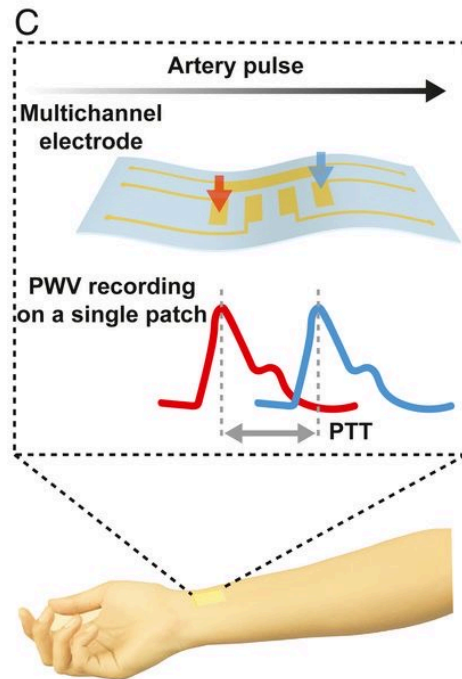
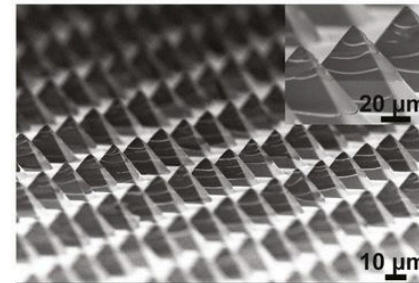
Wearable sensors



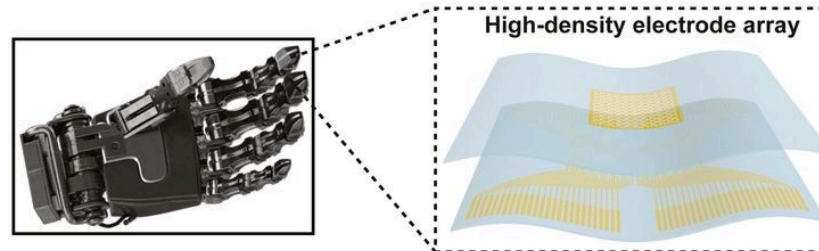
A
High-sensitivity & low-hysteresis sensor array



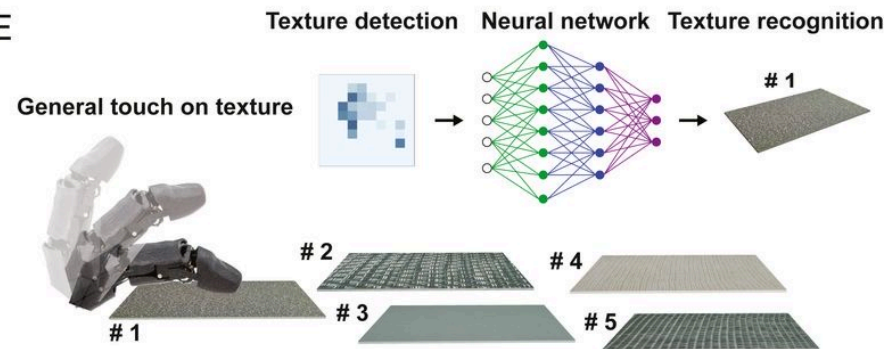
B



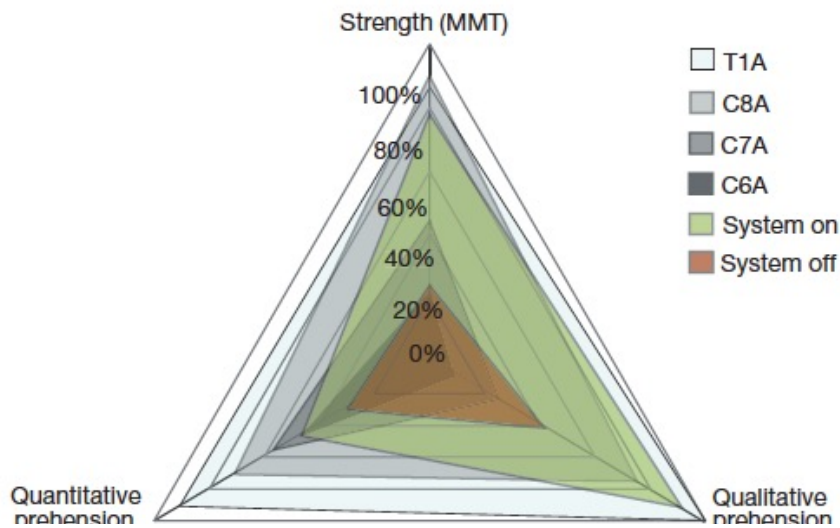
D



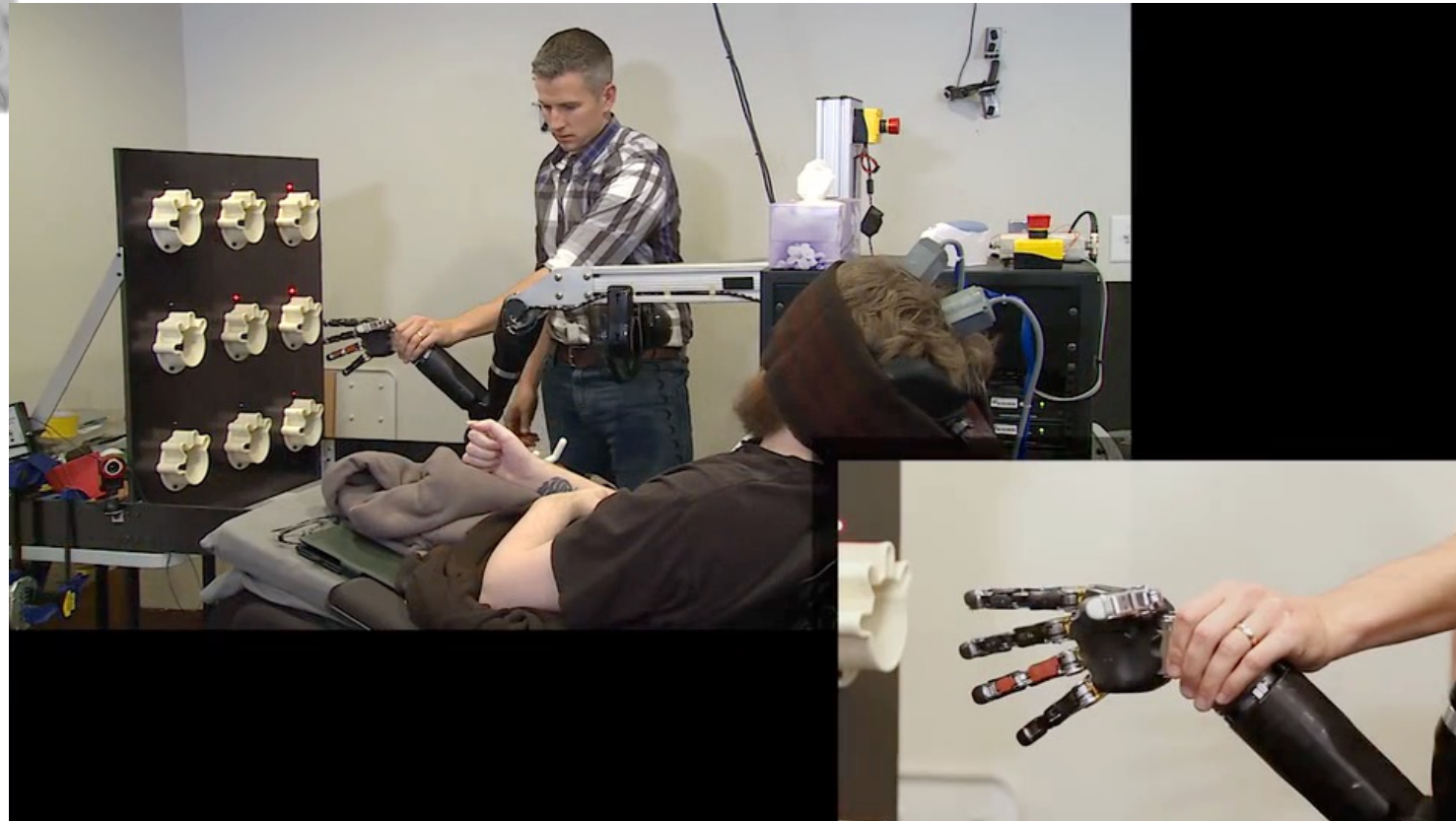
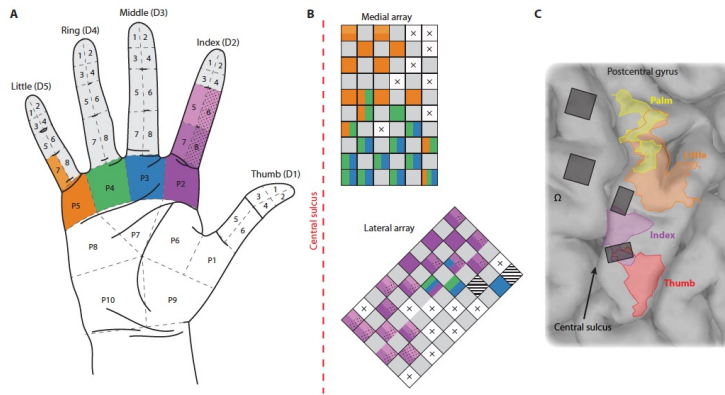
E



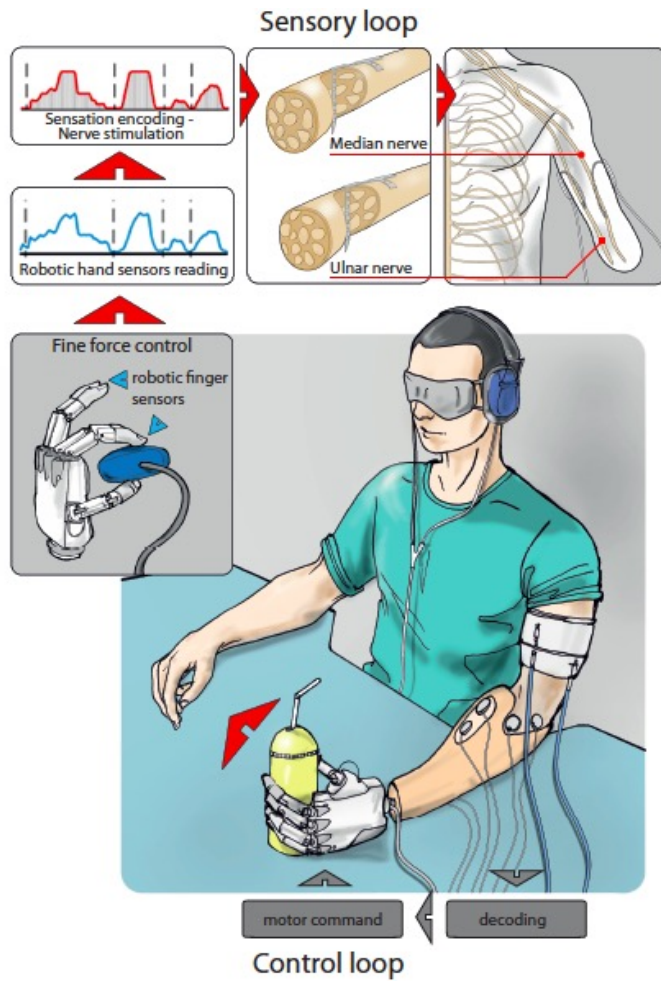
BMI-based neurorehabilitation

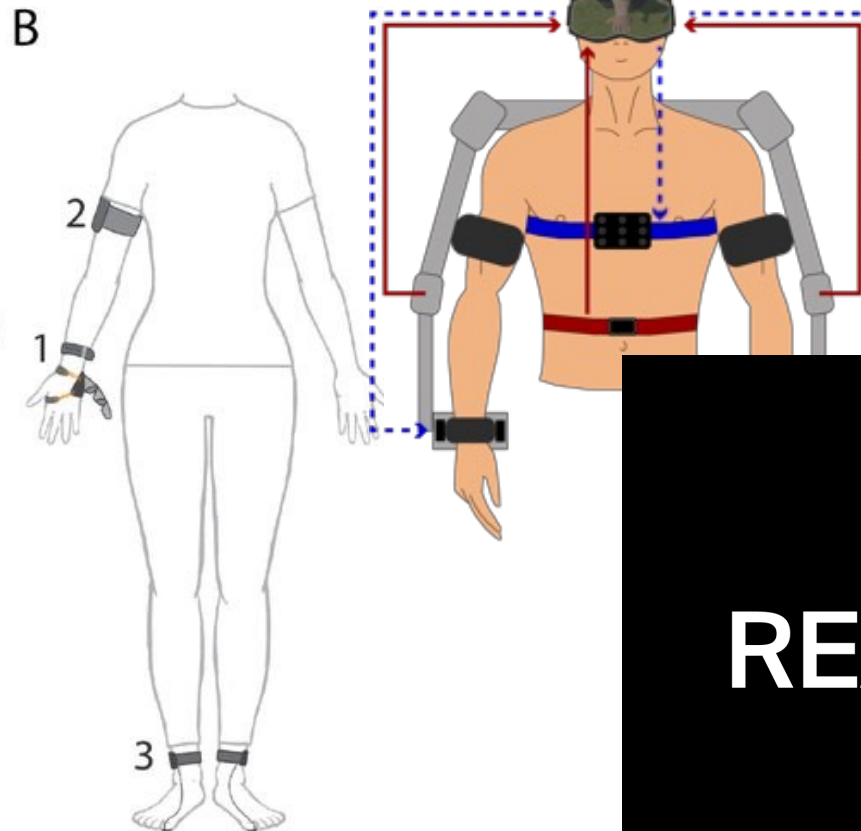


Sensory feedback



Sensory feedback

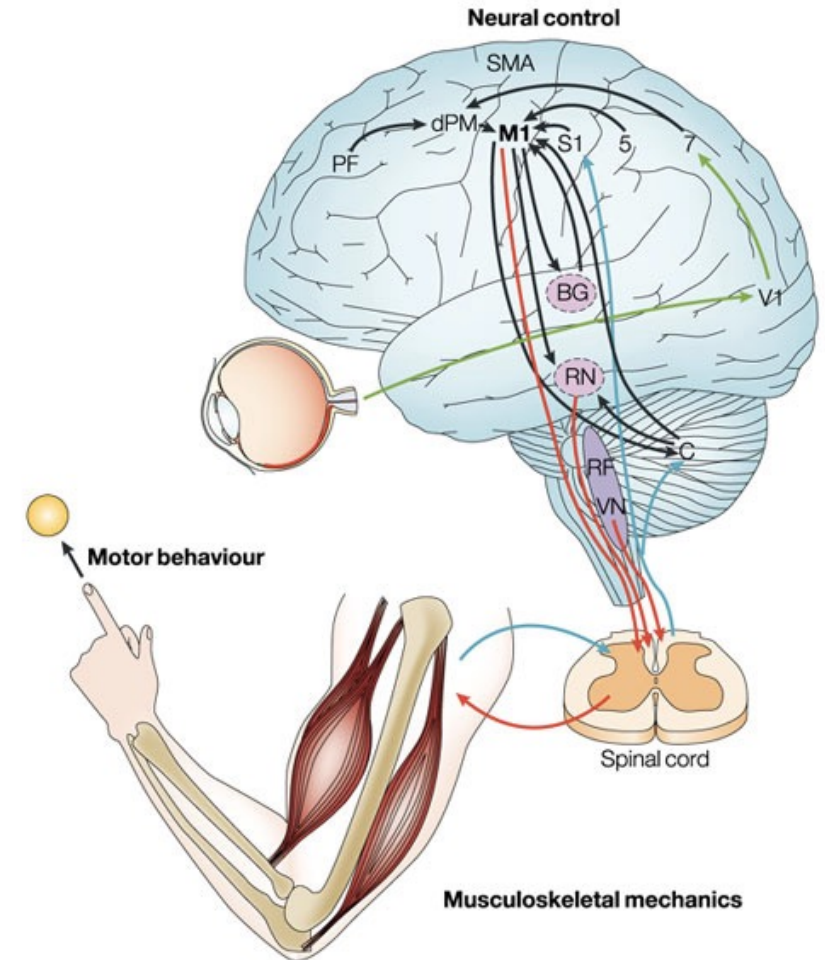
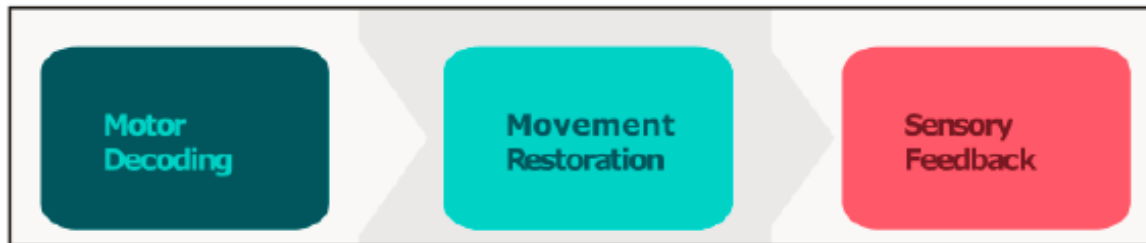




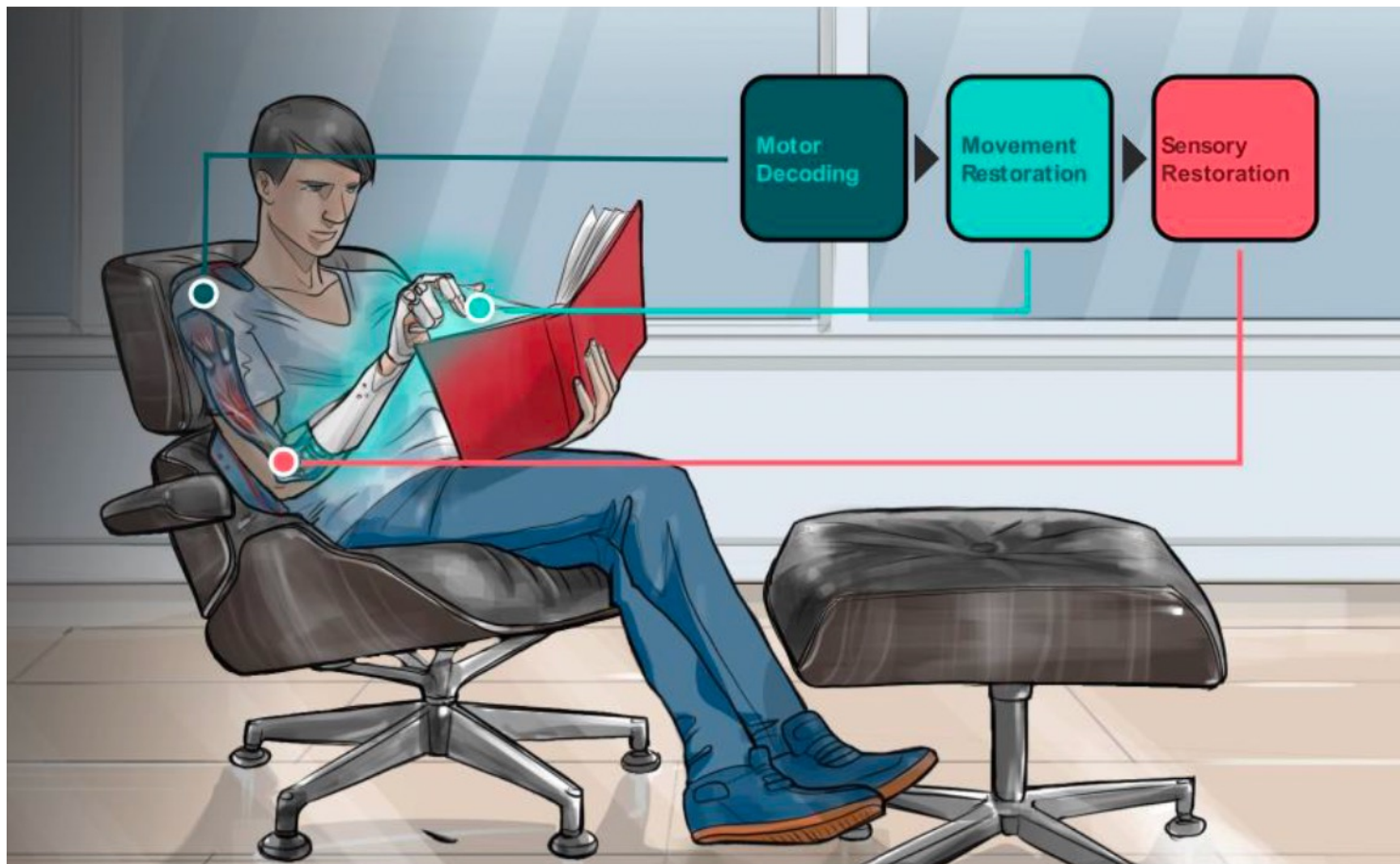
REACHING TASK

How to design a sensory-motor neuroprosthesis?

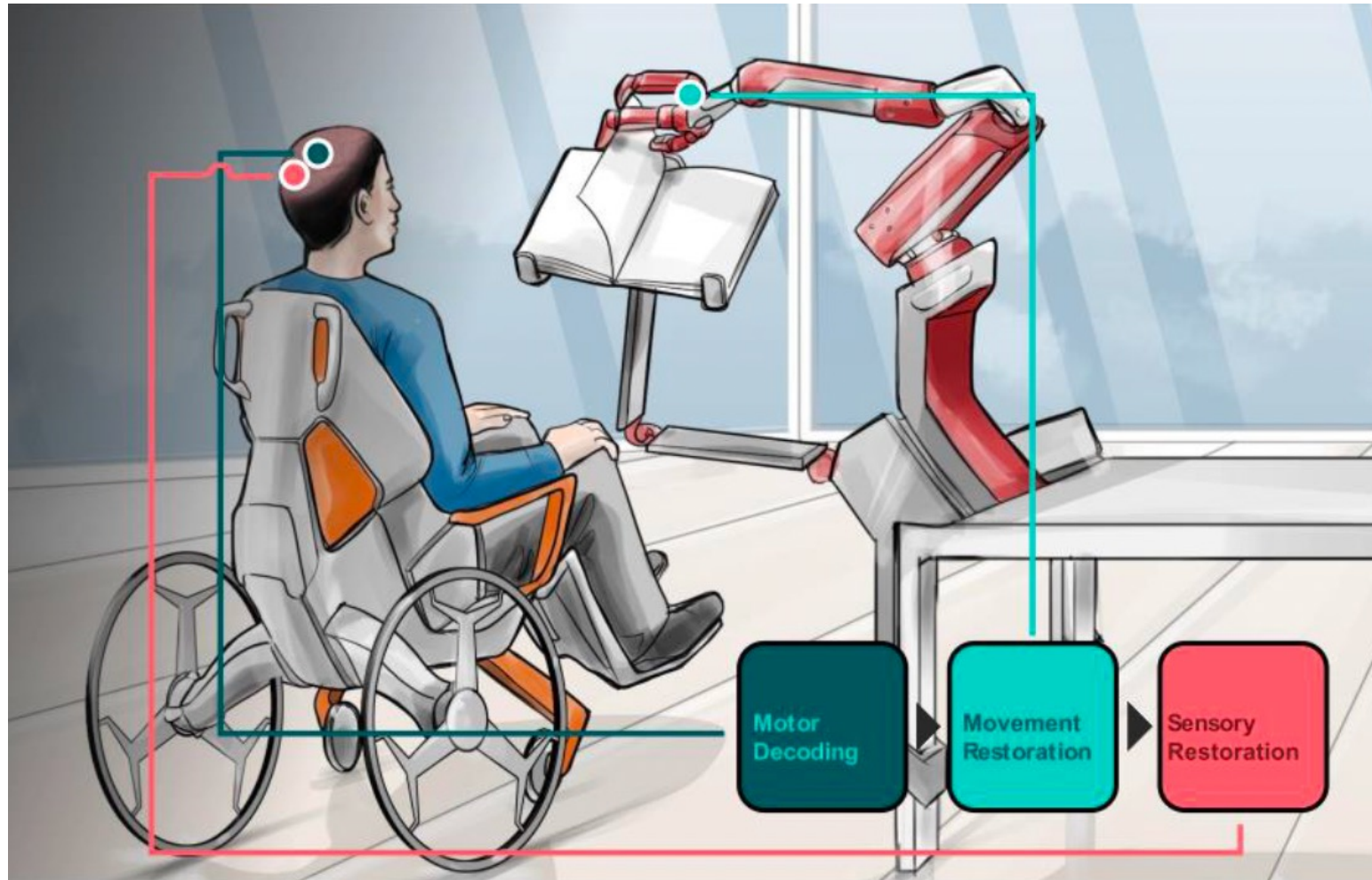
- Start from natural neural control of movement
- Try to replicate it



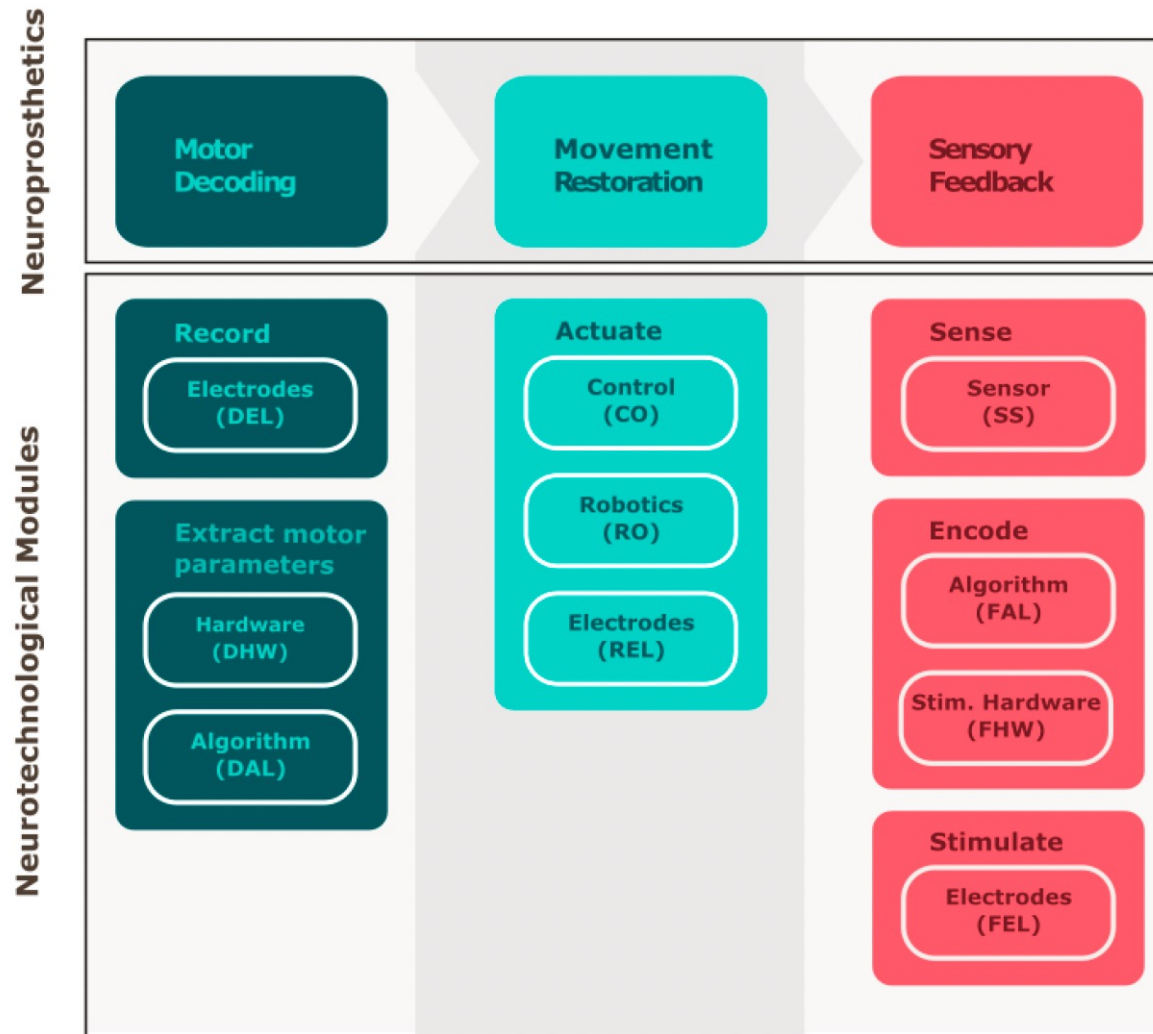
How to design a sensory-motor neuroprosthesis?



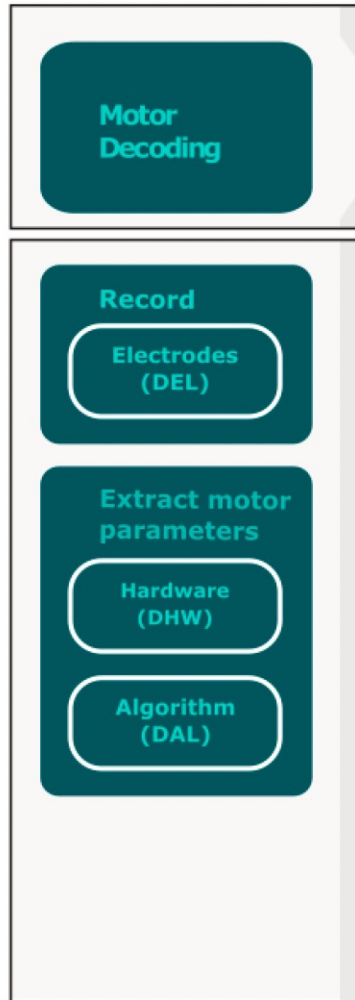
How to design a sensory-motor neuroprosthesis?



Neurotechnology modules



Motor decoding

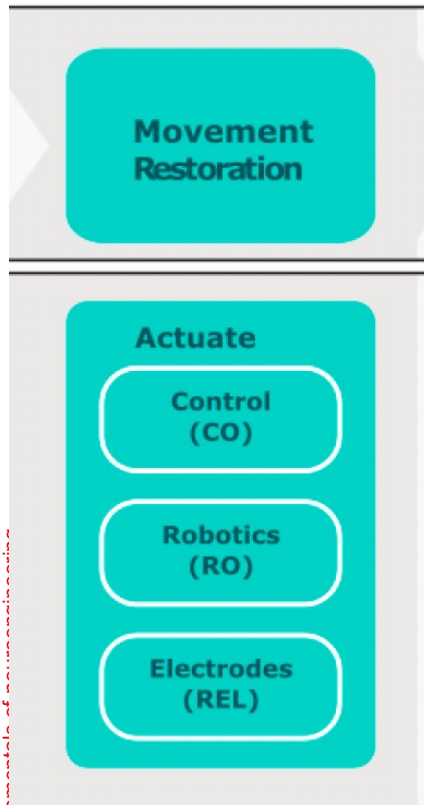


Understand the intention of the subject: grasping task? Locomotion speed? Etc.

Interface with the neuromuscular system to record electrophysiological or kinematic signals

Hardware to process the signals recorded

Software to process the signals recorded



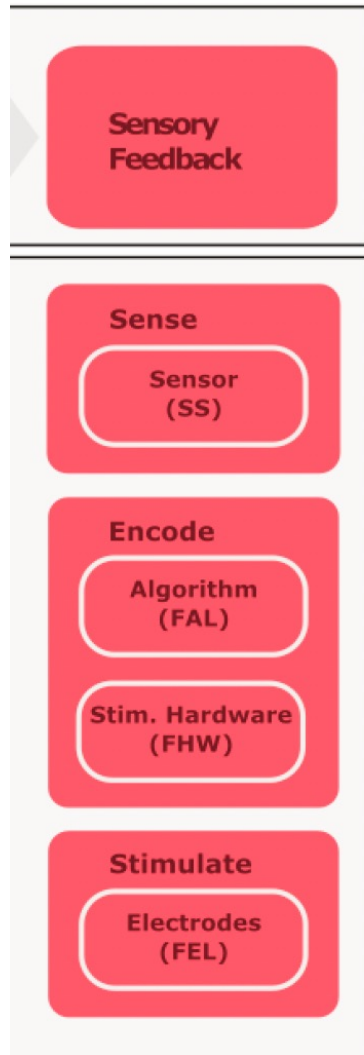
Restore specific movements impaired by neurological disorders or traumatic injuries

Use the motor intention detected to control the different actuation systems

Restore movements using robotic systems

Restore movements using electrical stimulation (muscle activation)

Sensory feedback



Restore the possibility to gather information about the world and the subject: touch? proprioception? Temperature? Etc.

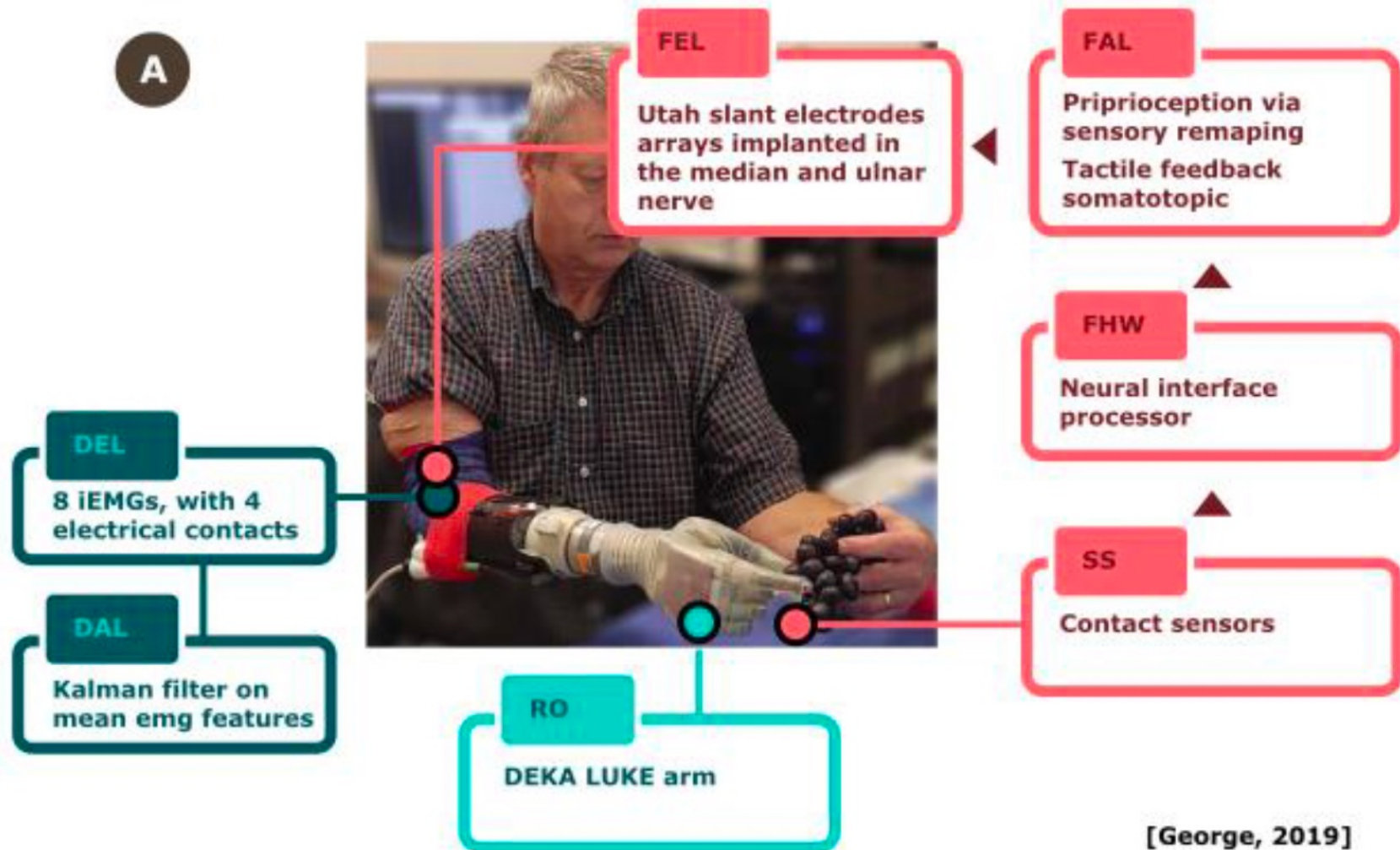
Artificial sensors to record information about the world and the subject

Software to translate the artificial sensory information into electrical stimulation parameters

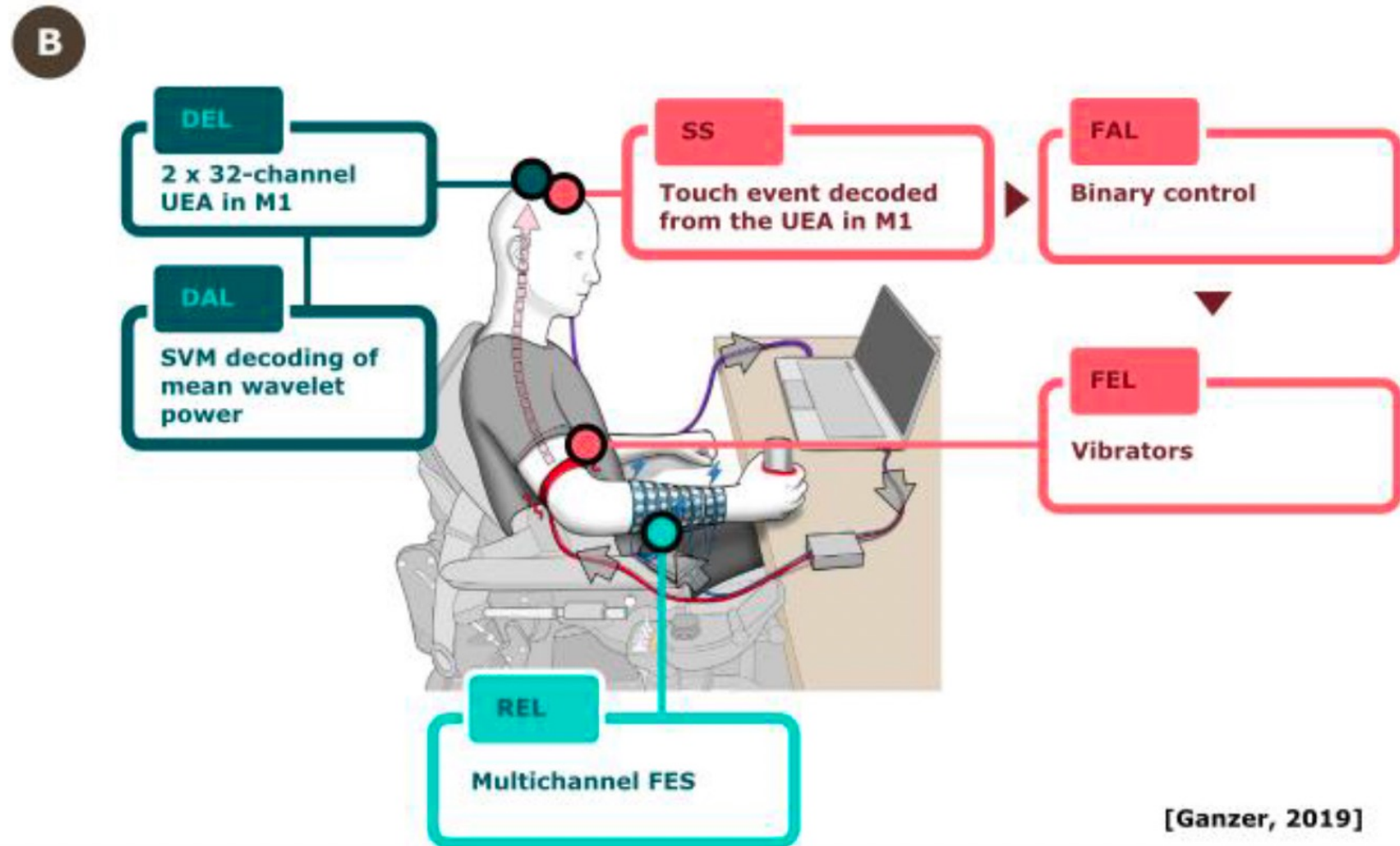
Hardware to stimulate the nervous system or the skin

