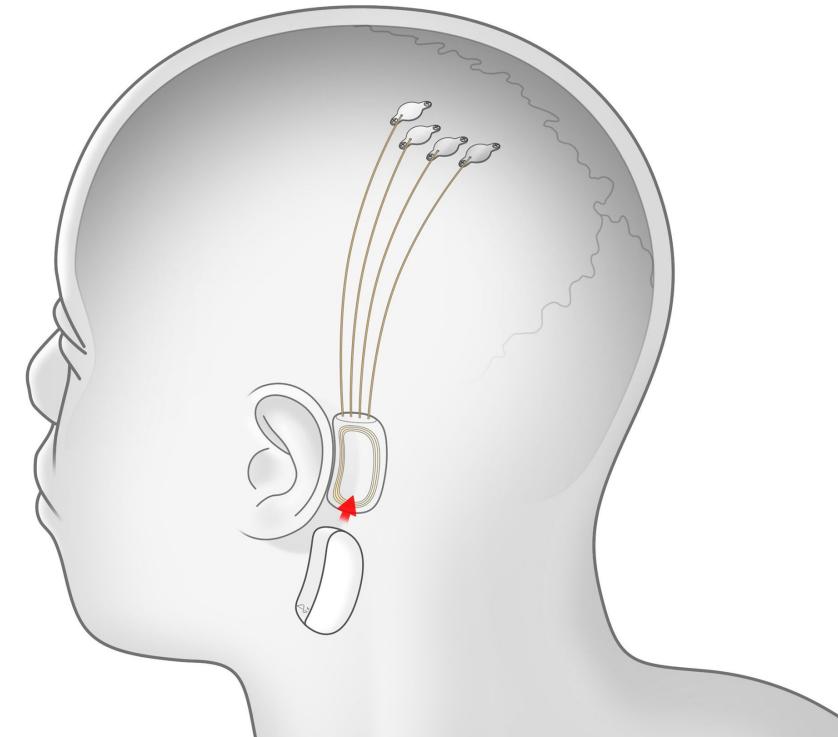


# Implantable and wearable human- machine interfaces

Silvestro Micera



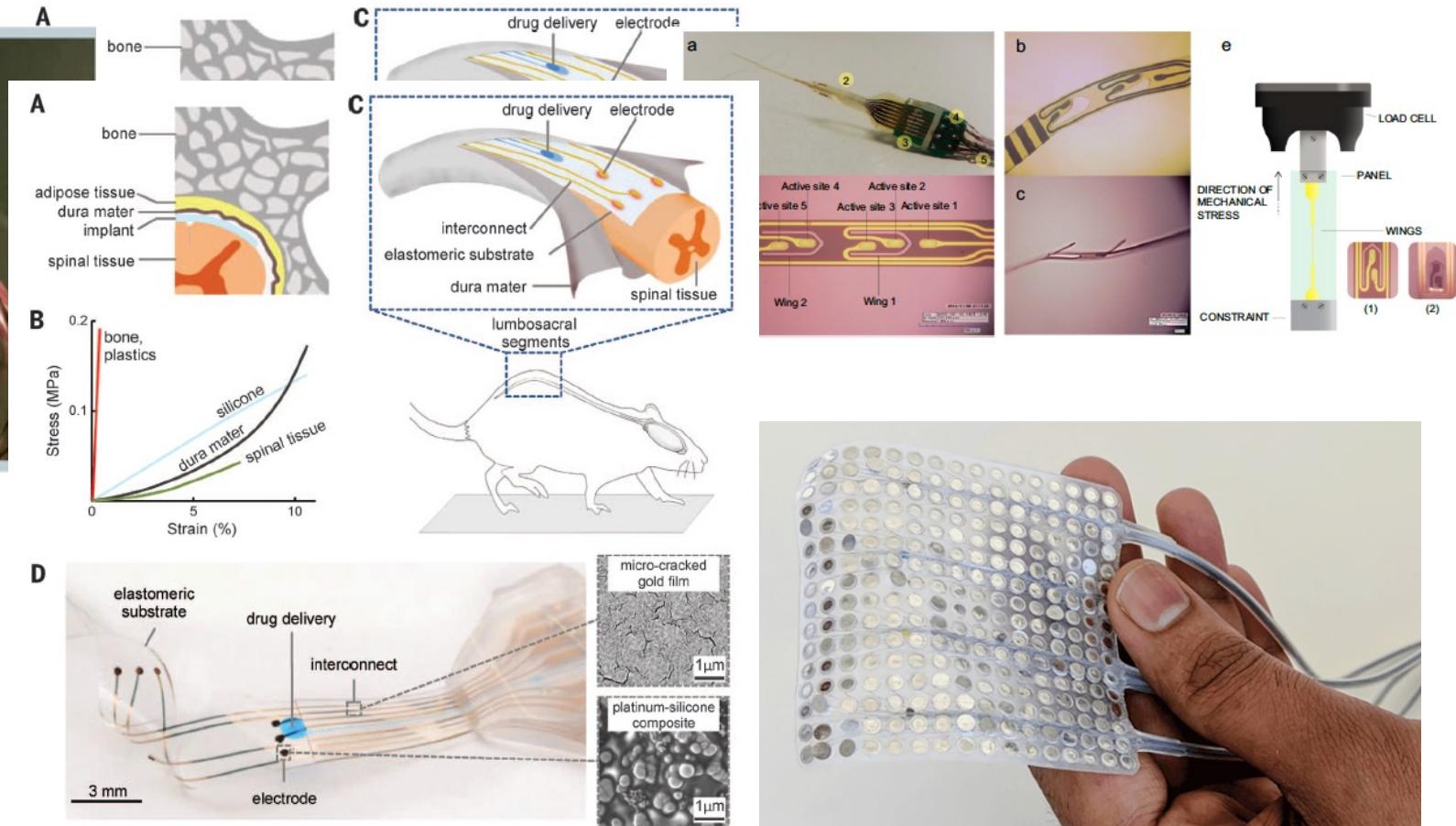
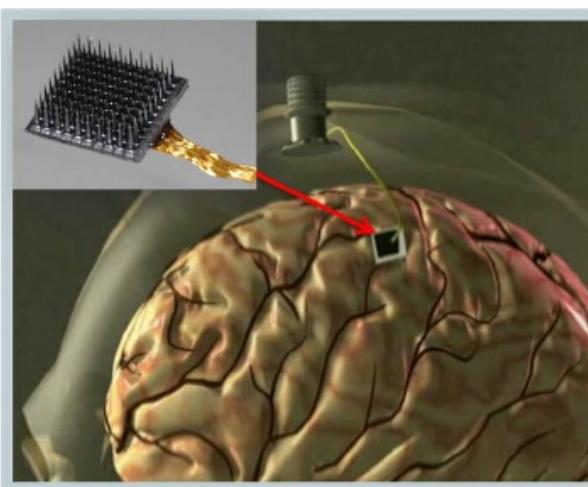
# Neural Engineering

2

- 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).

▪

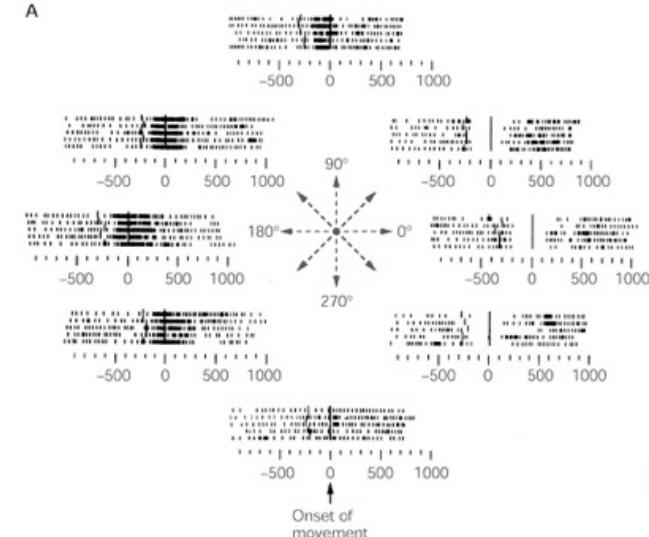
# Central and peripheral interfaces



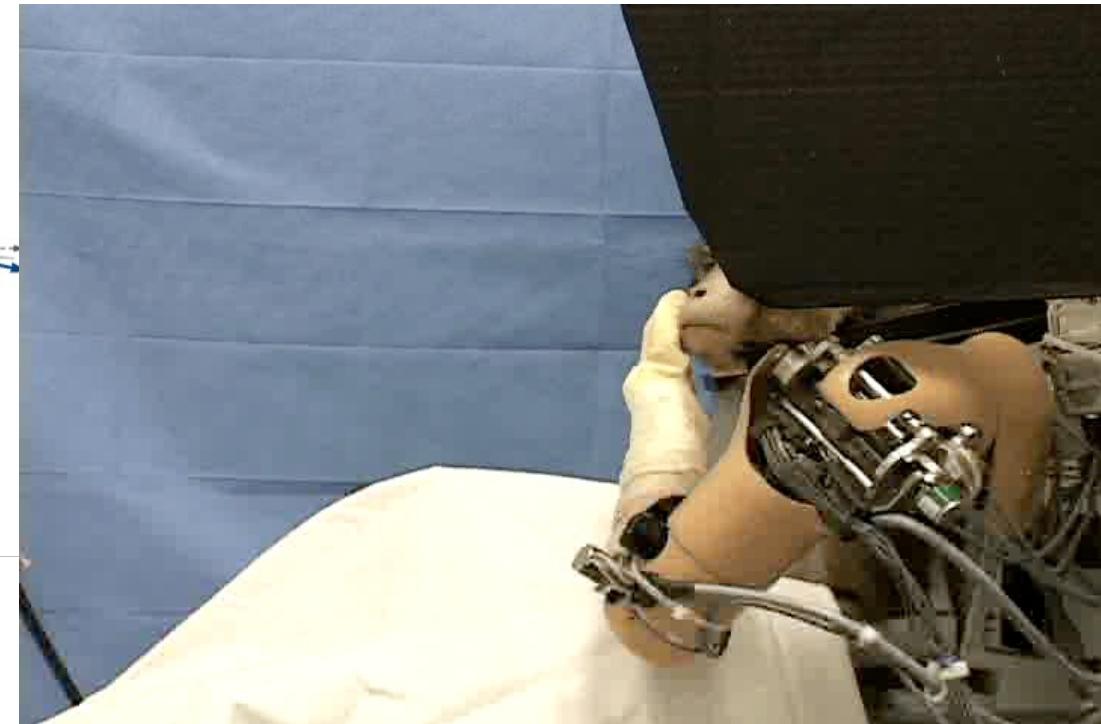
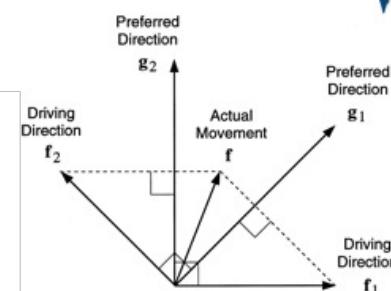
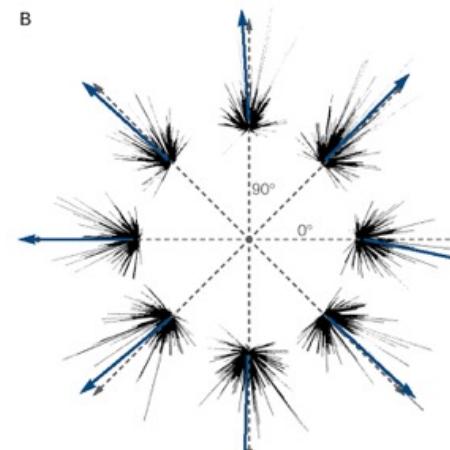
# Motor Neuroprosthetics

## Brain decoding

A



B



# Motor Neuroprosthetics

## Brain decoding

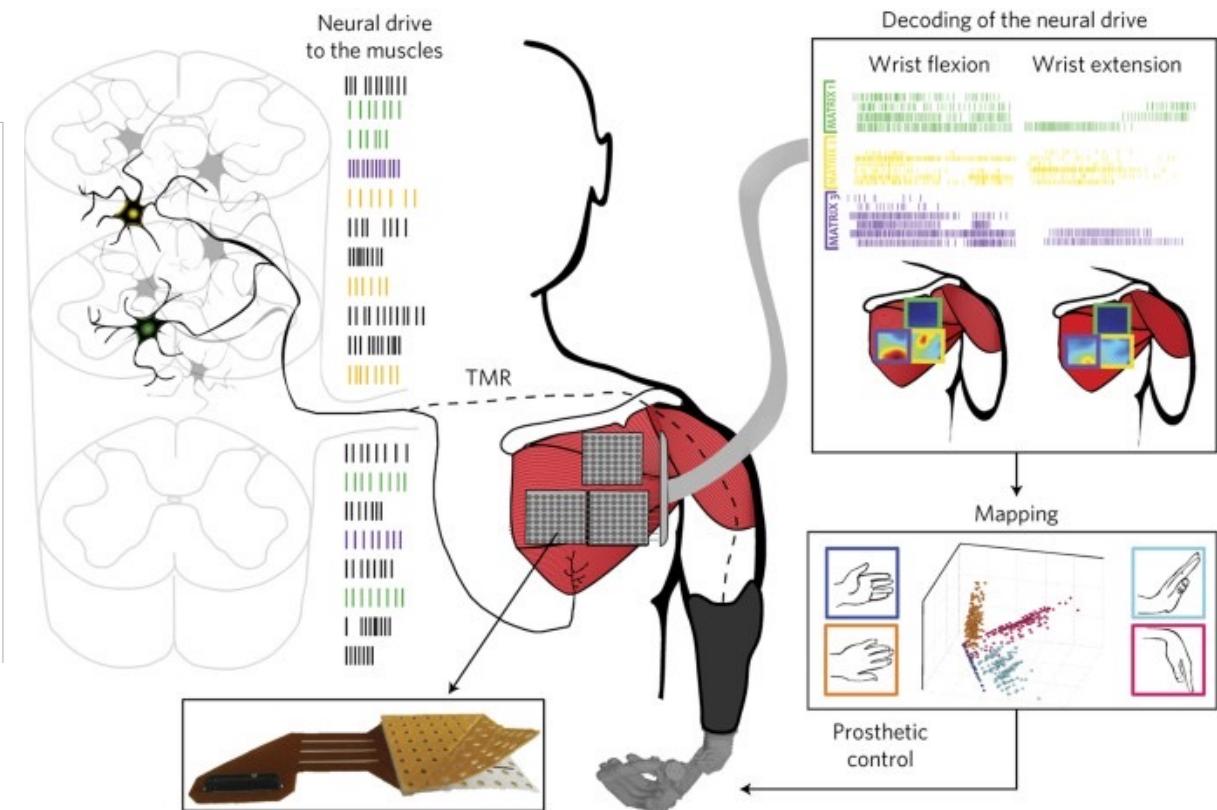
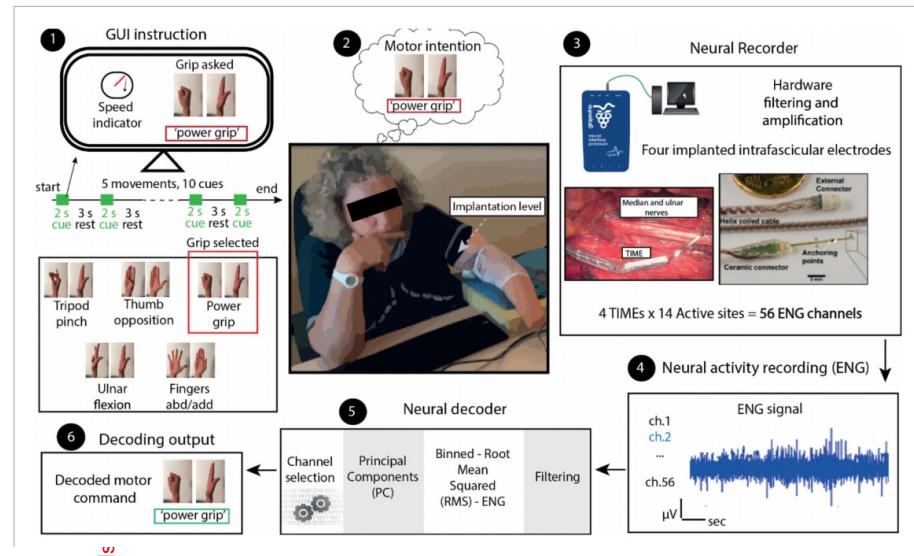
BrainGate Pilot Clinical Trial  
3D + Grasp Control of a Robotic Arm  
Participant S3  
Trial Day 1959 / 12 April 2011  
Hochberg *et al.*, 2012