Interface with the neuromuscular system or the skin to deliver the artificial sensation

Examples of Neuroprostheses

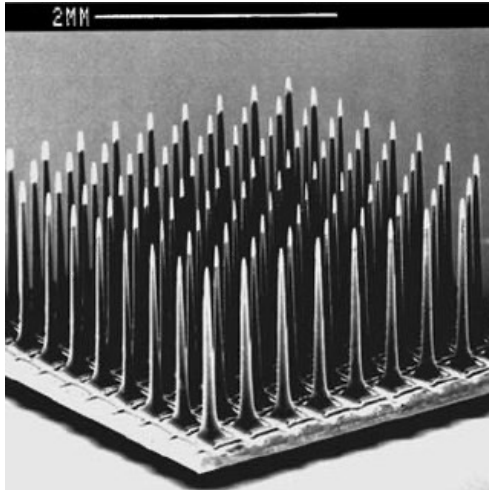


Examples of Neuroprostheses



Reusing (DEL-FEL)

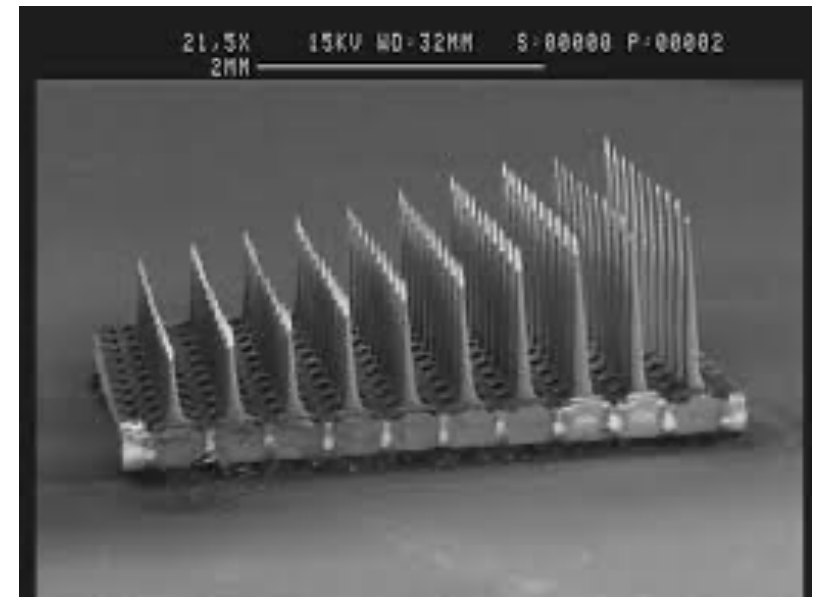
Utah Array



Motor (cortical) decoding

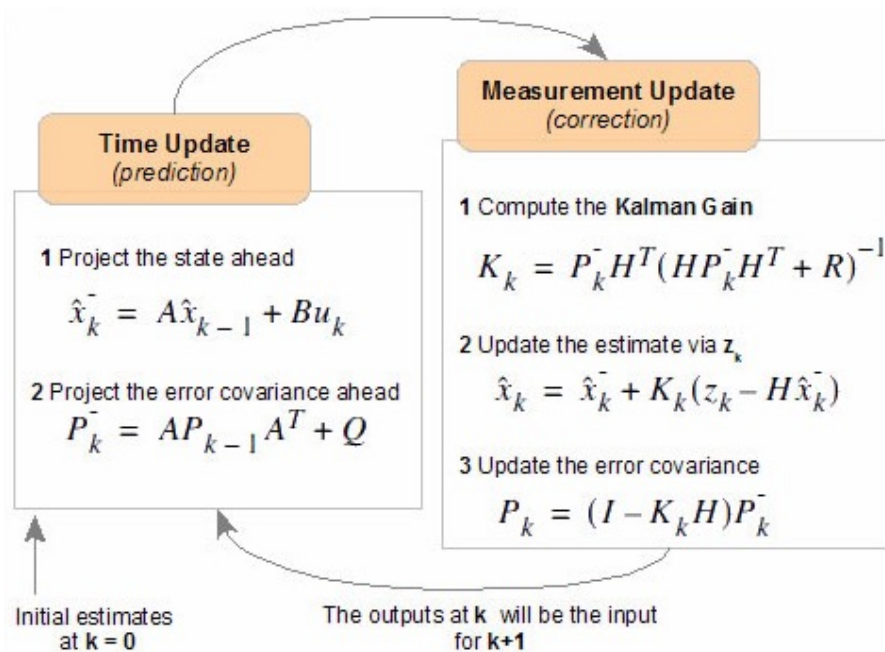
Sensory (cortical) feedback

SLANTED Utah Array

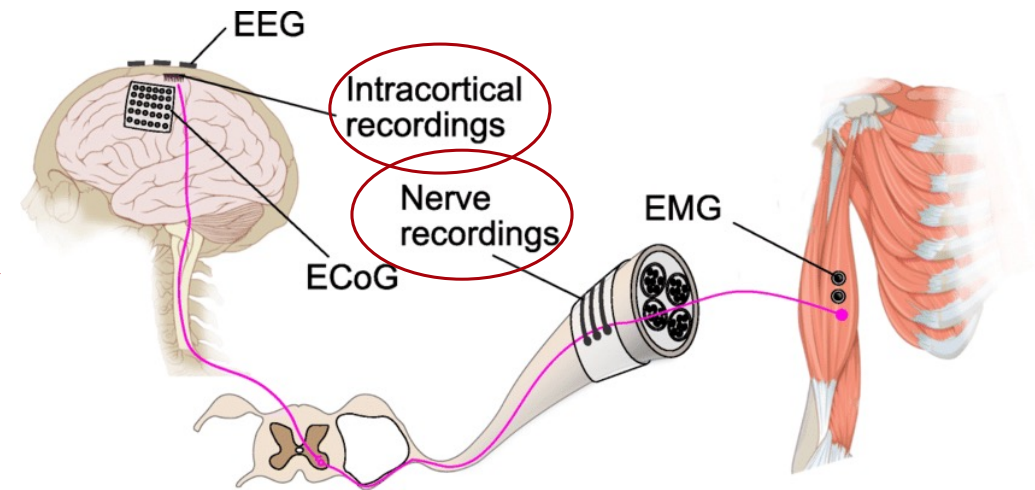


Motor (peripheral) decoding

Sensory (peripheral) feedback



Kalman filter



Decoding motor commands from cortical and peripheral signals



The Motivation

The loss of the upper limb is a traumatic event that changes the **quality of life** radically

Reduction of

- Ability in **reaching, grasping and manipulation**
- Ability in **sensing** through the sense of touch
- **Gesture** (communication)

Statistics

38% Transhumeral

31% Transradial

14% Partial hand

5% Fingers

...

...

1.7 million total number of amputees living in the U.S

65,000 upper limb amputations in the U.S. each year

27,000 hand amputation below the wrist in the U.S. each year

400 hand amputation below the wrist in Italy each year

Consequences

Few innovations in the past 50 years

Actual prostheses **do not satisfy** amputees' requirements and are very different from the natural model

The big challenges

Hand Prosthesis

How to design and develop a **more functional** and **naturally controlled** **prosthetics hand?**

Dexterity

Functionality

Reliability

...

...

UP Interface

How to **control** this dexterity?

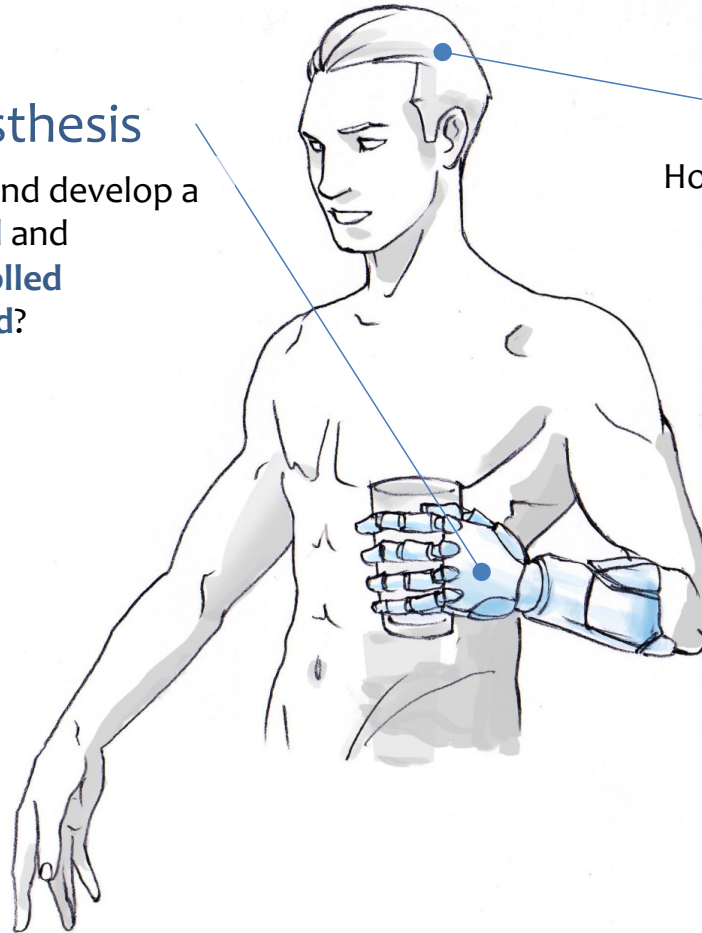
Sources

Cognitive Effort

Reliability

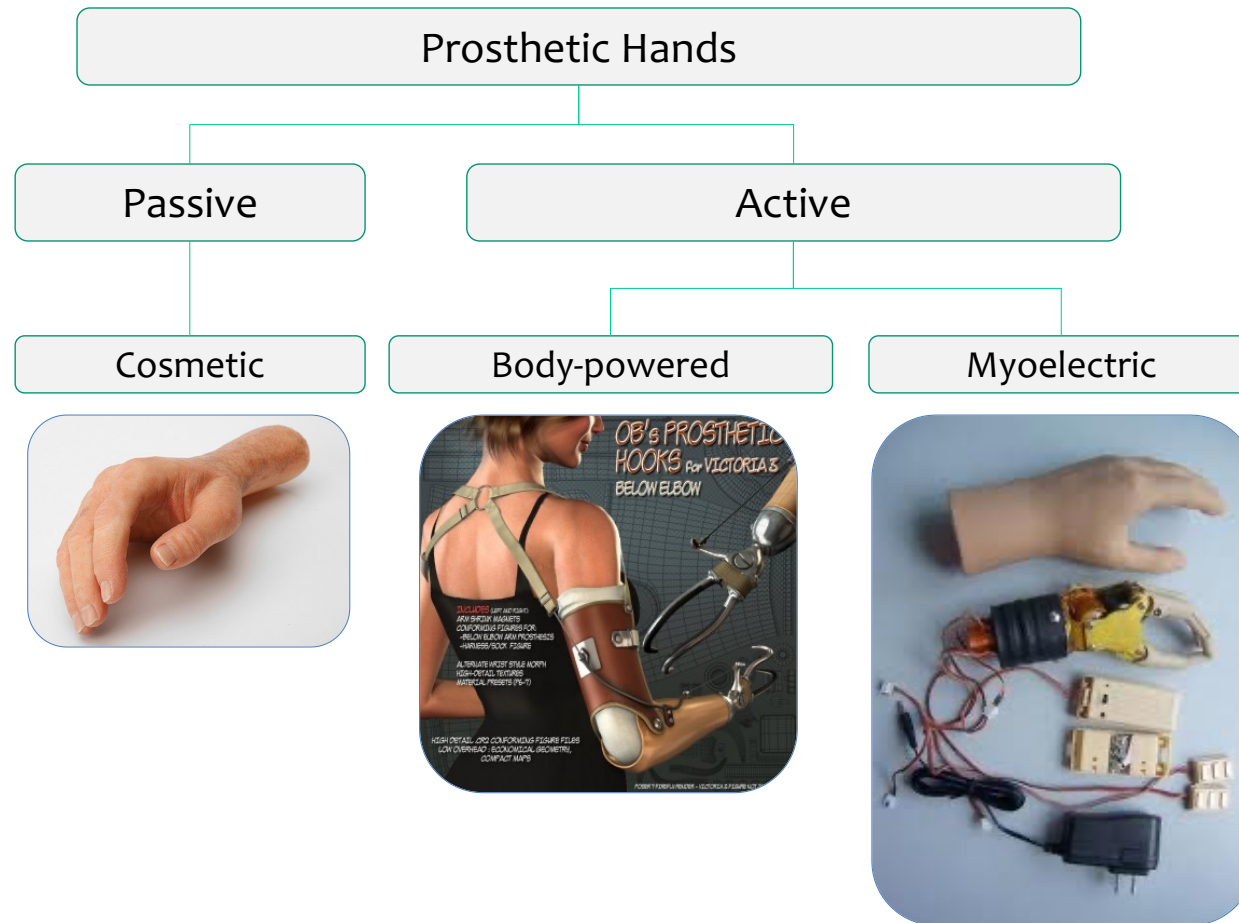
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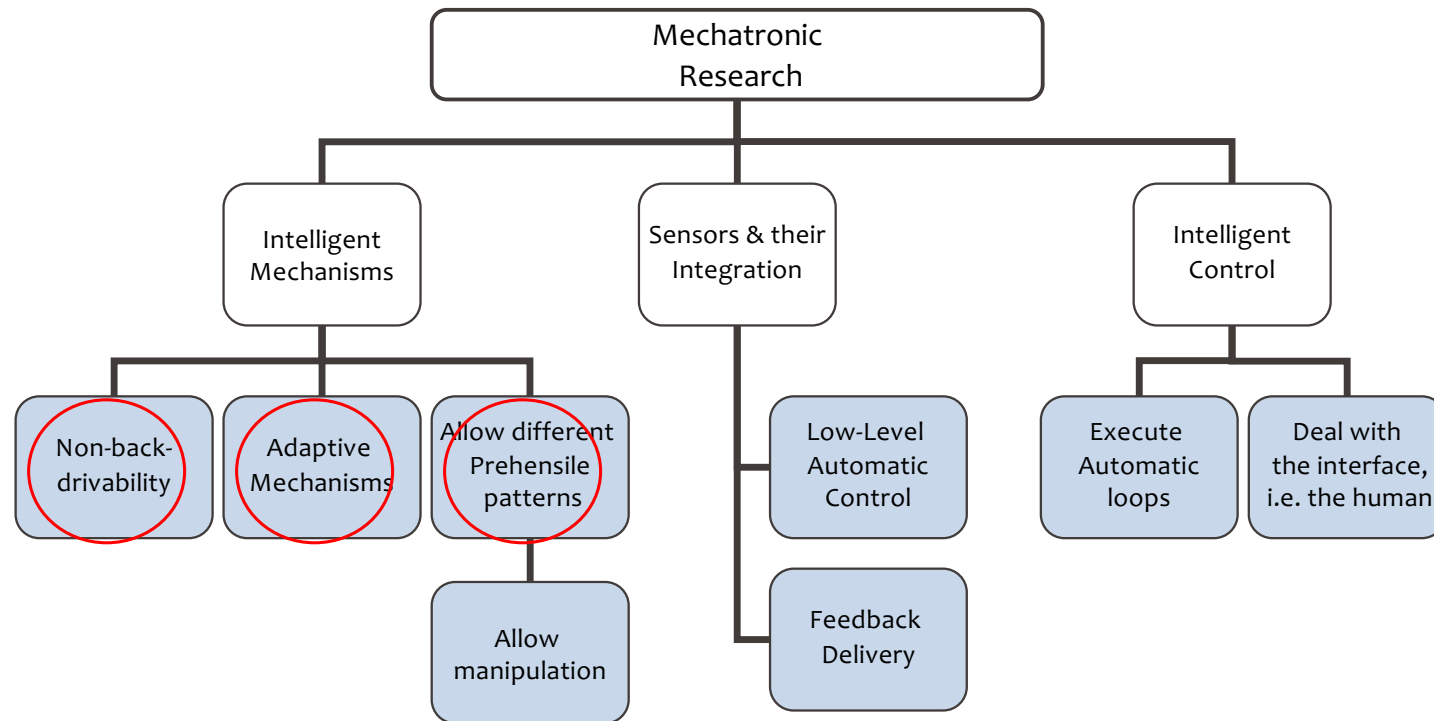


What can an amputee get today?

Hand Prosthesis



Key issues



Mechatronic

Design issues: adaptability

Problem: It's an hard task to **design, actuate, and control** a self-contained artificial hand with a number of degrees of freedom (DoF) equal or close to those in the biological human hand!

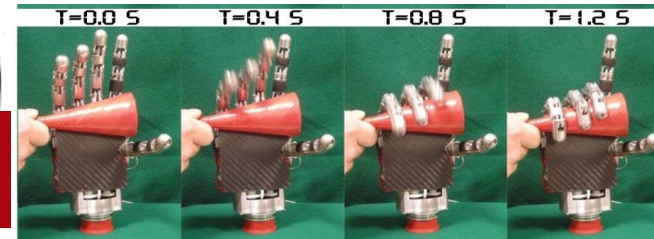
22 muscles

... + 18

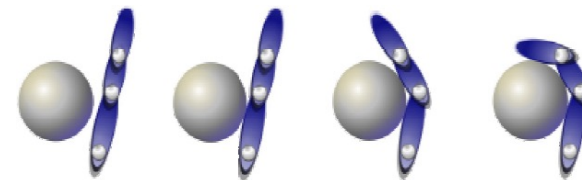
Adaptation also improves **grasp stability** as it increases the **contact areas** while grasping

Possible solutions (to simplify the problem):

- Cut DoFs; Rigidly couple DoFs;
- Implement adaptable mechanisms.

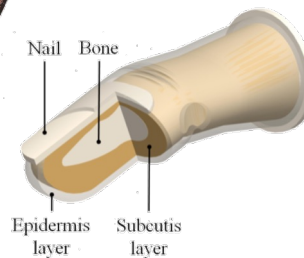


Hand adaptation mechanisms



Finger adaptation mechanisms

Phalanx adaptation mechanisms

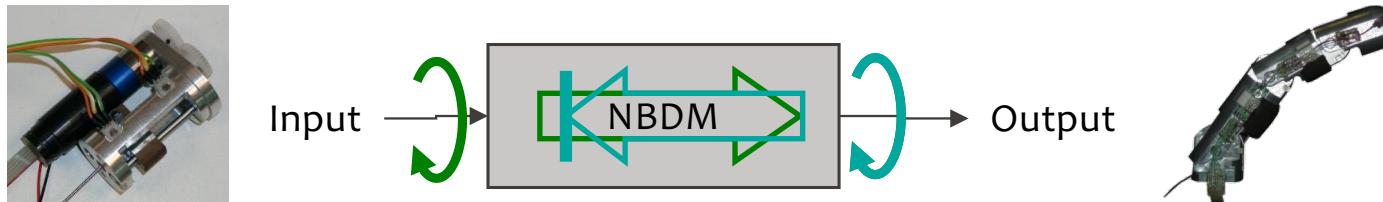


Underactuated mechanisms

Mechatronic

Design issues: non back drivability

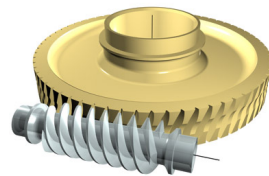
Mechanisms wherein motions generated by the input (motor) drive are **transmitted** to the output (i.e. fingers) and wherein motions originated from the output are **blocked**



In a prosthesis it allows to maintain the grasp once the power supply is switched off
Non back drivable transmission = Power saving!= key in prosthetics!



Lead Screw



Worm Gear



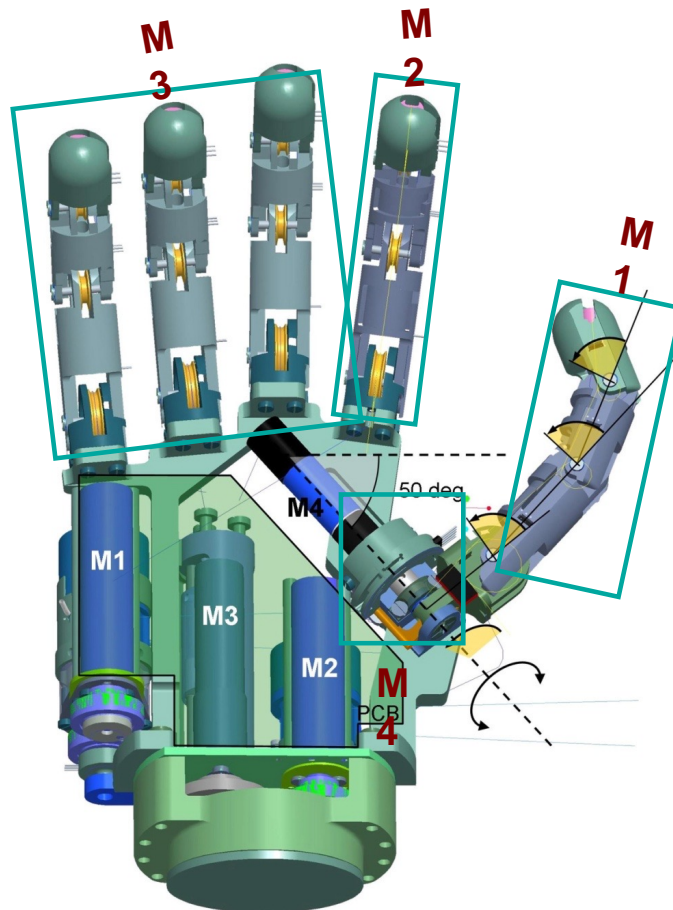
Gear heads with high
reduction rate



Brakes/
clutches

Case Study

The SmartHand prototype



The SmartHand at glance

Mechanical Spec

Weight	600 gr
Size	Human inspired
Degrees of freedom	16
Degrees of actuation	4
Full flexion speed	<1.5 s
Tendon max active force	45 N
Grasp force (Cyl, Lat, Lift)	<30, <5, 100 N

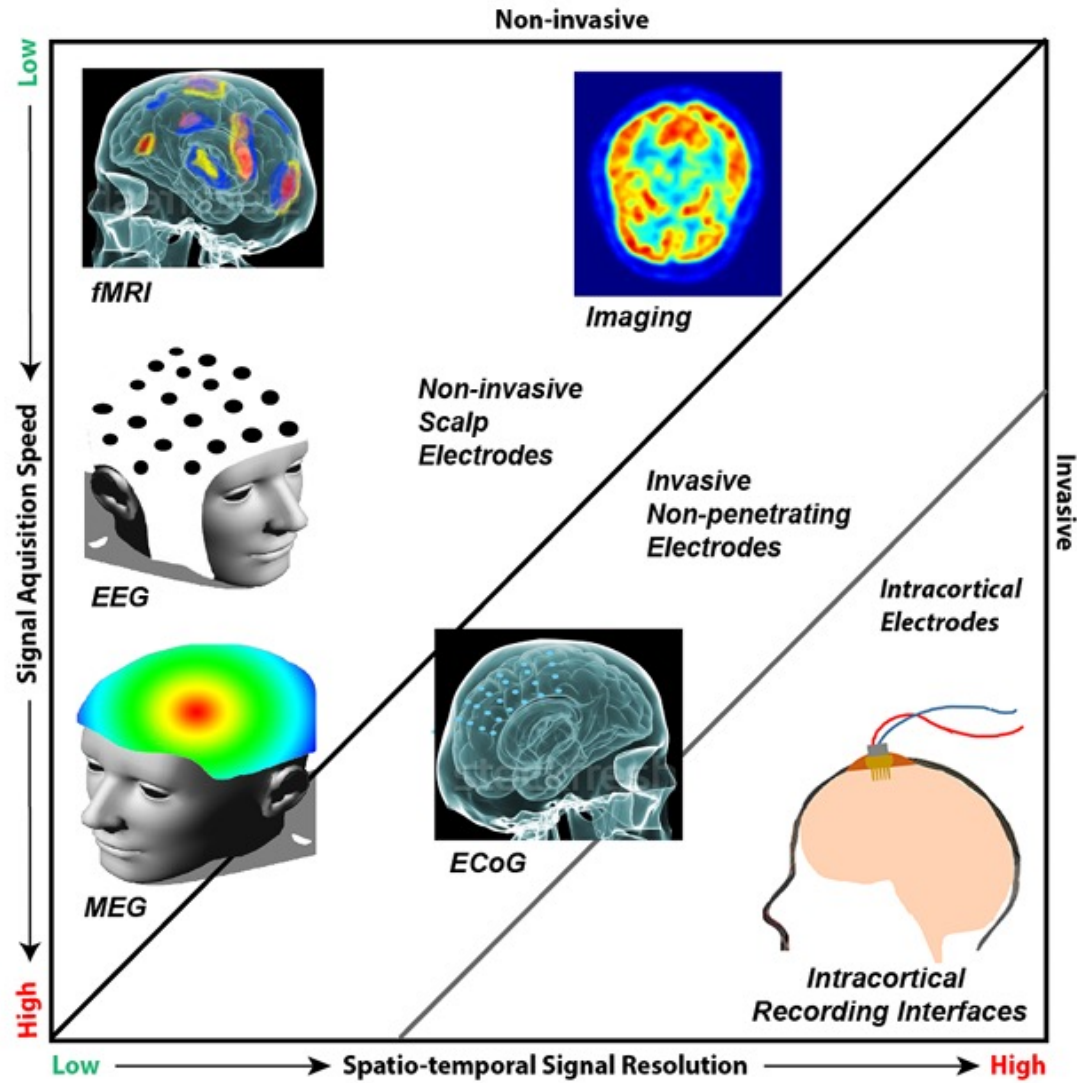
Sensory System

Position (digital encoder)	4
Position (Joint Hall sensors)	15
Position (Potentiometer)	2
Tension Sensors (strain gauges)	5
Limit switch (digital)	8

Electrical Spec

Power req.	12V / 3A
Control loops	Position and tension (1 kHz)
Reading delays	< 1 ms
Total preset grasps	10 (programmable)
Communication	RS232 / USB

Cortical signals



Ginaseka et al, 2015

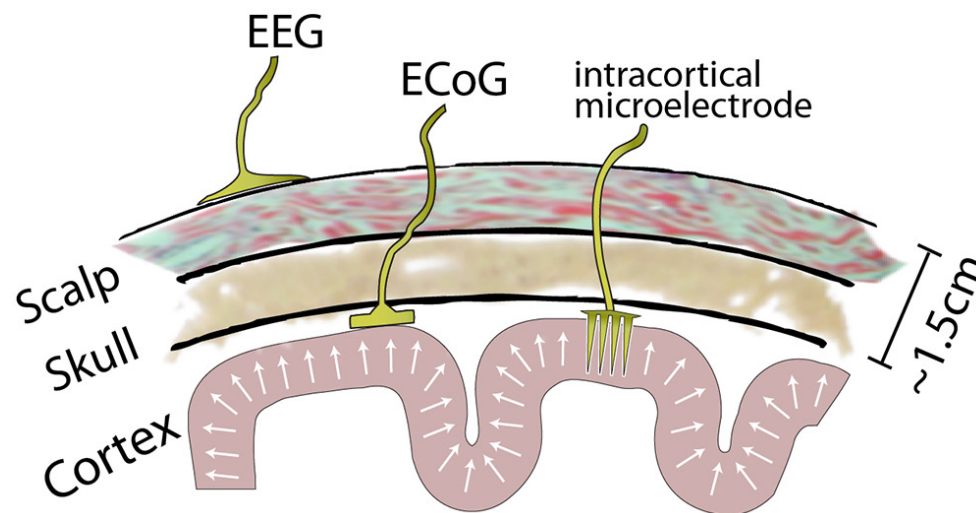
Cortical signals

Electric current contributions from all active cellular processes within a volume of brain tissue generate a potential, V_e (a scalar measured in Volts), with respect to a reference potential

The difference in V_e between two locations gives rise to an electric field (a vector whose amplitude is measured in Volts per distance)

Electric fields can be monitored by extracellularly placed electrodes with submillisecond time resolution

The biophysics related to extracellular field recording measurements is well understood.



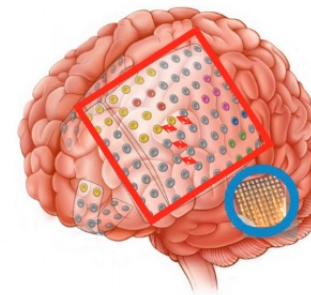
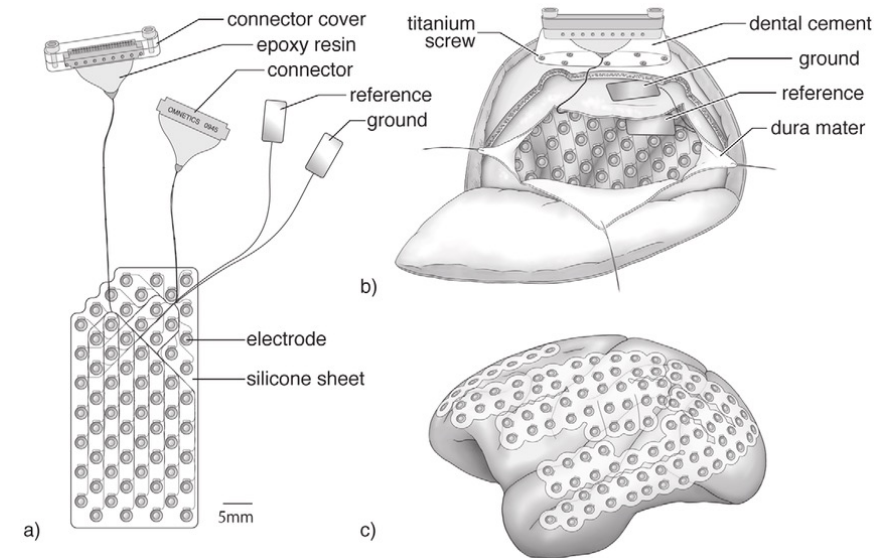
Buzsáki et al, 2012

Cortical signals - ECoG

Electrocorticography (ECoG) is a type of electrophysiological monitoring that uses electrodes placed directly on the exposed surface of the brain to record electrical activity from the cerebral cortex

In contrast, conventional electroencephalography (EEG) electrodes monitor this activity from outside the skull

ECoG may be performed either in the operating room during surgery (intraoperative ECoG) or outside of surgery (extraoperative ECoG).



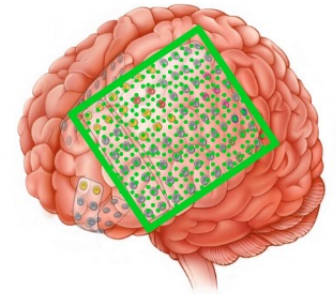
Current ECoGs

- Large area
- Low resolution



Current μ ECoGs

- Small area
- High resolution



BMSEED lahrpECoGs

- Large area
- High resolution

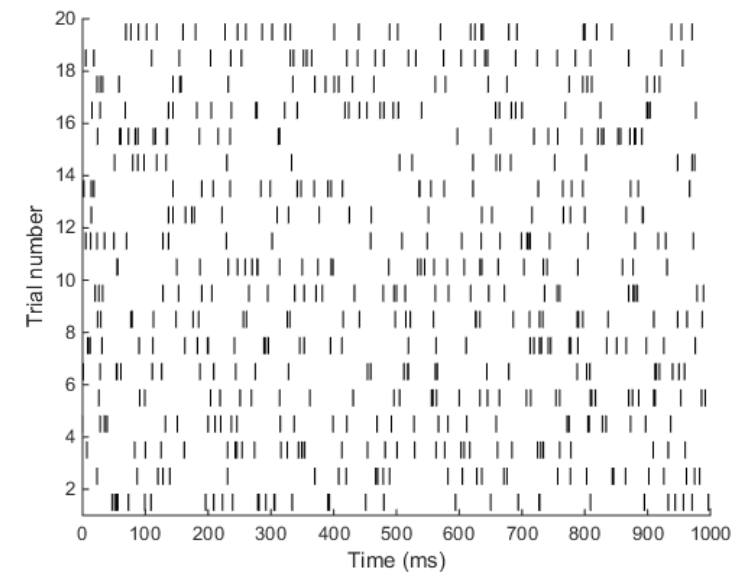
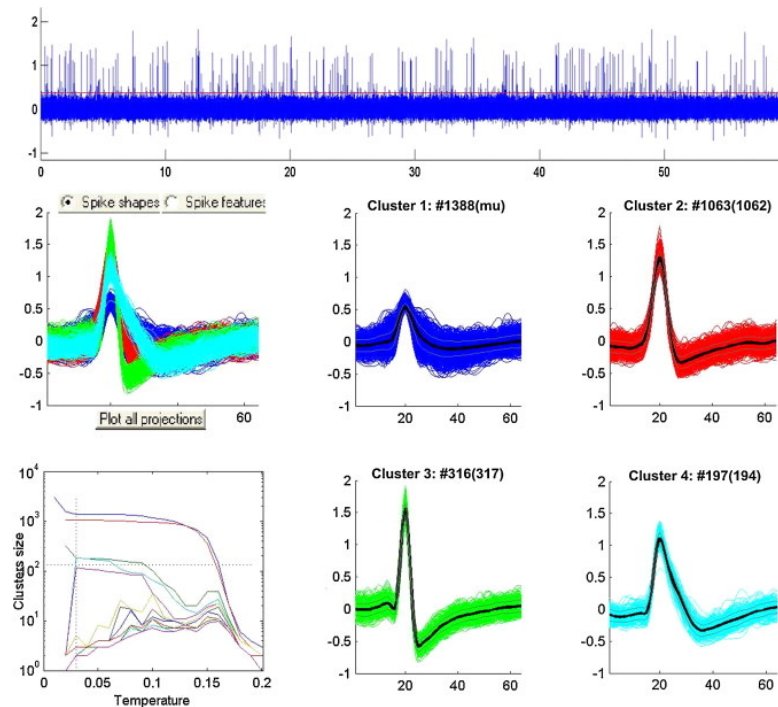


Cortical signals – Intracortical signals

Cortical activity recorded using intracortical electrodes positioned in specific areas (very high spatial selectivity)

The main unit of information to extract is the cortical spike (spike detection)

Different shapes of spikes represent specific activities of different neurons around the electrodes (spike sorting)

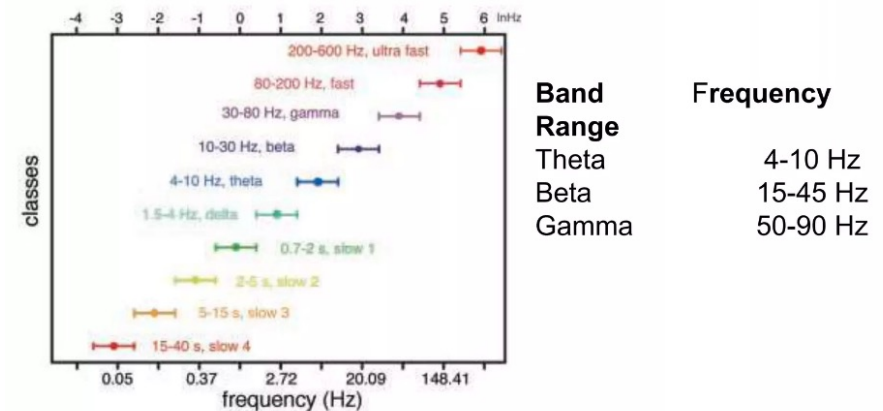
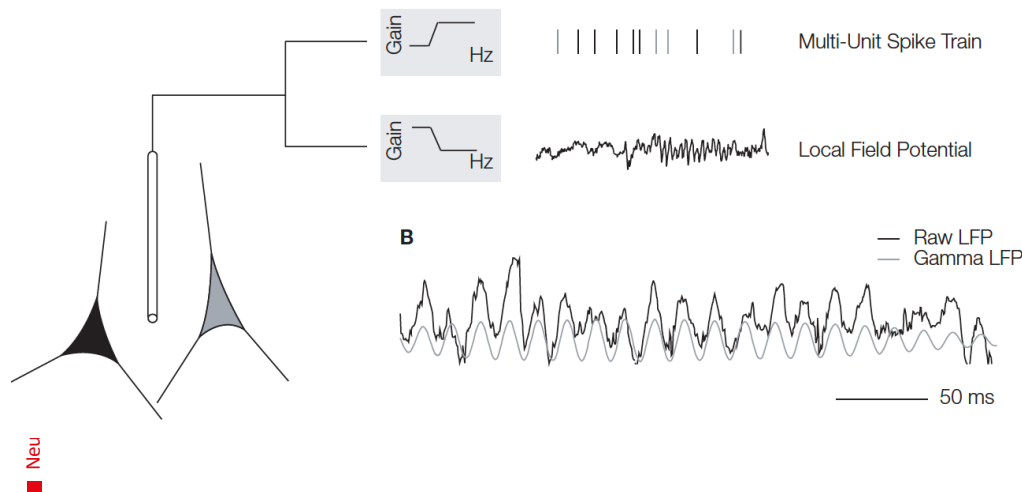


Cortical signals – Local field potentials

Local field potentials (LFP) are transient electrical signals generated in nervous and other tissues by the summed and synchronous electrical activity of the individual cells (e.g. neurons) in that tissue

LFP are 'local' because they are recorded by an electrode placed nearby the generating cells

They can be recorded, for example, via a microelectrode placed in the brain of a human or animal subject, or in an in vitro brain thin slice



Extraction of intracortical information

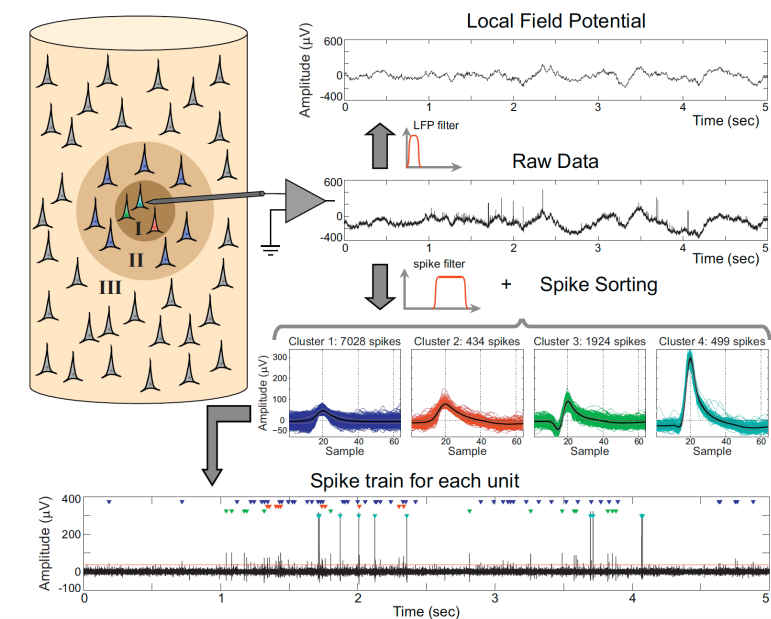
By bandpass filtering the signal, we obtain the activity of a few neurons close enough to the electrode plus background activity elicited by neurons further away from the tip

In the recorded bandpass filtered signal, the activity of different neurons is superimposed and it is important to extract the identities of the spikes corresponding to different neurons.