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

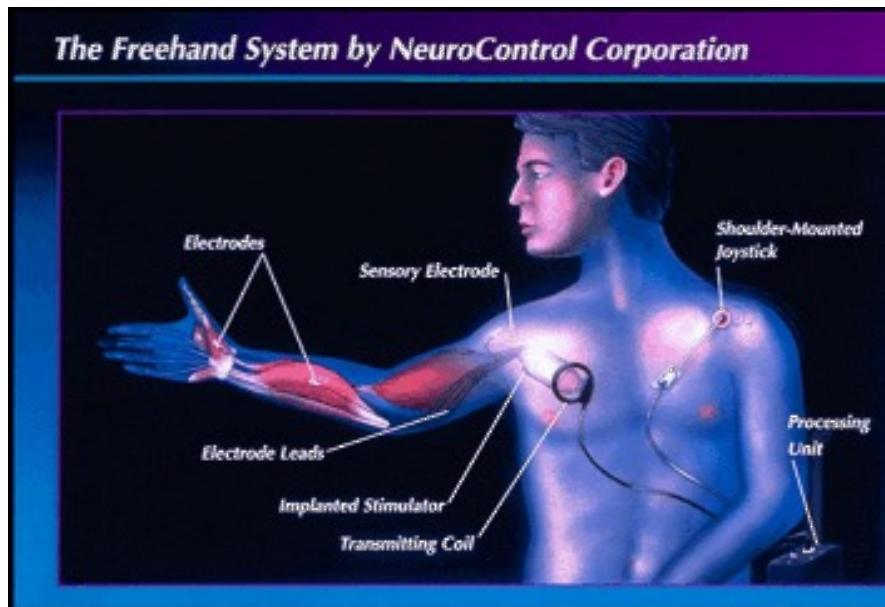
# Motor Neuroprosthetics

## Peripheral decoding

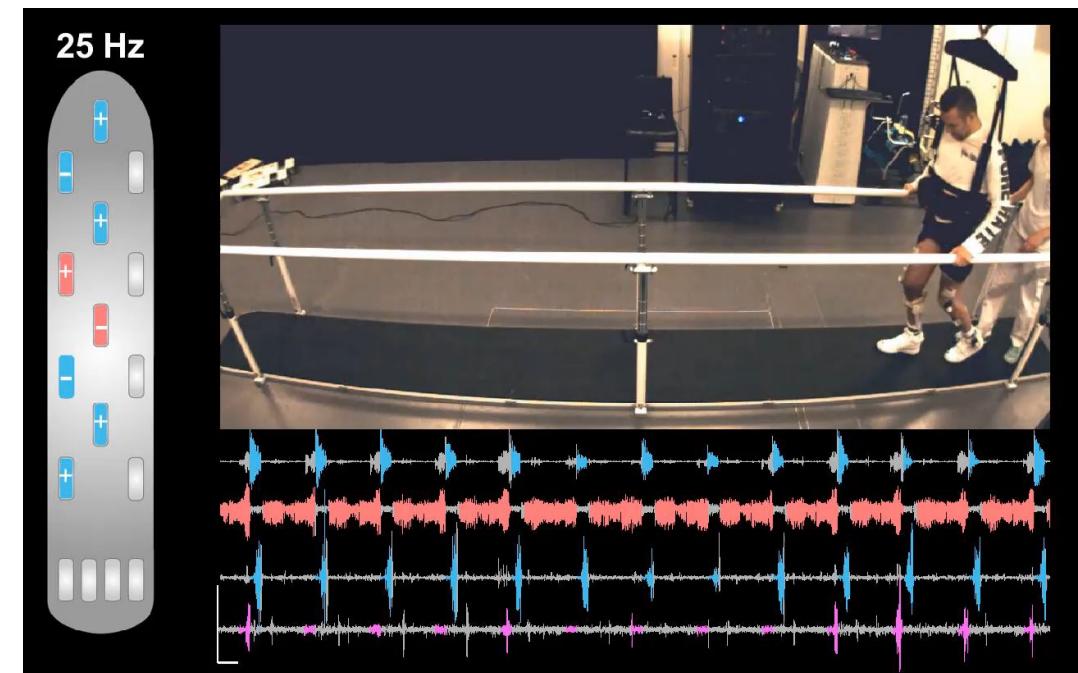
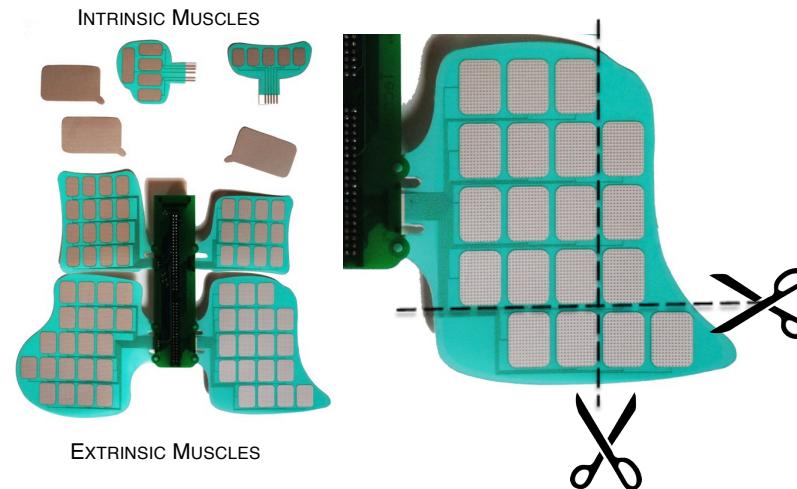


# Electrical stimulation (actuation)

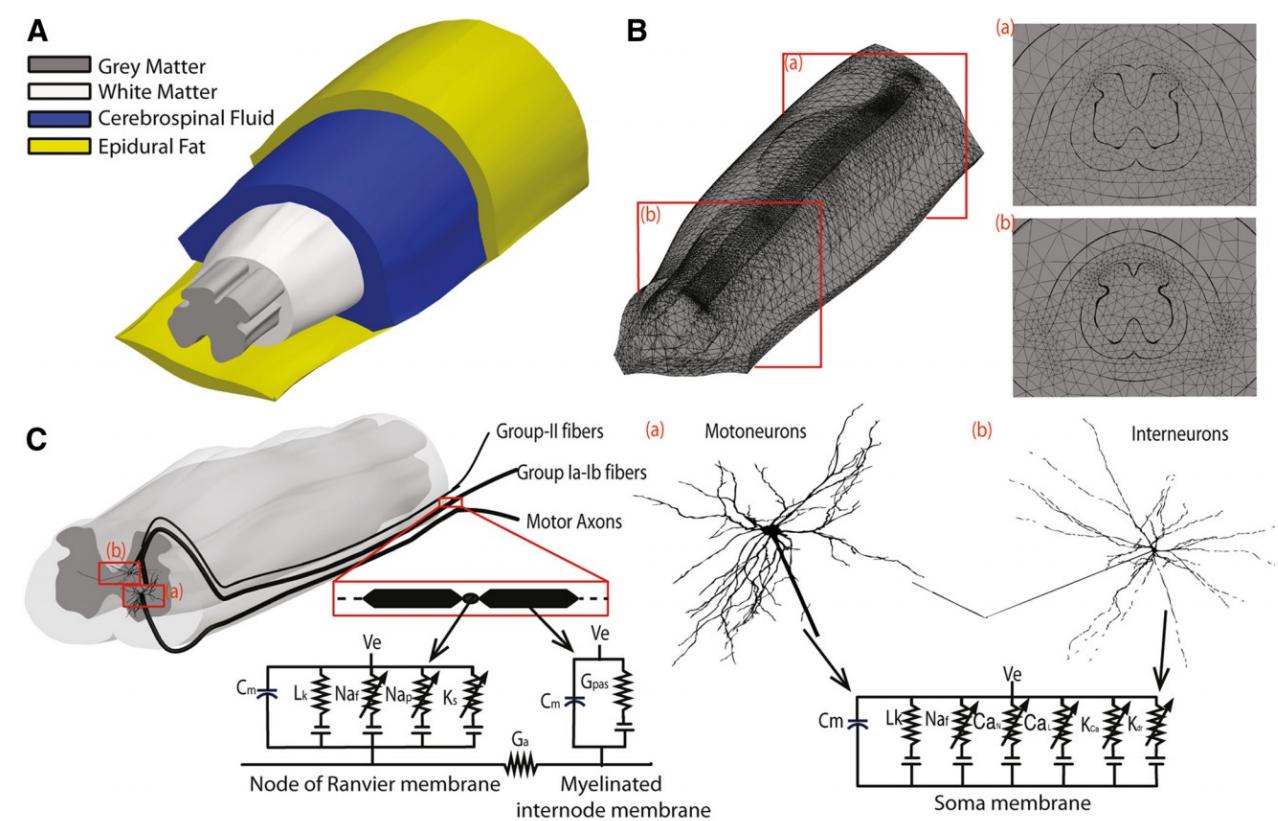
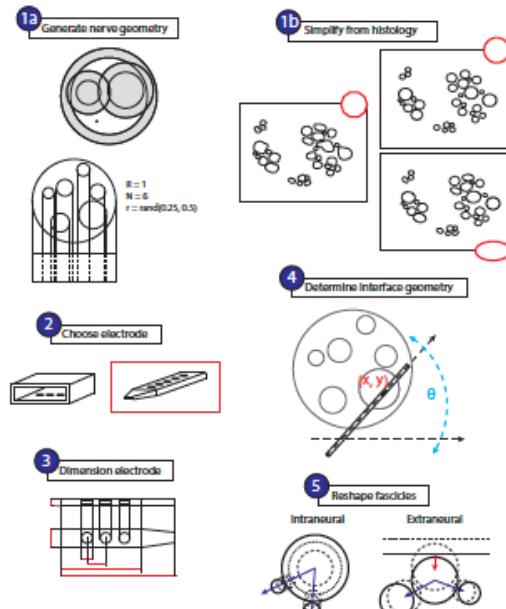
*The Freehand System by NeuroControl Corporation*



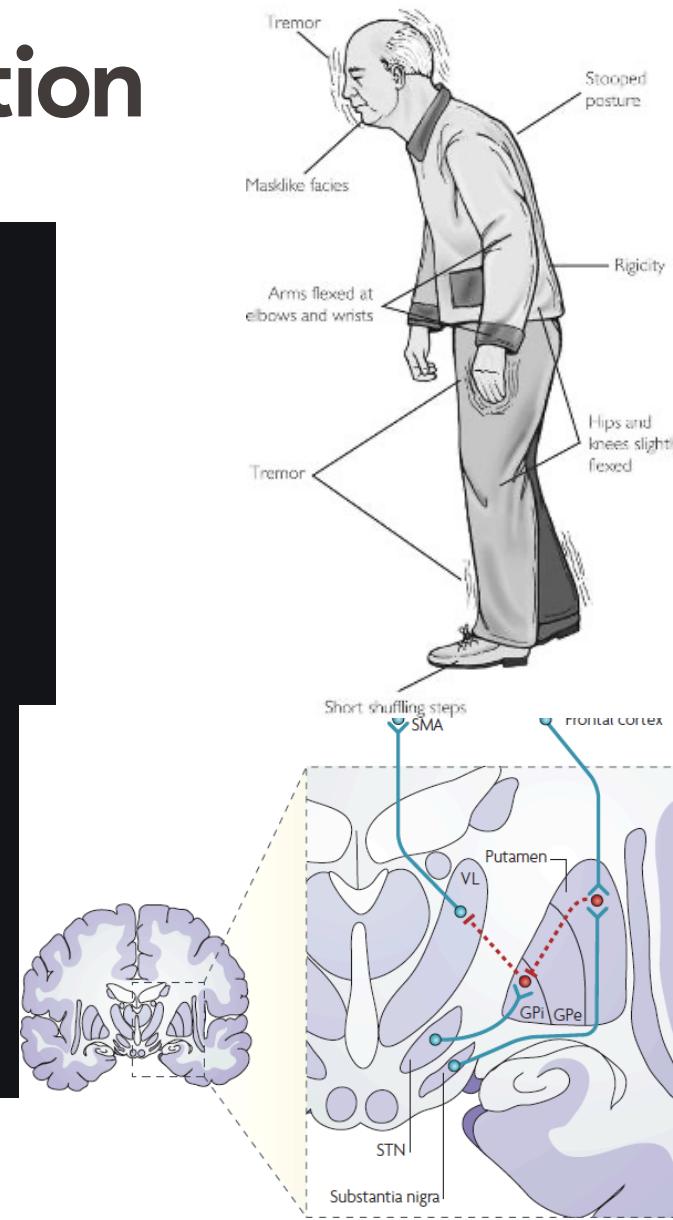
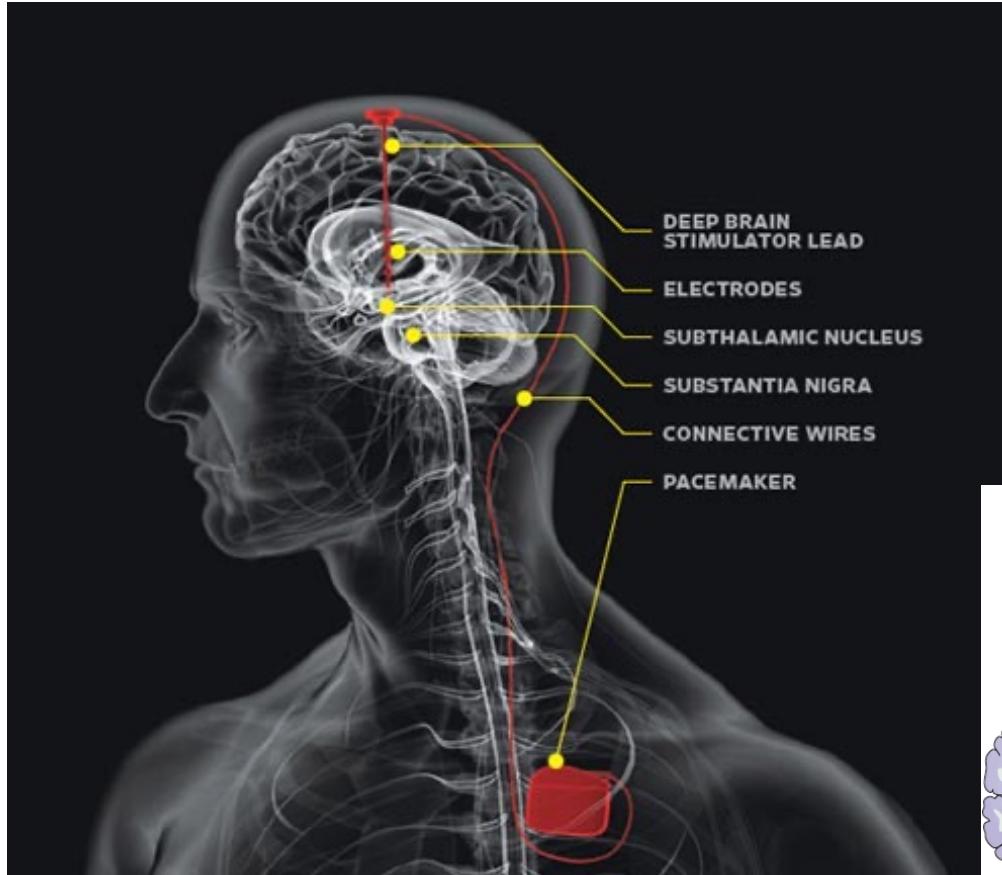
■ Fundamentals of neuroengineering