In principle, the spikes fired by a neuron recorded in a given electrode have a particular shape

The detected spikes are grouped into different clusters based on their shapes in a process known as Spike Sorting

Each cluster is then associated to a single unit (neuron), but some shapes cannot be separated due to a low signal to noise ratio, leading to a cluster associated with multiunit activity



Gonzalo Rey et al., 2015

Spike detection and sorting

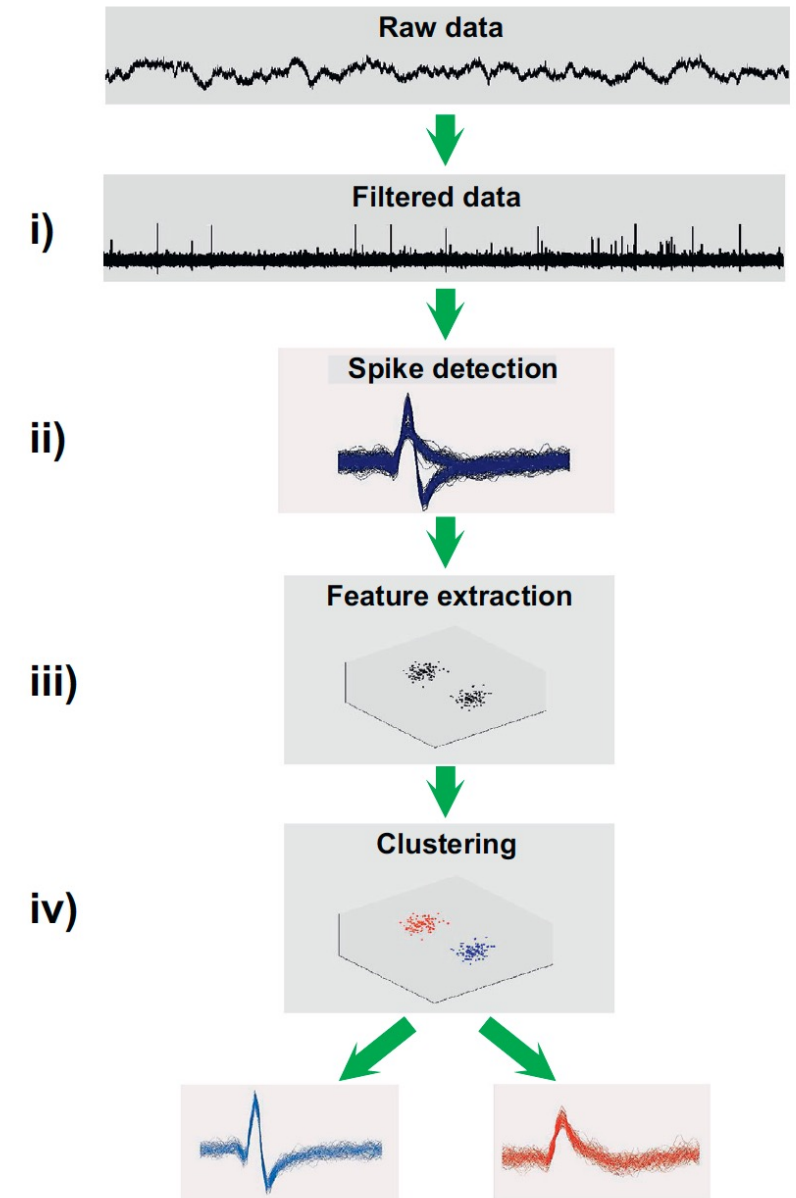
It should be noticed that the raw data is typically recorded using a hard-ware acquisition system that includes a first analog causal IIR (infinite impulse response) bandpass filter, e.g., between 0.3 Hz and 7500 Hz

For the purpose of spike detection and sorting, a second digital filter, e.g., between 300 Hz and 3000 Hz, is typically used

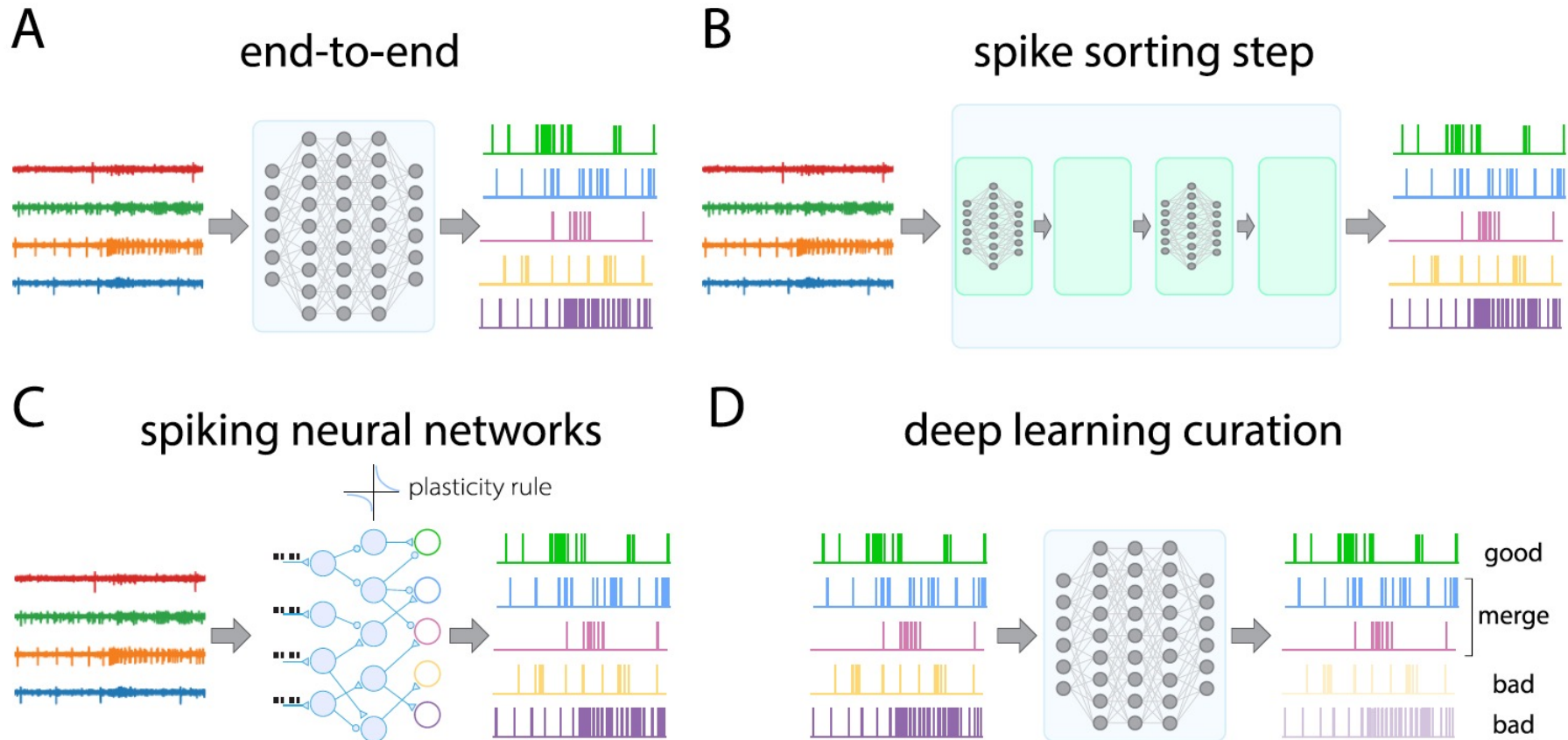
After filtering, spikes are easily visualized on top of background noisy activity and can be detected, for example, by using an amplitude threshold

If the value of the threshold is too small, noise fluctuations will lead to false positive events, if it is too large, low-amplitude spikes will be missed.

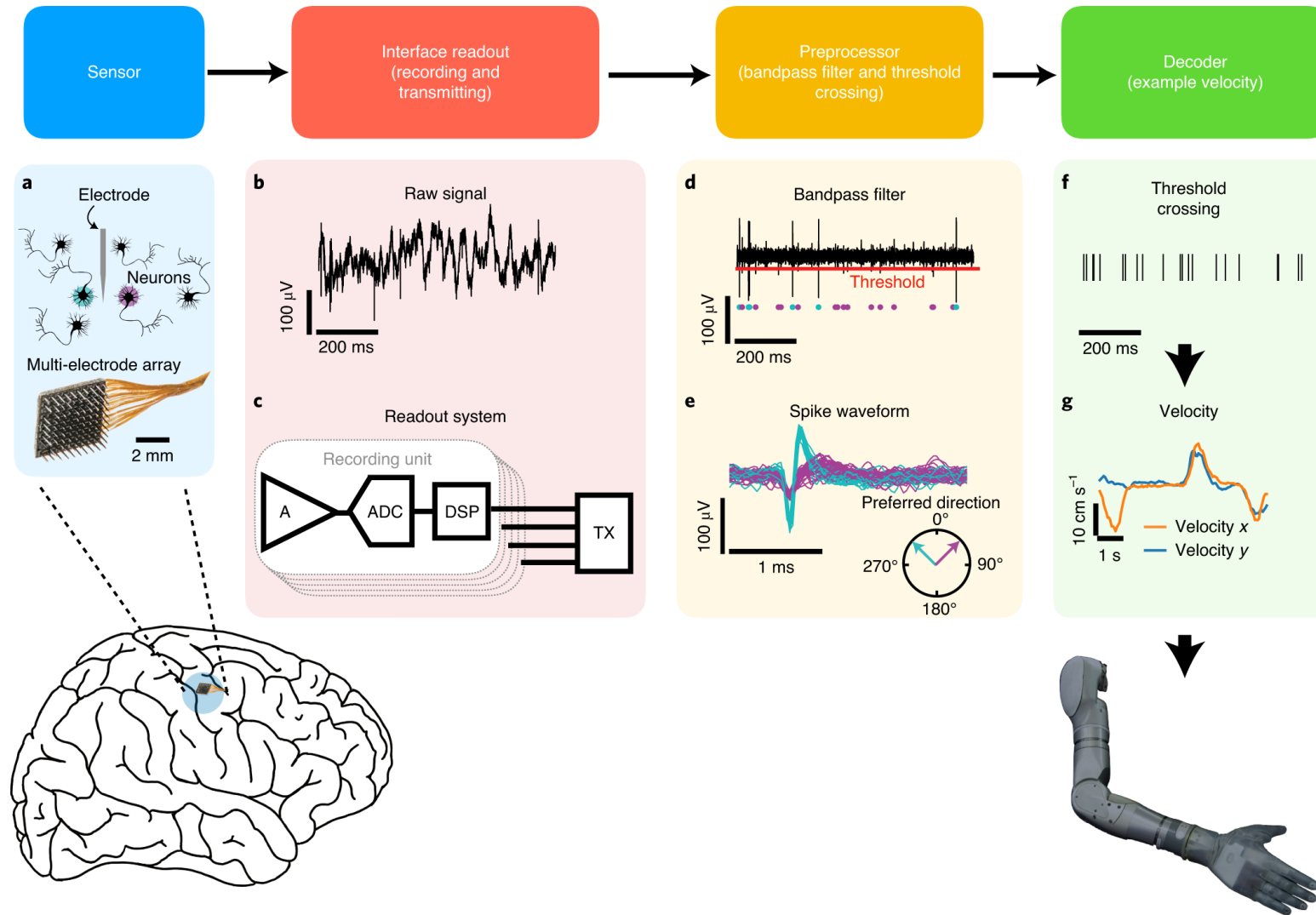
A threshold can be set manually, but since the detection tradeoff is related to the signal to noise ratio of the recording, it seems reasonable to look for an automatic threshold



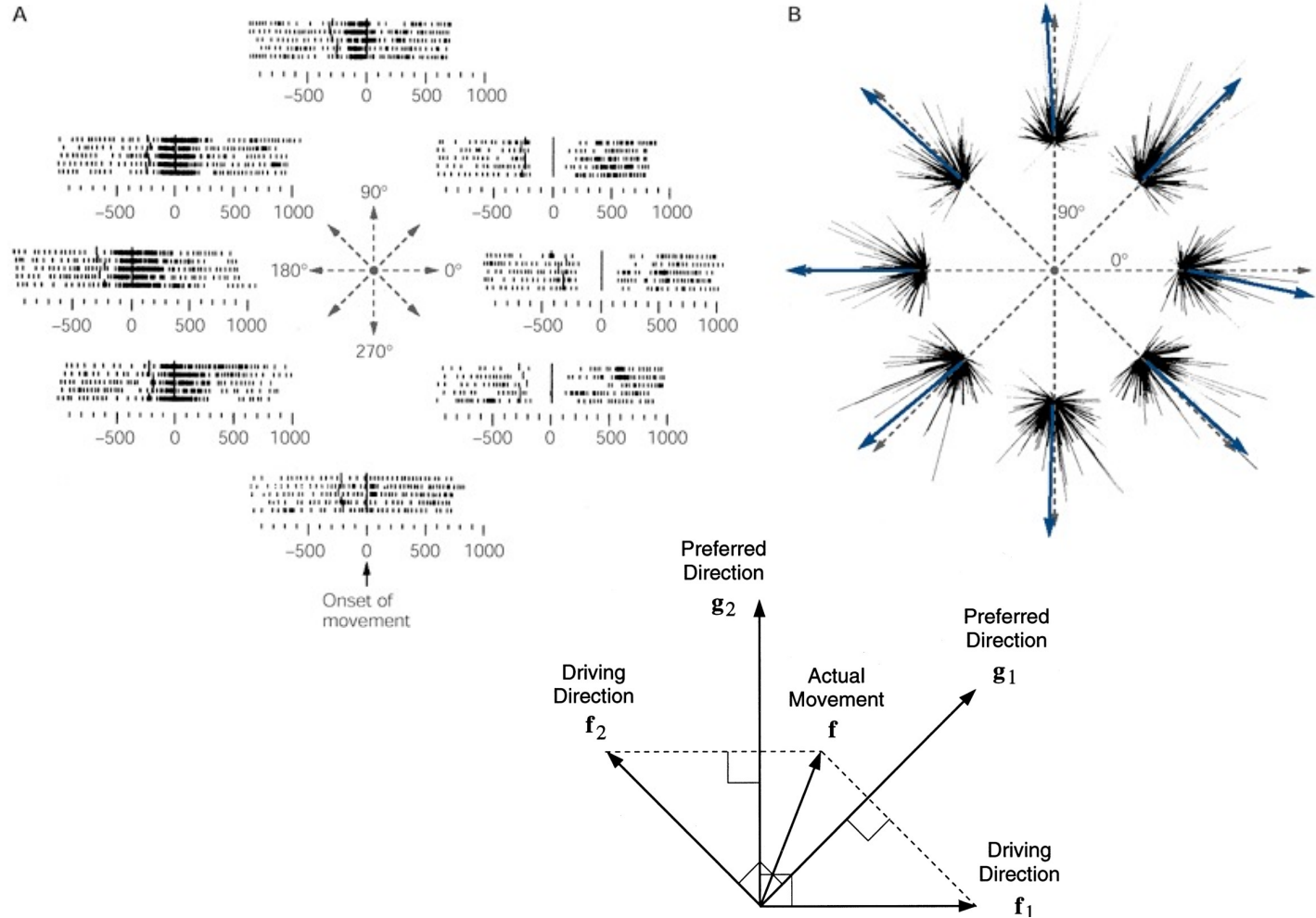
EPFL Deep learning for spike sorting



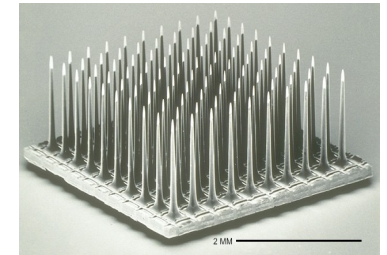
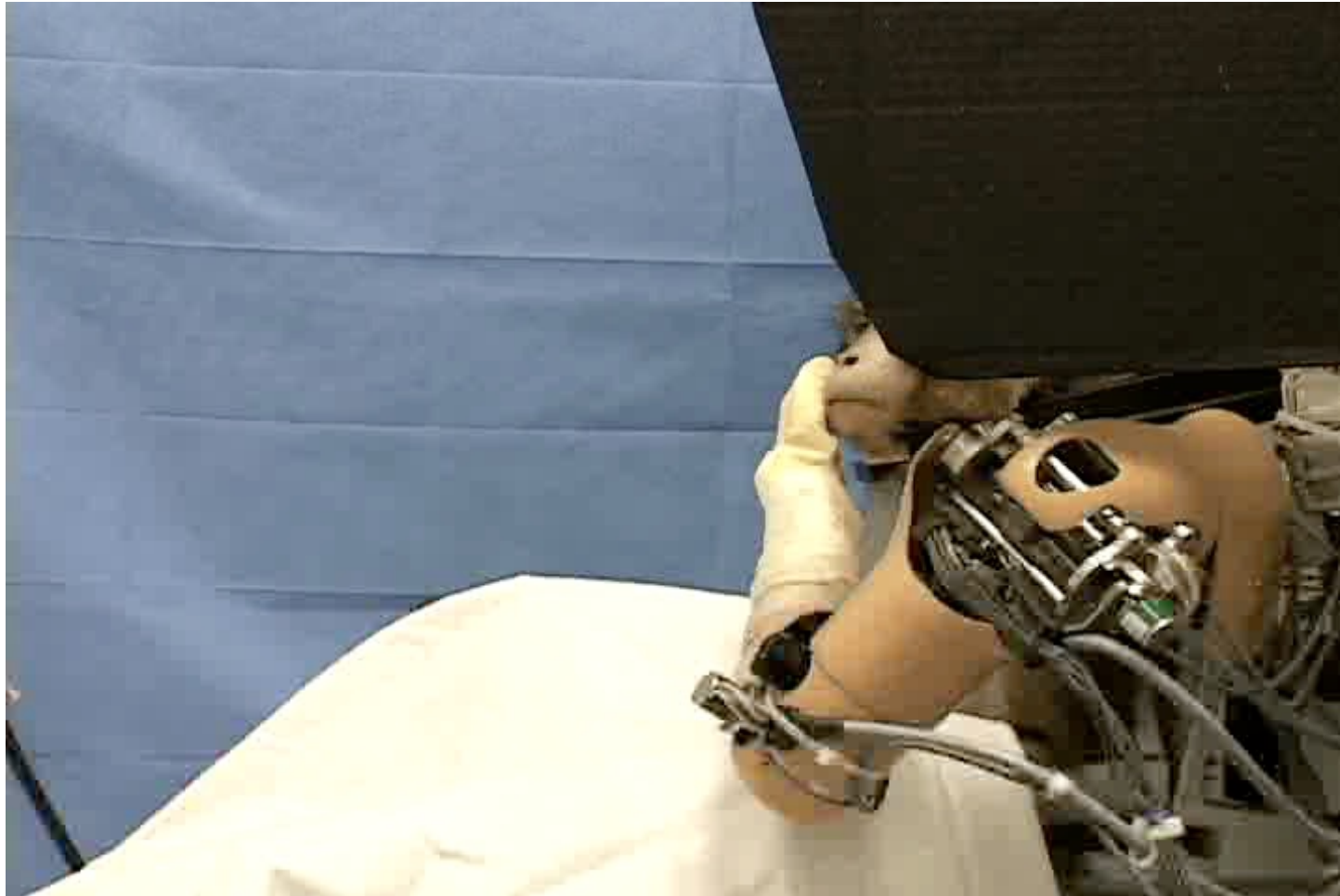
Brain decoding – General scheme



Extraction of 2D movements from M1



Extraction of movements from M1



Utah Array,
Cyberkinetics LTD

■ Schwartz and colleagues

Brain decoding – 3D robot control (with Kalman filters)

BrainGate Pilot Clinical Trial
3D + Grasp Control of a Robotic Arm
Participant S3
Trial Day 1959 / 12 April 2011
Hochberg *et al.*, 2012

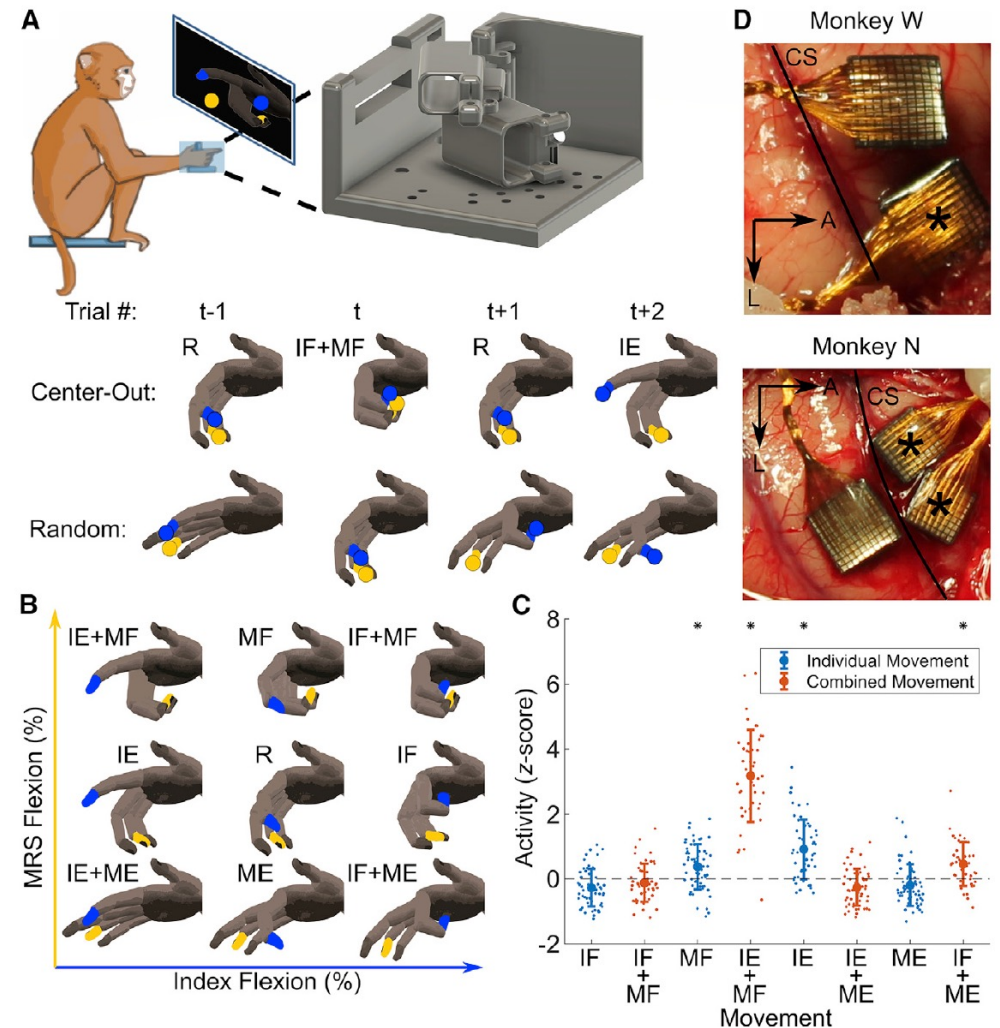


Caution: Investigational Device. Limited by Federal Law to Investigational Use.

Brain decoding of finger movements

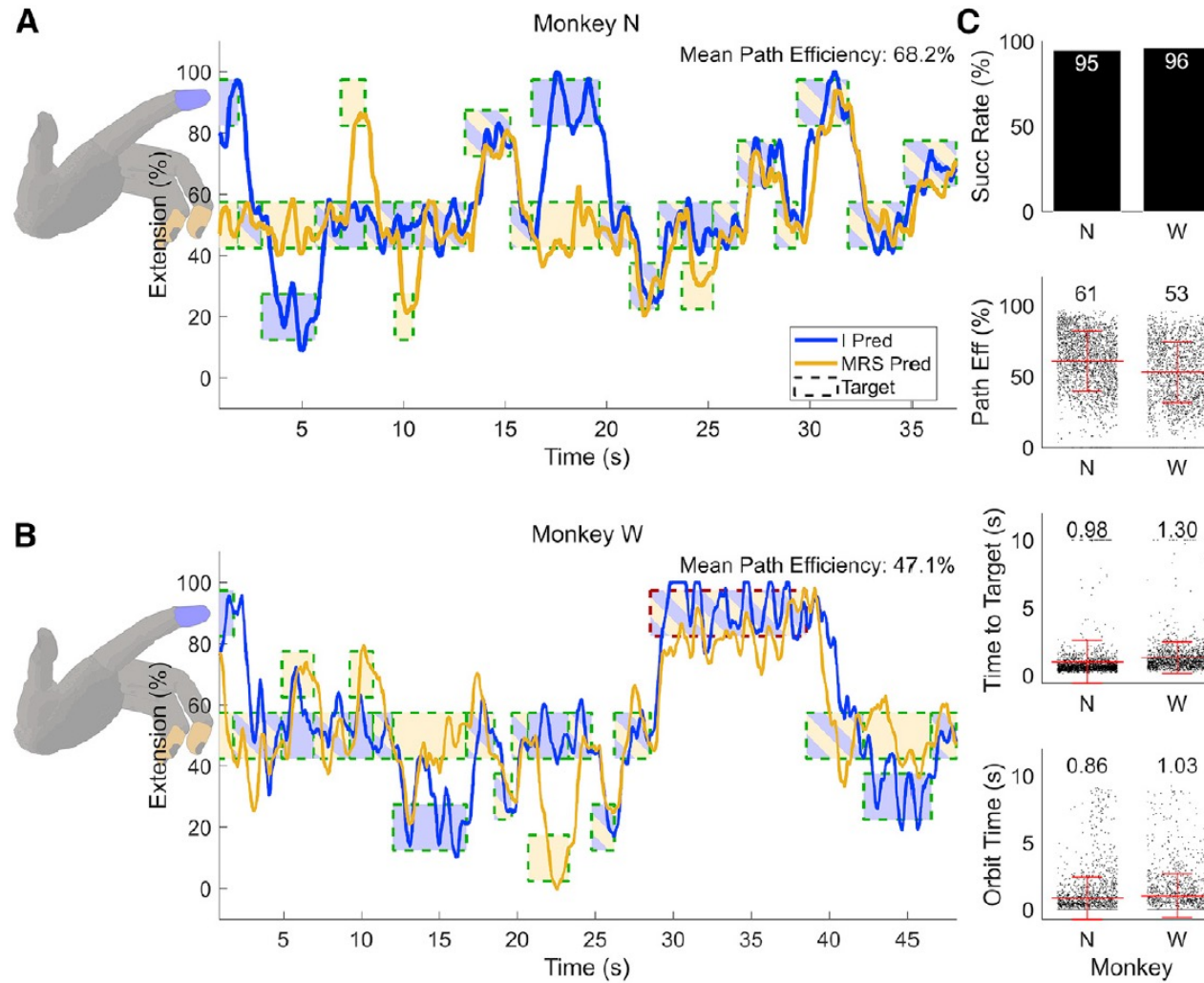
Fine, independent, and simultaneous online control of two systematically individuated groups of fingers within one hand to acquire two targets, one each for the index finger and the middle-ring-small (MRS) fingers, in a non-prehensile task

Processing of intracortical brain-machine interface in nonhuman primates using a Kalman filter



Nason et al., 2021

Brain decoding of finger movements

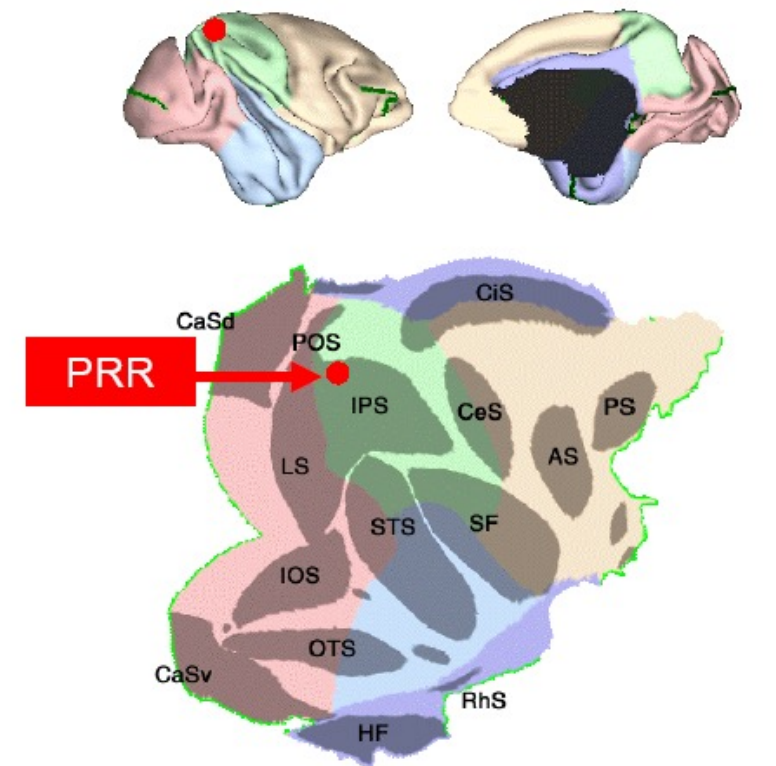


Brain decoding – High level areas

Even if most of the brain decoding approaches are based on recording from M1, other options are also possible

For example, recordings can be made at points along a major pathway for visually guided movement which begins in the extra striate visual cortex and passes through the parietal reach region (PRR) and area 5 to the dorsal premotor cortex (PMd) and then to the primary motor cortex

Although PRR is specialized for reaching movements, it represents the goals of the reach in visual coordinates

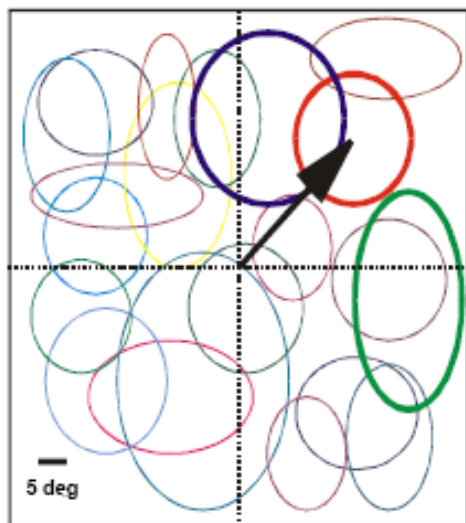


D. Van Essen, H. Drury (1998)

Musallam et al., 2007

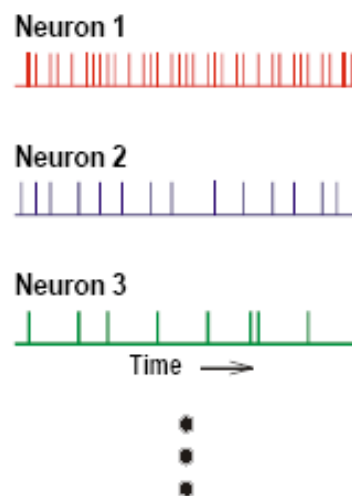
Brain decoding – High level areas

Estimating the Planned Reach Direction



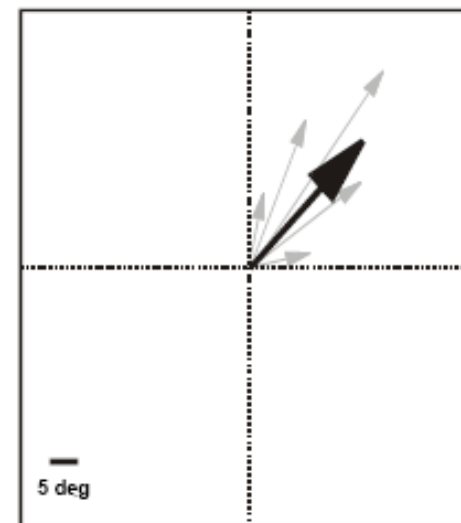
PRR receptive fields span workspace.

Complete set of reaches: $P(n|x)$



For any given reach...

... measure spike trains: n



Calculate probability of all reaches:

$$P(x|n) P(n) = P(n|x) P(x)$$

Select most probable: $\max (P(x|n))$

Brain decoding – High level areas

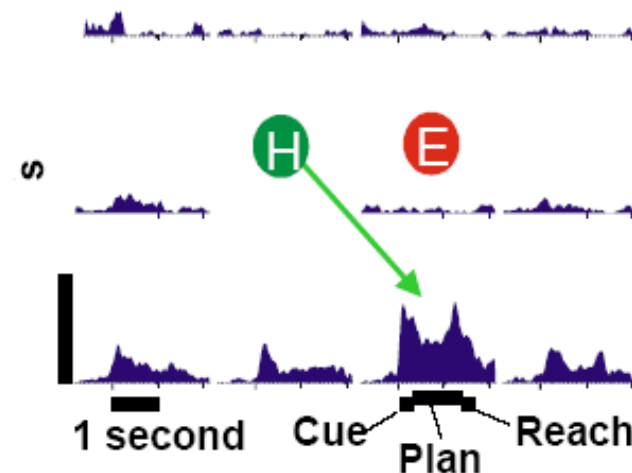
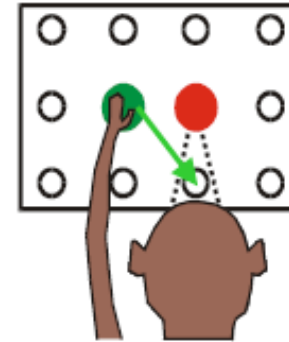
Potential Advantages of PRR Neurons for Prosthetic Systems

PRR neurons encode:

- The plan to reach to a target
- The plan for the upcoming reach
- The plan with respect to the eyes

PRR neurons may:

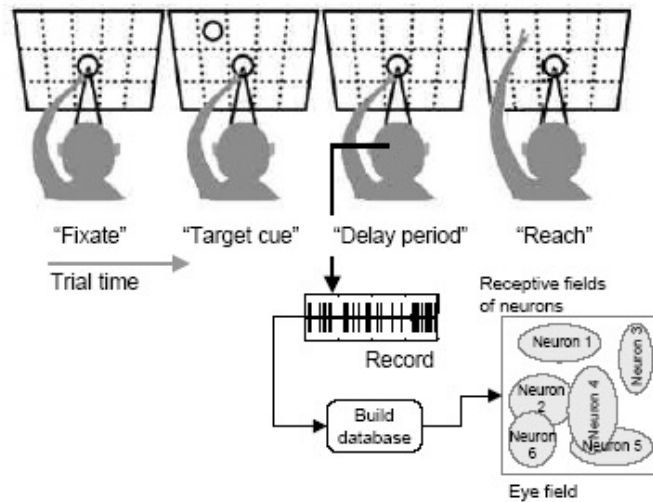
- not encode muscle forces
- reorganize little following injury
- adapt quickly to calibrate the system



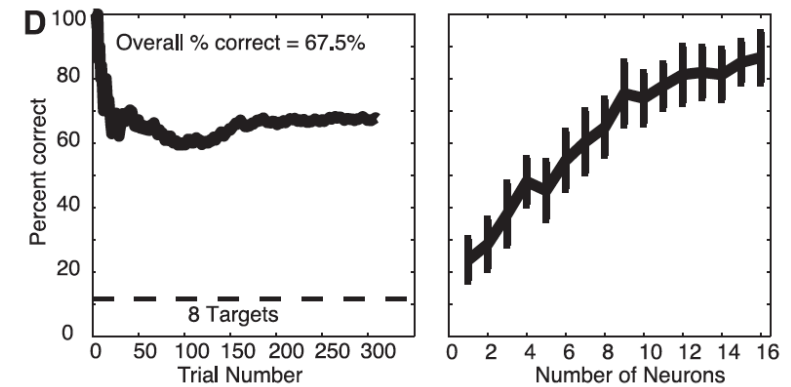
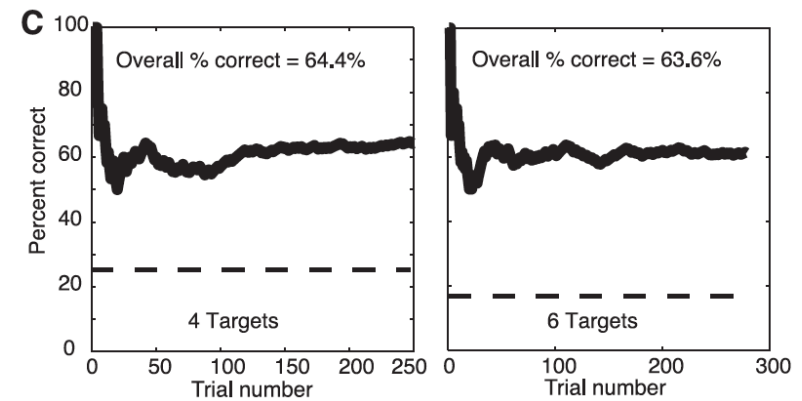
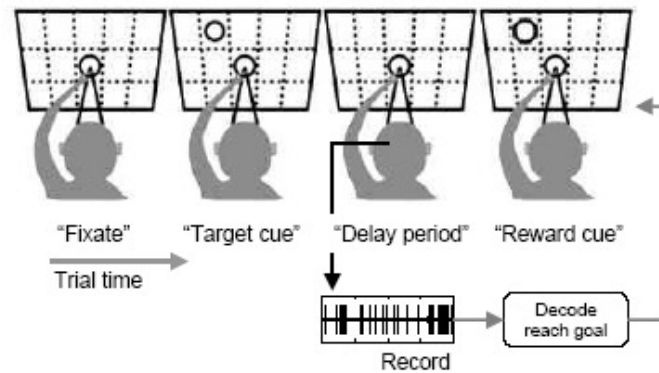
Batista, Buneo, Snyder, Andersen (1999) Science 285.