# Computational models

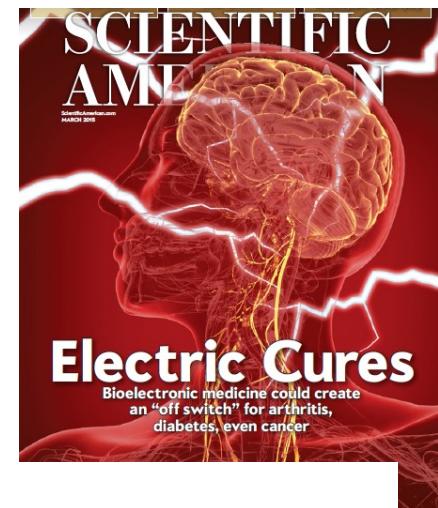
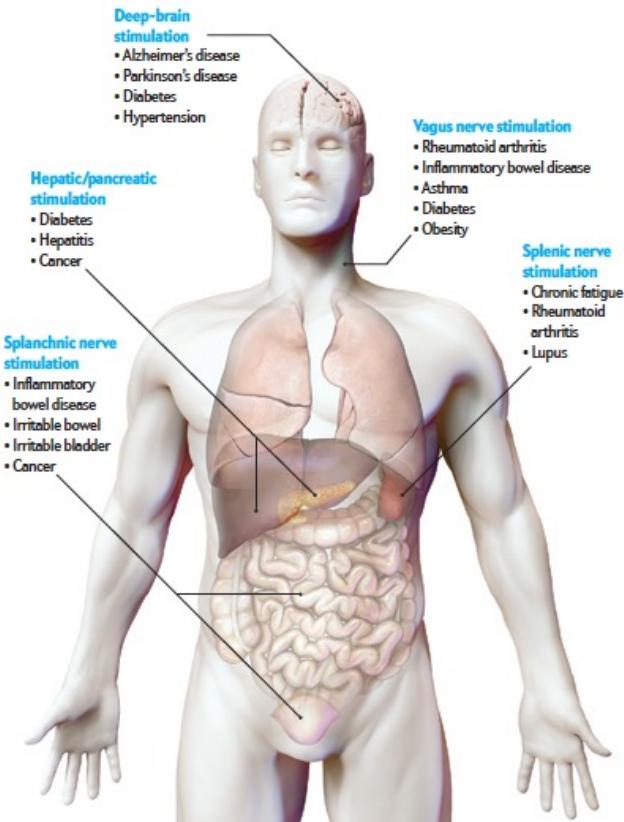


# Deep Brain Stimulation



- 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

■ Fundamentals of neuroengineering

**A** High-sensitivity & low-hysteresis sensor array

Soft substrate

**B**

20  $\mu\text{m}$

10  $\mu\text{m}$

**C**

Artery pulse

Multichannel electrode

PWV recording on a single patch

PTT

**D**

High-density electrode array

**E**

Texture detection

Neural network

Texture recognition

General touch on texture

# 1

# 2

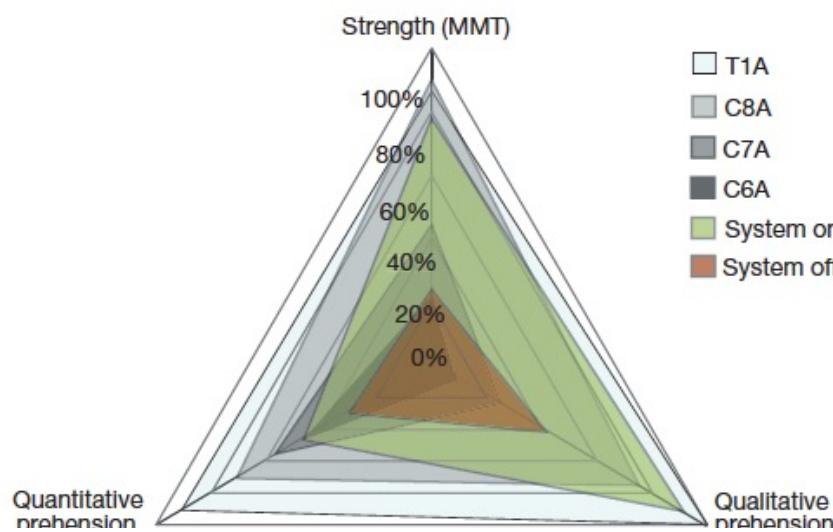
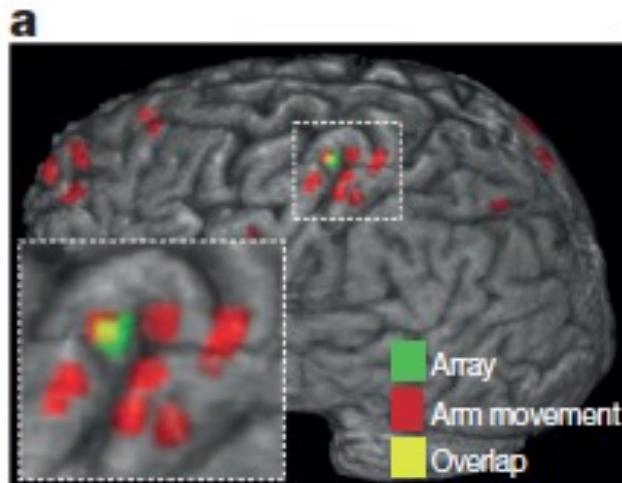
# 3

# 4

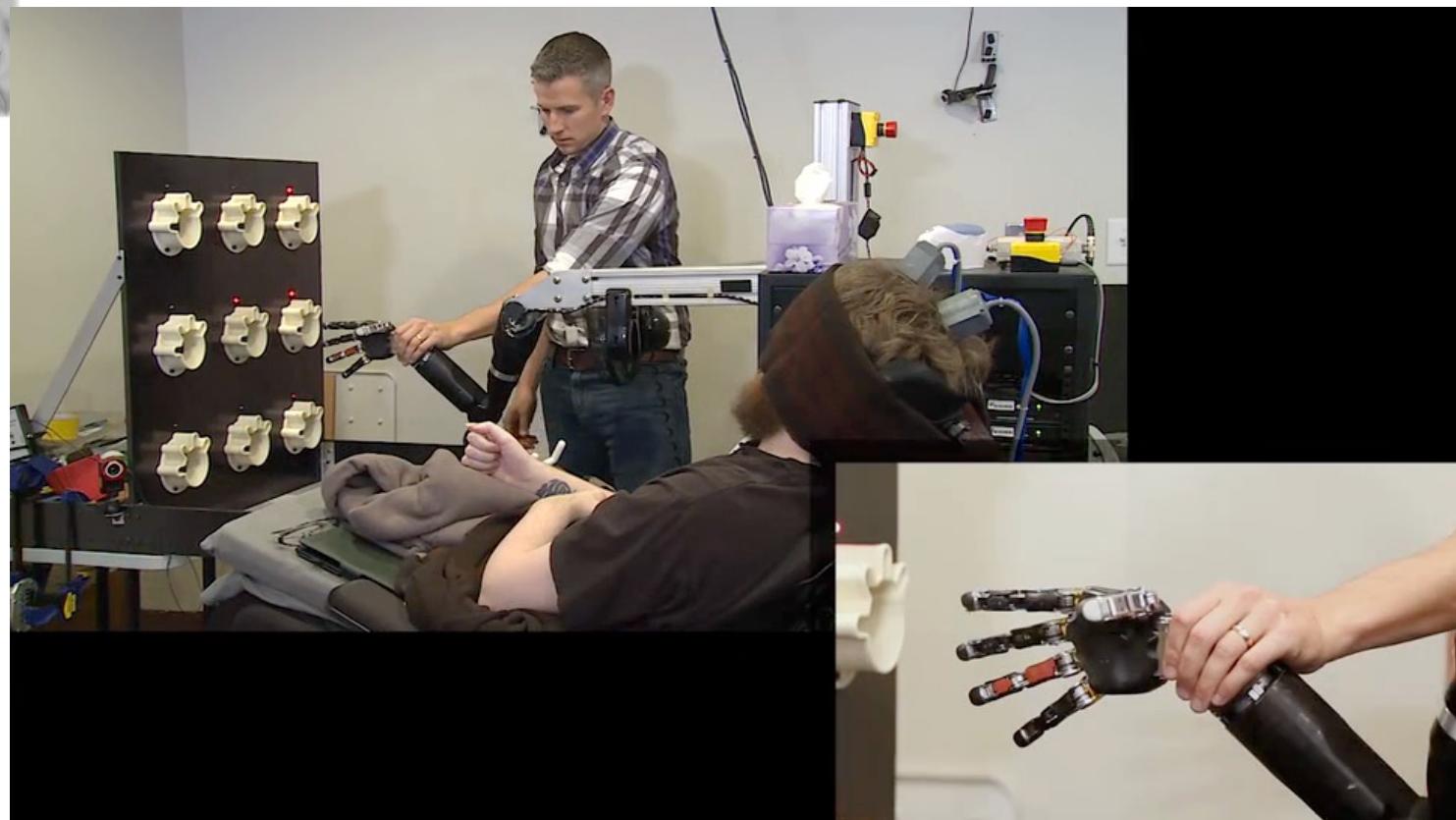
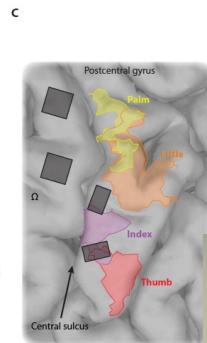
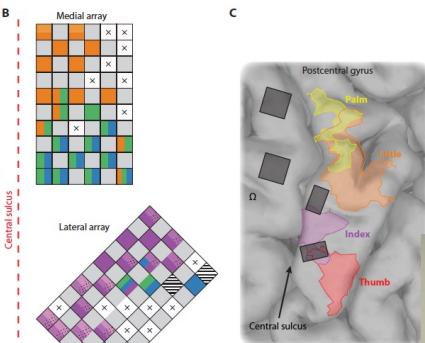
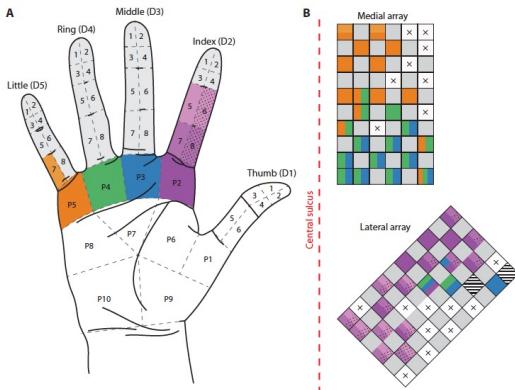
# 5



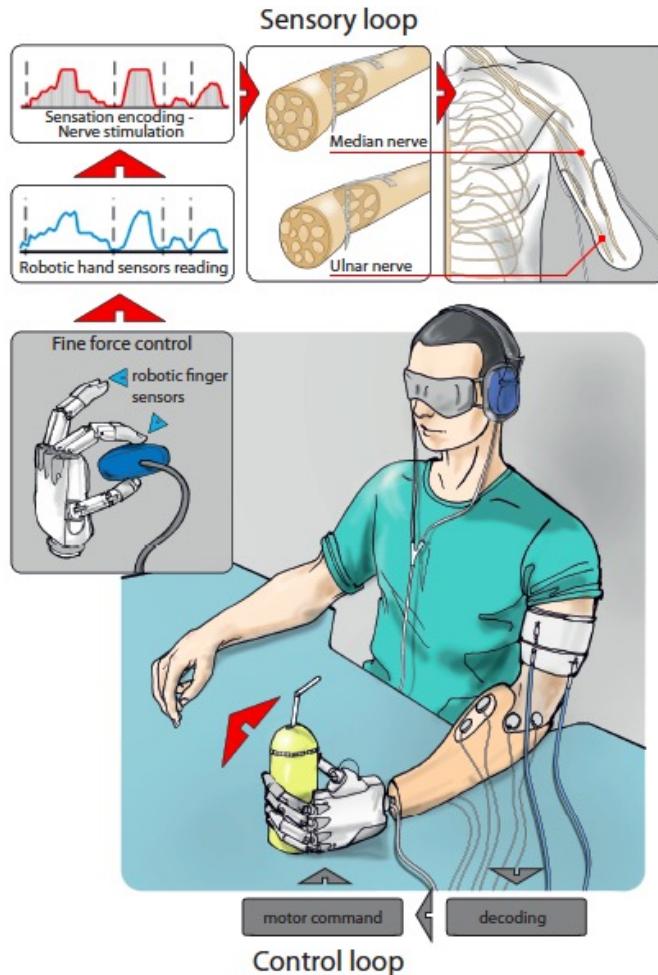
# BMI-based neurorehabilitation



# Sensory feedback



# Sensory feedback

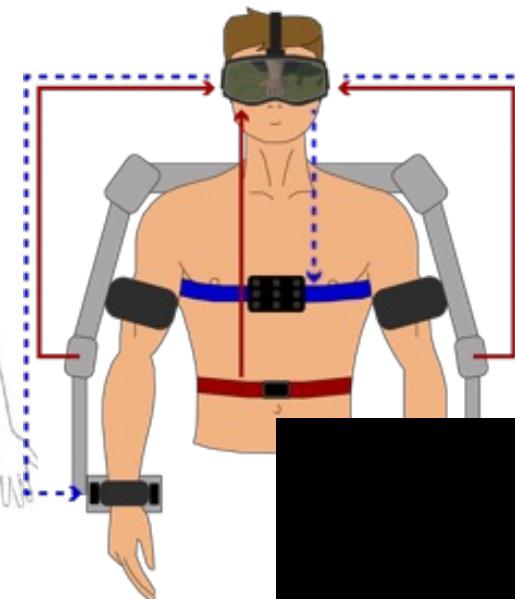
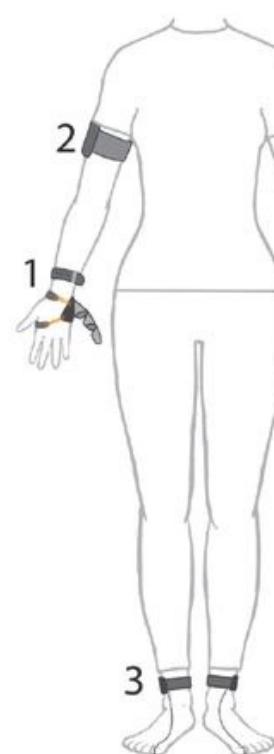