Brain decoding – High level areas

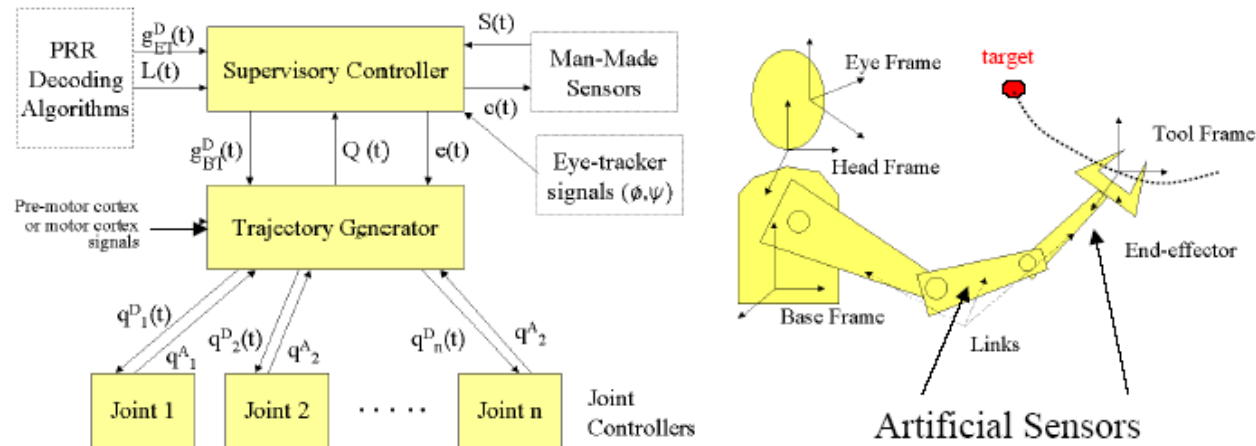
① Reach Task



② Brain Control Task



EPFL Brain decoding – High level areas



Key variables

- intended reach location
- intentional and cognitive mind state
- external sensor variables

Decoding high-level control information can be “easier” BUT it requires the developed of **shared-control** mechanisms with the robotic system

EPFL ECoG signals

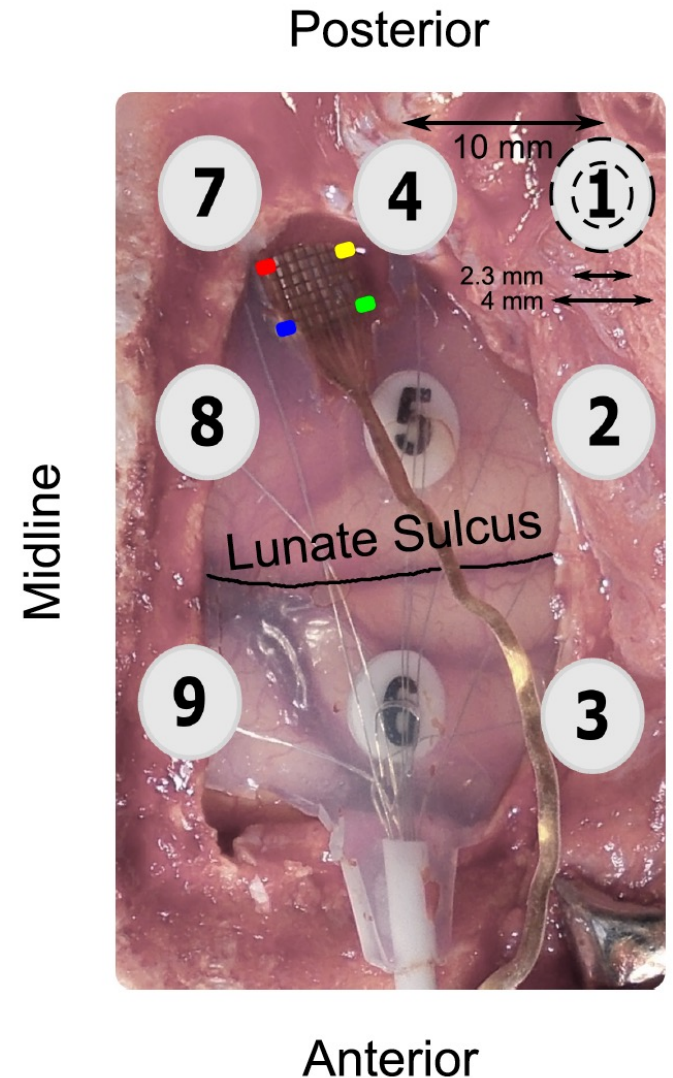
Electrocorticogram (ECoG) refers to the signal obtained from macroelectrodes (typically 2–3 mm in diameter)

It has been mainly used to be placed directly on the pial surface of cortex of epileptic patients for localization of the seizure focus

It is important to understand the spatial spread of ECoG arrays

To address these issues, hybrid electrode array that allowed to simultaneously record MUA, LFP, and ECoG was designed

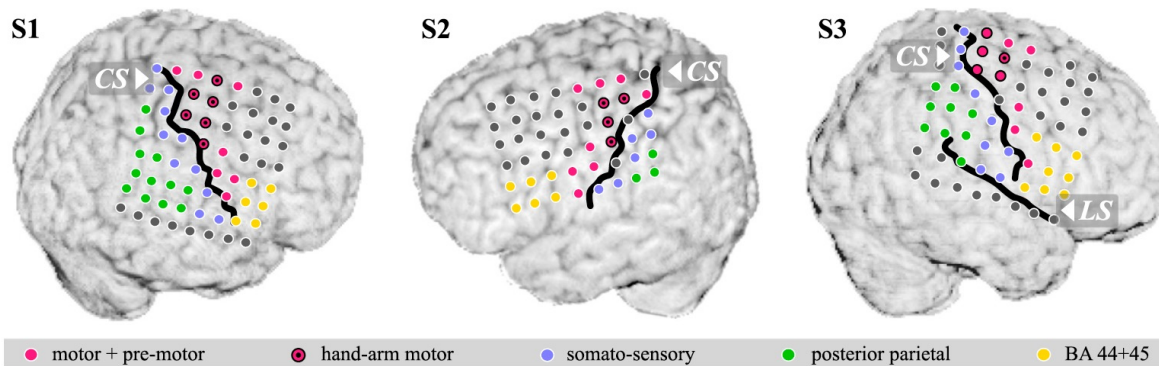
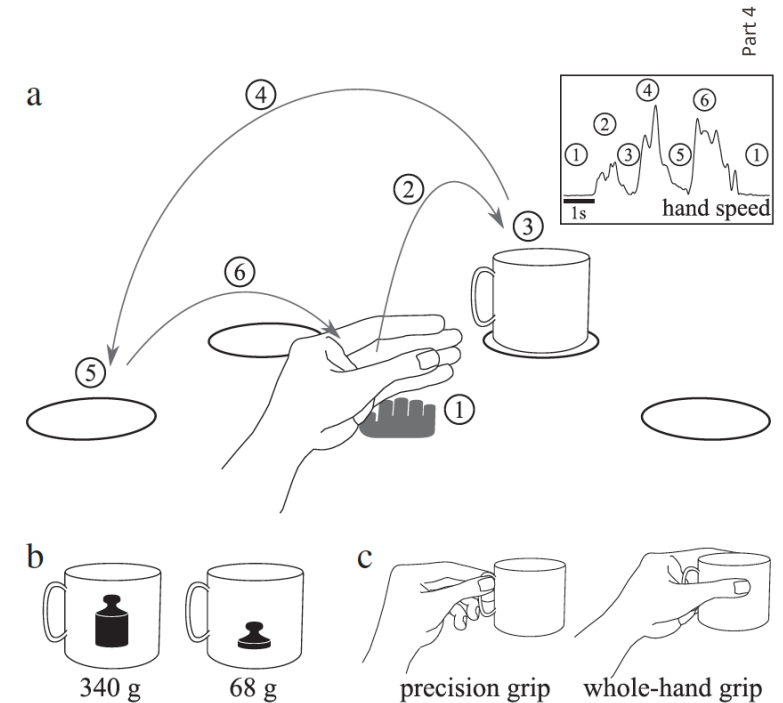
A computational model was used to estimate the spatial spread of LFP and ECoG



EPFL ECoG-based grasping decoding

The goal was to verify whether ECoG signals can be used to decoding two different grasp types (precision vs. whole-hand grip) in natural reach-to-grasp movements in single-trials

Self-paced movement execution in a paradigm accounting for variability in grasped object position and weight was chosen to create a situation similar to everyday settings.



Pistohl et al., 2012

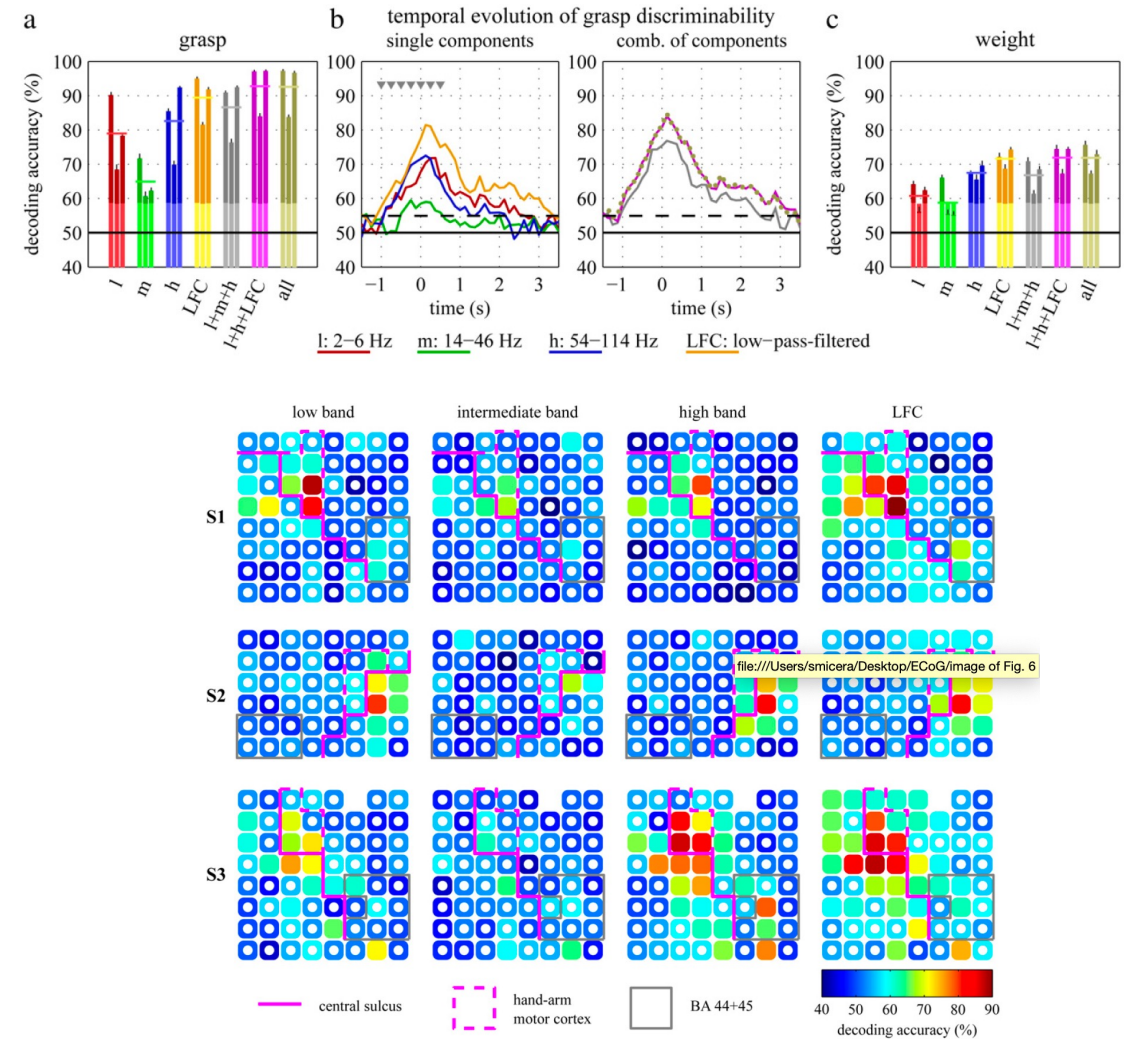
ECoG-based grasping decoding

Three informative signal components (low-pass-filtered component, low-frequency and high-frequency amplitude modulations) were identified which allowed for accurate decoding of precision and whole-hand grips.

Importantly, grasp type decoding generalized over different object positions and weights

Within the frontal lobe, informative signals predominated in the precentral motor cortex and could also be found in the right hemisphere's homologue of Broca's area

We conclude that ECoG signals are promising candidates for BMIs that include the restoration of grasping movements.



EPFL ECoG-based exoskeleton control

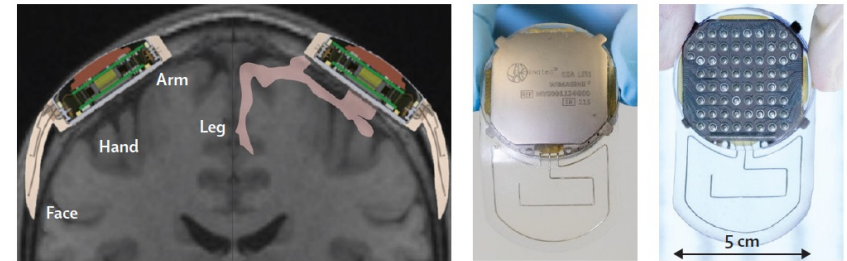
The researchers recruited a 28-year-old man, who had tetraplegia following a C4–C5 spinal cord injury

Two bilateral wireless epidural recorders, each with 64 electrodes, were implanted over the upper limb sensorimotor areas of the brain

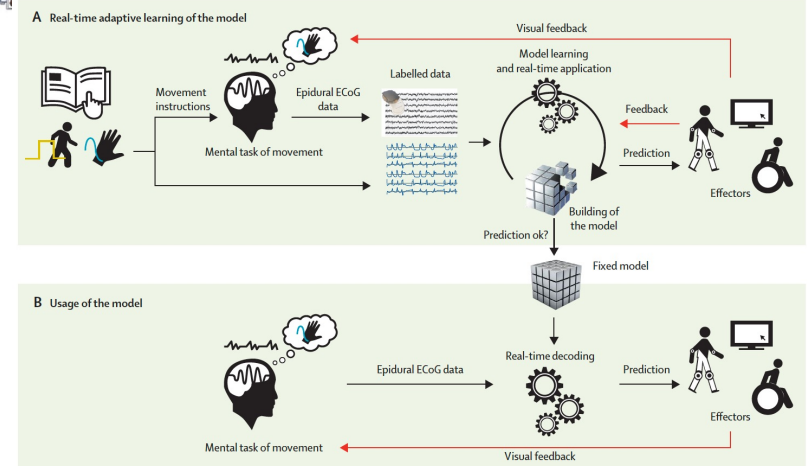
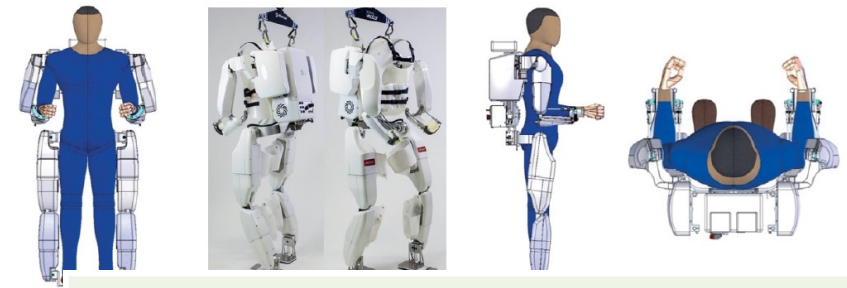
Epidural electrocorticographic (ECoG) signals were processed online by an adaptive decoding algorithm to send commands to effectors (virtual avatar or exoskeleton)

Throughout the 24 months of the study, the patient did various mental tasks to progressively increase the number of degrees of freedom.

B WIMAGINE wireless recorder



C EMY exoskeleton



EPFL ECoG-based exoskeleton control



EPFL EMG interface for robotic systems

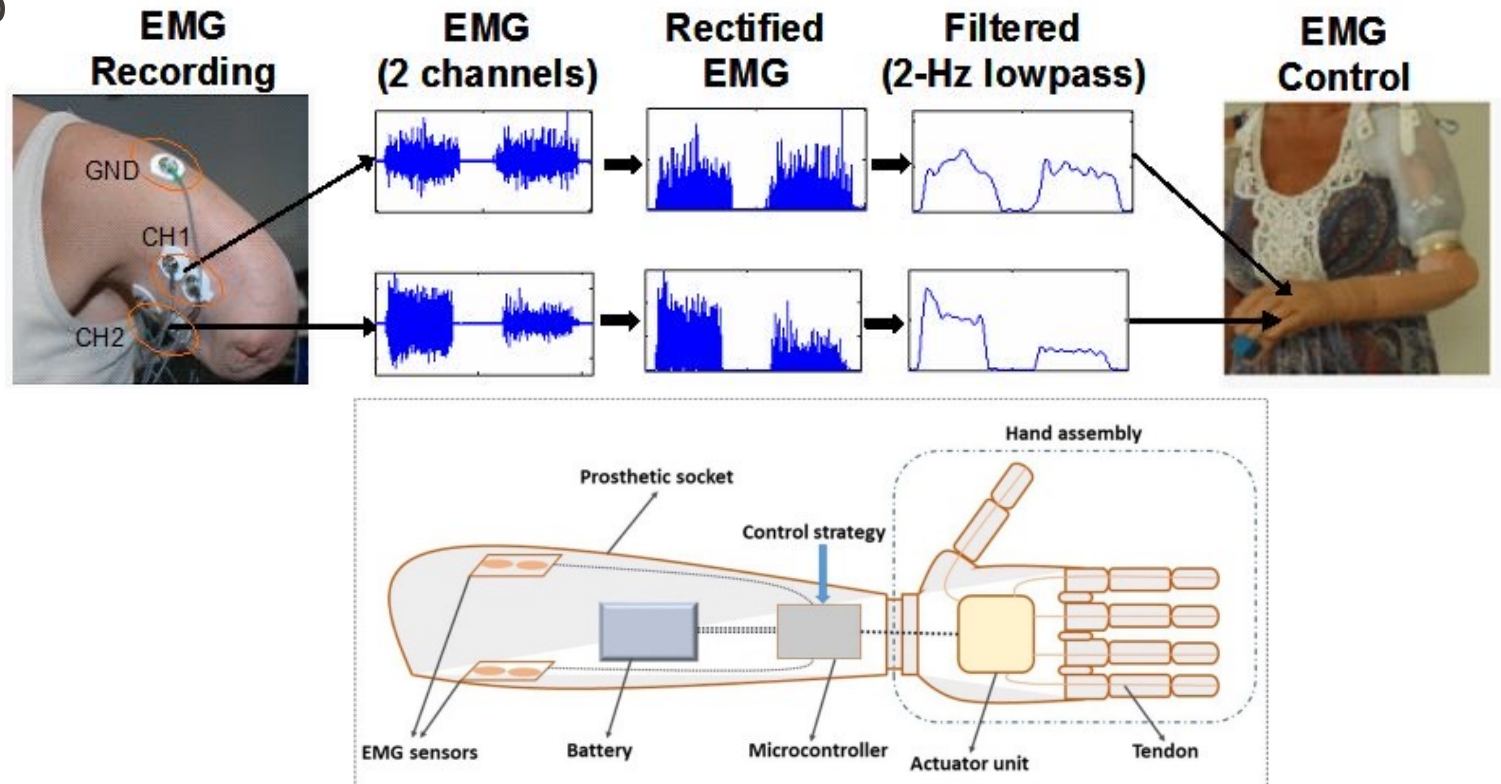
How to use EMG signals for this goal

- Residual skills of the user?
- Intended movement to control?
- Are the muscles actuating this movement still controllable?
- Rehabilitation or Assistance?
- Noninvasive or implantable?
- Proportional control?
- Pattern Recognition?
- Blind Source Separation? (HD-EMG)

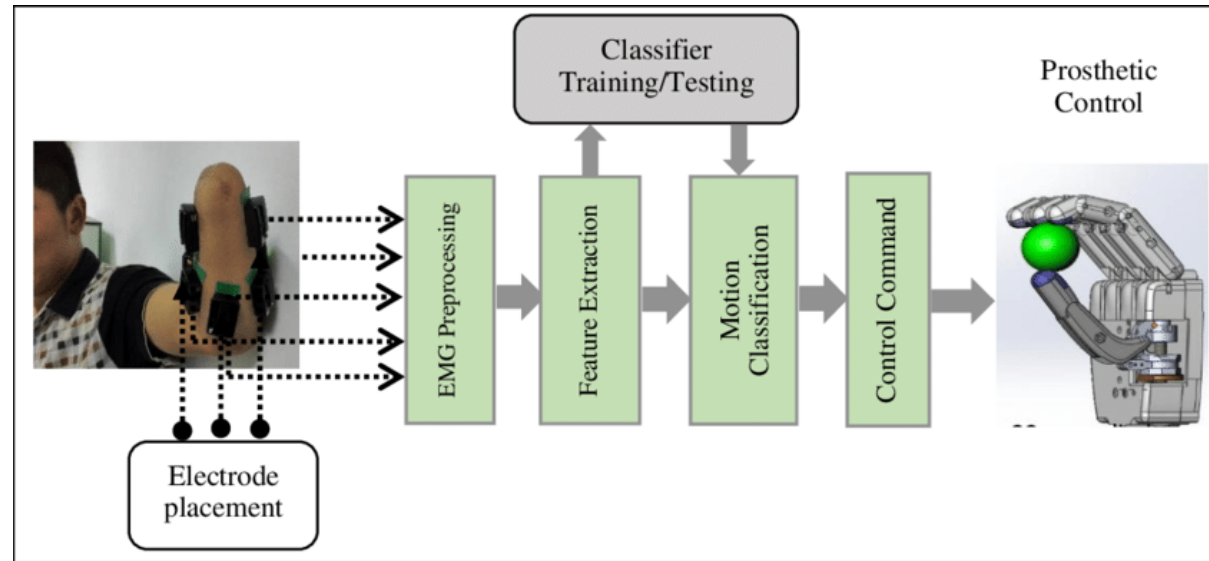
EPFL Hand prosthesis – Proportional control

N antagonist muscles are used to control 1 degree of freedom of the prosthesis (hand opening/closing). Often biceps/triceps or wrist extension/flexion

An increased number of required movements makes very difficult to use this ap



EPFL Hand prosthesis – Pattern recognition



In this case, the muscles naturally involved in the specific movement (e.g. ECR for the extension of the wrist) are no more available

For this reason, “not- homologous” voluntary movements of the subject have to be coded as prosthesis movements (e.g. extension of the elbow for the extension of the wrist)

This approach requires a quite long training phase and makes very difficult for the subject to easily control more than two degrees of freedom

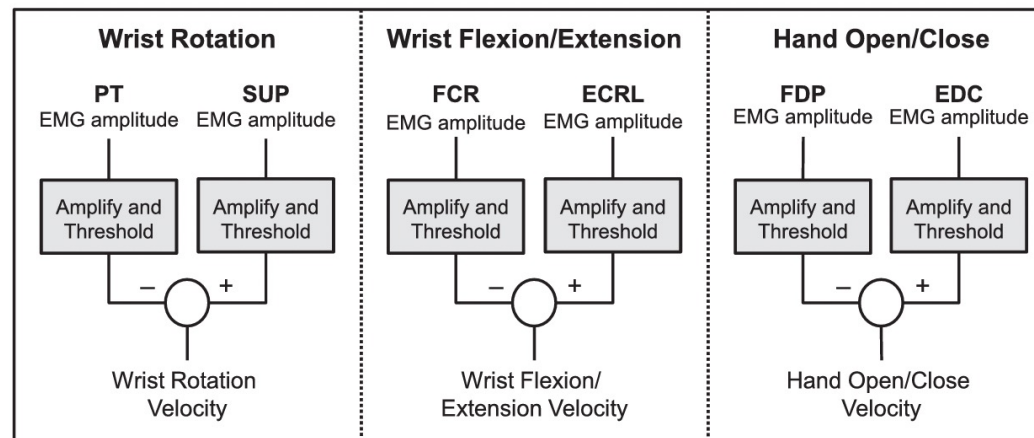
EPFL Intramuscular EMG (iEMG) control

Clinically available myoelectric control strategies do not allow simultaneous movement of multiple degrees of freedom (DOFs)

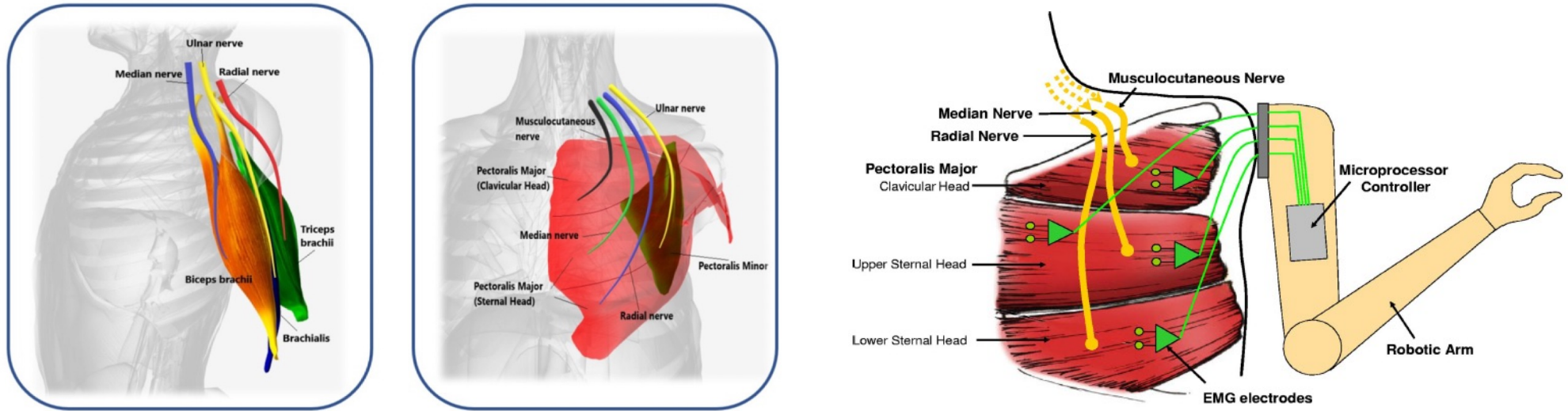
The use of implantable devices that record intramuscular EMG signals could overcome this constraint

Intramuscular EMG signals can be recorded using percutaneous fine wire electrodes inserted using needles

The use of iEMG can allow to use proportional control (but of course also pattern recognition)



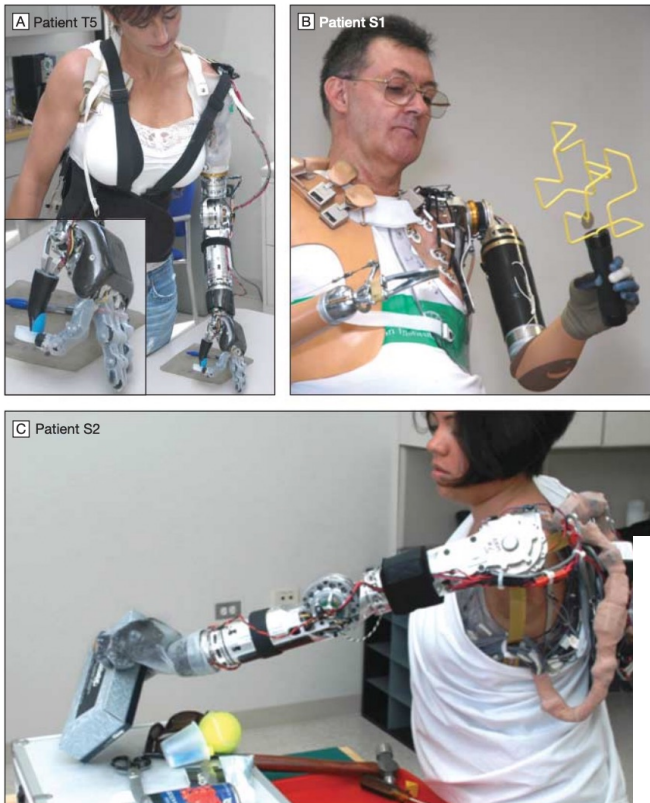
EPFL Targeted muscle reinnervation (TMR)



A surgical technique called targeted muscle reinnervation (TMR) transfers residual arm nerves to alternative muscle sites

After reinnervation, these target muscles produce electromyogram (EMG) signals on the surface of the skin that can be measured and used to control prosthetic arms

EPFL Targeted muscle reinnervation (TMR)



Subjects showed statistically better performance in the Southampton Hand Assessment Procedure ($p=0.04$) and the Clothespin relocation task ($p=0.02$)

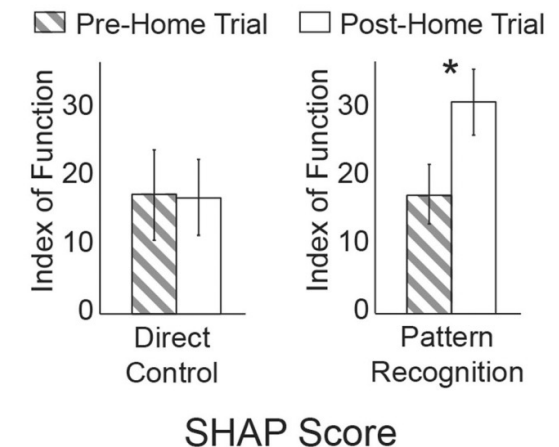
Notably, these tests required movements along 3 degrees of freedom.

Seven of 8 subjects preferred pattern recognition control over direct control

Results demonstrate that pattern recognition is a viable option and has functional advantages over direct control.

Subject	Direct Control Wear Time (hrs)	Pattern Recognition Wear time (hrs)	Number of Recalibrations	Preference of Control
S1	41	15	7	PR
S2	280.1	301.6	39	PR
S3	196.8	183.6	73	PR
S4	254.6	366.9	56	PR
S5	91.4	85.1	10	PR
S6	54.9	27.9	20	DC
S7	157.7	128.5	18	PR
S8	33.2	73.0	38	PR

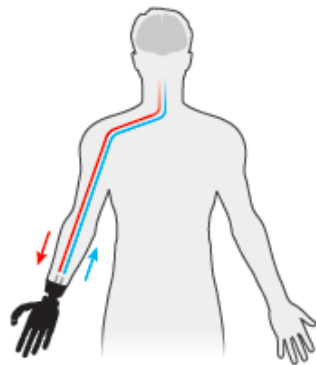
Table 2. Wear time, recalibration and control preference.



Hargrove et al., 2017

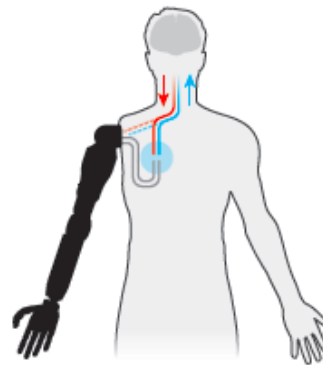
Sensory feedback

Real-time, and natural feedback from the hand prosthesis to the user is essential in order to enhance the control and functional impact of prosthetic hands in daily activities, prompting their full acceptance by the users



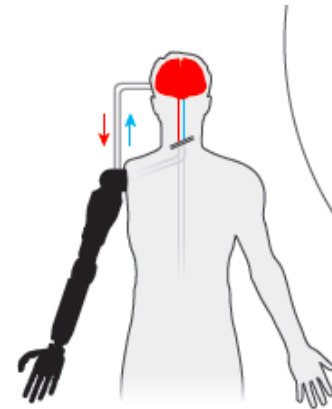
Use the remaining nerves

Electrical leads from the prosthetic's sensors stimulate nerves in the person's stump that once served the real limb.



Move the nerves

Re-routed nerves grow new endings into muscle and skin, where external devices translate signals going to and from the prosthesis.

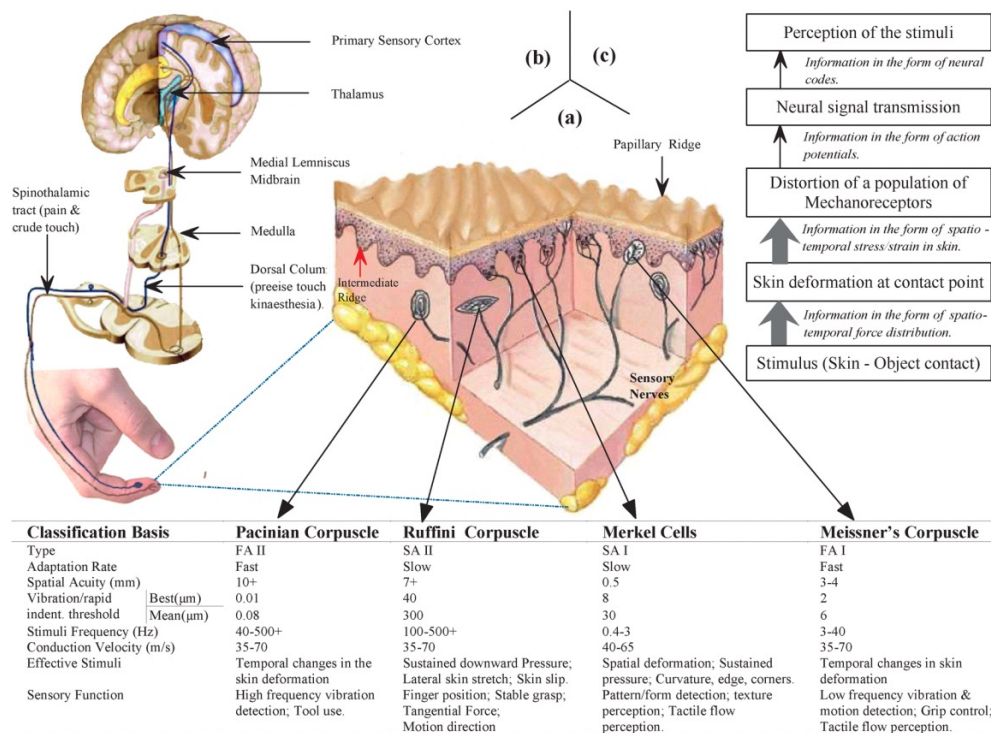


Stimulate the brain

Sensory signals are routed around a severed spinal cord and into the brain, where they produce sensations by direct stimulation of the cortex.

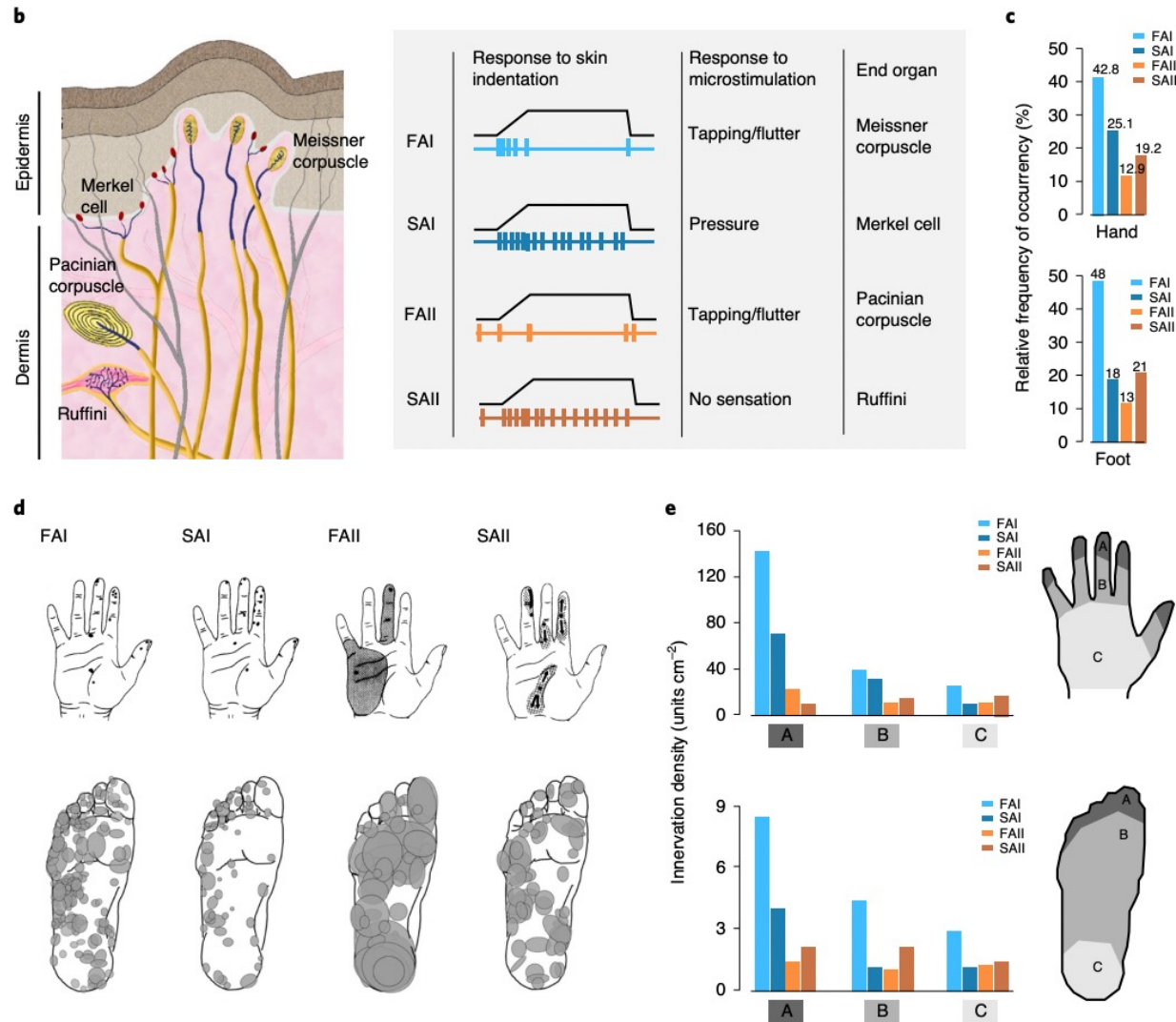
Kwok, Nature, 2013

Human touch system

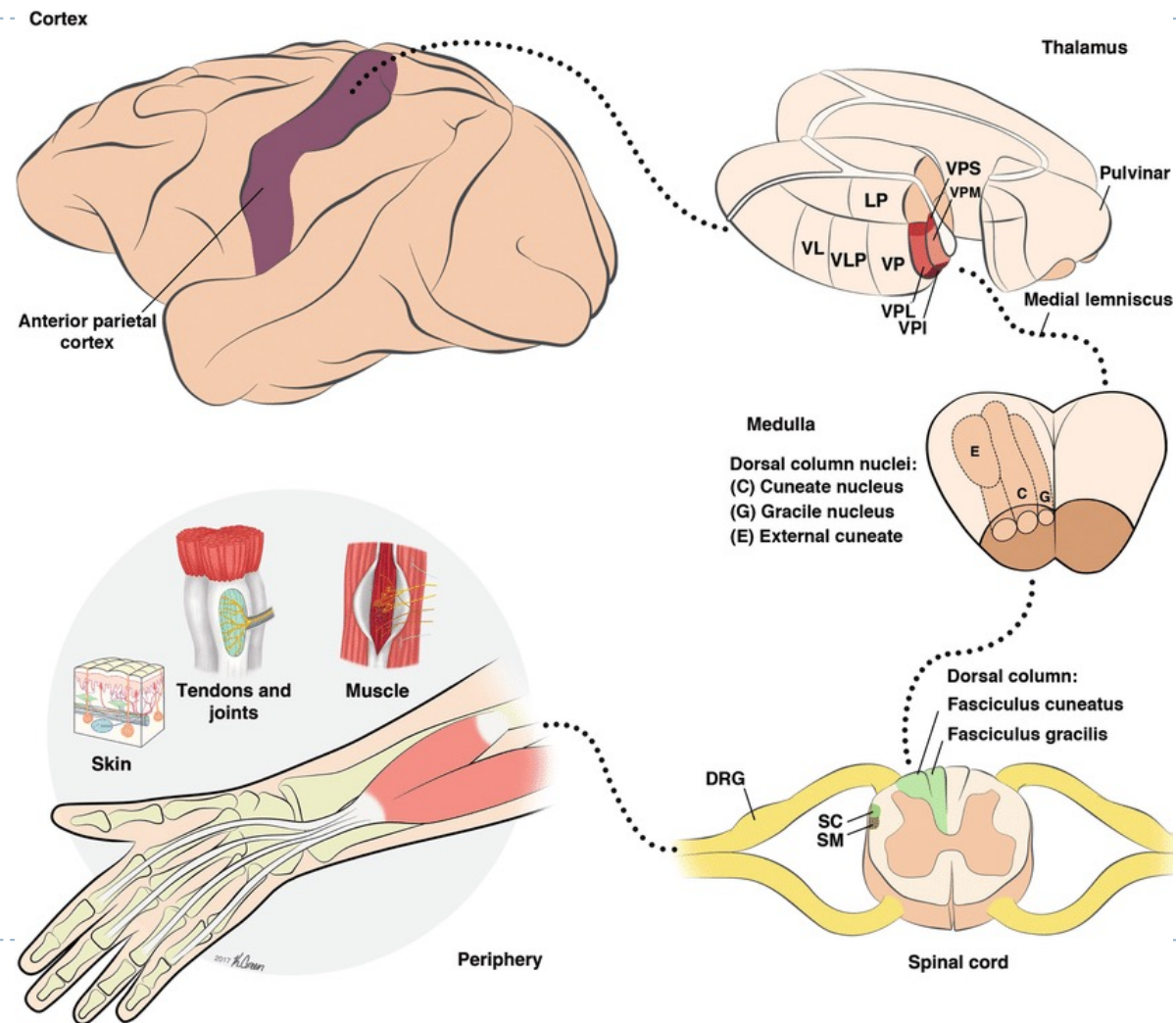


- During object manipulation and tactile exploration, the glabrous skin of the hand undergoes complex spatiotemporal mechanical deformations, which in turn, drive very precise spiking responses in individual afferents
- Coarse object features, such as edges and corners, are reflected in spatial patterns of activation in slowly adapting type I (SAI) and rapidly adapting (FA) fibers, which are densely packed in the fingertip
- At the same time, interactions with objects and surfaces elicit high-frequency, low-amplitude surface waves that propagate across the skin of the finger and palm and excite vibration-sensitive Pacinian (PC) afferents all over the hand

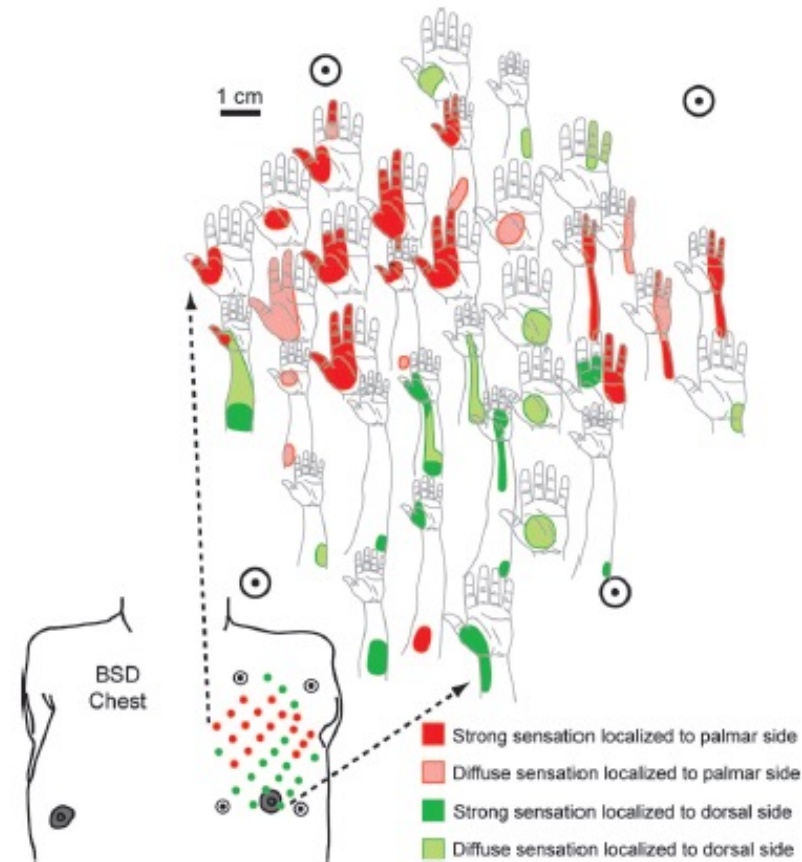
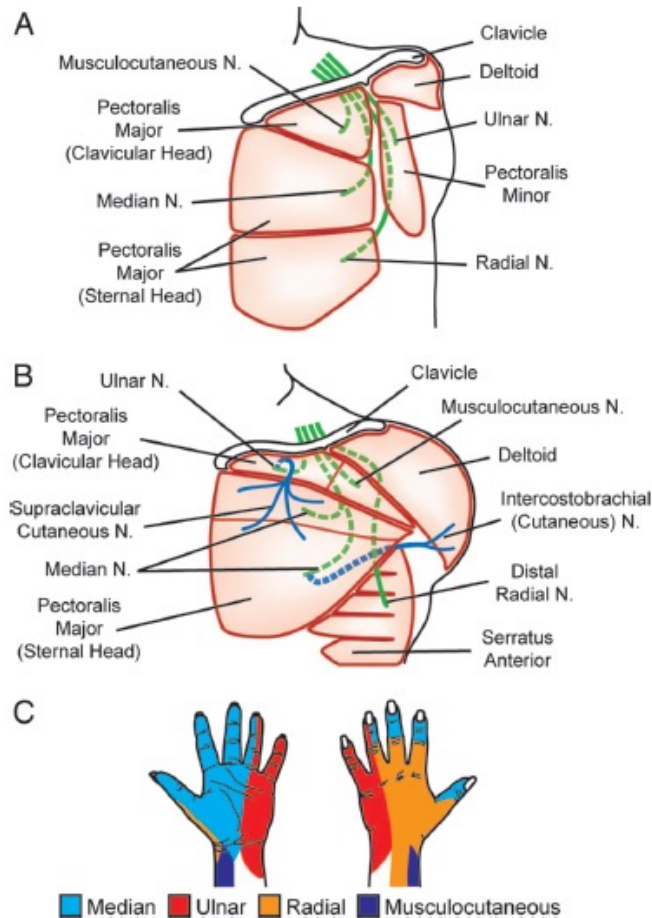
Human touch system



Human touch system

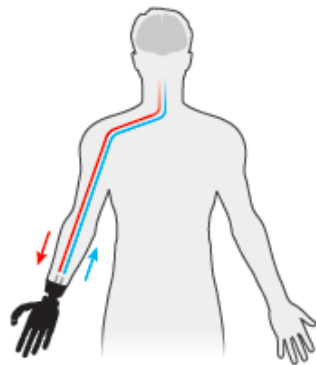


Targeted Muscle Reinnervation



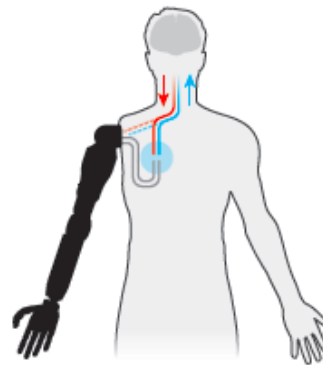
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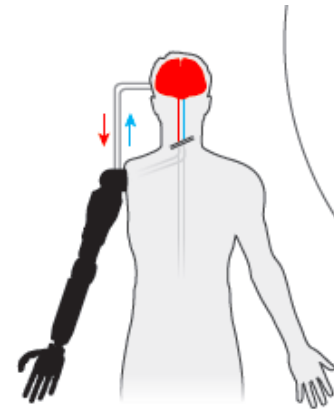
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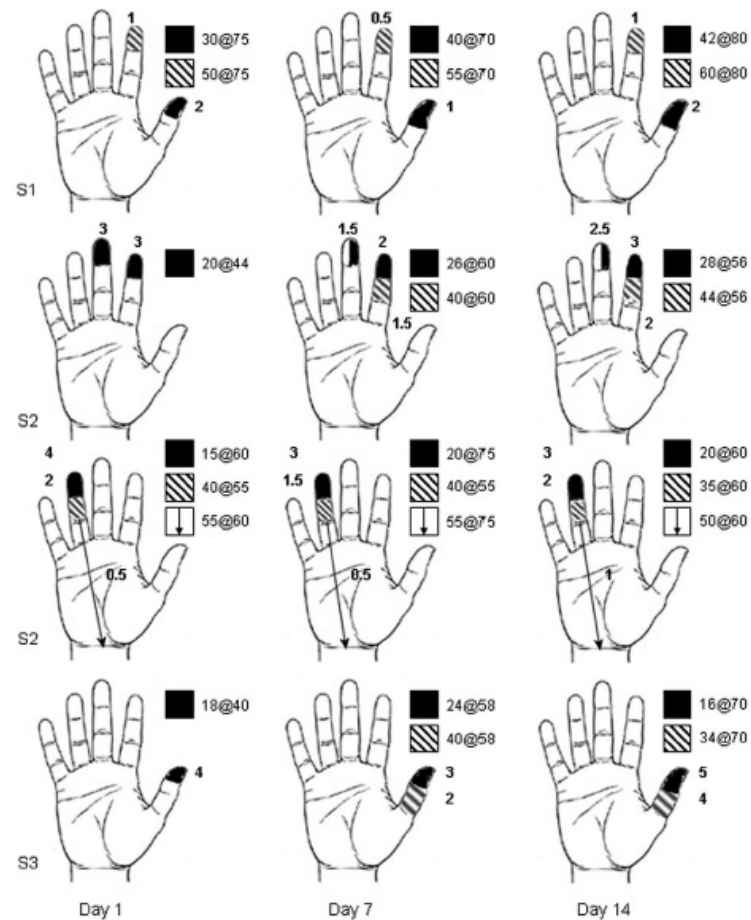
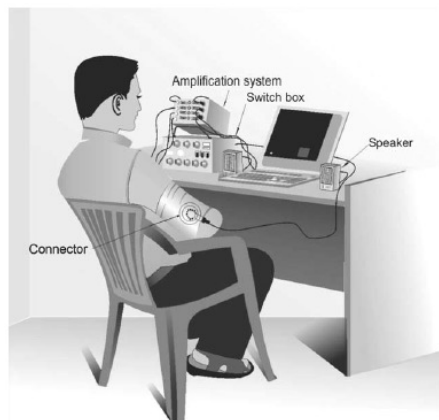
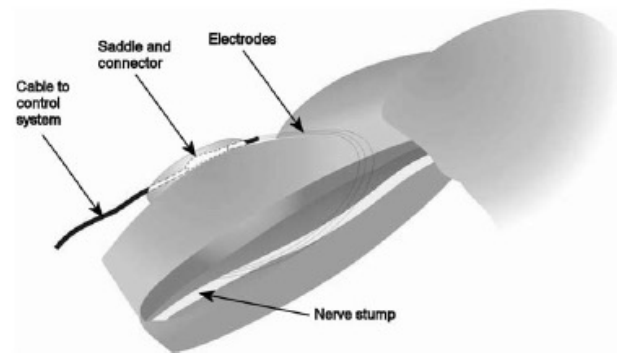


Stimulate the brain

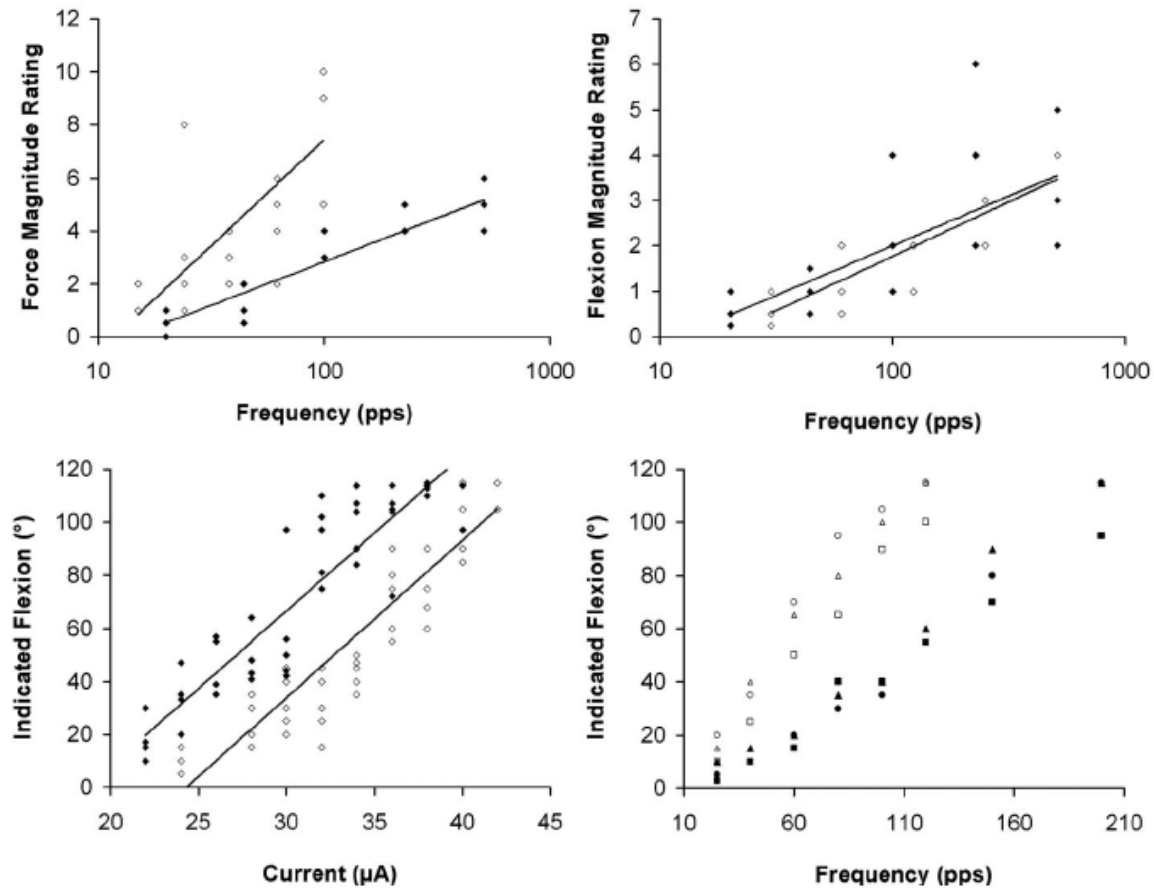
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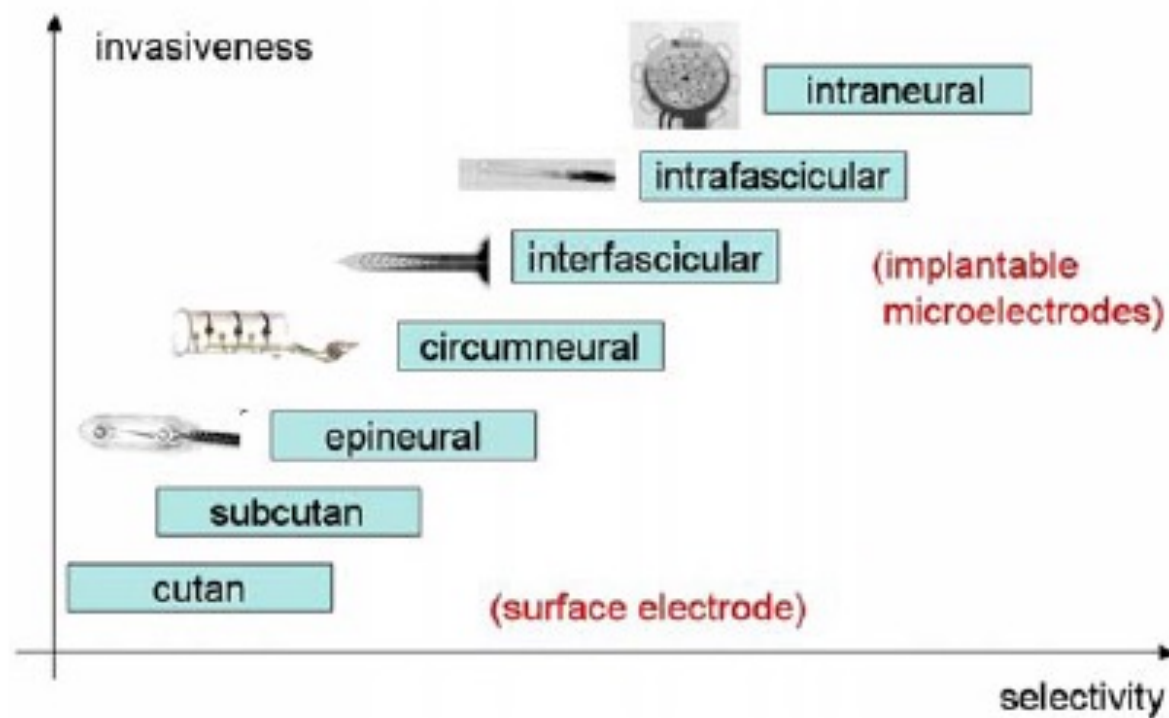
First intraneural experiment



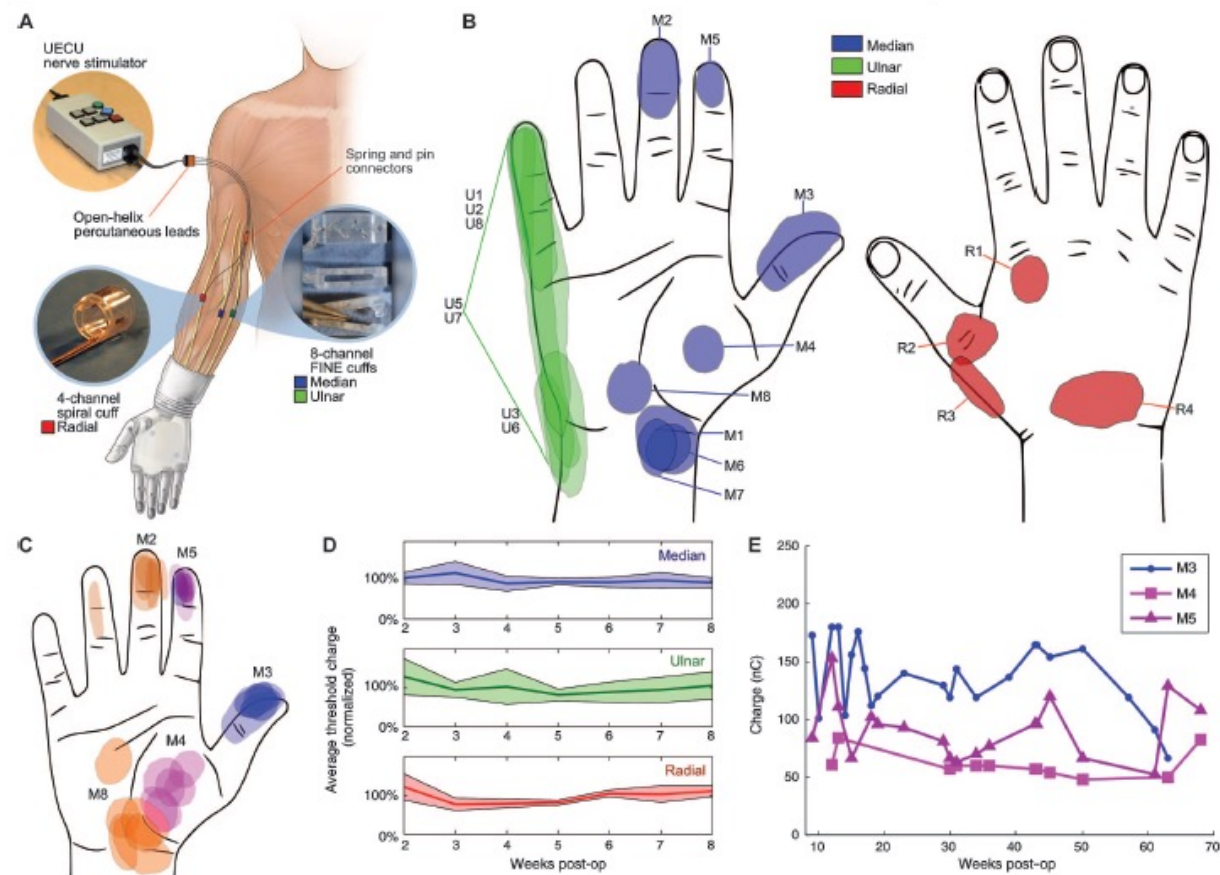
First intraneural experiment



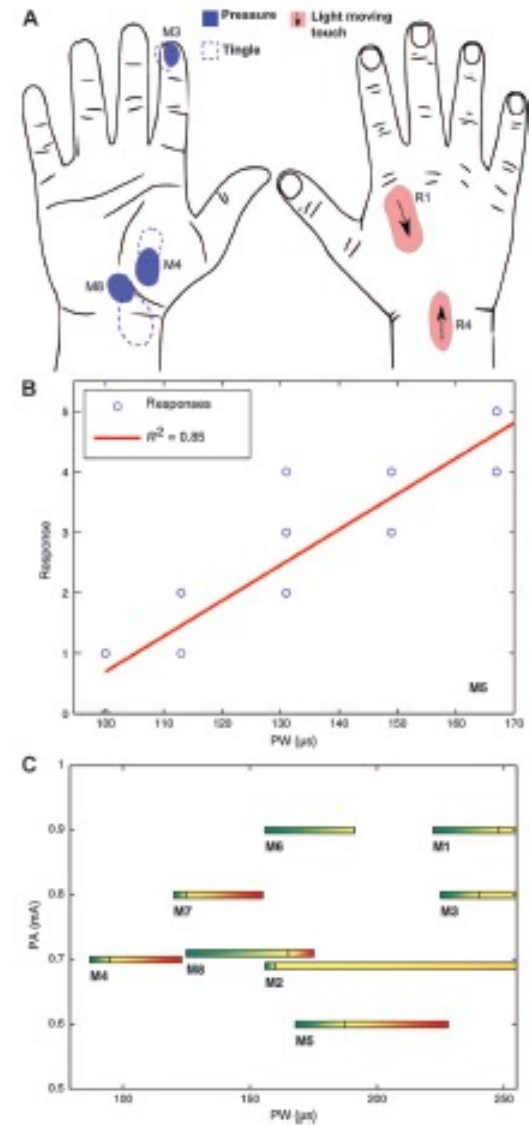
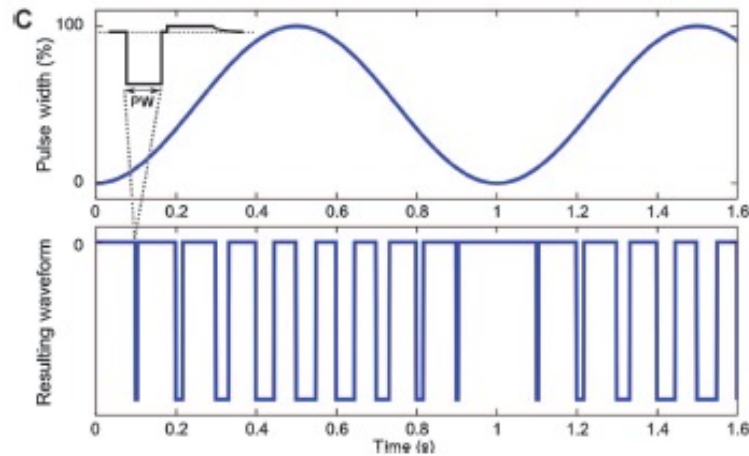
Peripheral implantable electrodes



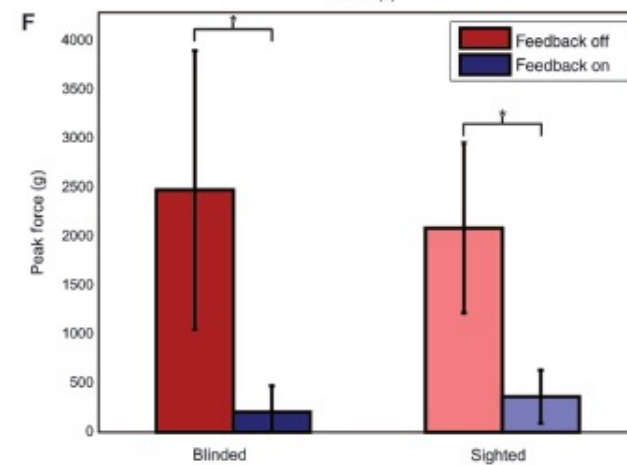
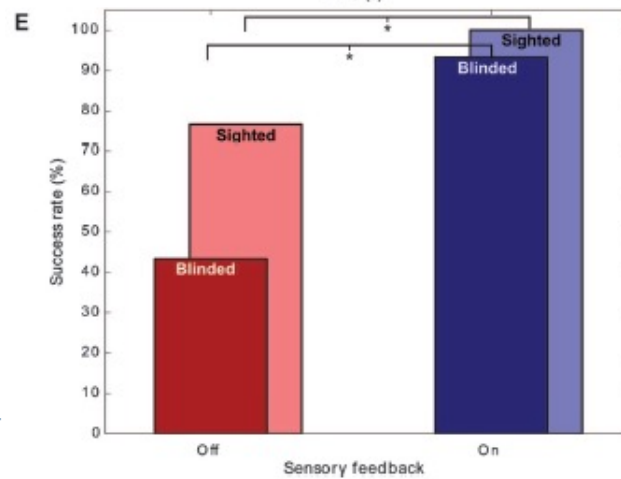
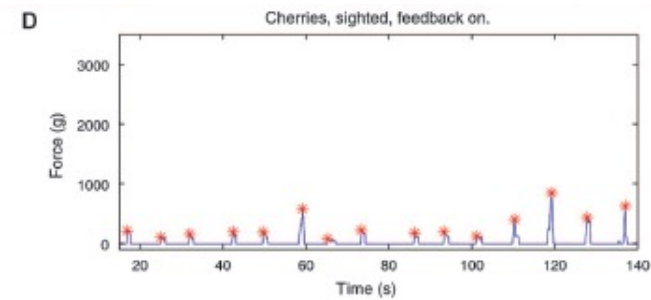
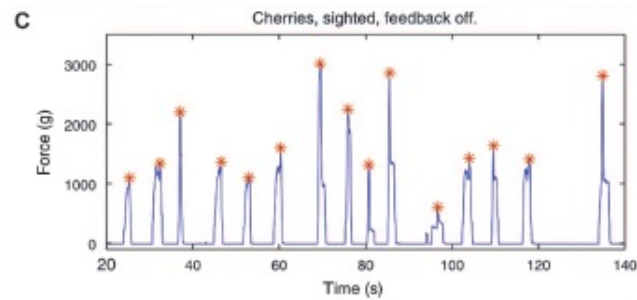
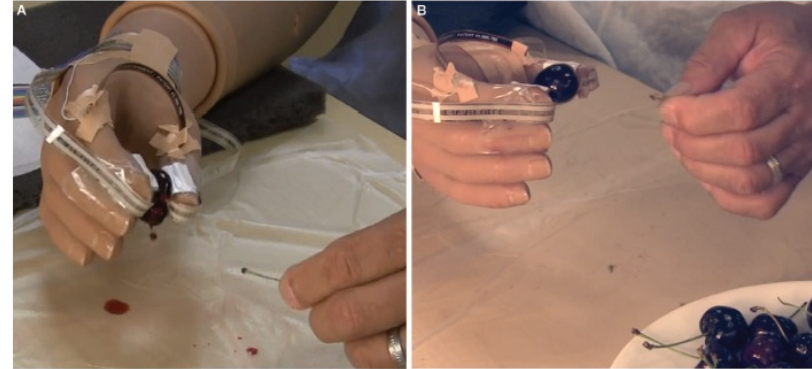
Sensory feedback using FINE electrodes



Sensory feedback using FINE electrodes



Sensory feedback



Short-term implant of TIMEs in an amputee



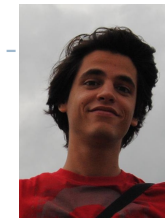
P.M. Rossini



S. Raspopovic



M. Capogrosso



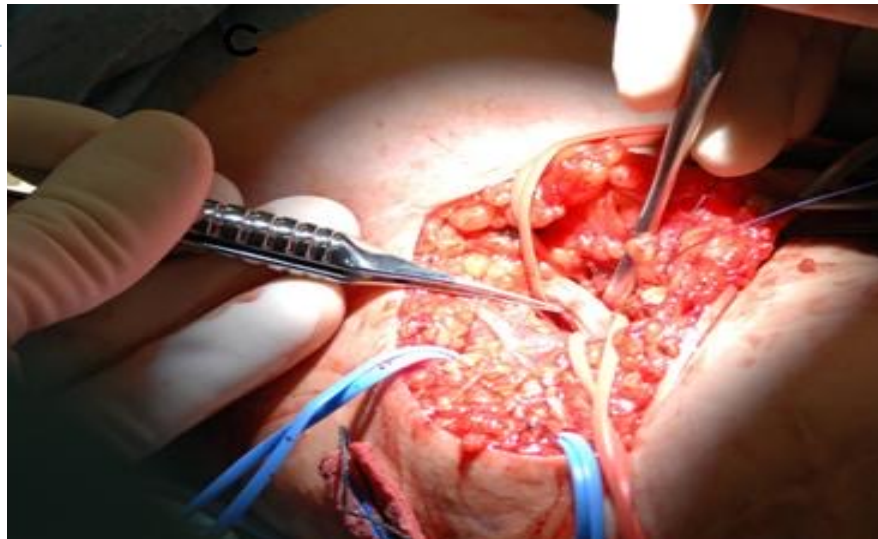
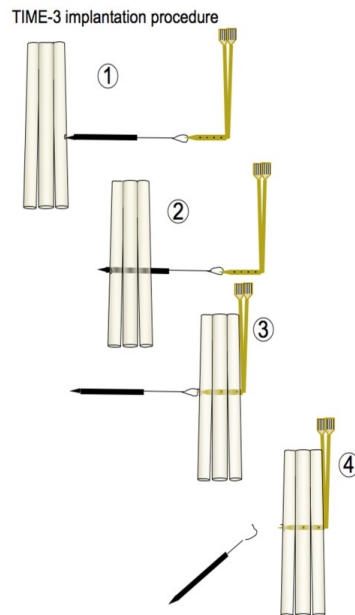
M. Bonizzato

- 35 year old man, from Denmark
- trans-radial amputation in 2004 (fireworks accident during family celebration)
- Subjects resistant to pharmacological therapy and with no neuropathies (evaluated by Electroneurography) or other systemic diseases affecting brain/spinal cord/nerves
- Subjects with no neuropsychiatric disorders, evaluated by neuropsychological and psychiatric tests (WAIS-R, CES-D, MMPI-2)
- FOUR week implant



TIME implant

- **Nerves to implant:**
 - ✓ Median nerve
 - ✓ Ulnar nerve
- **Number of electrodes:**
 - ✓ 2 for each nerve

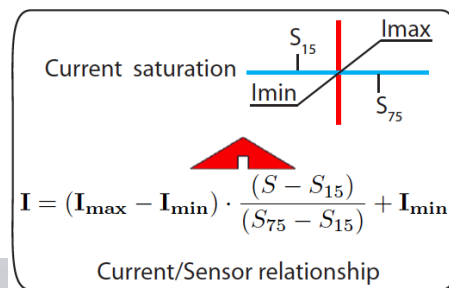


▪Surgical technique:

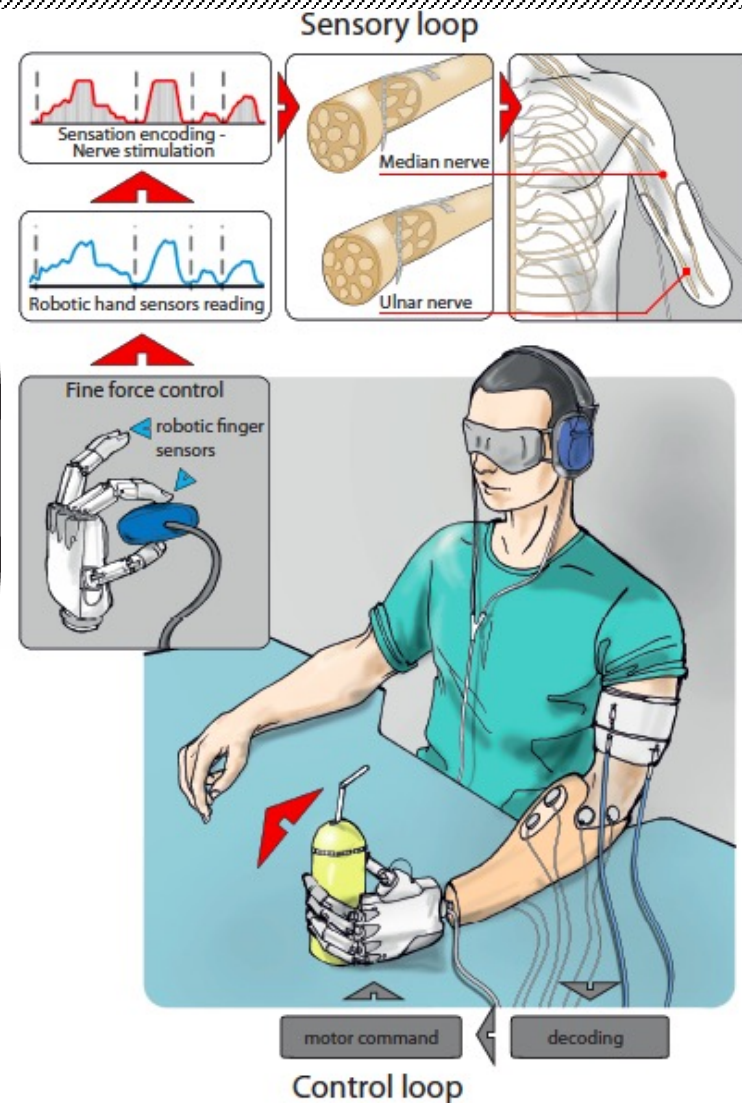
- ✓ General anesthesia
- ✓ skin incision (medial edge of the biceps muscle-15 cm)
- ✓ Exposition of the ulnar and median nerves
- ✓ epineural microdissection
- ✓ TIME electrodes inserted under surgical microscope using a guiding needle
- ✓ 8-0 suture used to fix the electrodes to the epineurium
- ✓ Subcutaneous pockets

Closed-loop control based on sensory feedback

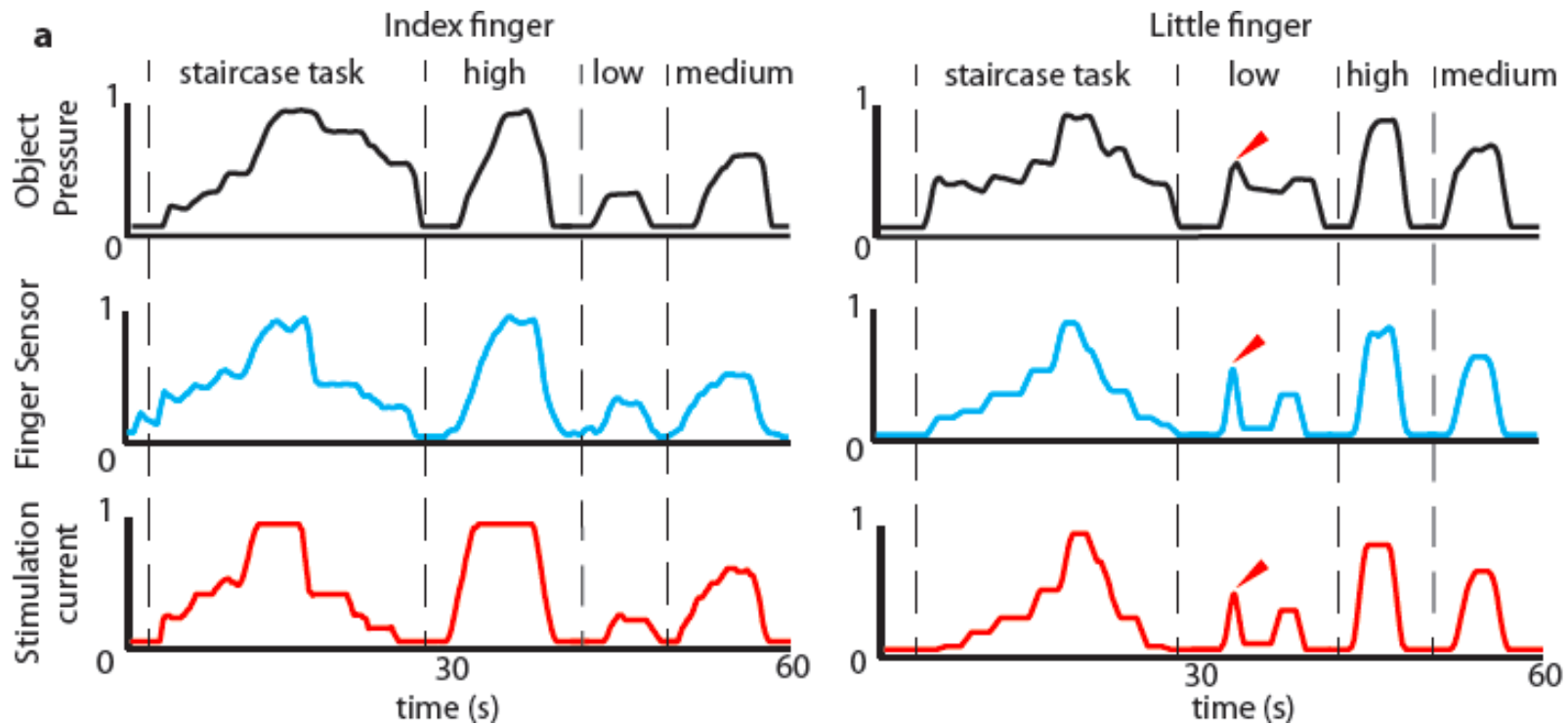
- Test the possibility for the subject to use the sensory information during closed-loop control and manipulation experiments



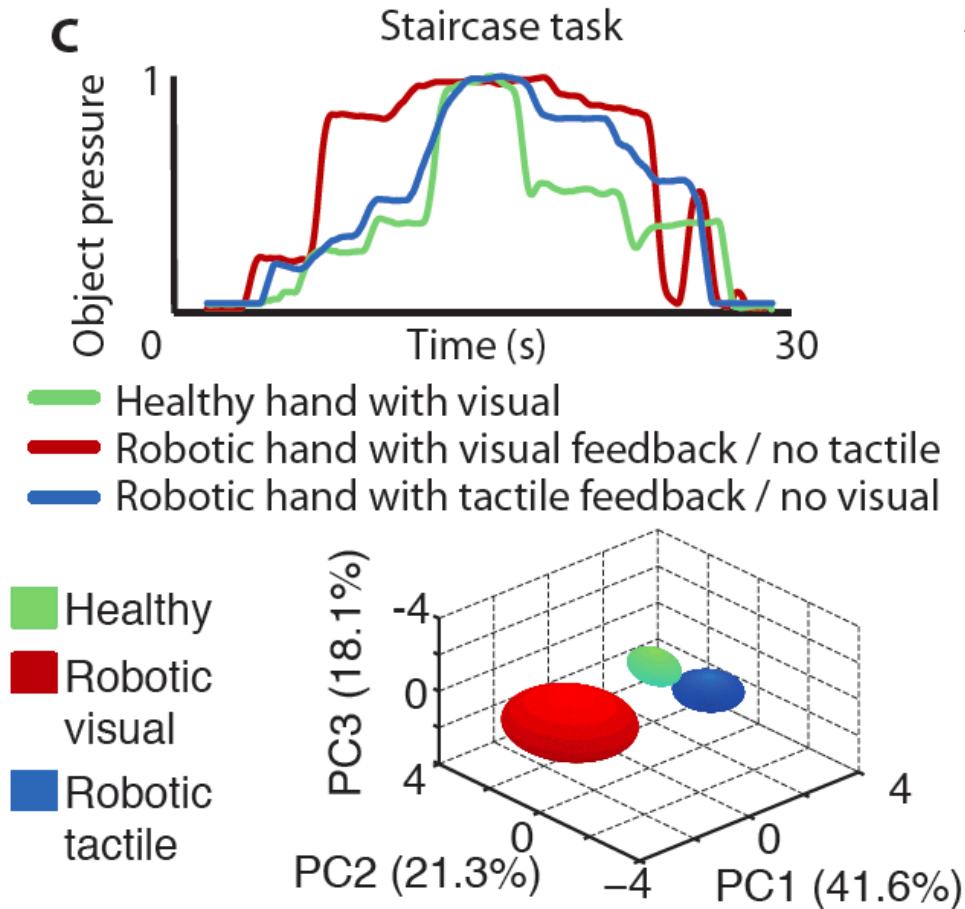
Azzurra dexterous hand
(Prensilia srl)