# Human augmentation

A



B



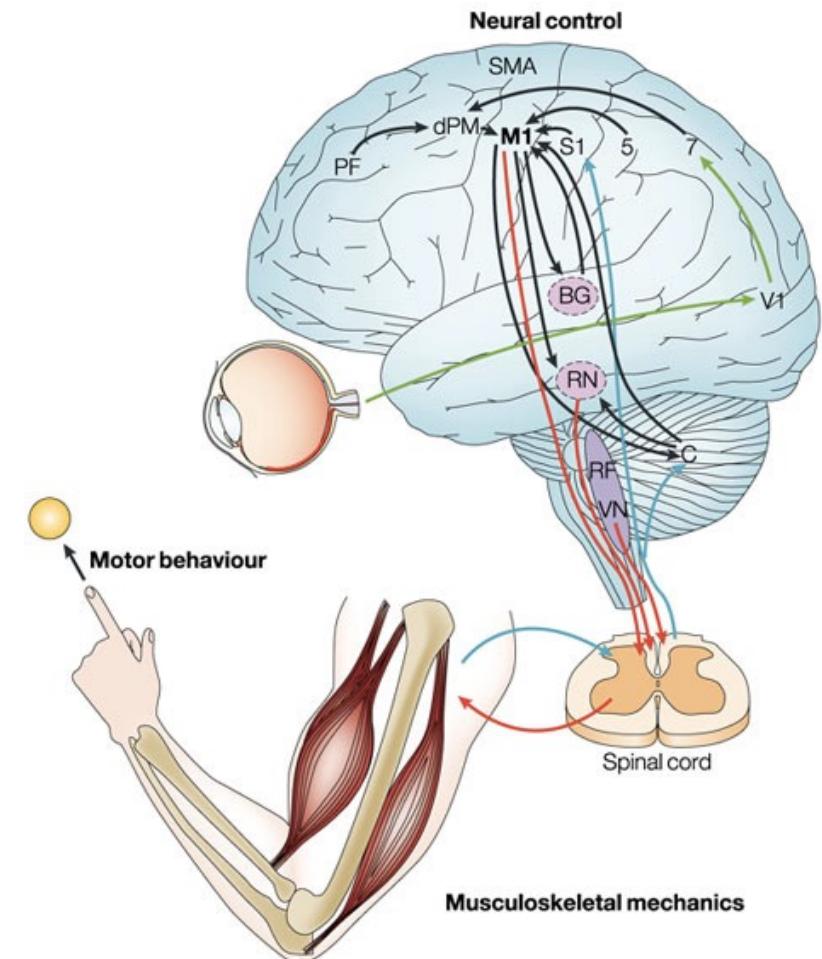
REACHING TASK

# How to design a sensory-motor neuroprosthesis?

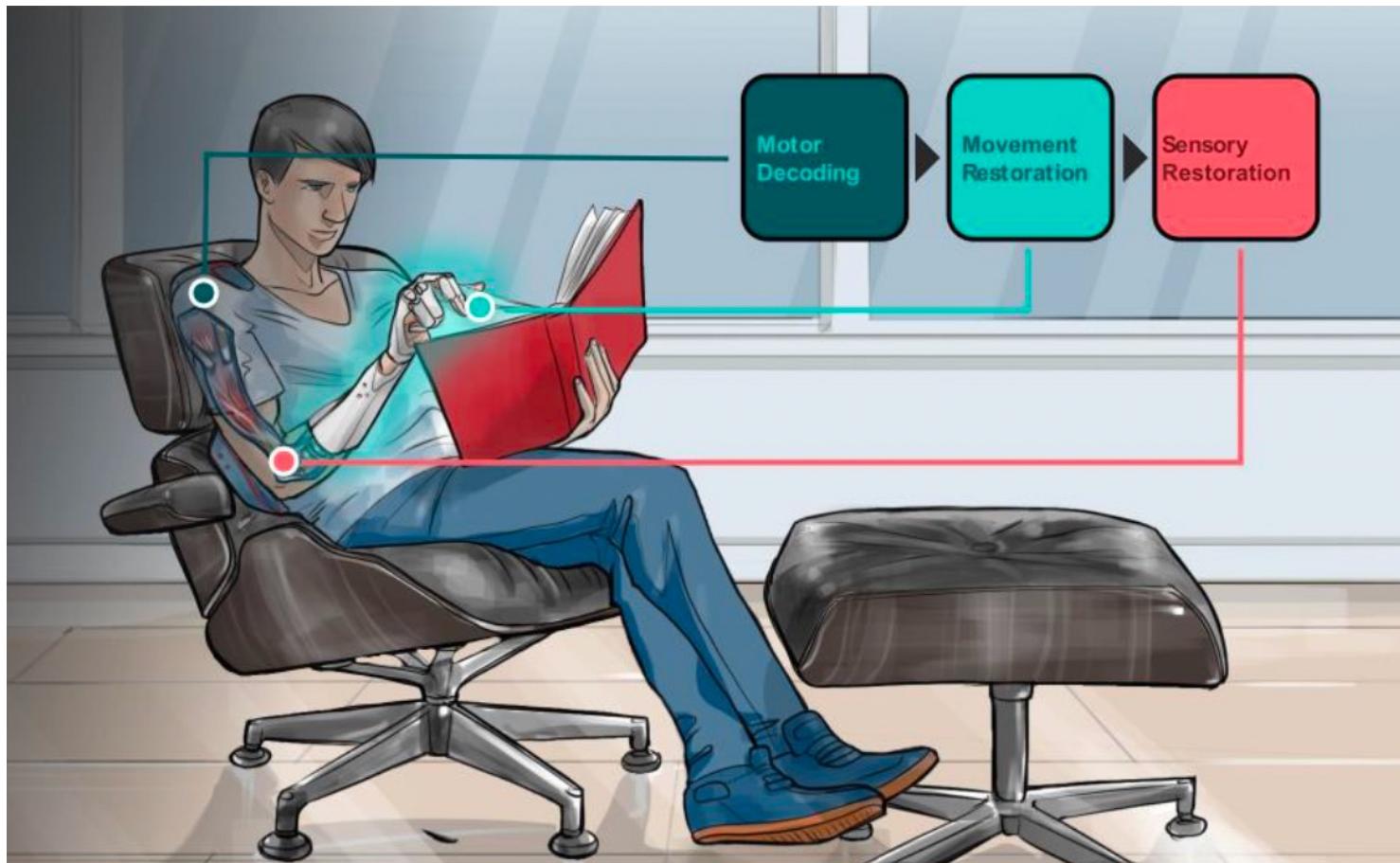
- Start from natural neural control of movement
- Try to replicate it



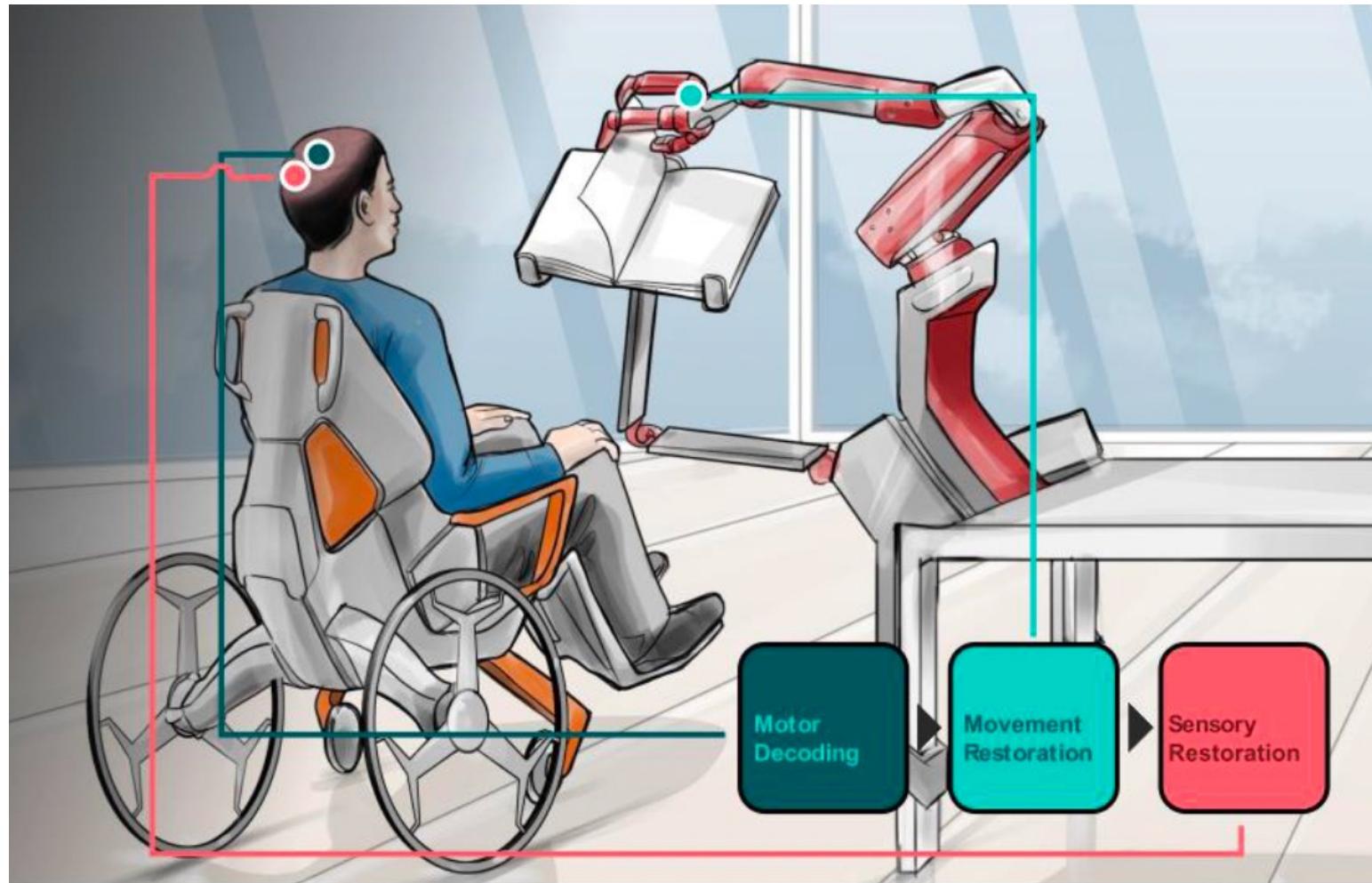
■ Fundamentals of neu



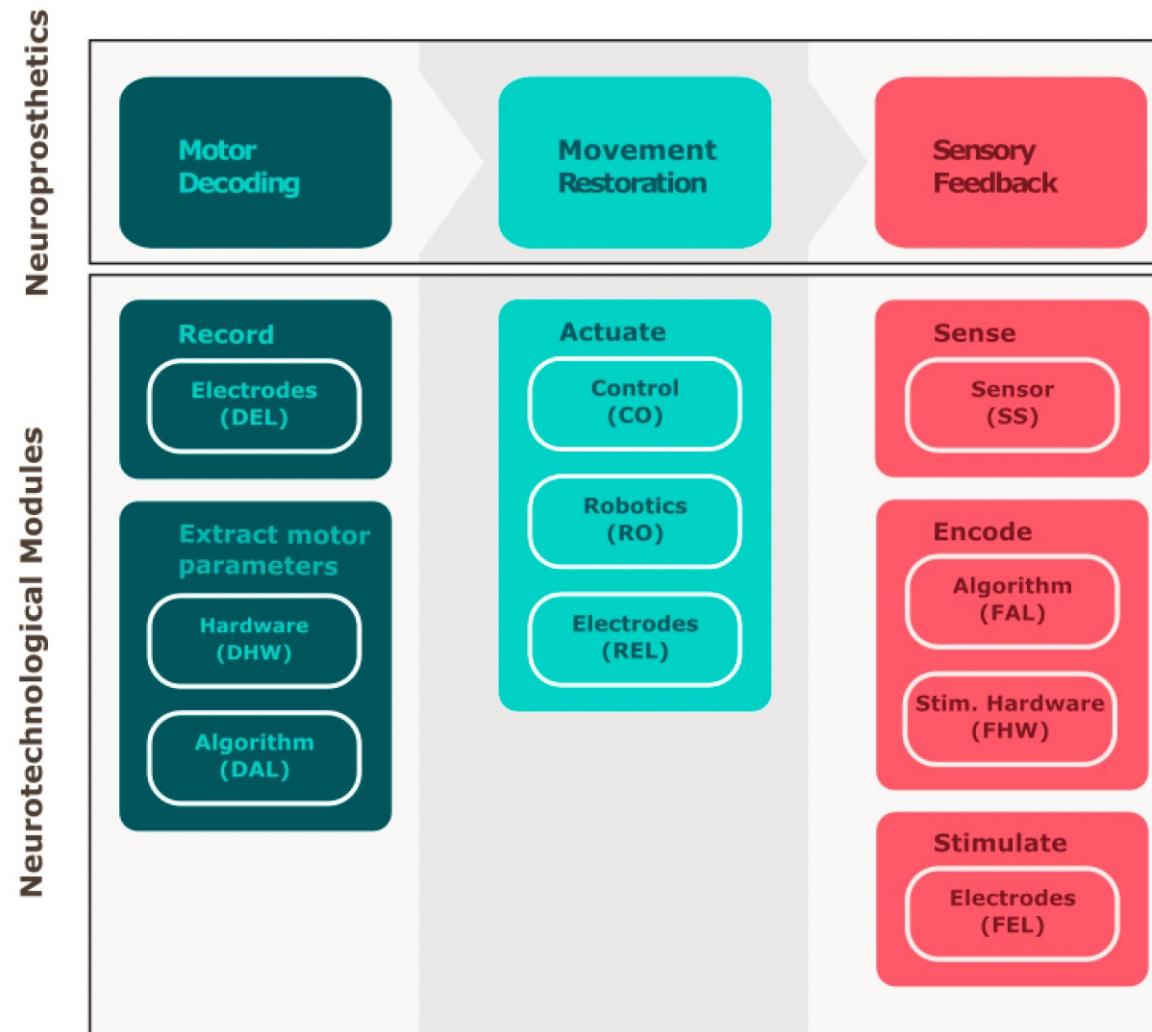
# How to design a sensory-motor neuroprosthesis?



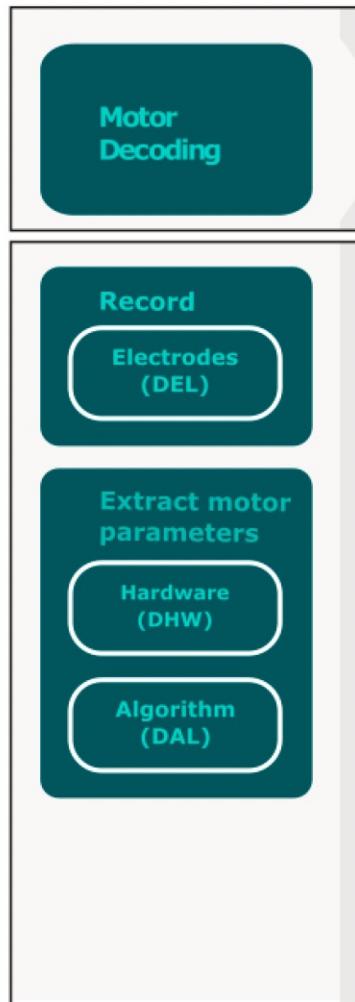
# How to design a sensory-motor neuroprosthesis?



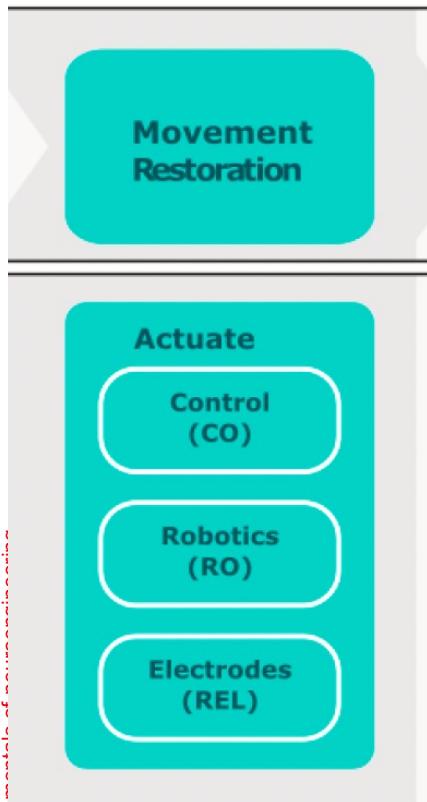
# Neurotechnology modules



# Motor decoding



# Movement restoration



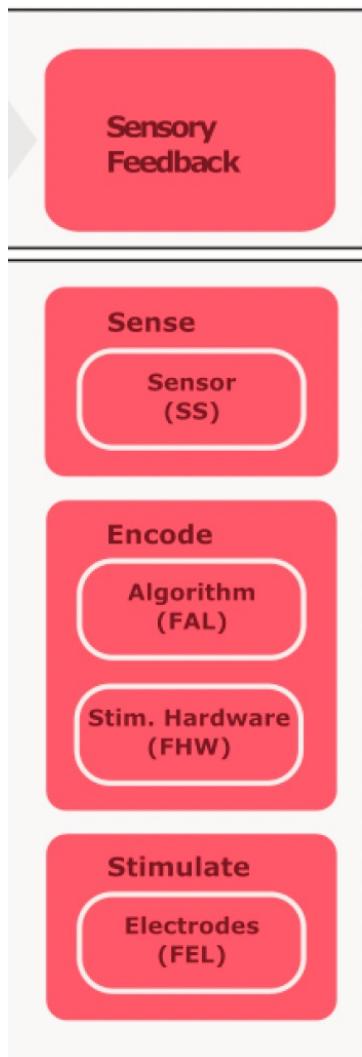
Restore specific movements impaired by neurological disorders or traumatic injuries

Use the motor intention detected to control the different actuation systems

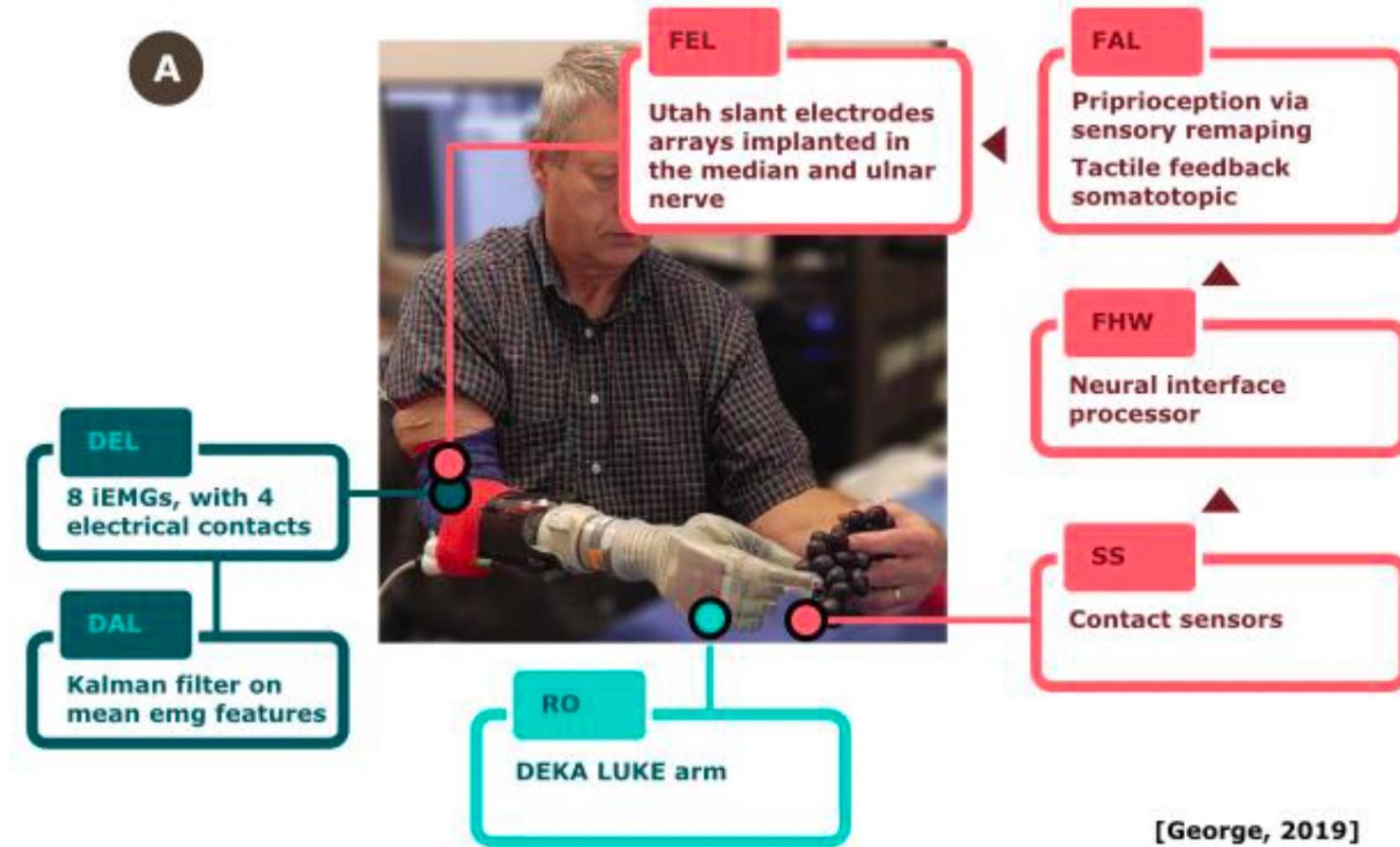
Restore movements using robotic systems

Restore movements using electrical stimulation (muscle activation)

# Sensory feedback

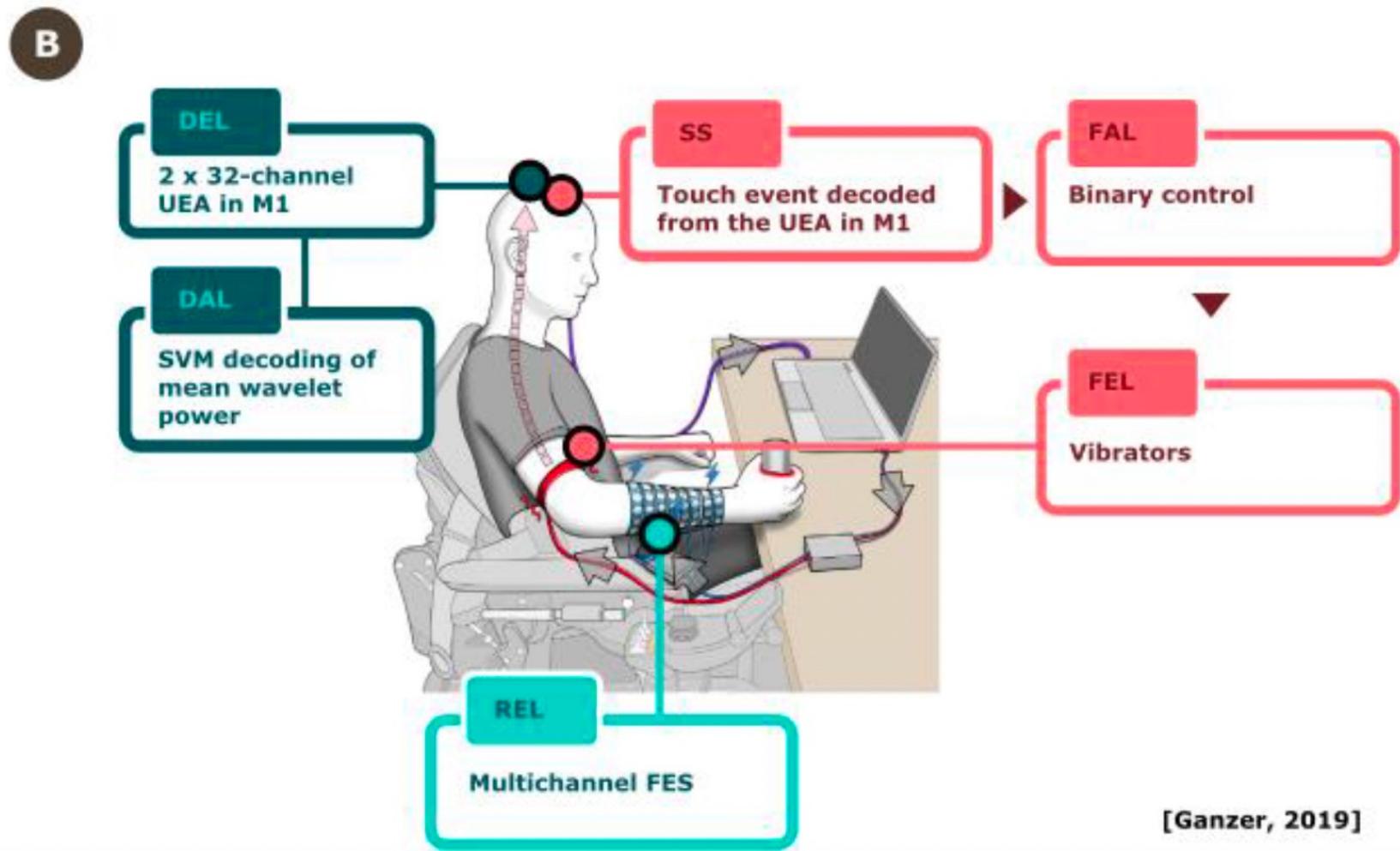


# Examples of Neuroprostheses



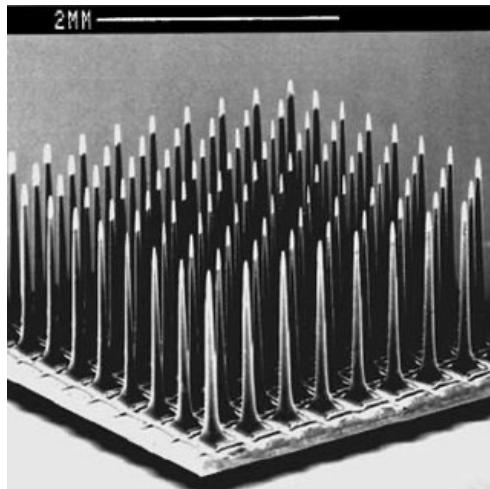
[George, 2019]

# Examples of Neuroprostheses



# Reusing (DEL-FEL)

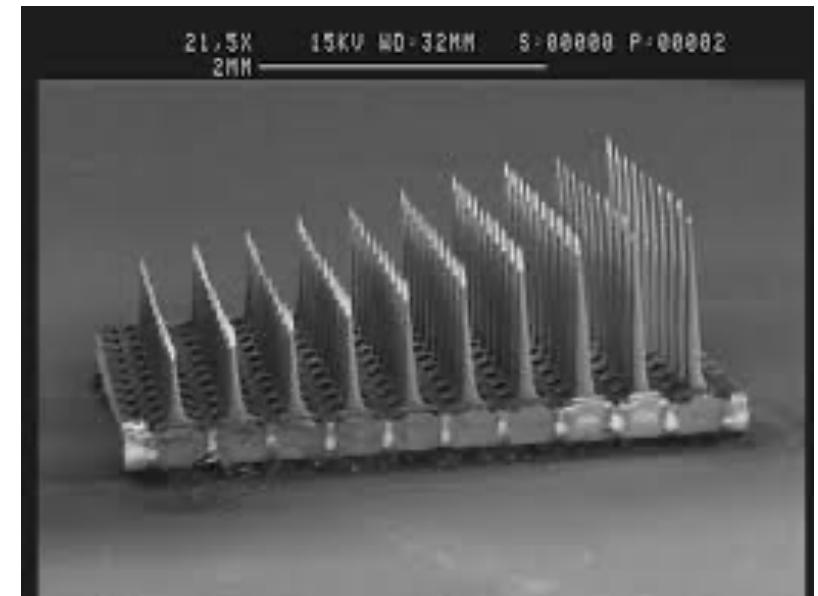
## Utah Array



Motor (cortical) decoding

Sensory (cortical) feedback

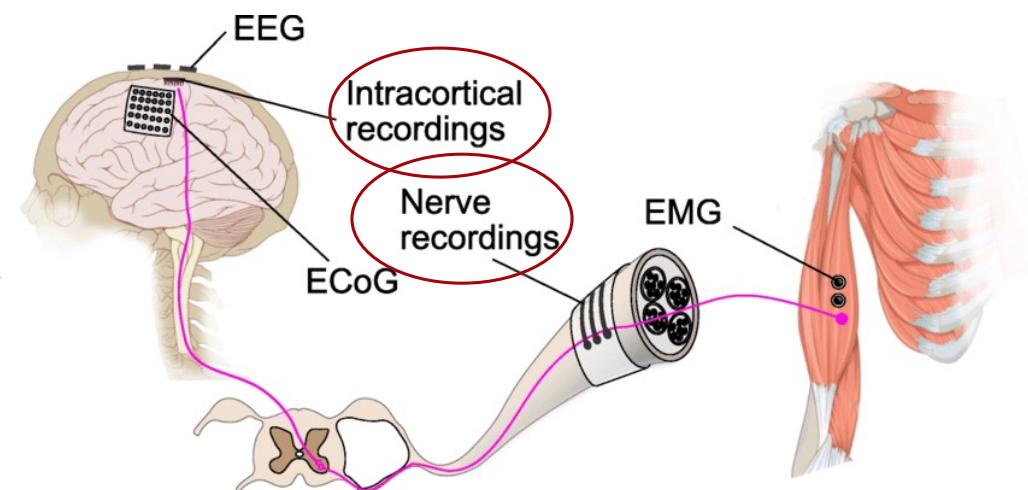
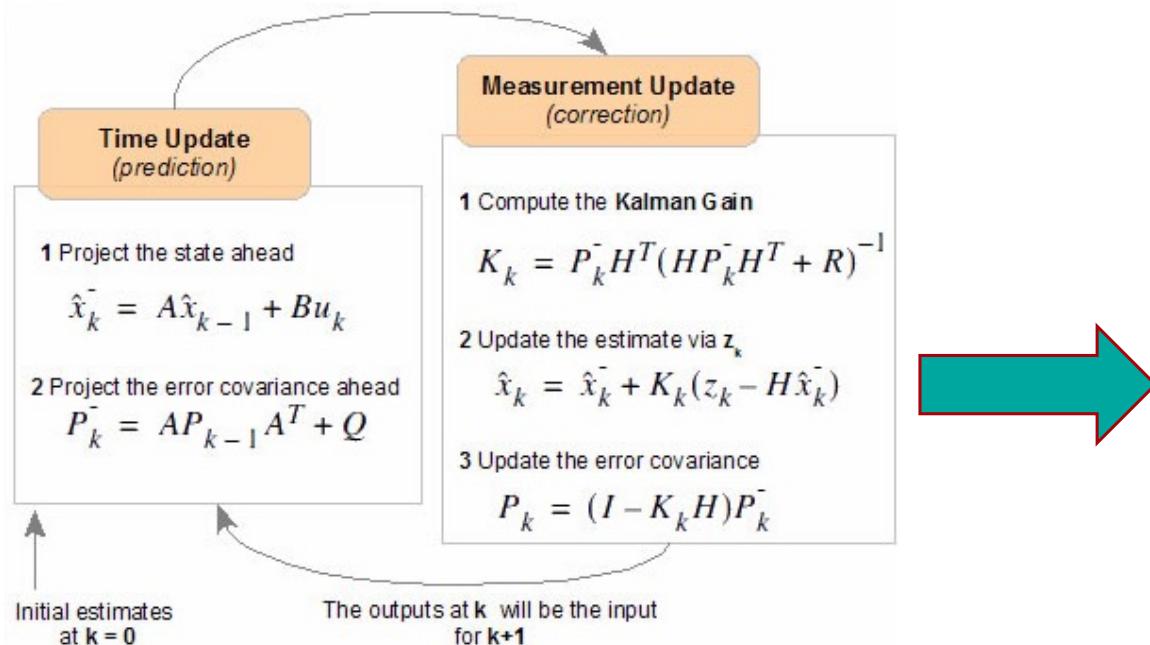
## SLANTED Utah Array



Motor (peripheral) decoding

Sensory (peripheral) feedback

# Reusing (DAL)



**Decoding motor commands from cortical and peripheral signals**

# Bionic artificial hand



# 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

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

31% Transradial

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

14% Partial hand

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

5% Fingers

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?**

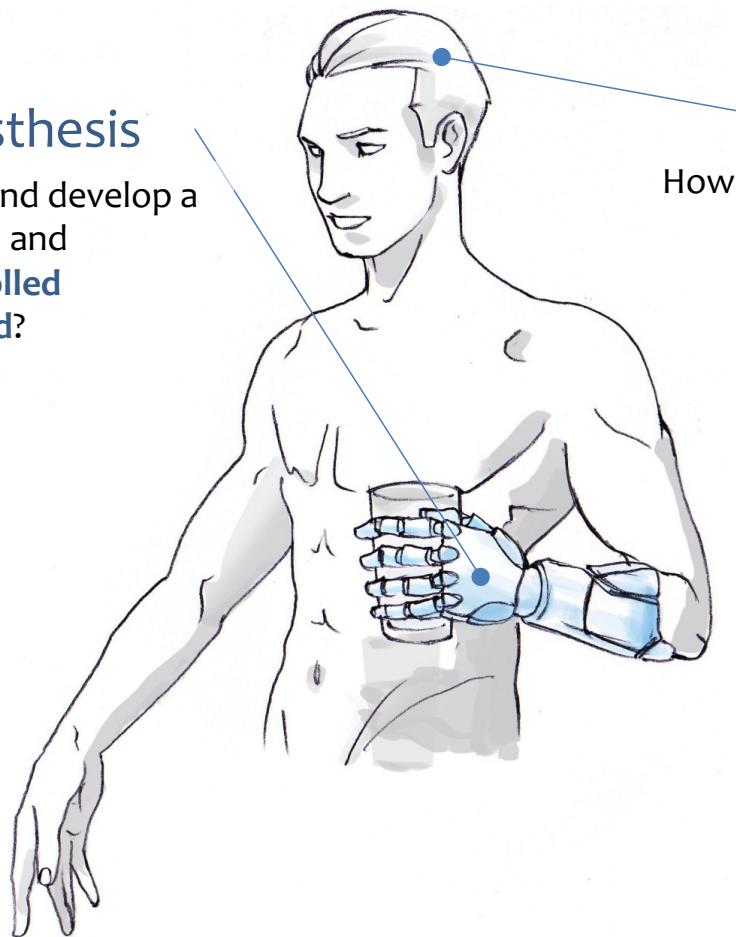
*Dexterity*

Functionality

Reliability

...