Selection of grasping force levels

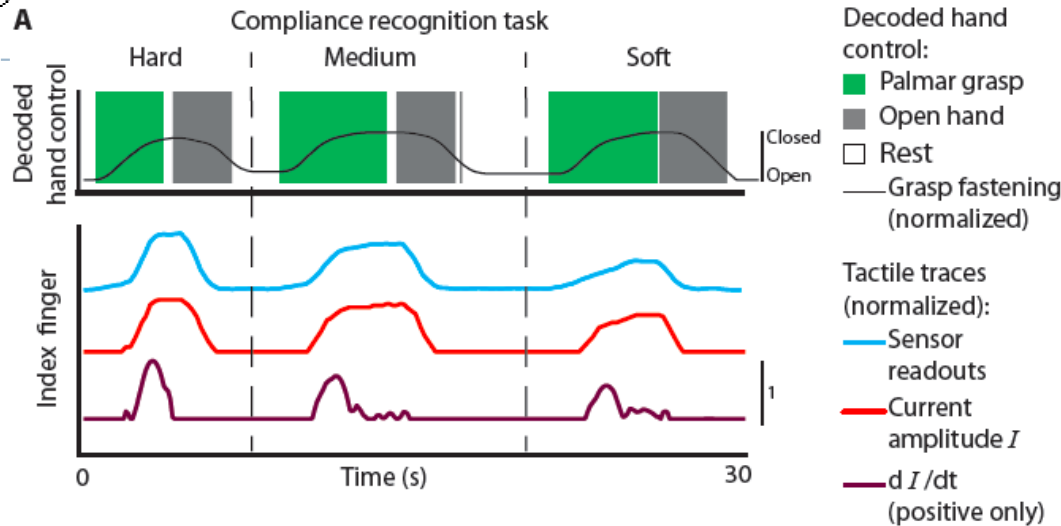


Modulation of grasping force



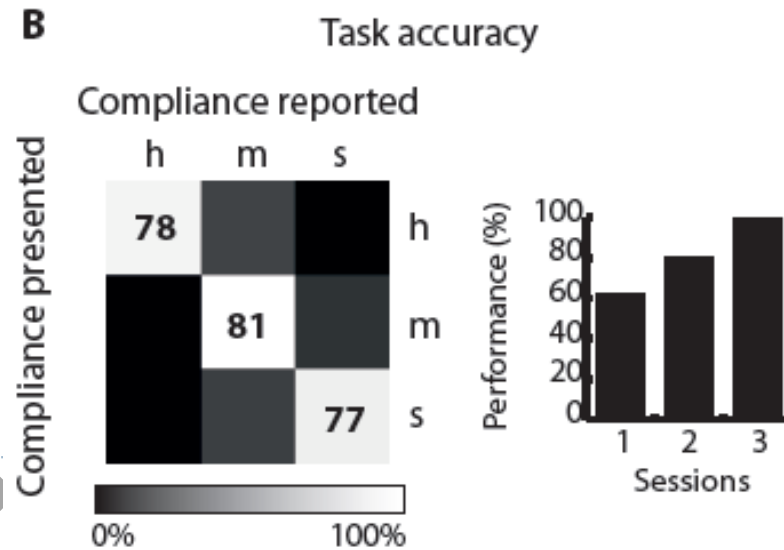
The artificial sensory feedback allowed the user to achieve performance close to the natural ones

Compliance recognition



Three objects with different stiffness properties

Quite good performance and interesting learning ability



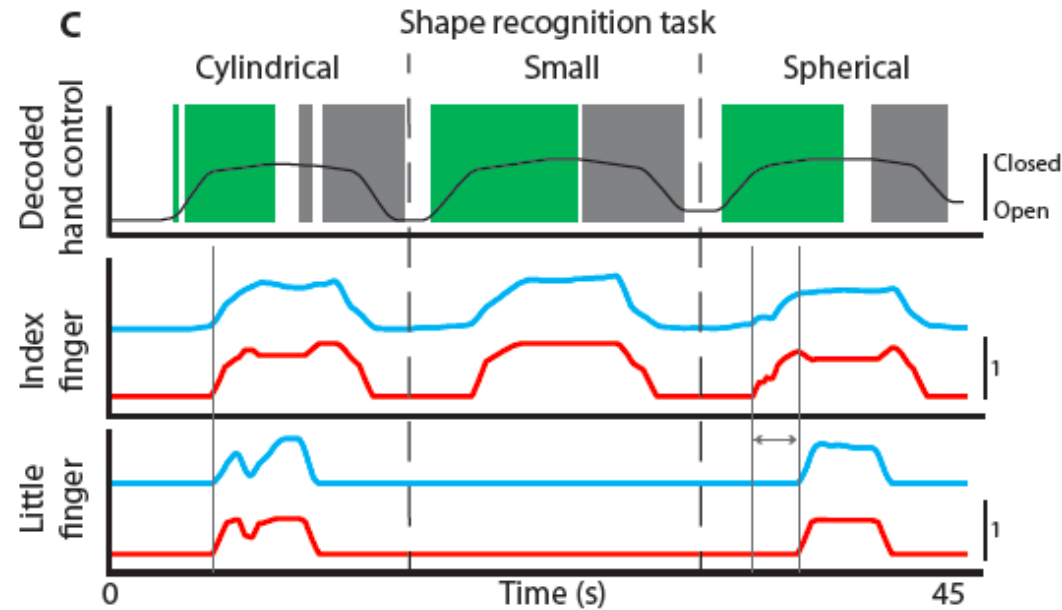
Shape recognition

Decoded hand control:

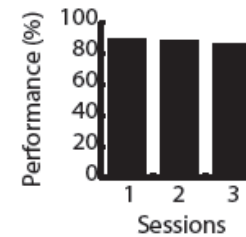
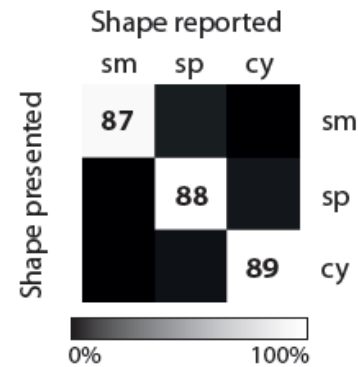
- Palmar grasp
- Open hand
- Rest
- Grasp fastening (normalized)

Tactile traces (normalized):

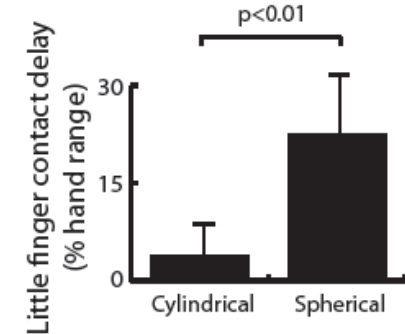
- Sensor readouts
- Current amplitude I
- dI/dt (positive only)



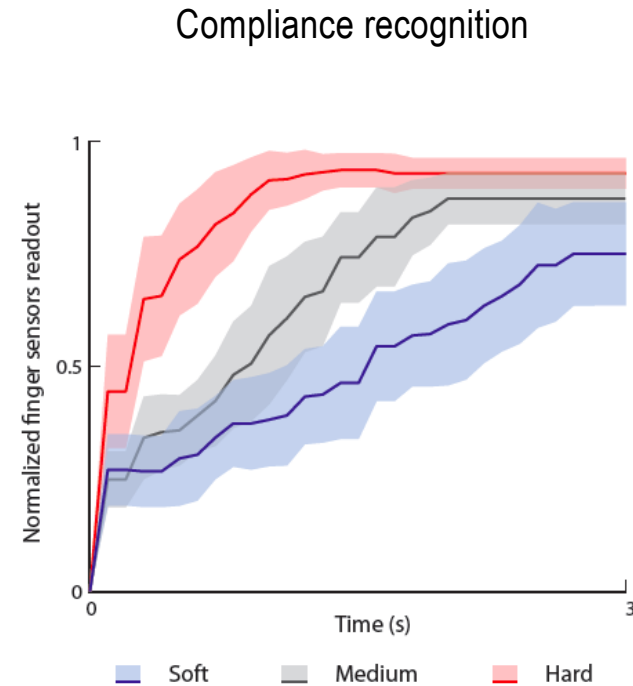
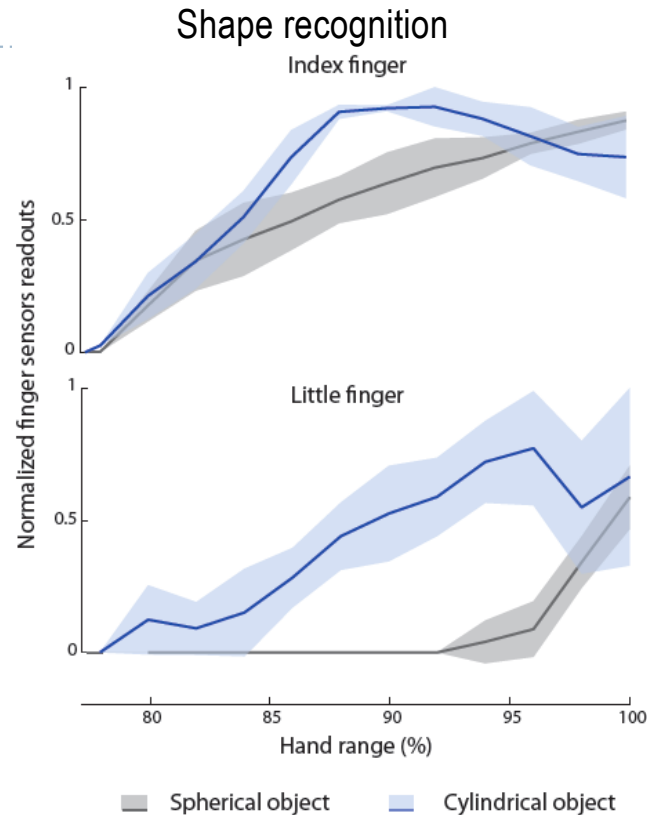
D Task accuracy



Shape discrimination analysis

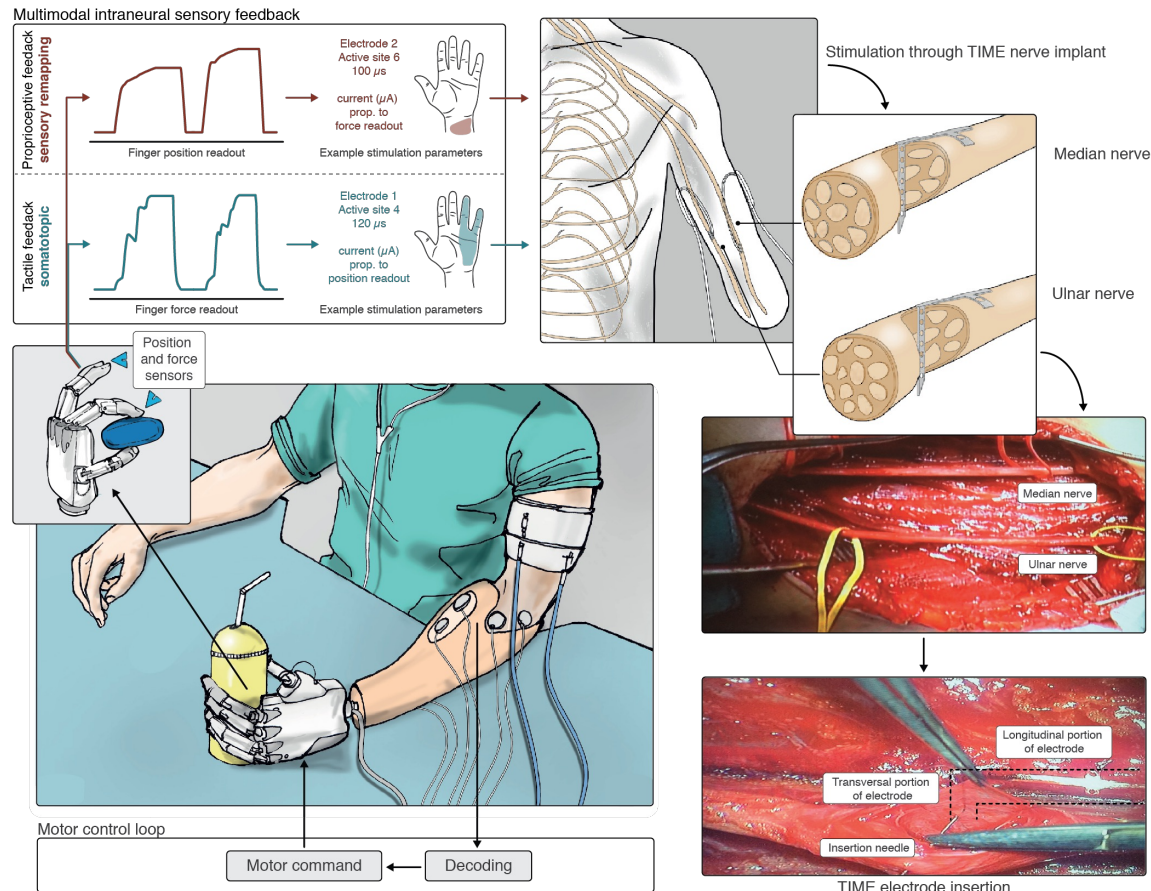


Why this is possible?



Different force profiles were provided to the users using the afferent stimulation
→ this is **NOT** on-off sensation!

Restoration of proprioception and tactile feedback



Restoration of proprioception and tactile feedback

a Experimental setup

vs – very small



s – small



l – large



vl – very large



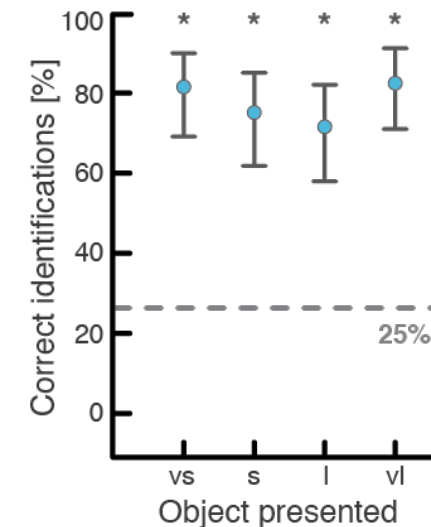
b

Task performance with proprioception only (n=2)



Subject's answer	Object presented			
	vs	s	l	vl
vl				83
l			72	
s		75		
vs	82			

Overall performance: **78% correct**



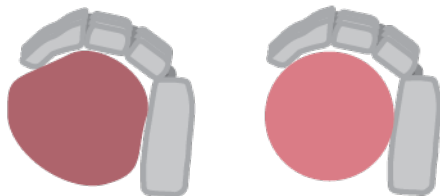
Restoration of proprioception and tactile feedback

a Experimental setup

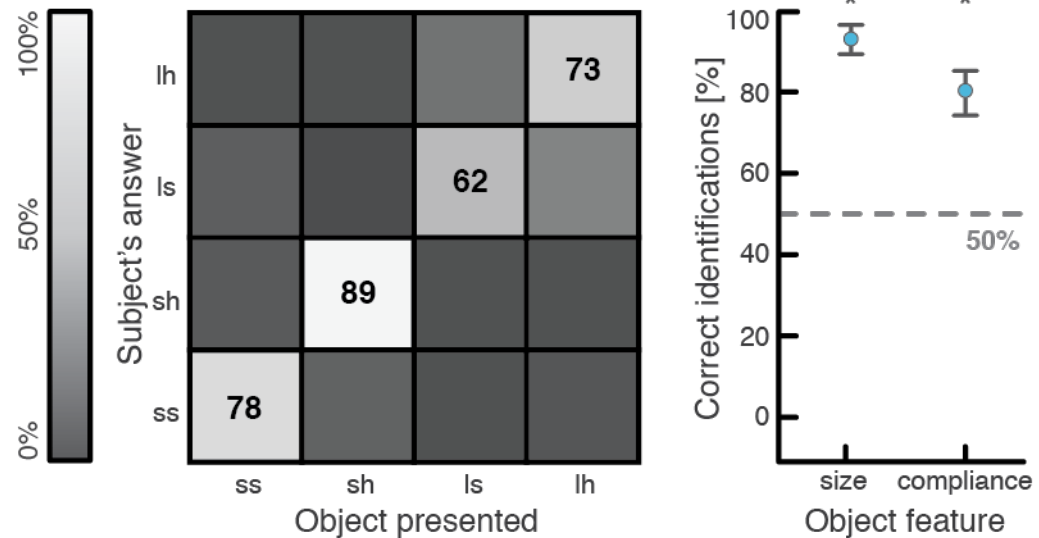
ss – small soft sh – small hard



ls – large soft lh – large hard

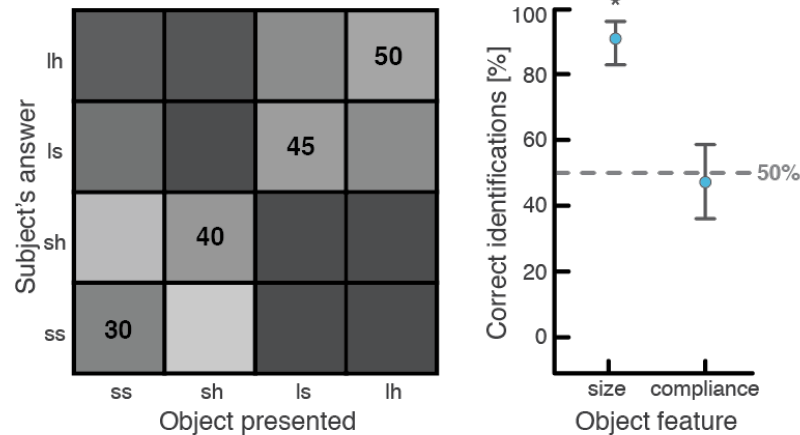


b Task performance with touch and proprioception (n=2)



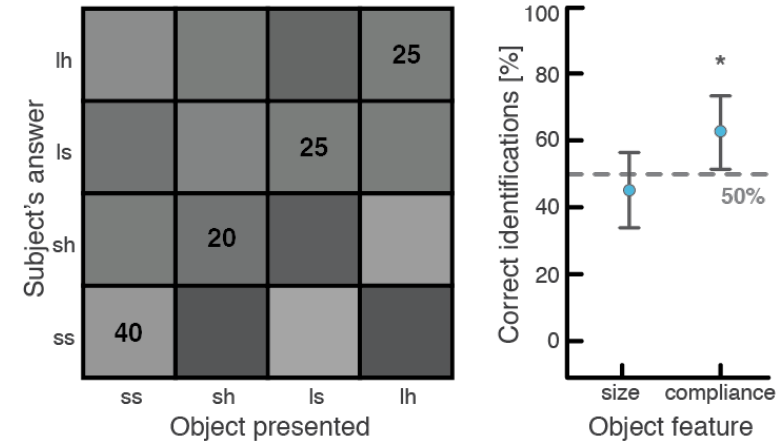
Restoration of proprioception and tactile feedback

c Proprioception only control condition (n=1)

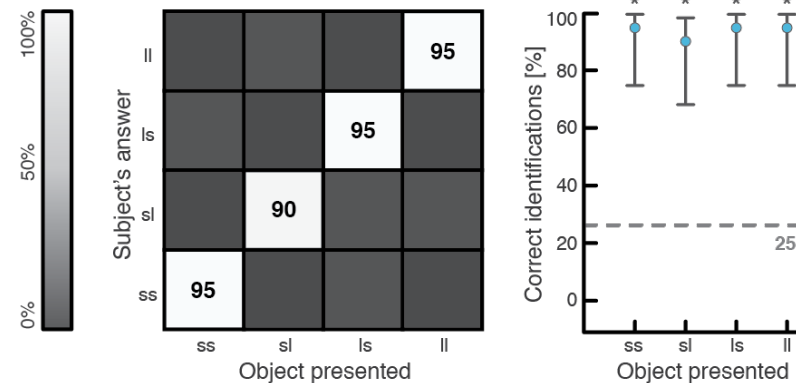


Overall performance: **41.3% correct**

e Touch only control condition (n=1)

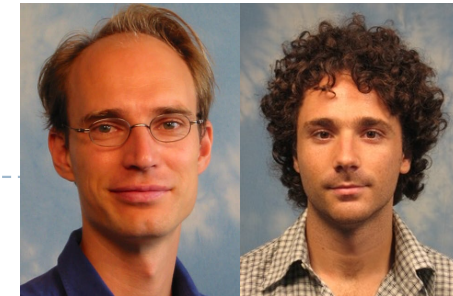


Multi-joint proprioception task (n=1)



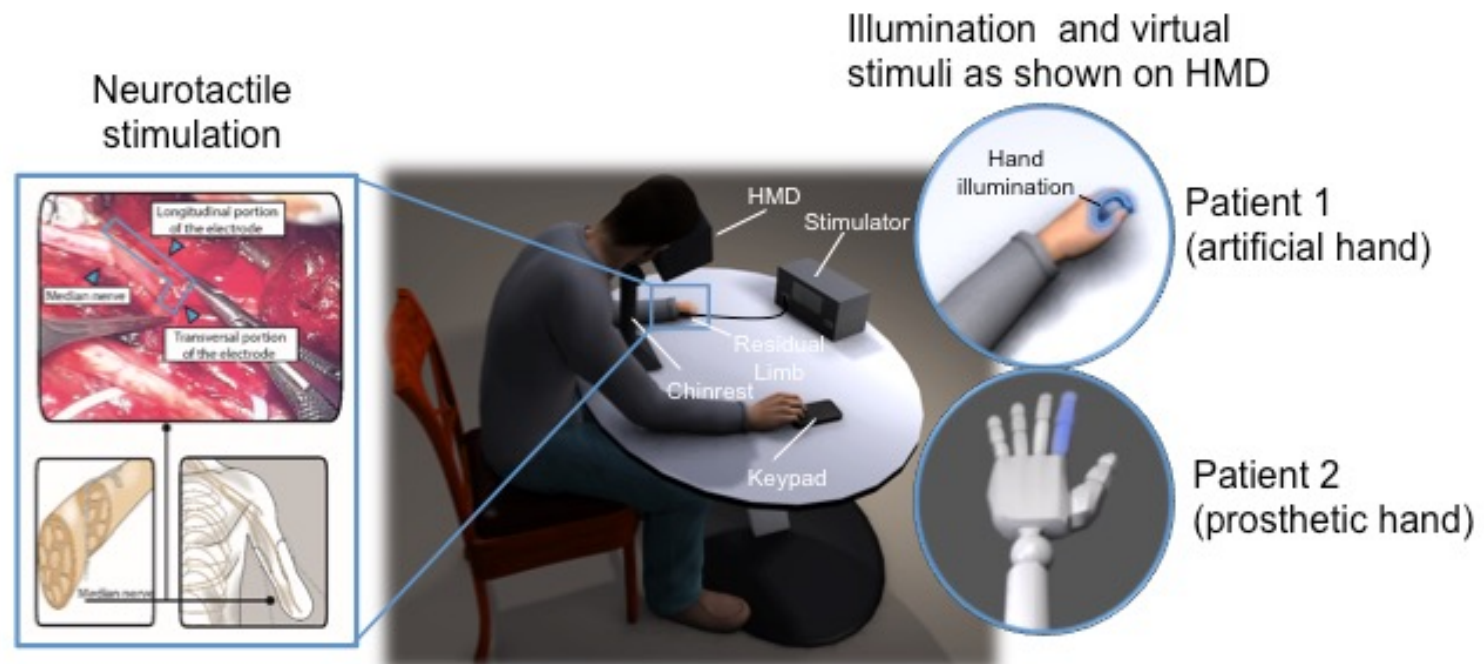
Overall performance: **93.7% correct**

Embodiment

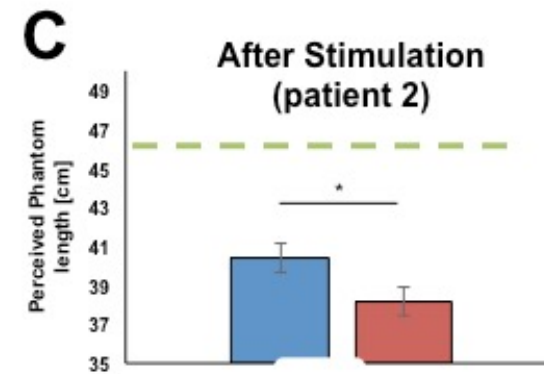
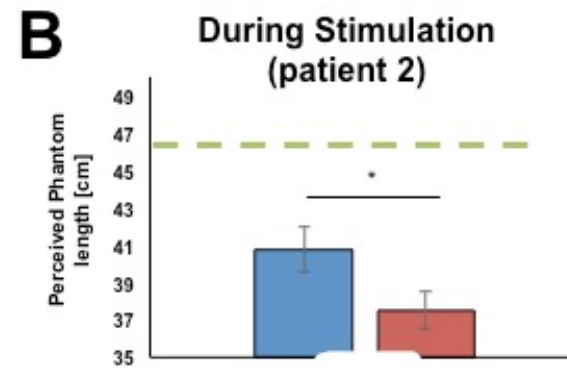
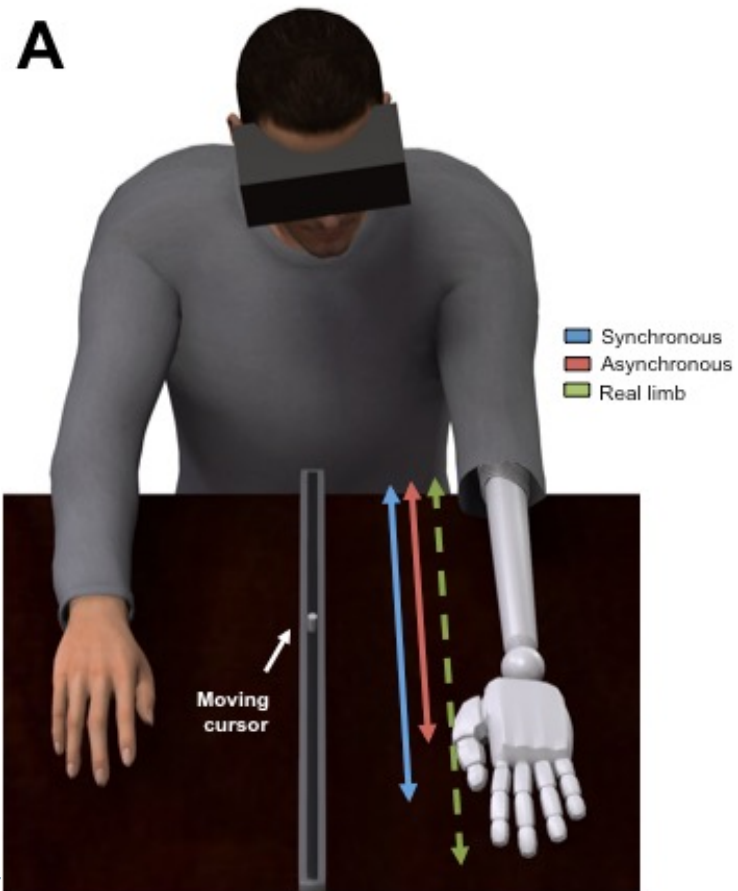


O. Blanke

G. Rognini



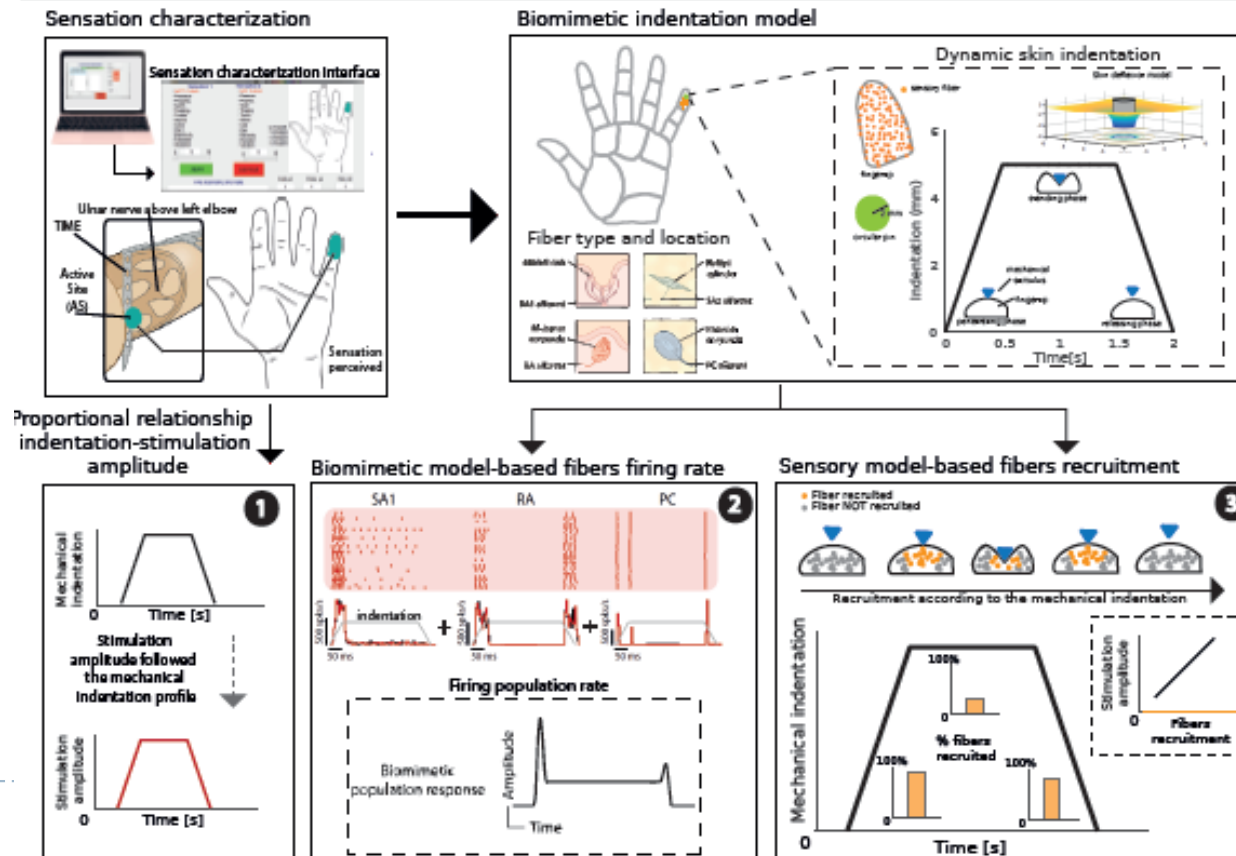
Embodiment



Biomimetic encoding strategy

Step 1: Biomimetic model-based approach and parameters generation

We identified electrode active site which elicits sensations in the locations corresponding to the fingertip. Then, we simulated a mechanical skin indentation using the biomimetic model. The model outcomes were the firing population activity generated by the combination of all the fibers (SA, RA, PC) response and the number of sensory fibers recruited during the skin indentation. We also generated the stimulation amplitudes following a proportional relationship with the mechanical stimulus as used in (16).



Biomimetic encoding strategy

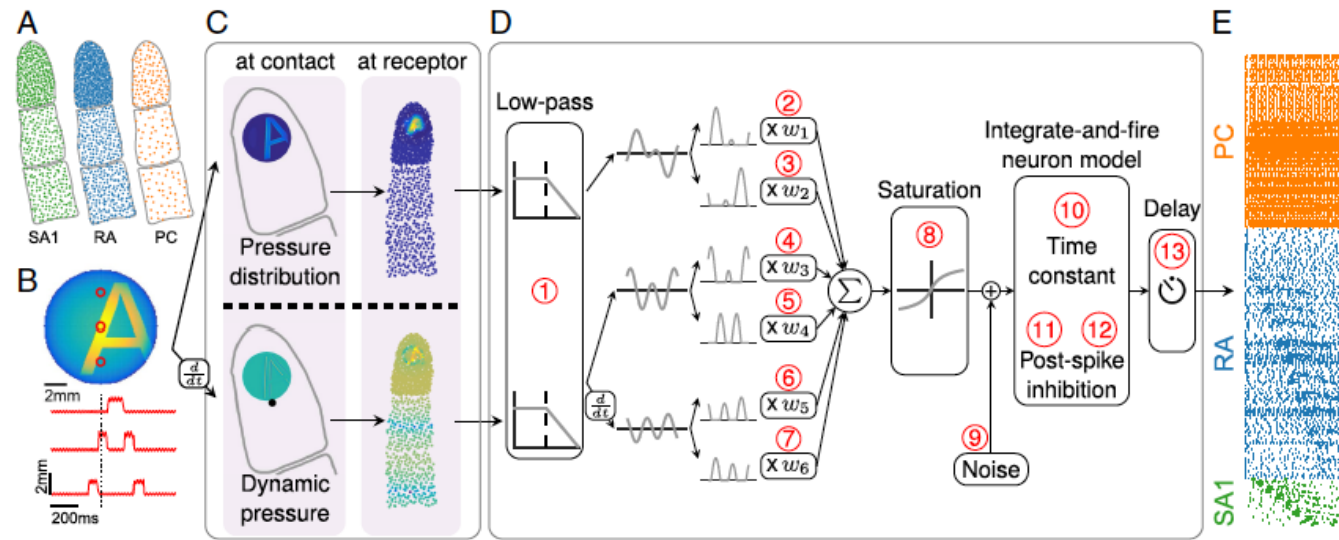
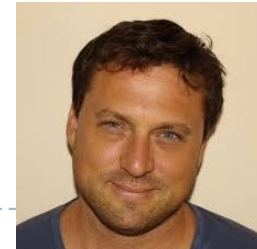


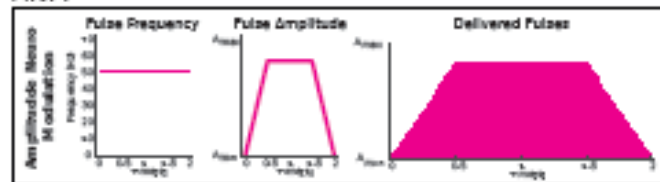
Fig. 1. Overview of the model. (A) Receptors are distributed across the skin given the known innervation densities of SA1, RA, and PC afferents. (B) The stimulus—in this case, a vibrating embossed letter A scanned across the skin—is defined as the time-varying depth at which each small patch of skin (here dubbed a pin) is indented (with a spatial resolution of 0.1 mm). The traces in Lower show the time-varying depth at the three locations on the skin indicated by the red dots in Upper. (C) The mechanics model relies on two parts: (Upper) modeling the distribution of stresses using a quasistatic elastic model and (Lower) modeling dynamic pressure and surface wave propagation. Left shows the surface deformation of the skin, and Right shows the resulting pattern of stresses at the location of the receptors. (D) The spiking responses are determined by leaky IF models using different sets of up to 13 parameters (marked in red numbers) for individual SA1, RA, and PC afferents fit based on peripheral recordings to skin vibrations. Adapted from ref. 71. (E) The output of the model is the spike train of each afferent in the population. Raster of the response of the afferent population sampled as in A to the stimulus shown in B (only active afferents are included). Note that the SA1s (in contact) only encode the spatial aspect of the stimulus, that the PCs encode from the whole finger phase-lock with the 200-Hz vibration, and that the RAs show mixed spatial and vibration responses.

Biomimetic encoding strategy

Step 2: Sensory encoding strategies

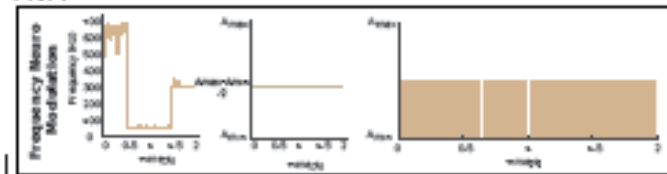
Different encoding strategies in which only one stimulation feature is modulated (Single feature) or both frequency and amplitude of the stimuli are simultaneously modulated (Hybrid). We converted the firing population rate generated by the biomimetic model in the frequency of the intraneural stimulation (FNM, HNM-1 and HNM-2). The stimulation amplitude was converted using the mechanical stimulus (ANM and HNM-1) or the fibers recruitment (HNM-2). The pulse-width was always fixed to 60 μ s.