...



## UP Interface

How to **control** this dexterity?

Sources

Cognitive Effort

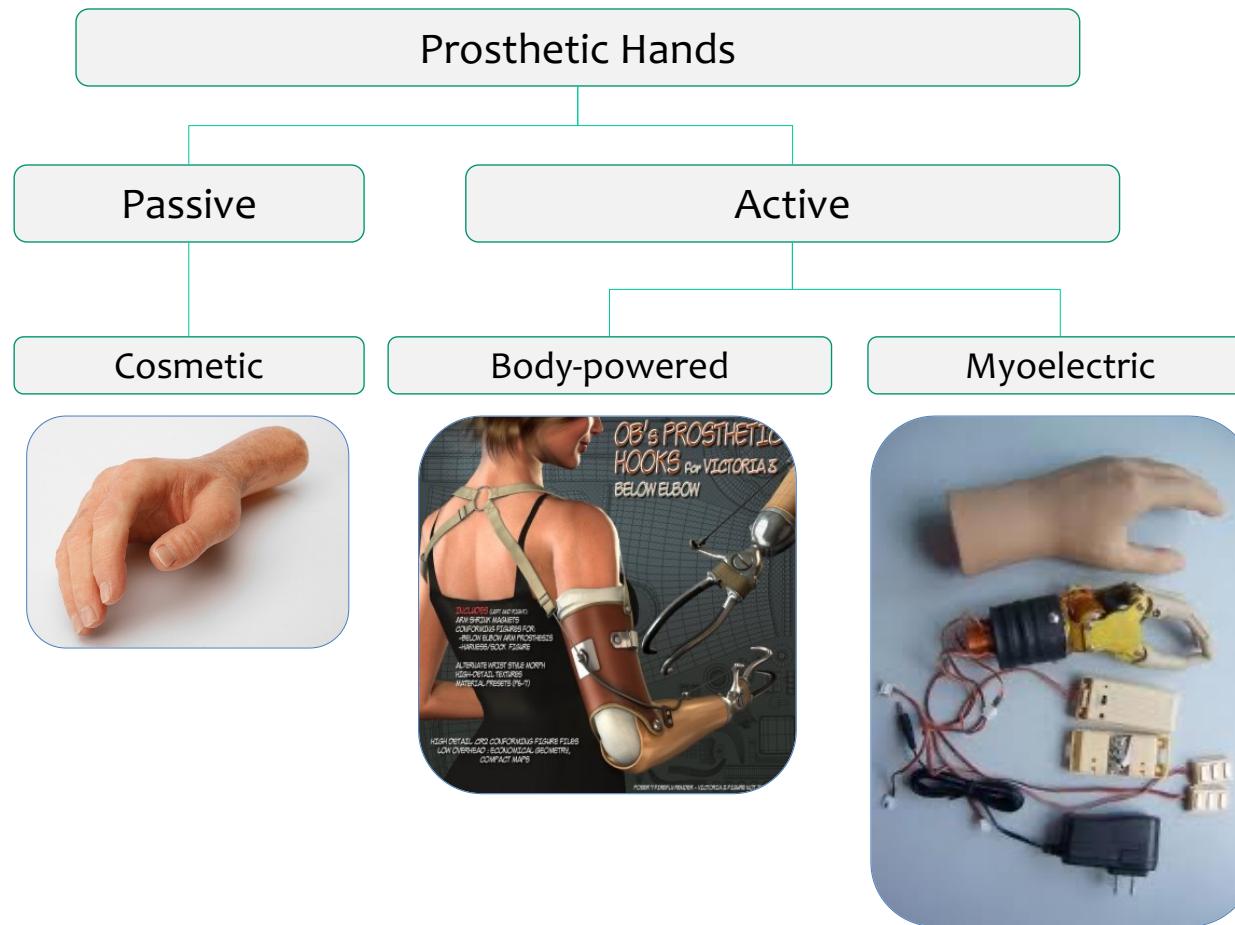
Reliability

...

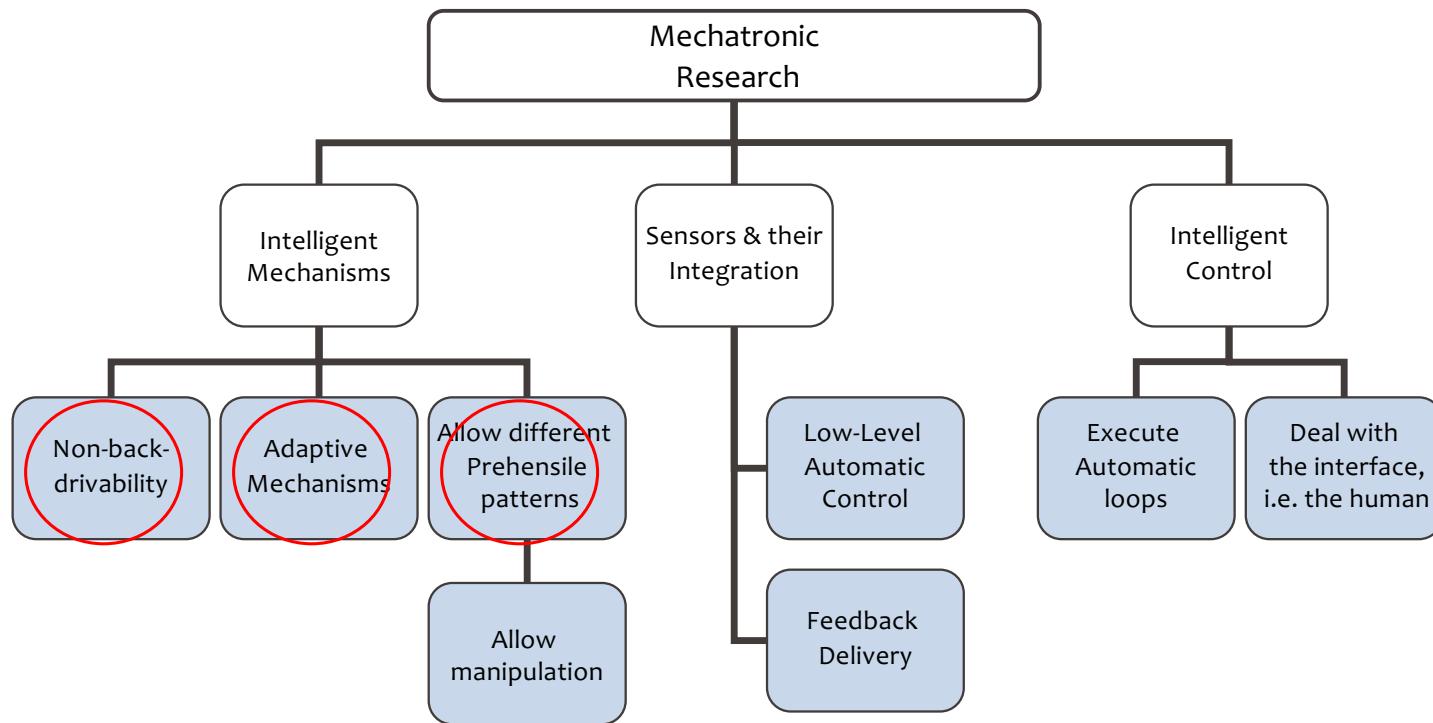
...

# What can an amputee get today?

## Hand Prostheses



# Key issues

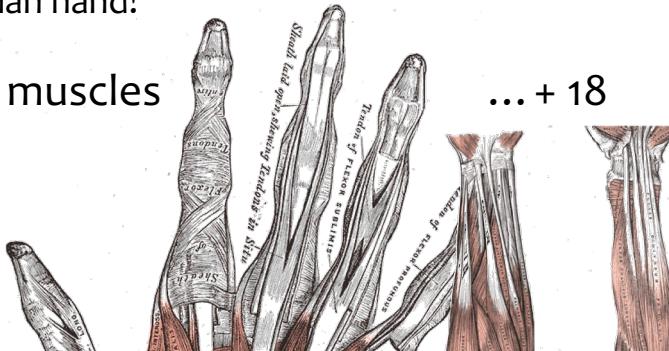


# Mechatronic

## Design issues: adaptability

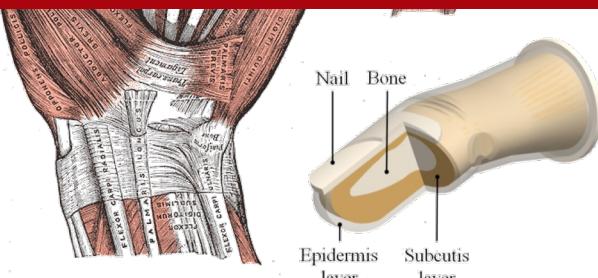
**Problem:** It's an hard task to **design, actuate, and control** a self-contained artificial hand with a number of degrees of freedom (DoF) equal or close to those in the biological human hand!

22 muscles



... + 18

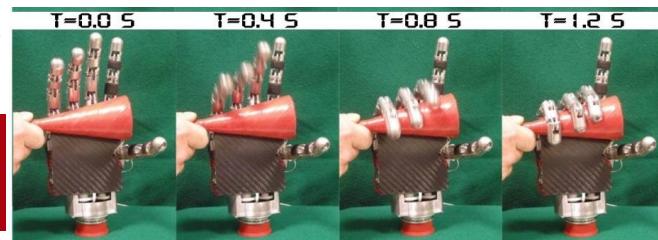
Adaptation also improves **grasp stability** as it increases the **contact areas** while grasping



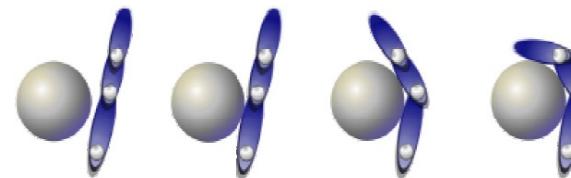
Phalanx adaptation mechanisms

Possible solutions (to simplify the problem):

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



Hand adaptation mechanisms



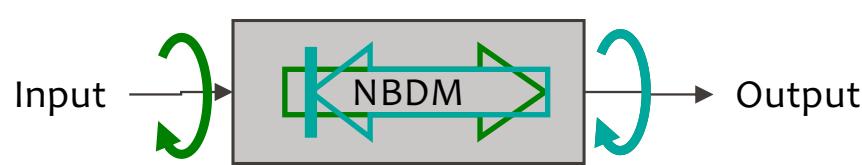
Finger adaptation mechanisms

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

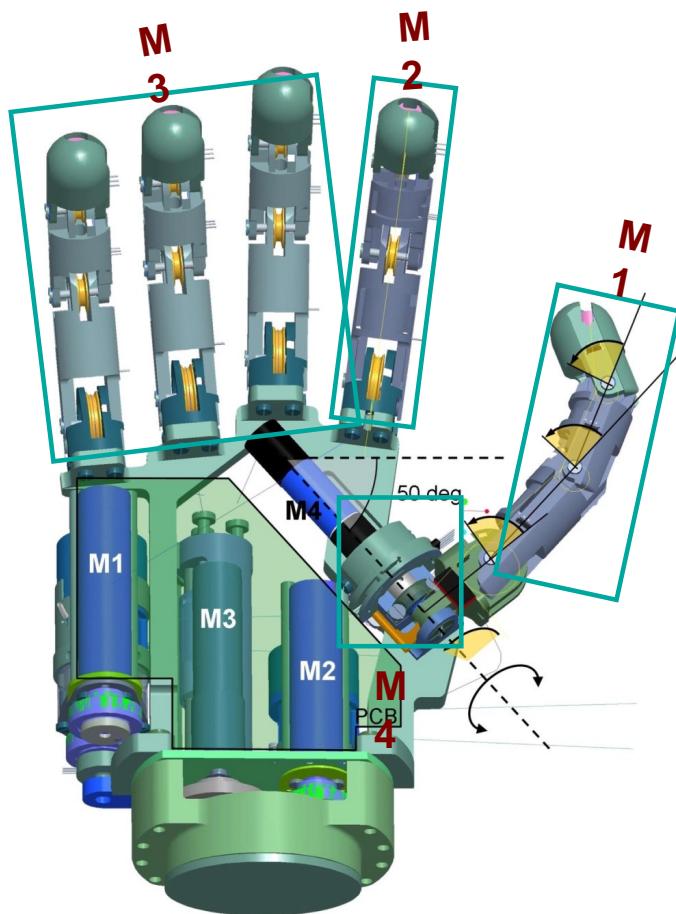


Gear heads with high reduction rate



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

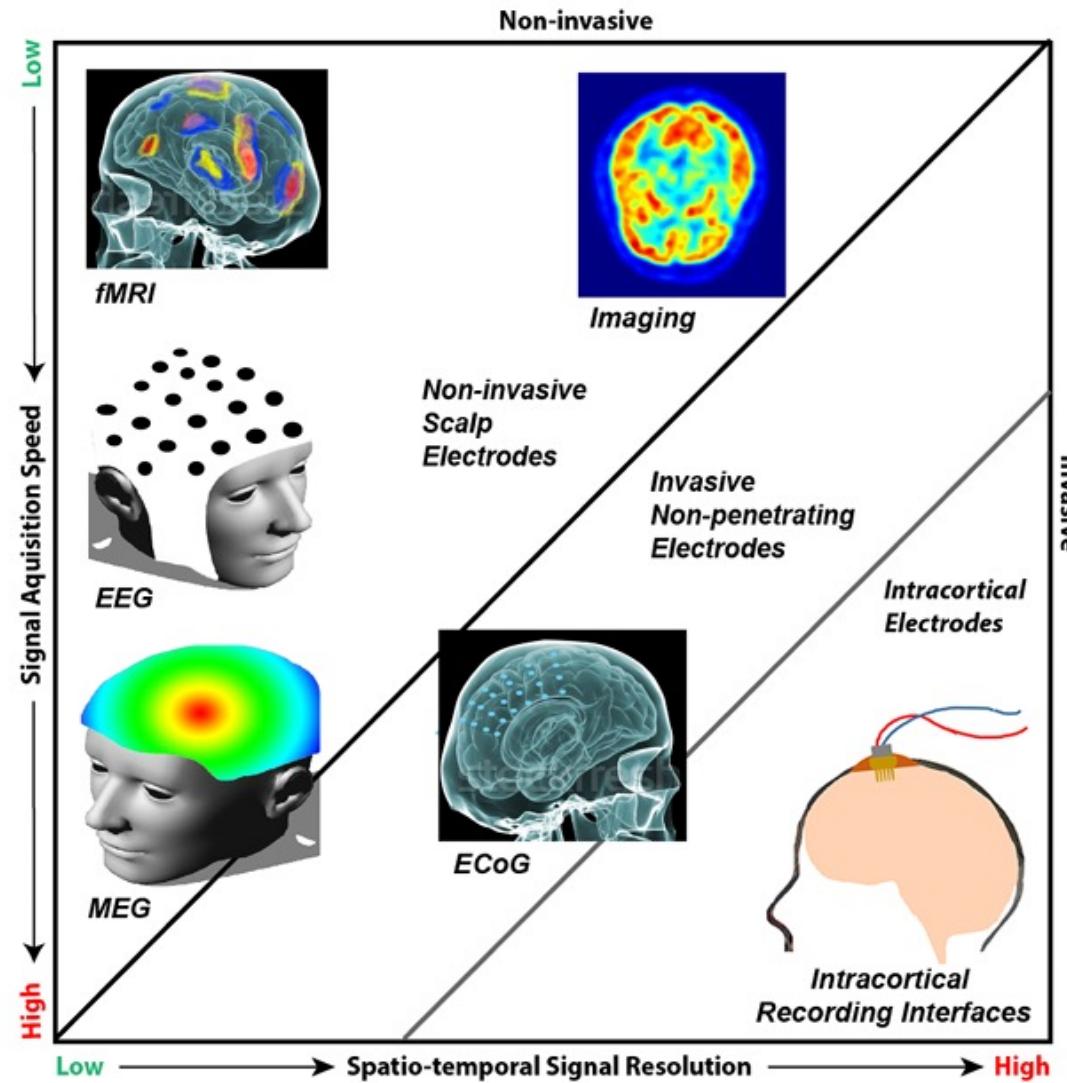
## Sensory System

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

# Cortical signals



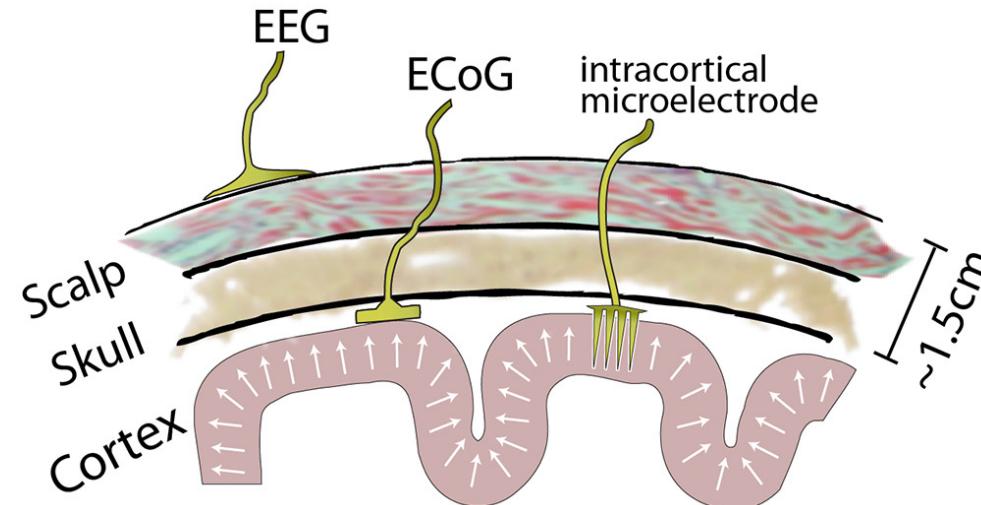
# Cortical signals

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.



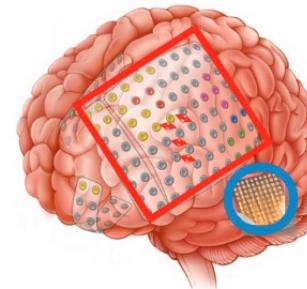
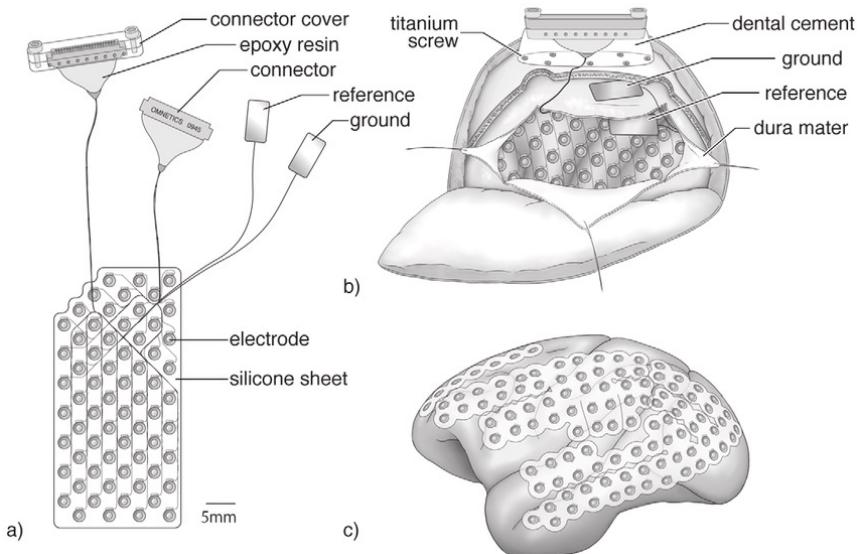
Buzsáki et al, 2012

# Cortical signals - ECoG

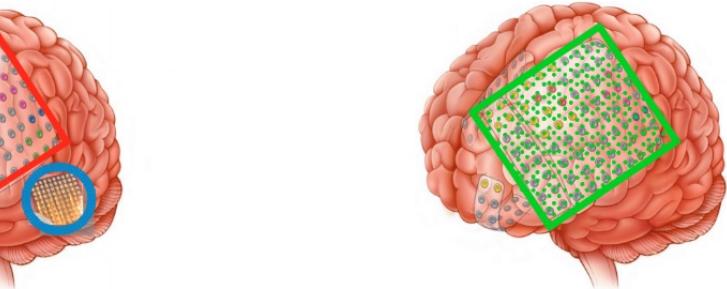
Electrocorticography (ECoG) is a type of electrophysiological monitoring that uses electrodes placed directly on the exposed surface of the brain to record electrical activity from the cerebral cortex

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

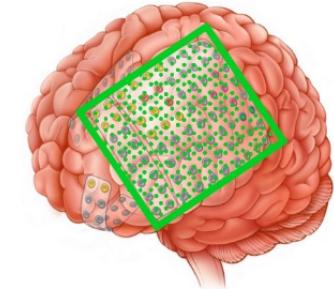
ECoG may be performed either in the operating room during surgery (intraoperative ECoG) or outside of surgery (extraoperative ECoG).



**Current ECoGs**  
•Large area  
•Low resolution



**Current  $\mu$ ECoGs**  
•Small area  
•High resolution



**BMSEED IahruECoGs**  
•Large area  
•High resolution

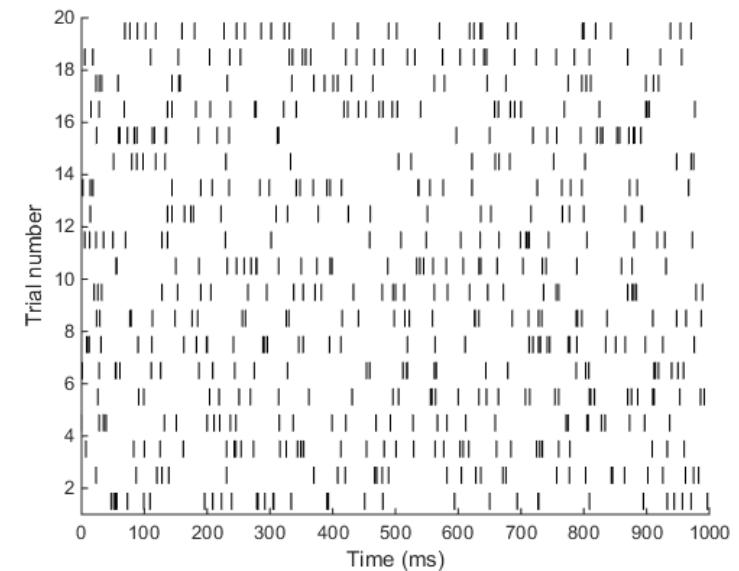
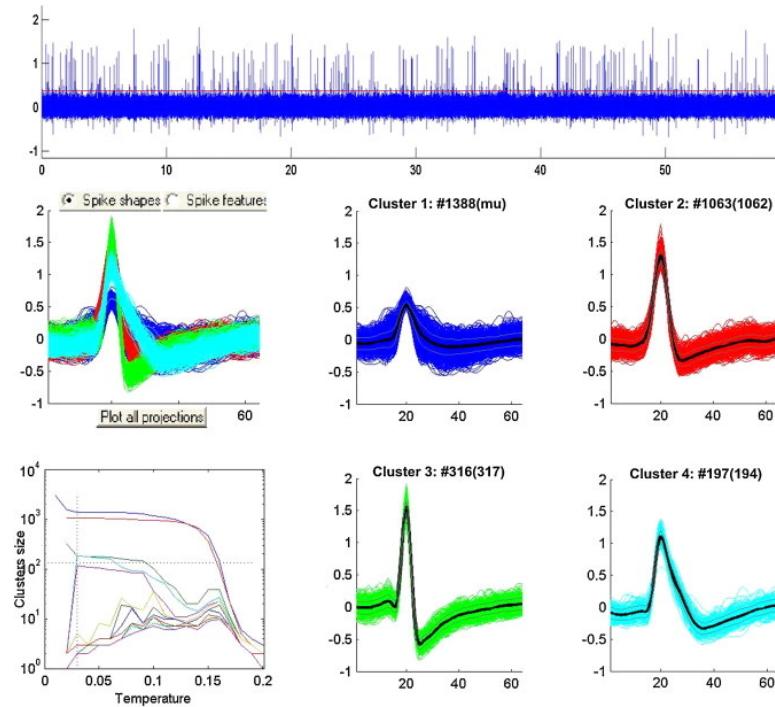


# Cortical signals – Intracortical signals

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)

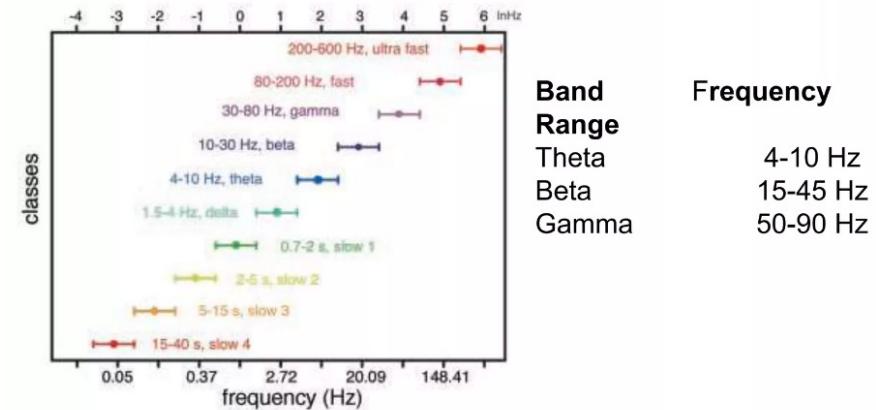
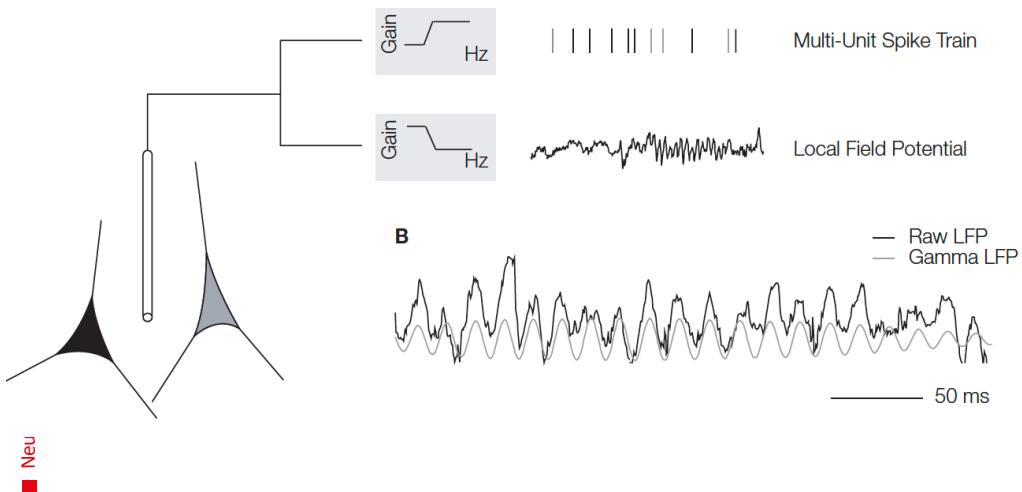


# Cortical signals – Local field potentials

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

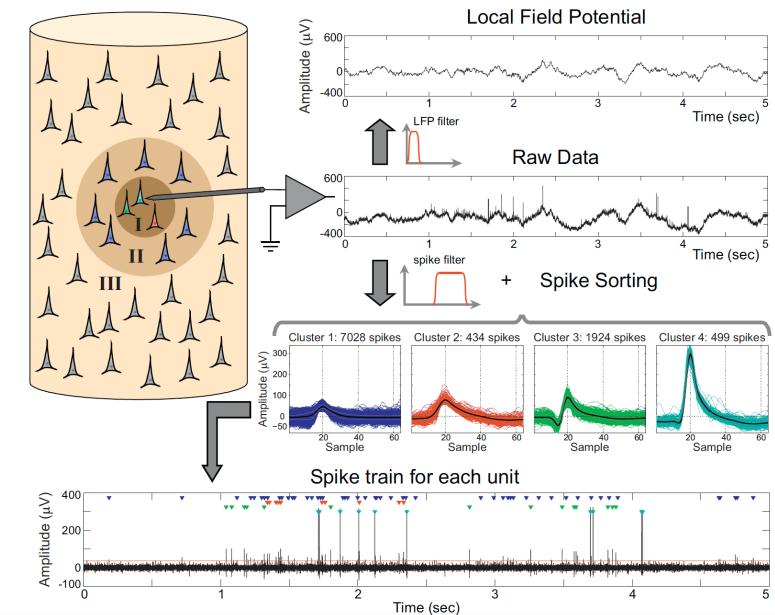
By bandpass filtering the signal, we obtain the activity of a few neurons close enough to the electrode plus background activity elicited by neurons further away from the tip

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

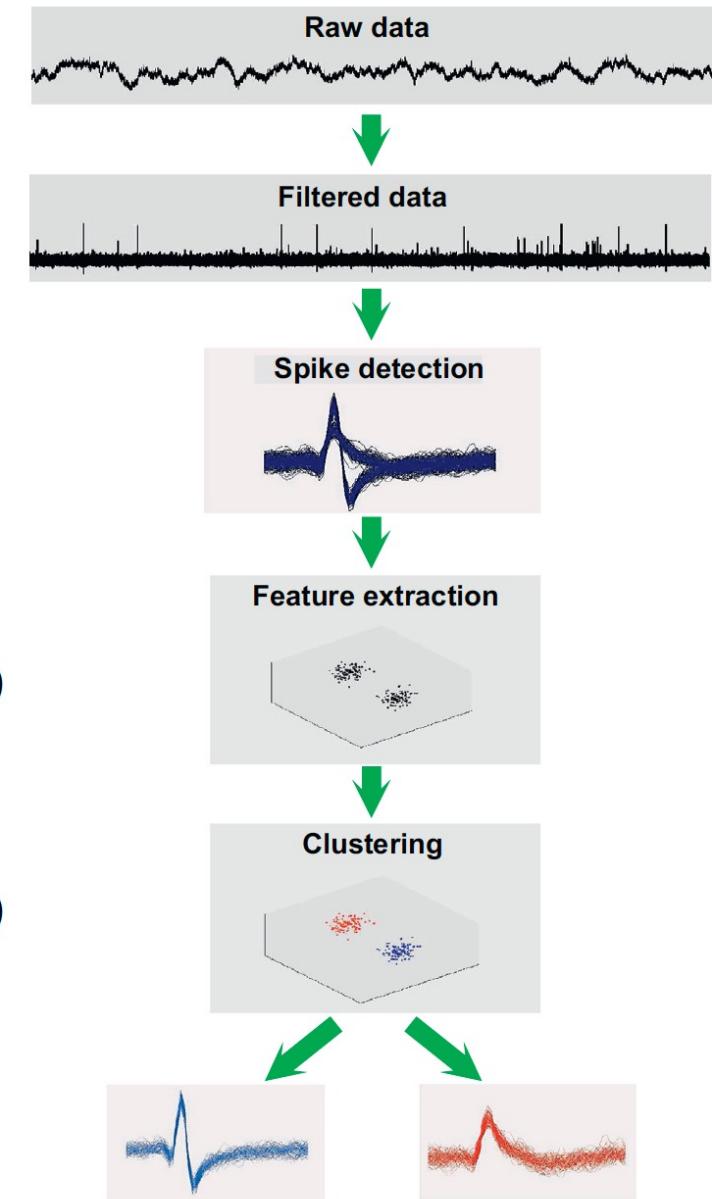
It should be noticed that the raw data is typically recorded using a hard-ware acquisition system that includes a first analog causal IIR (infinite impulse response) bandpass filter, e.g., between 0.3 Hz and 7500 Hz