ANM



1

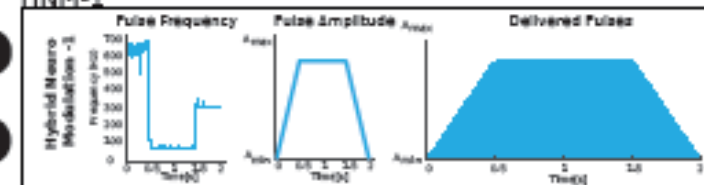
FNM



2

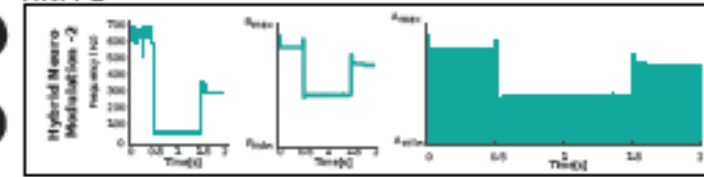
Single feature approaches

HNM-1



1
+

HNM-2

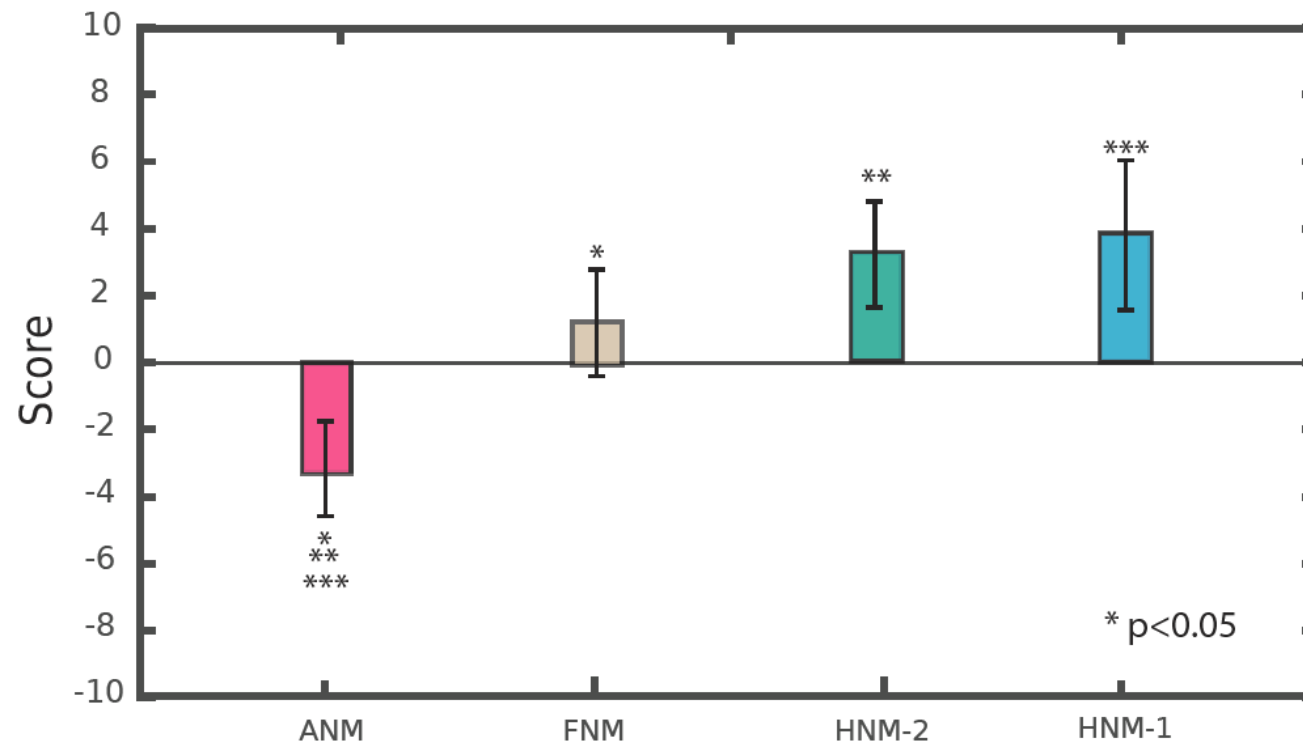


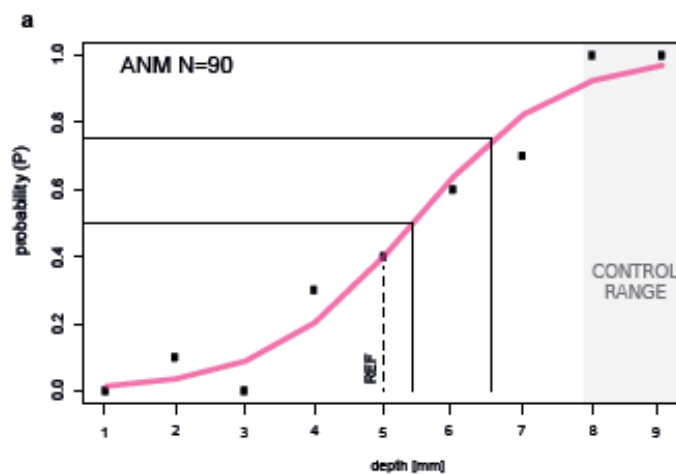
2
+

Hybrid approaches

Biomimetic encoding strategy

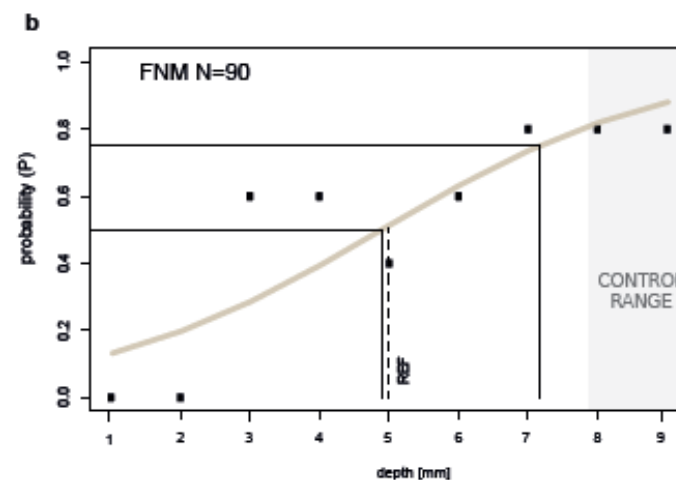
b Perceived naturalness among different encoding strategies N=16





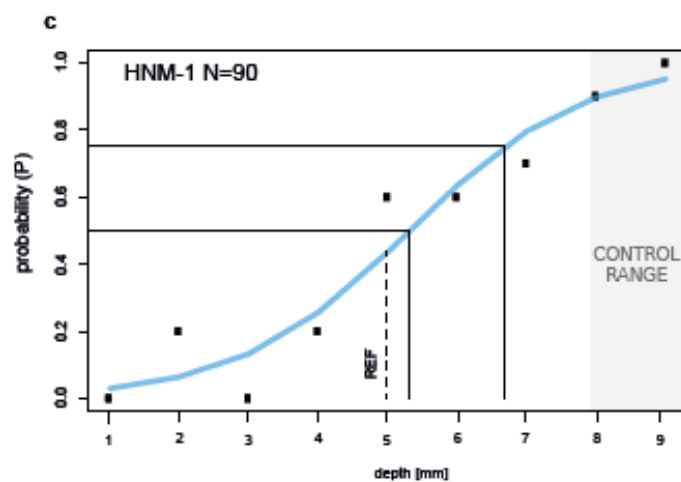
Point of Subjective Equality (PSE): 5.51 mm

Just-Noticeable Difference (JND): 1.01 mm



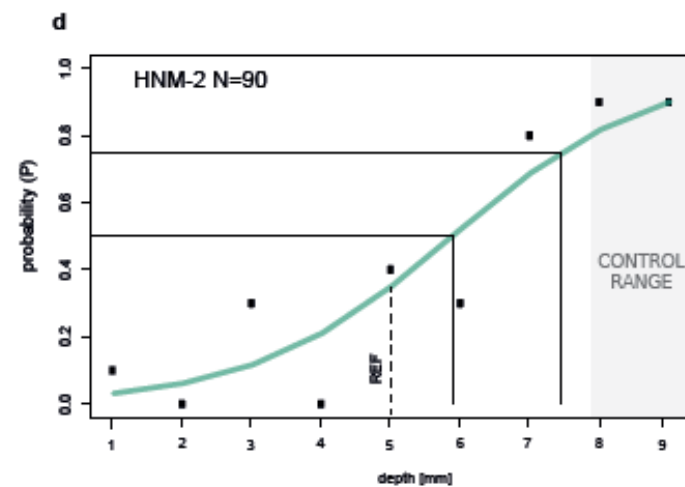
Point of Subjective Equality (PSE): 4.87 mm

Just-Noticeable Difference (JND): 2.26 mm



Point of Subjective Equality (PSE): 5.31 mm

Just-Noticeable Difference (JND): 1.35 mm



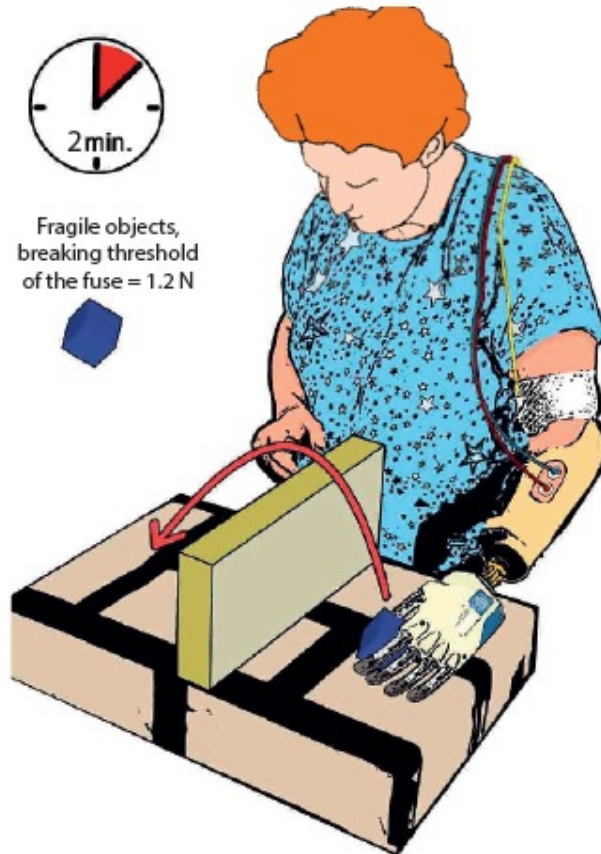
Point of Subjective Equality (PSE): 5.87 mm

Just-Noticeable Difference (JND): 1.55 mm

a Setup - Virtual Eggs Test (VET)

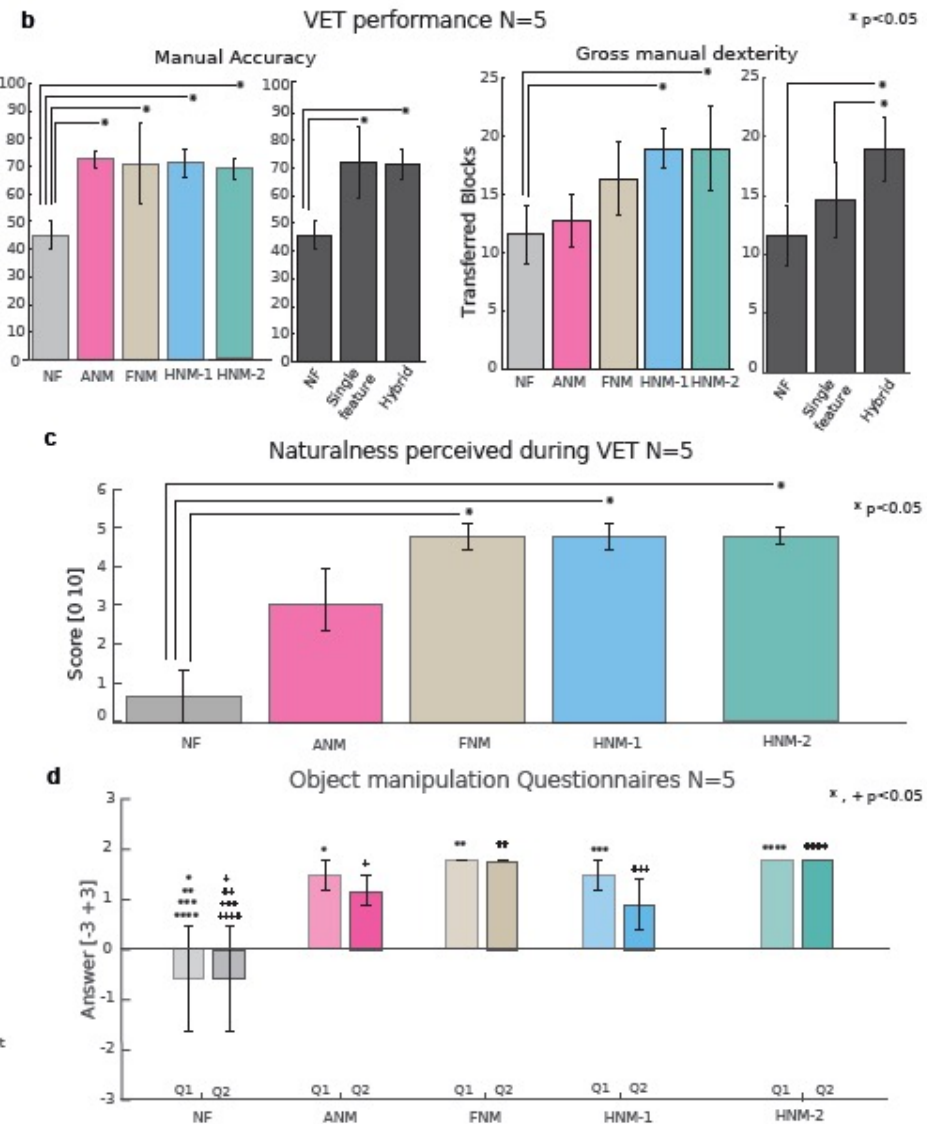


Fragile objects,
breaking threshold
of the fuse = 1.2 N

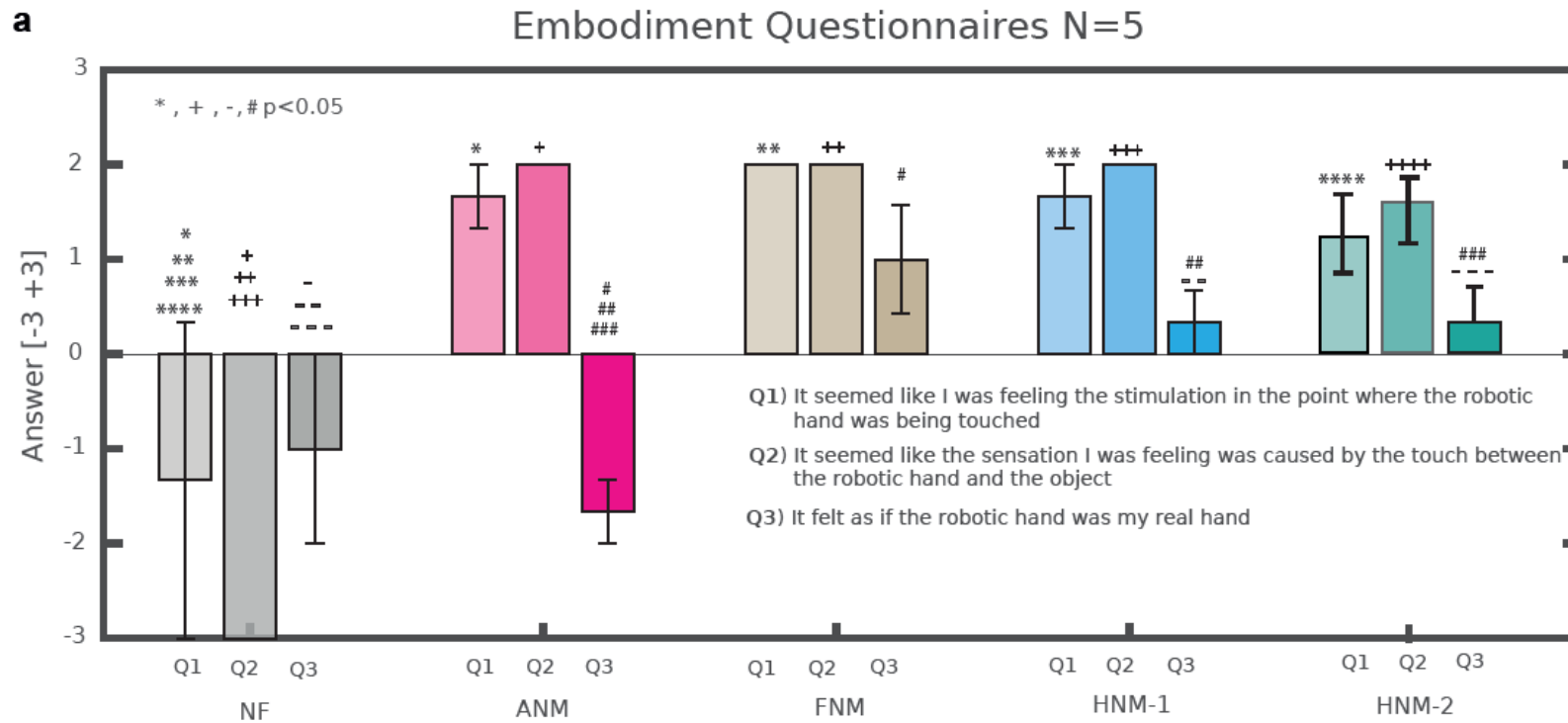


Q1) It seemed like I was grasping a real object

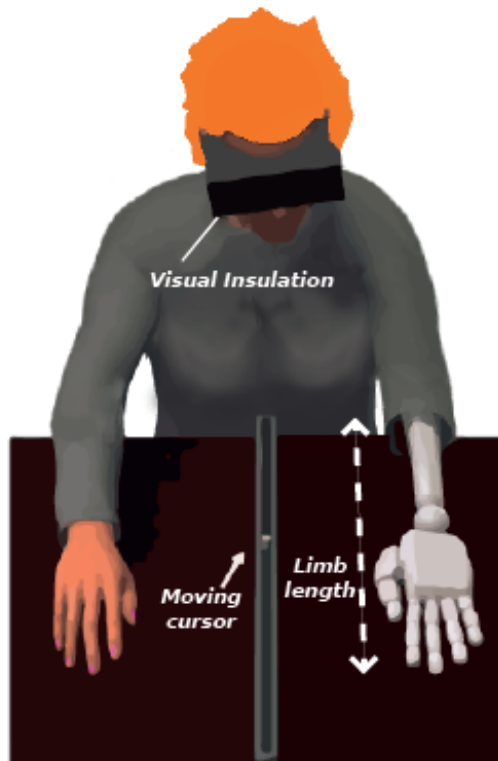
Q2) I felt the intensity of the grasping force applied by the robotic hand on the object



Biomimetic encoding strategy



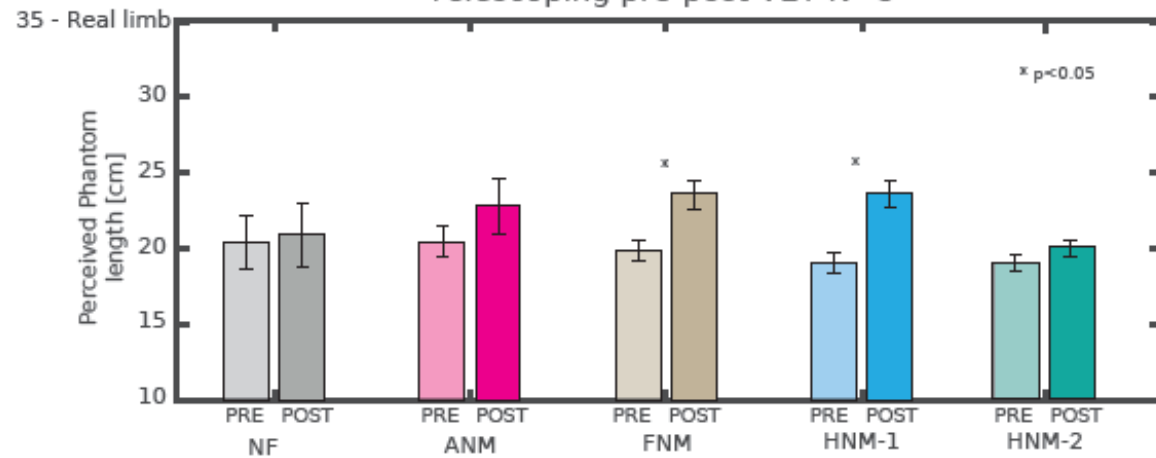
a Telescoping task setup



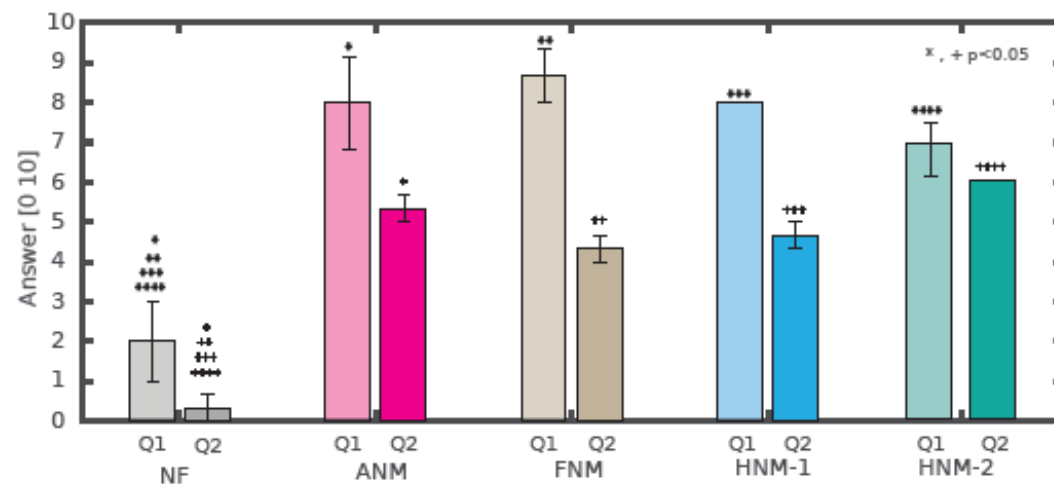
Q1) It seemed like the phantom hand had changed orientation as the robotic hand

Q2) I felt my phantom arm longer

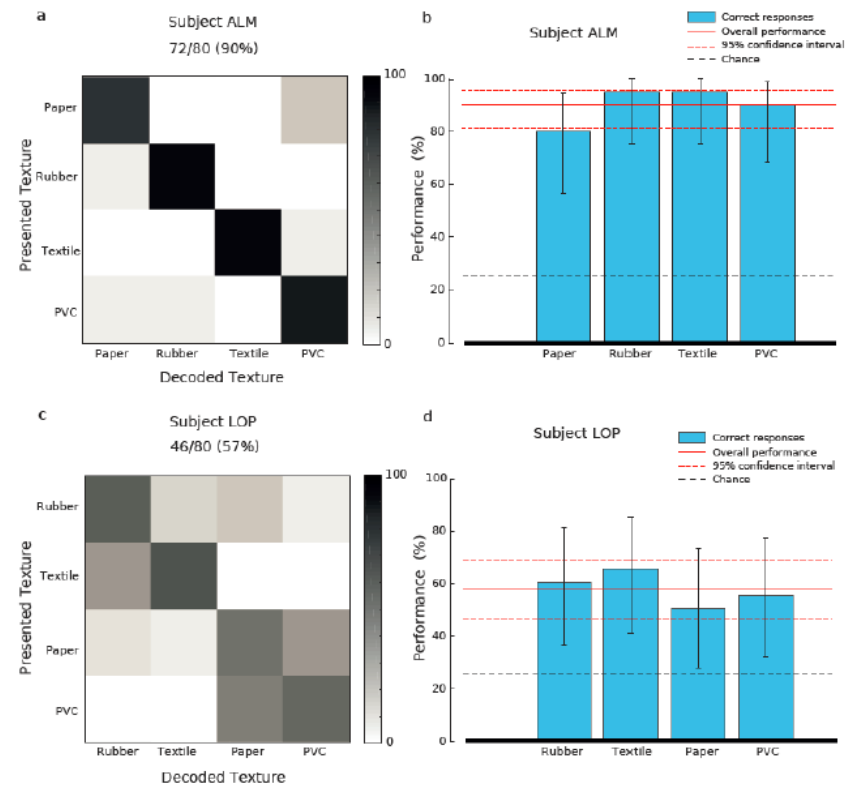
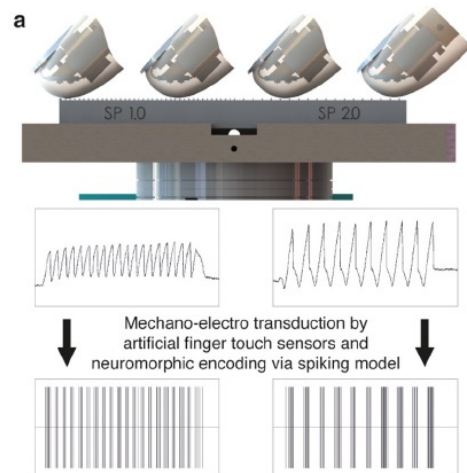
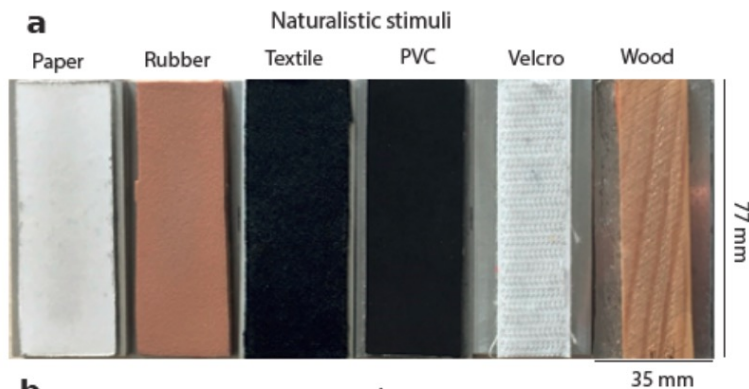
b Telescoping pre-post VET N=5



c Phantom limb dimension perceptions Questionnaires N=5

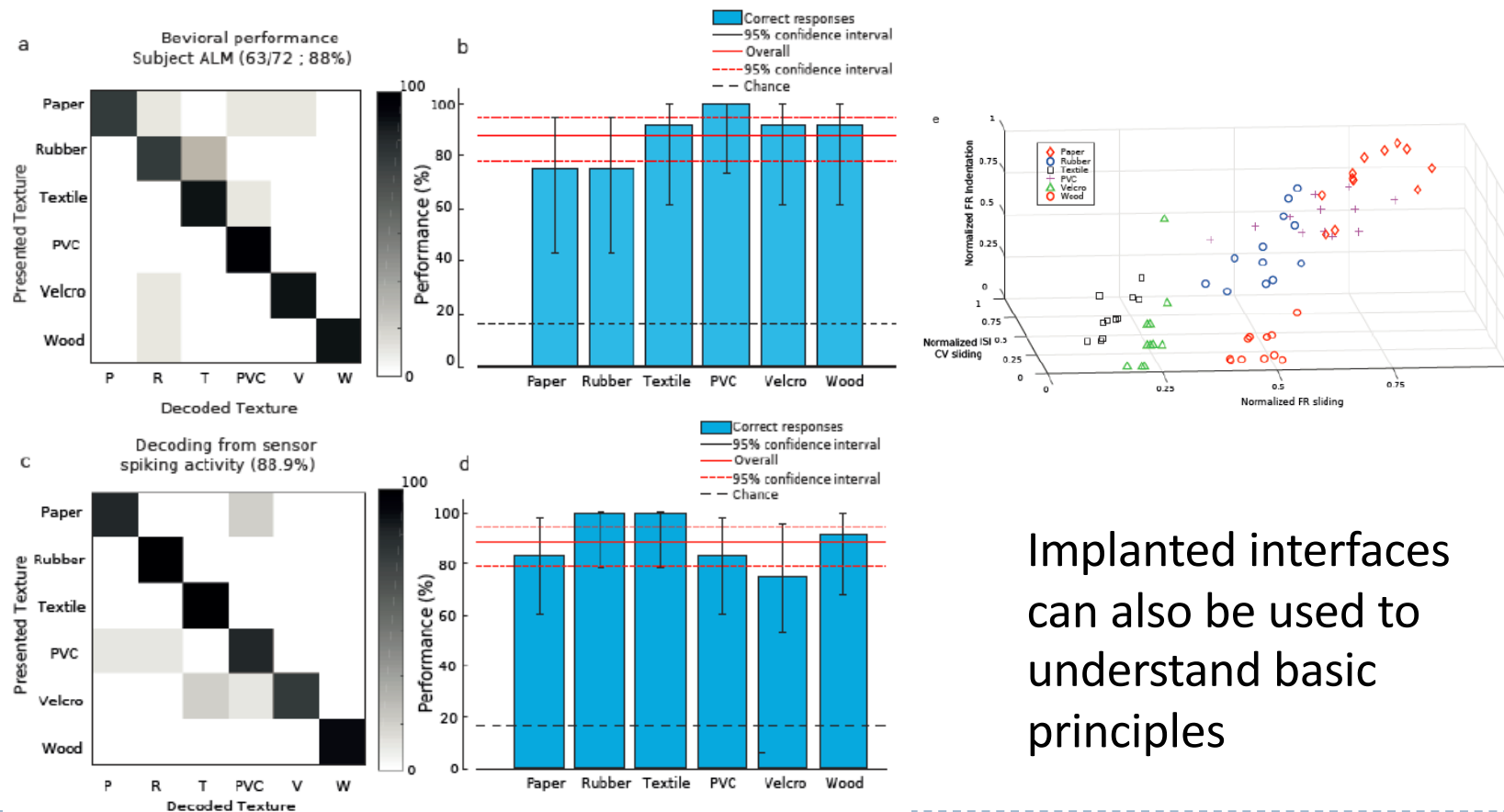


Restoring perception of real textures

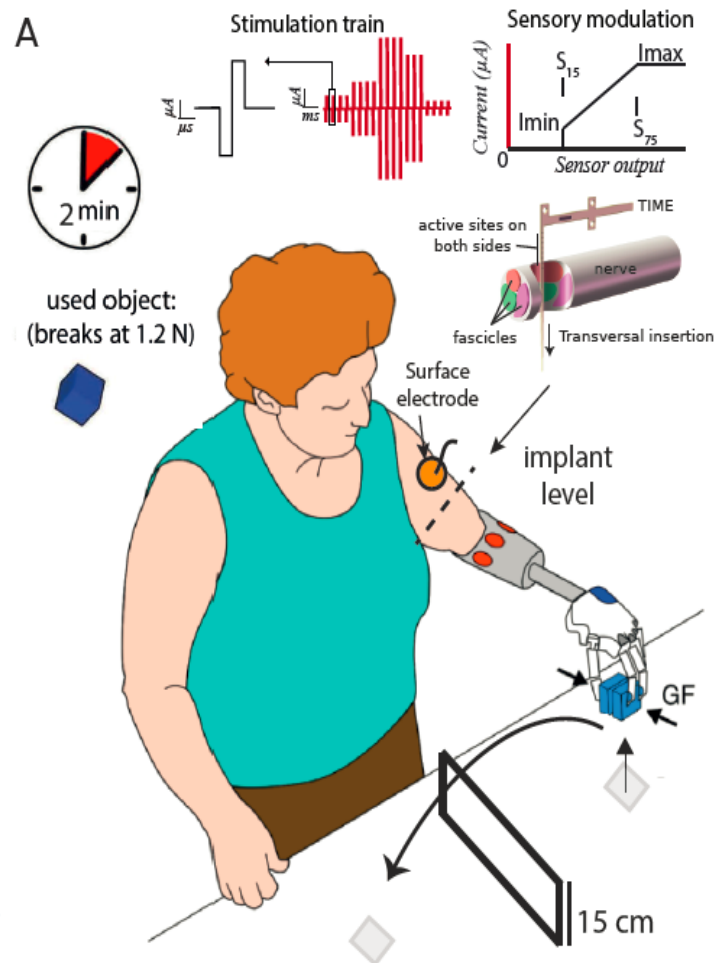


Oddo et al., eLIFE, 2016
Mazzoni et al., Sci Rep, 2019

Restoring perception of real textures



Effects of cognitive load



B Induced sensations & stimulation parameters

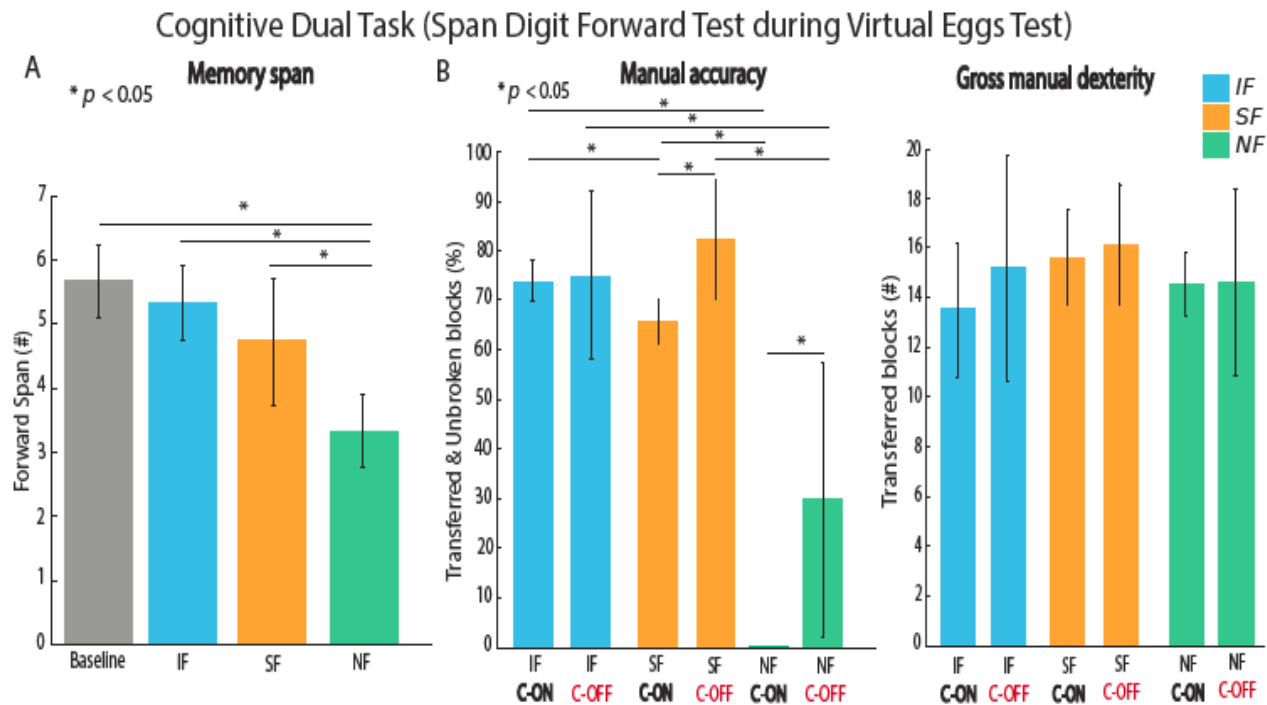
Intraneural sensory Feedback (IF)

sensation type	vibration
sensation intensity	$S_{min} = 1, S_{max} = 8$
electrode position	proximal part of ulnar nerve above elbow
amplitude	$A_{min} = 200 \mu A, A_{max} = 300 \mu A$
pulse-width	80 μs
frequency	50 Hz

Superficial sensory Feedback (SF)

sensation type	electricity
sensation intensity	$S_{min} = 1, S_{max} = 8$
electrode position	on the skin of the left arm
amplitude	$A_{min} = 100 \mu A, A_{max} = 500 \mu A$
pulse-width	200 μs
frequency	50 Hz

Effects of cognitive load



Bidirectional neurocontrolled leg protheseses



Above the knee

Below the knee

Leg Prosthetics

Utah Bionic Leg

Powered Knee Module
Weight: 1.6 kg
Range of Motion: 120 deg
Max Torque: 150 Nm
Max Speed: 500 deg/s
Build Height: 255mm

Standard Connection
Allows adjustment of
prosthesis build height
and ankle
inversion/eversion to
patient using standard
prosthetic components

Powered Ankle-Toe Module
Weight: 1.6 kg
Range of Motion - Ankle: 40 deg
Range of Motion - Toe: 45 deg
Max Torque: 150 Nm
Max Speed: 350 deg/s
Build Height: 165 mm



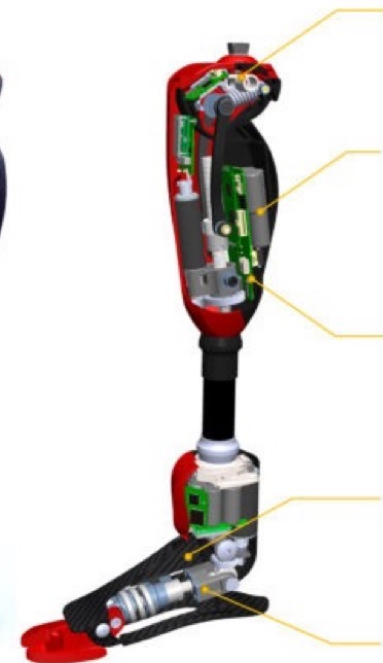
Passively Variable Transmission
Continuously changes the motor
gearing based on the applied
load to optimize motor function
and battery life

Lithium-Ion Battery
Enables combined 12,800 steps
on level ground and 40 flights of
stairs on a single charge, or
hybrid mode allows for indefinite
activity with battery
regeneration during walking

Artificial Sensing and Control
Embedded computers and
sensors execute control loops up
to 2,000 times per second to
optimize the prosthesis behavior
based on the user's movement

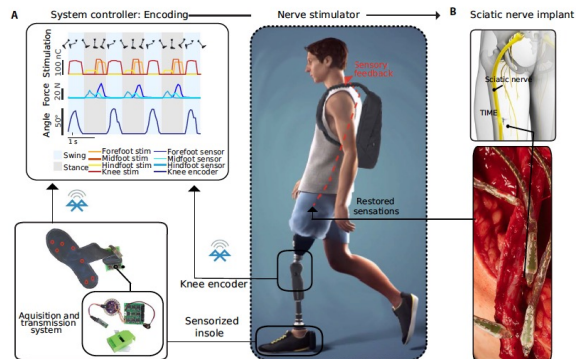
Carbon Fiber Foot Case
A lightweight, high strength
carbon fiber foot shell contains
the electromechanical actuation
system

Bioinspired Artificial Tendon
An artificial tendon connects the
toe and the ankle joint to allow
for biomimetic foot mechanics
during walking



Bidirectional neurocontrolled leg protheses

Sensory feedback



■ i4LIFE – Intraneural sti

Enhancing functional abilities and cognitive integration
of the lower limb prosthesis

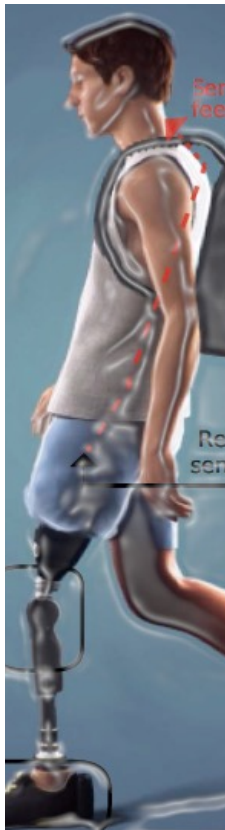
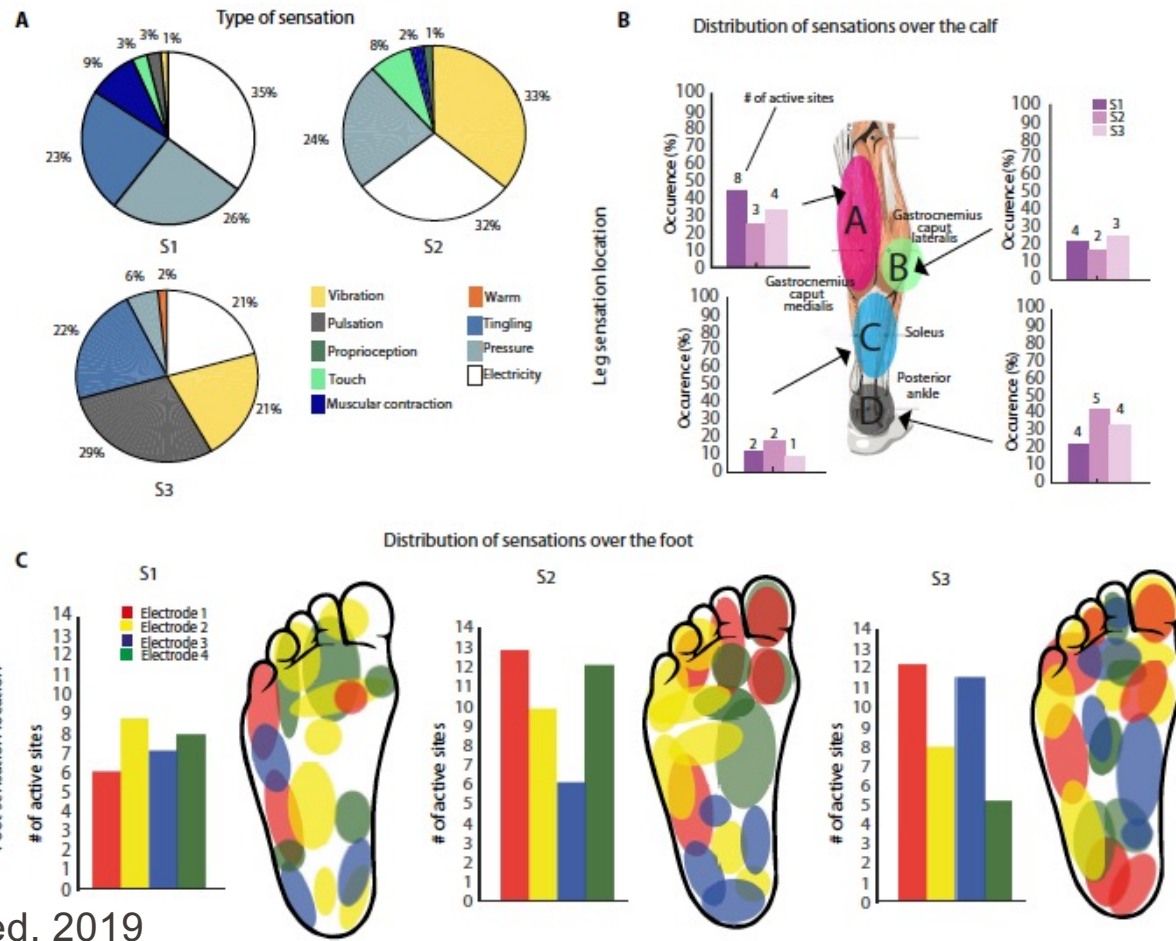
Movie S2:

Neuroprosthesis working
principle and active tasks

Caution: Investigational device

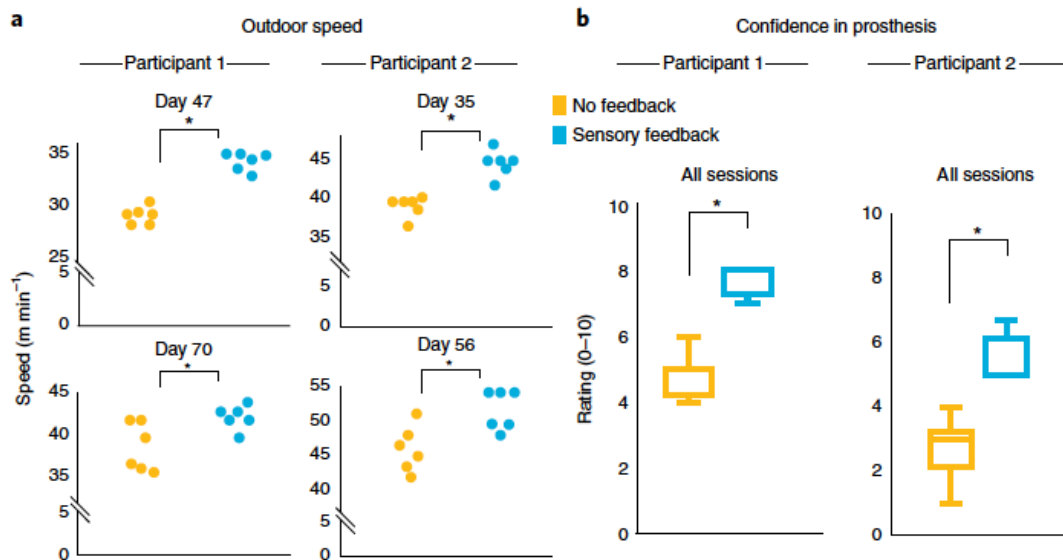
Bidirectional neurocontrolled leg protheses

Sensory feedback



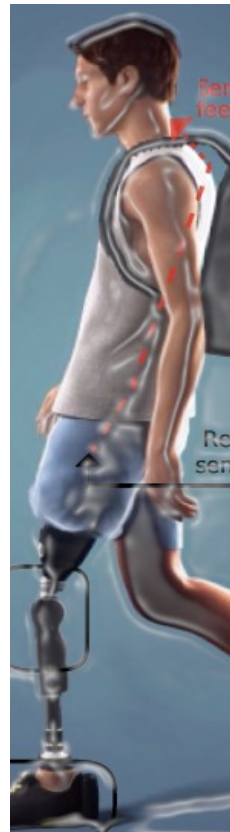
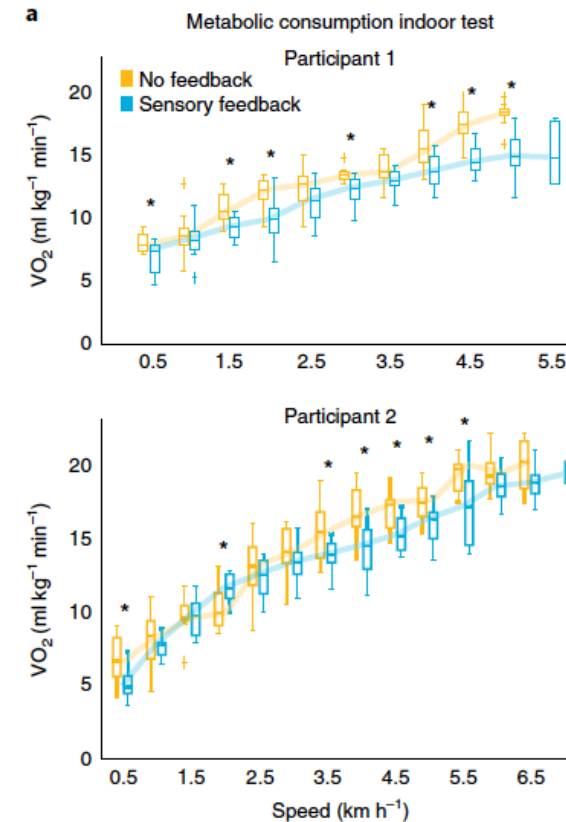
Bidirectional neurocontrolled leg protheses

Sensory feedback



Walking speed and self-reported confidence increased while mental and physical fatigue decreased for both participants

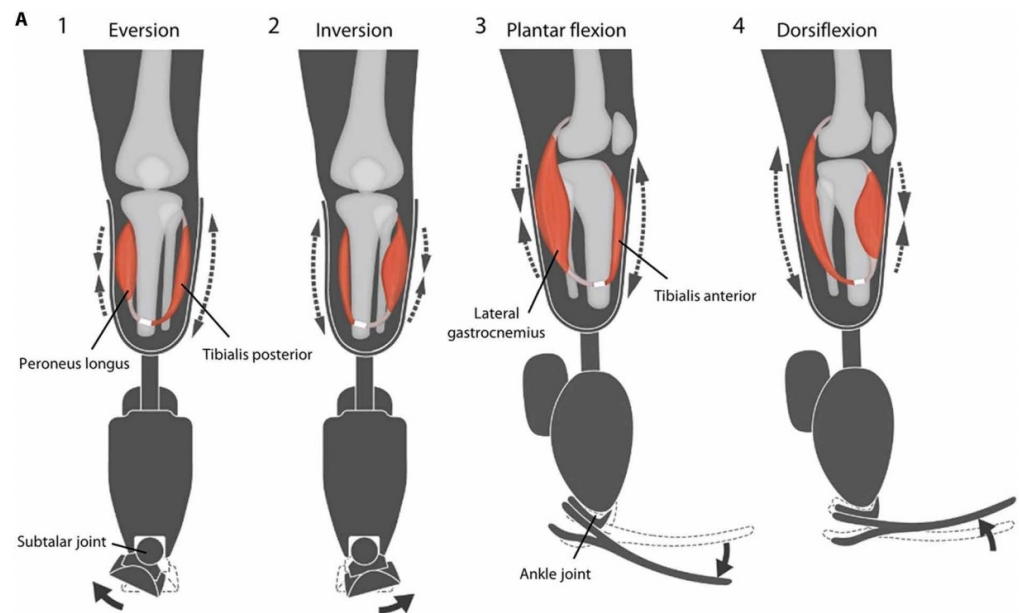
Participants exhibited reduced phantom limb pain with neural sensory feedback.



Petrini et al., Nature Medicine, 2019

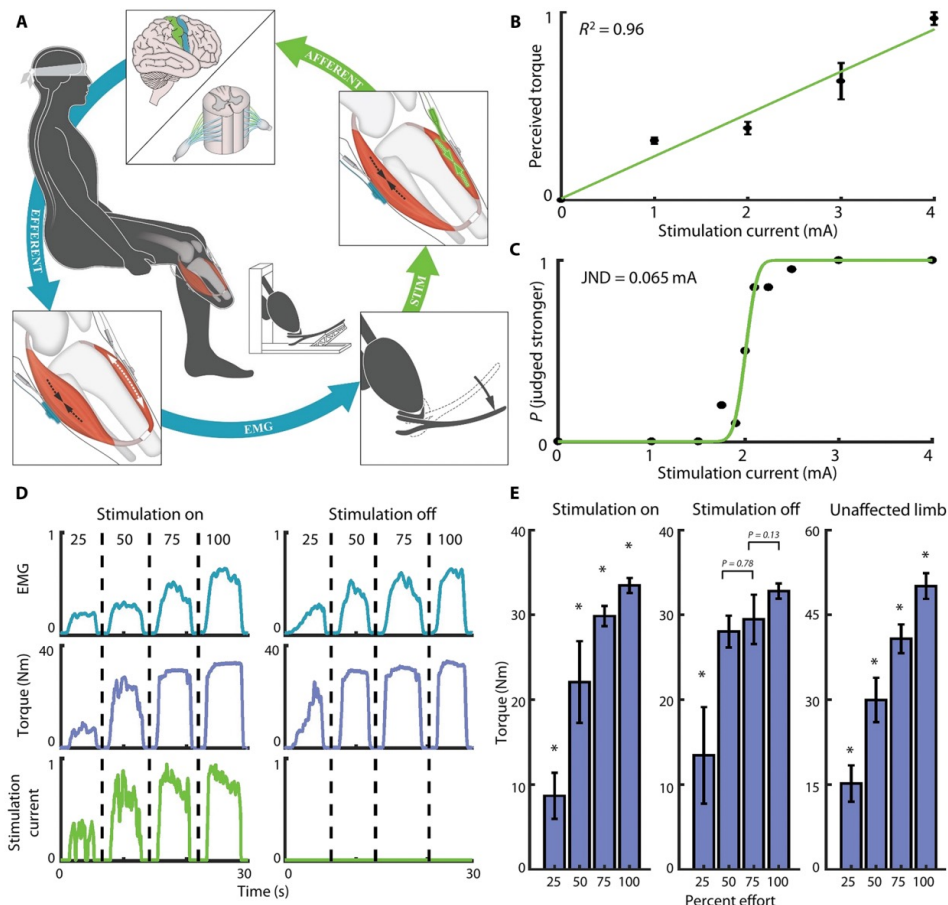
Agonist-antagonist myoneural interface

- As a methodology of improving efferent (neural pathways that relay commands from the central nervous system to a muscle or other end organ) prosthetic control and providing afferent proprioceptive sensation, we present an agonist-antagonist myoneural interface (AMI)
- An AMI is made up of an agonist and an antagonist muscle tendon connected mechanically in series: When the agonist contracts, the antagonist is stretched and vice versa
- The purpose of an AMI is to control and interpret proprioceptive feedback from a bionic joint.



Clites et al., Science Trans Med, 2018

Agonist-antagonist myoneural interface – Closed-loop torque control

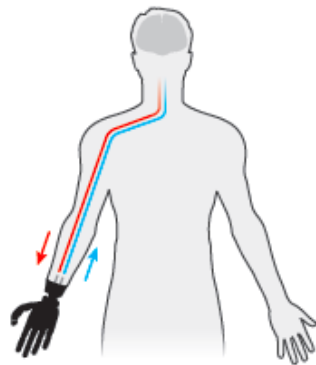


- (A) Schematic of the prosthesis-in-the-loop control architecture, in which afferent feedback of prosthetic joint torque is provided via FES of the antagonist muscle. The patient perceives this stimulation as a natural sensation of ankle torque
- (B) Magnitude estimation of perceived dorsiflexion torque as a function of stimulation current delivered to the tibialis anterior
- (C) Discrimination performance as a function of differences in stimulation current
- (D) Representative sample traces of lateral gastrocnemius EMG (blue), torque (purple), and stimulation current (green) during closed-loop torque control trials for the "stimulation on" (n = 79 total trials) and "stimulation off" (n = 79 total trials) cases
- (E) Summary data for closed-loop torque control trials in each of the stimulation on (n = 79 trials), stimulation off (n = 79 trials), and "unaffected limb" (n = 80 trials) cases

Clites et al., Science Trans Med, 2018

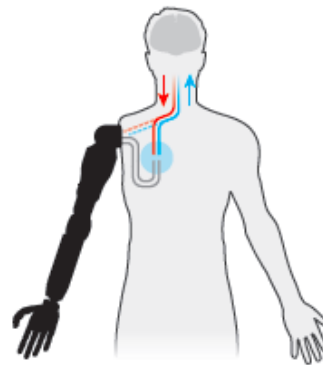
Sensory feedback

Real-time, and natural feedback from the hand prosthesis to the user is essential in order to enhance the control and functional impact of prosthetic hands in daily activities, prompting their full acceptance by the users



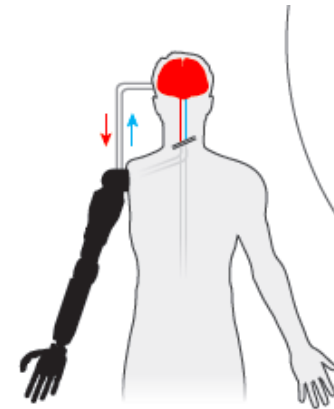
Use the remaining nerves

Electrical leads from the prosthetic's sensors stimulate nerves in the person's stump that once served the real limb.



Move the nerves

Re-routed nerves grow new endings into muscle and skin, where external devices translate signals going to and from the prosthesis.

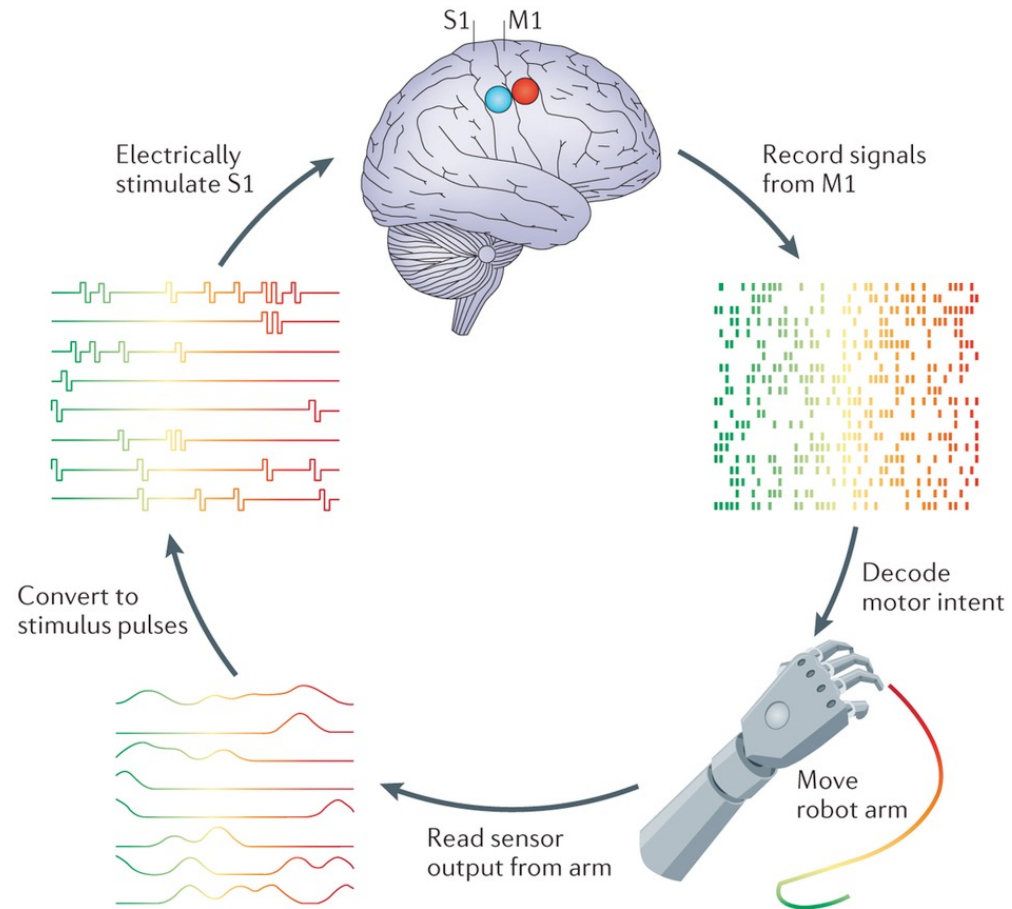


Stimulate the brain

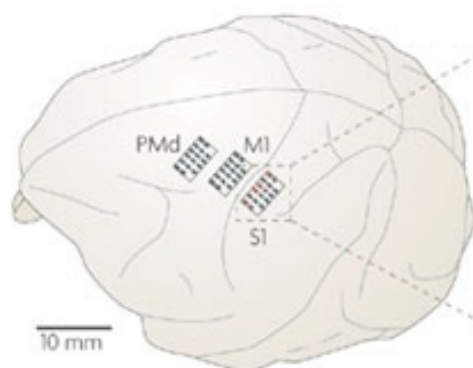
Sensory signals are routed around a severed spinal cord and into the brain, where they produce sensations by direct stimulation of the cortex.

Kwok, Nature, 2013

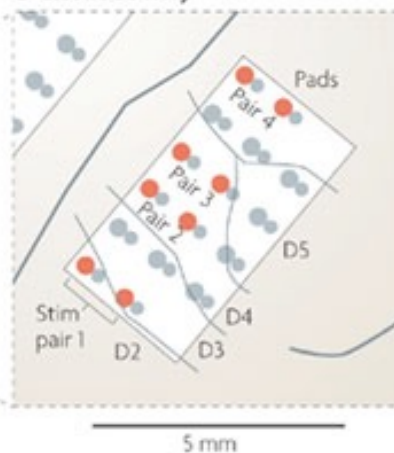
Brain-to-machine-to-brain interface



a Implantation sites



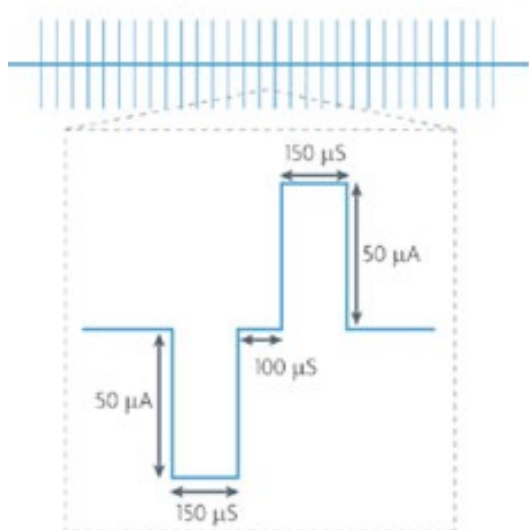
b Electrode array



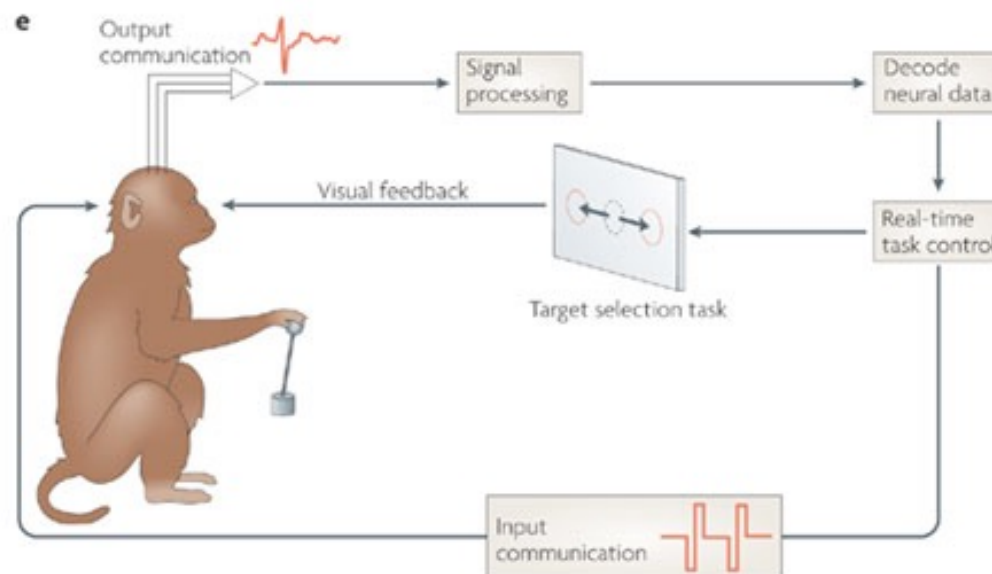
c Receptive fields



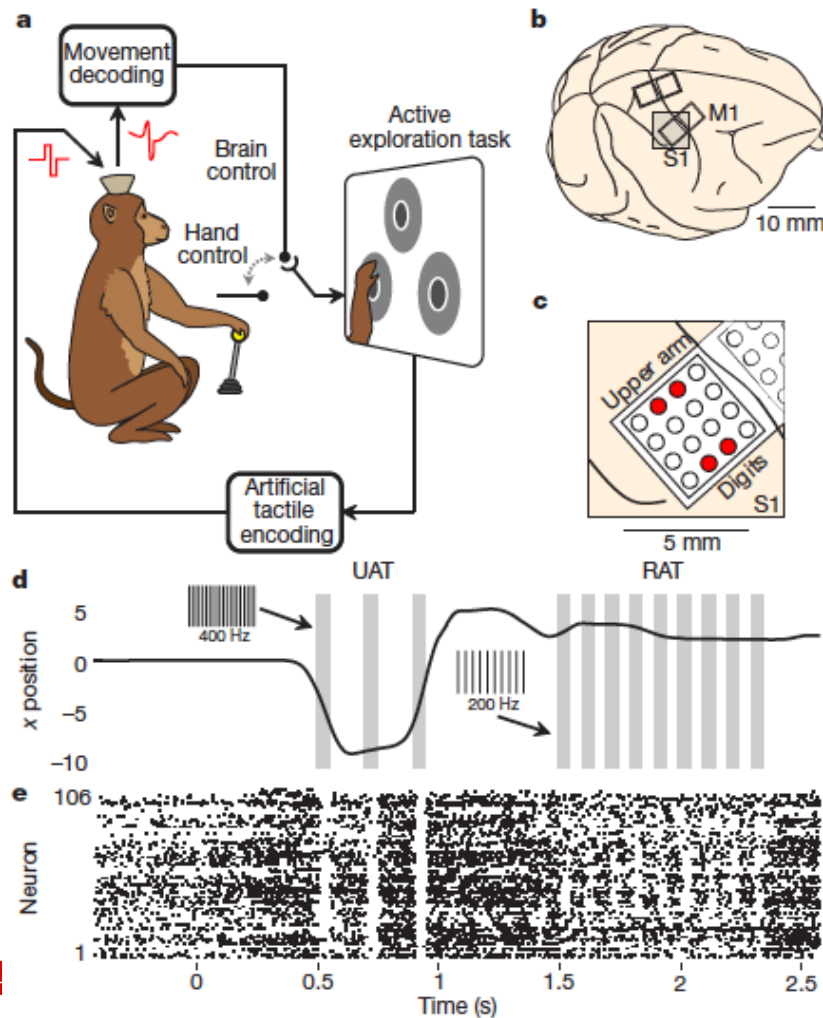
d Stimulation pattern



e



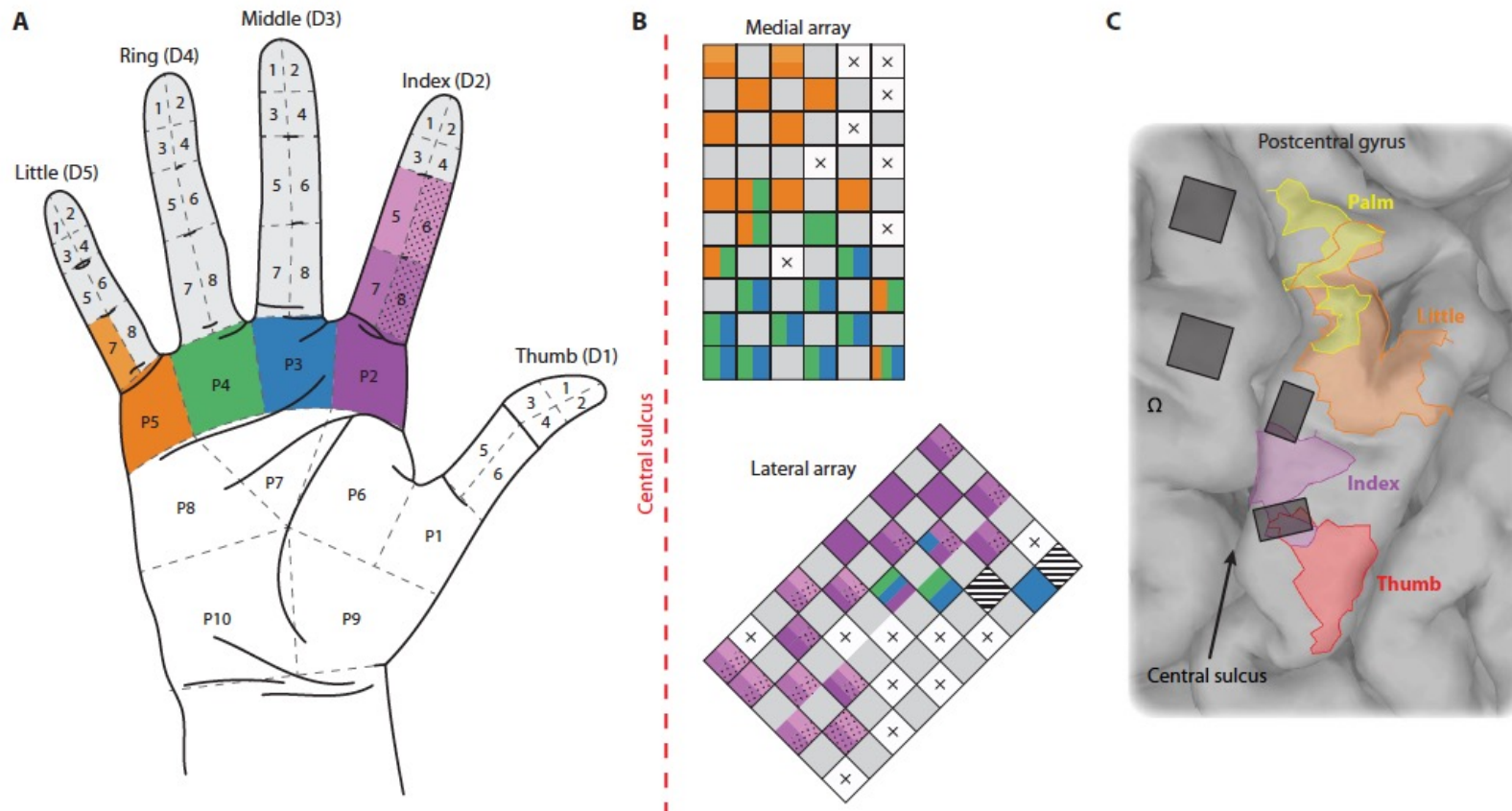
Intracortical sensory feedback



Intracortical sensory feedback is possible but the performance are still limited

O'Doherty et al., 2011

Brain-to-machine-to-brain interface in a quadriplegic subject



Brain-to-machine-to-brain interface in a quadriplegic subject

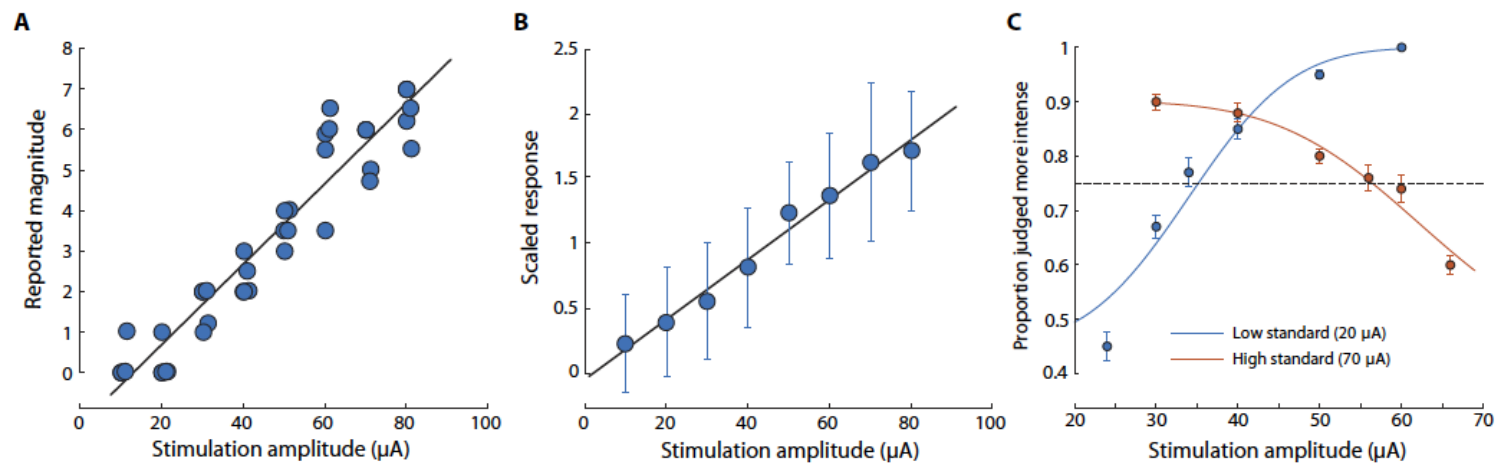
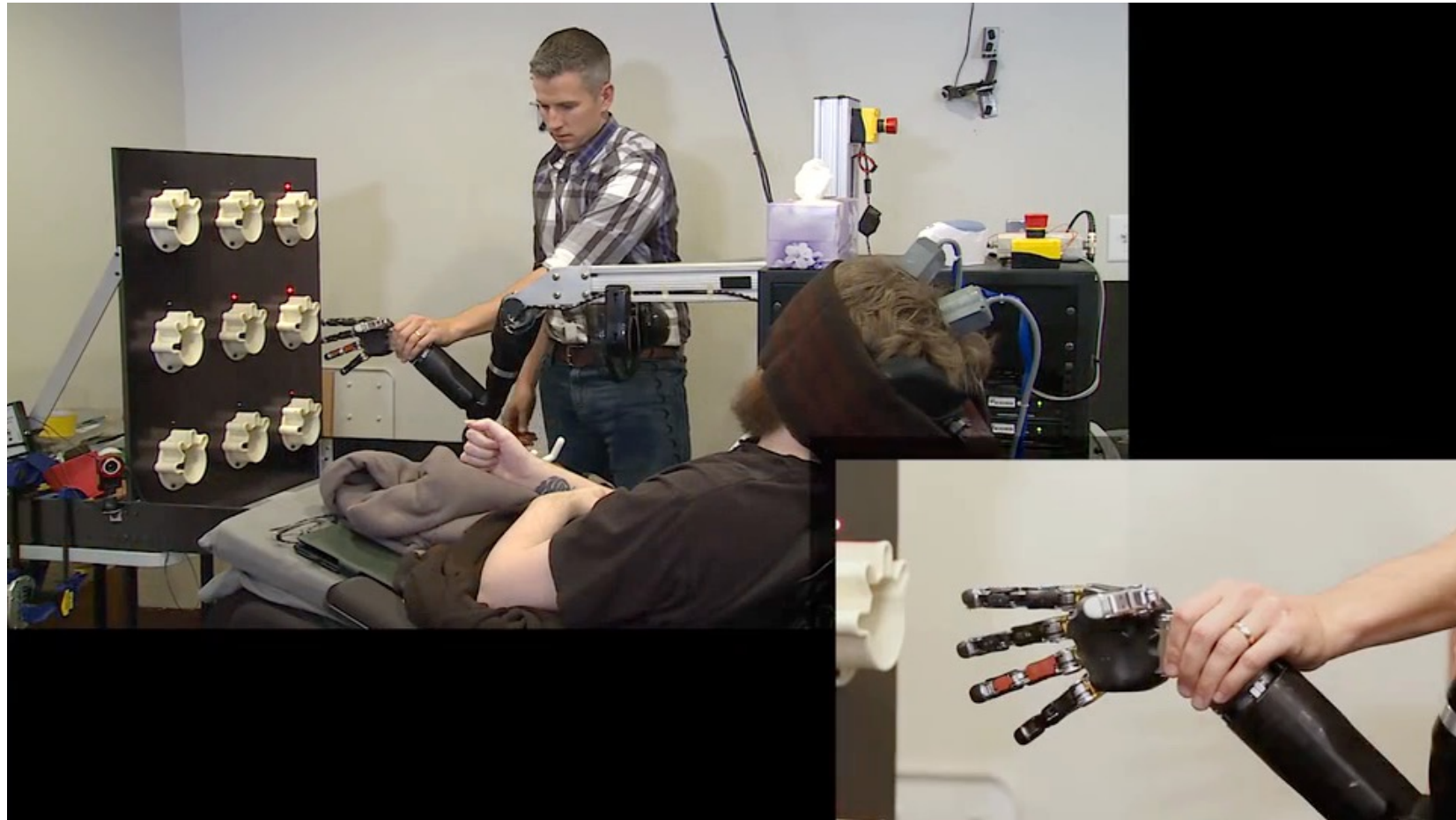


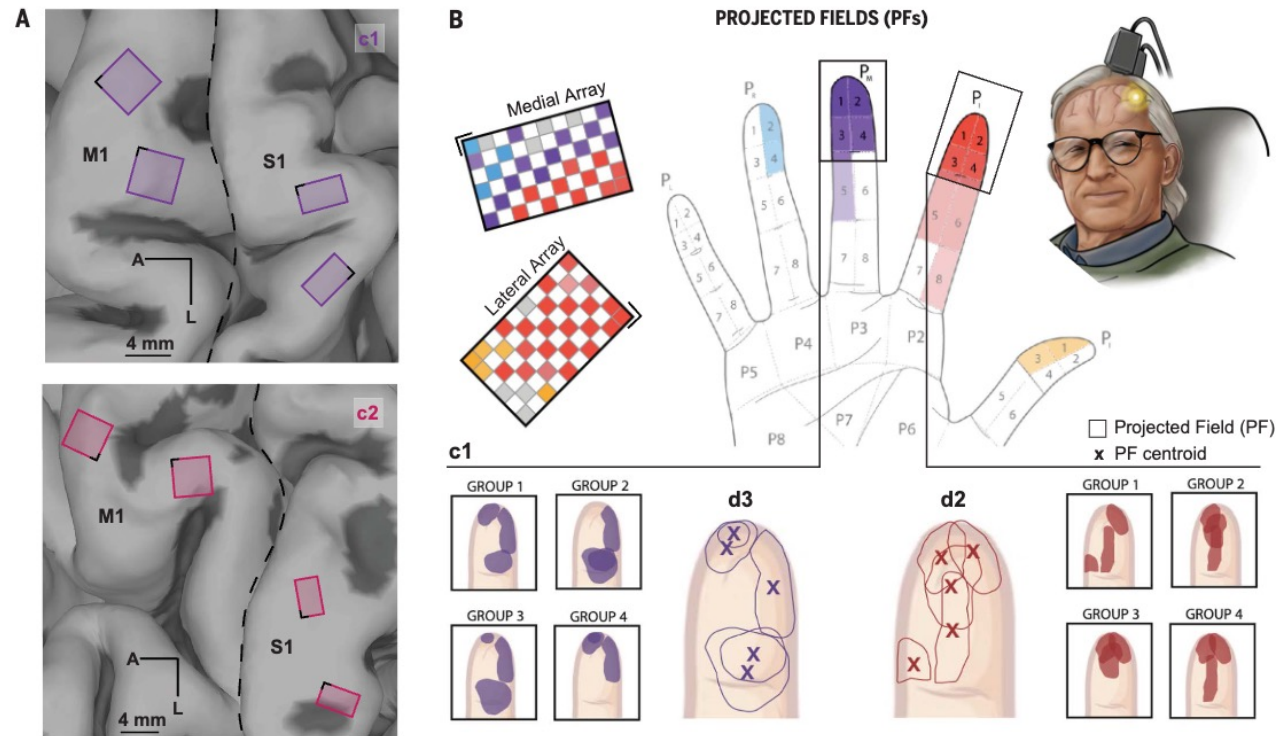
Table 2. Accuracy of prosthetic finger discrimination. The percentage of times that sensations were reported to originate from a specific finger (columns) when each prosthetic finger was touched (rows).

	Reported D2	Reported D3	Reported D4	Reported D5
Actual D2	96.9 \pm 7.2%	1.5 \pm 5.3%	1.5 \pm 5.3%	0%
Actual D3	0%	73.5 \pm 18.1%	21.9 \pm 18.4%	0%
Actual D4	0%	18.5 \pm 22.8%	73.1 \pm 24.6%	6.5 \pm 16.8%
Actual D5	0%	3.1 \pm 7.2%	3.1 \pm 10.7%	93.9 \pm 12.1%

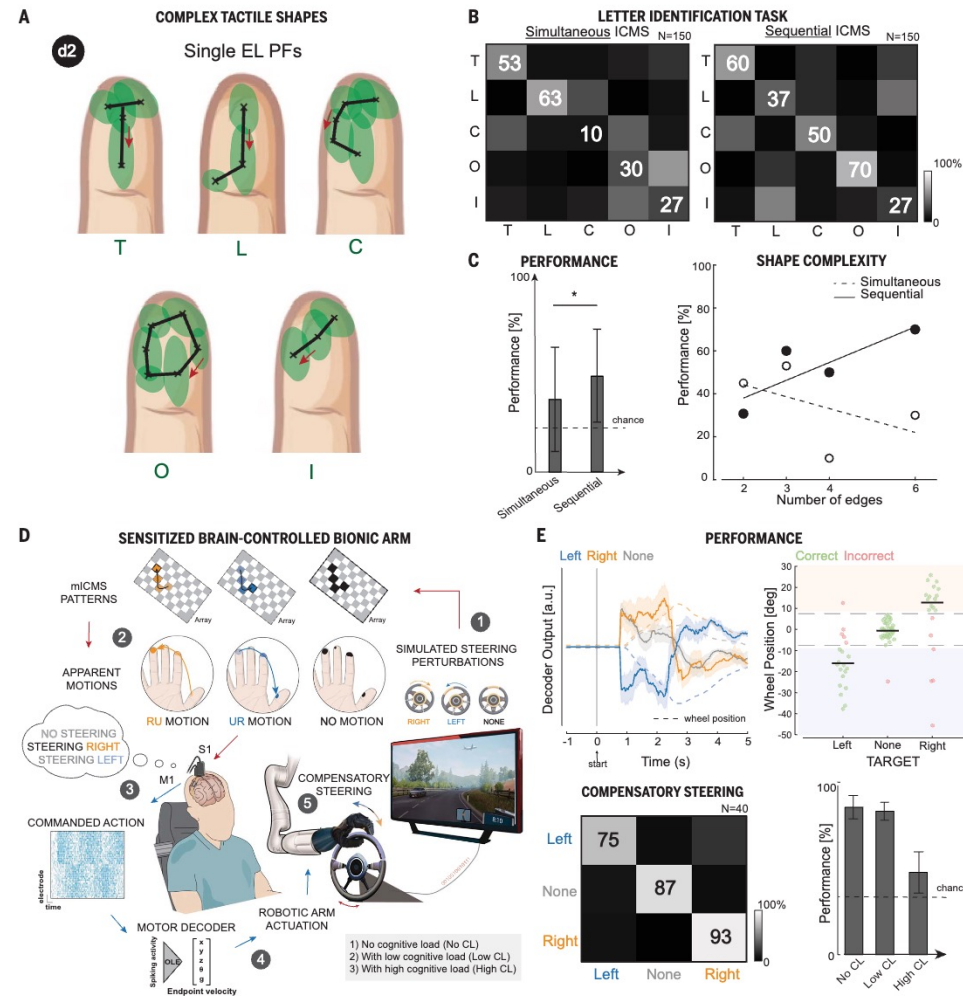
Brain-to-machine-to-brain interface in a quadriplegic subject



Brain-to-machine-to-brain interface in a quadriplegic subject



Brain-to-machine-to-brain interface in a quadriplegic subject



Brain-to-machine-to-brain interface in a quadriplegic subject