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

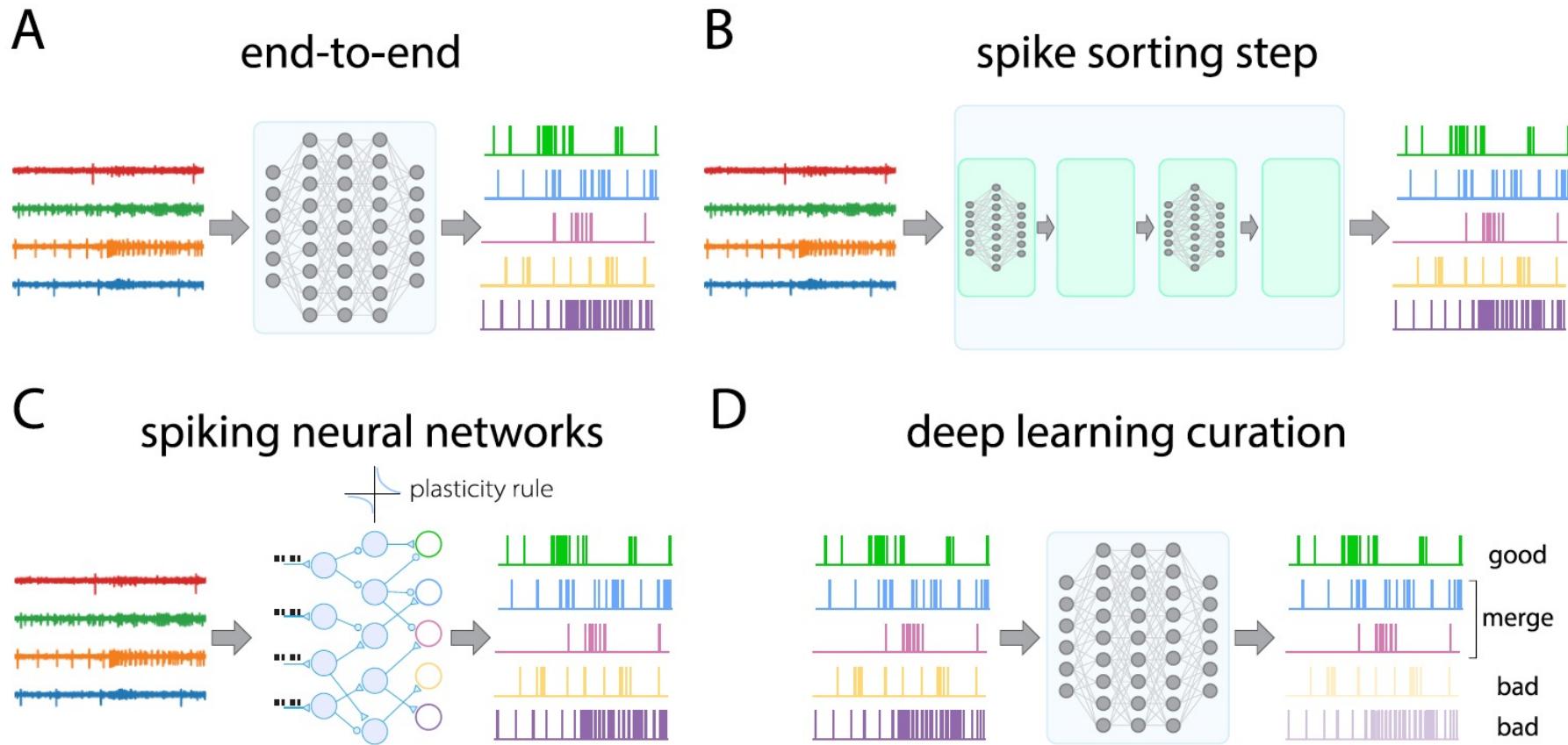
After filtering, spikes are easily visualized on top of background noisy activity and can be detected, for example, by using an amplitude threshold

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.

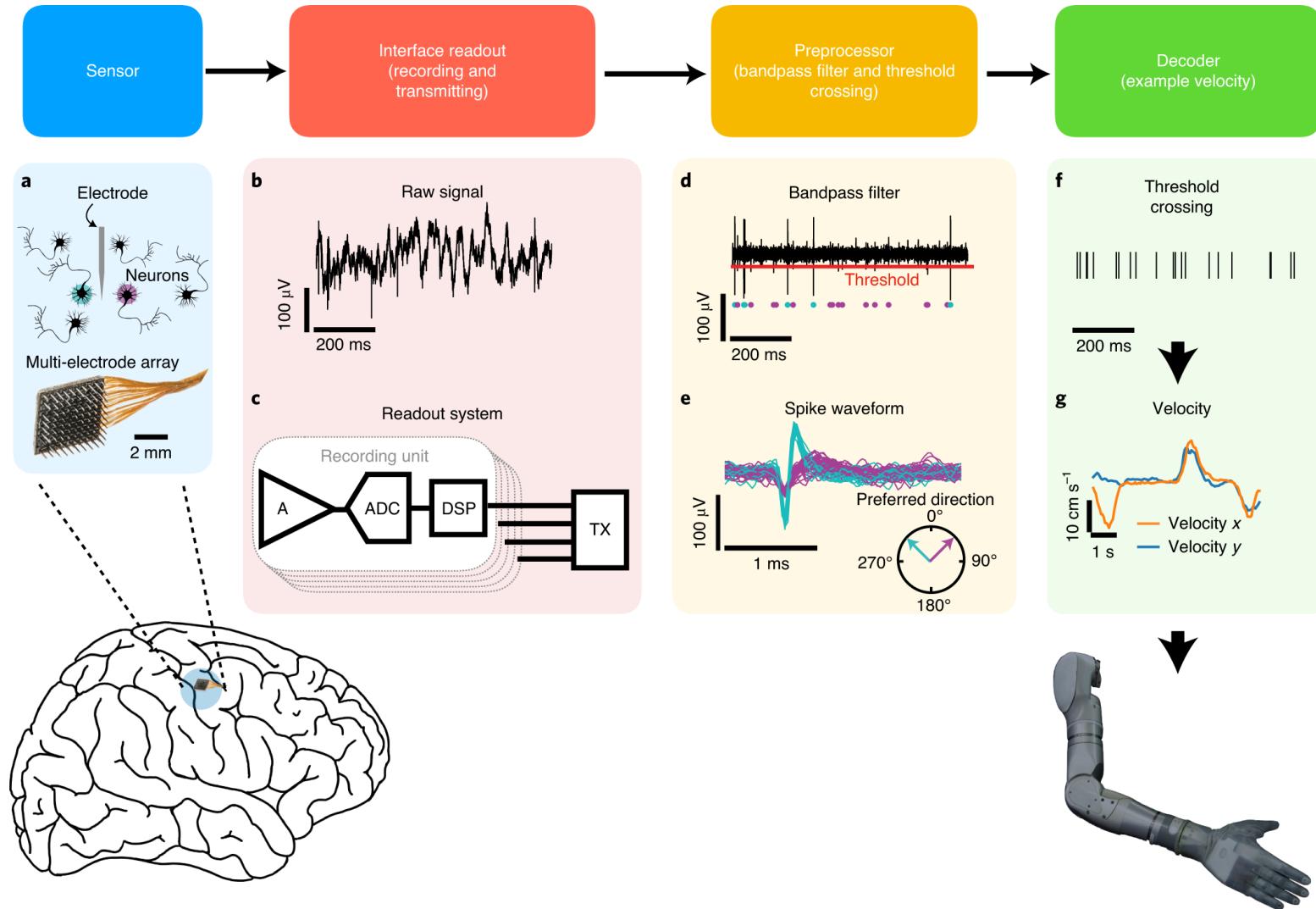
A threshold can be set manually, but since the detection tradeoff is related to the signal to noise ratio of the recording, it seems reasonable to look for an automatic threshold



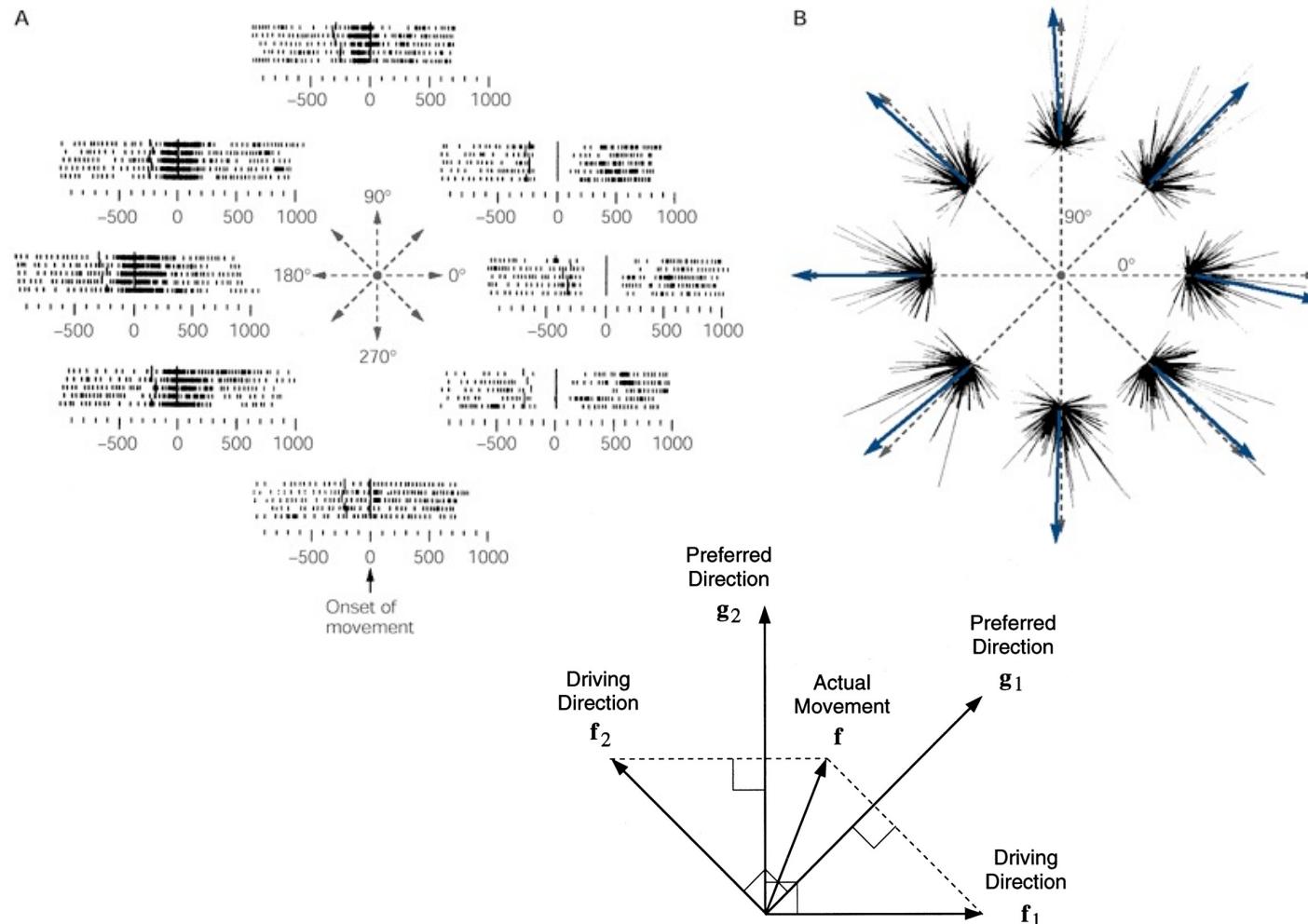
# Deep learning for spike sorting



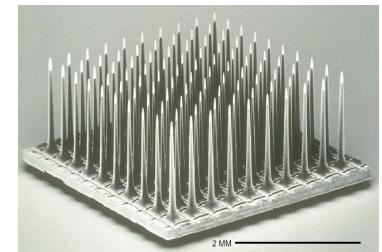
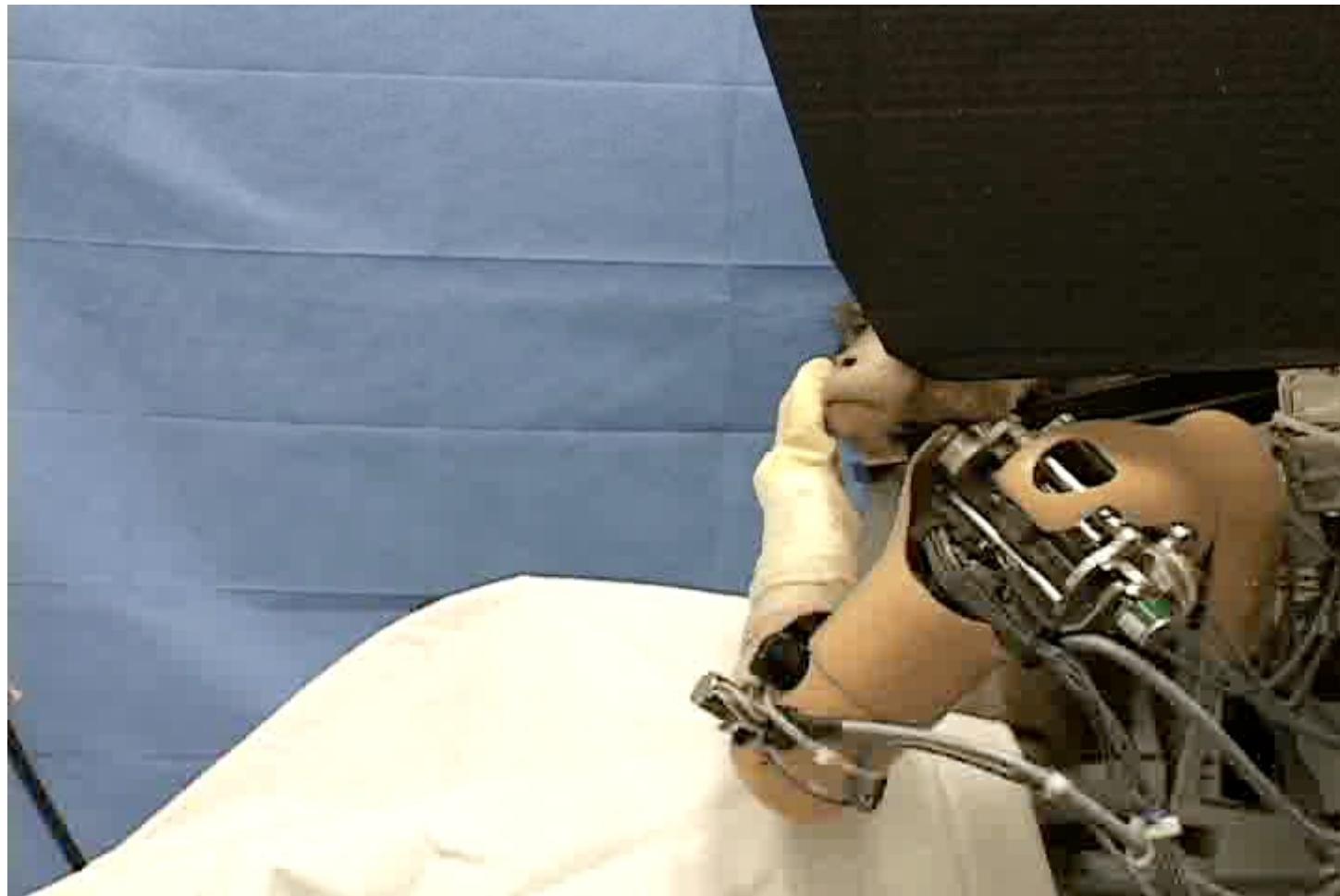
# Brain decoding – General scheme



# 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)

46

Part 4

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.

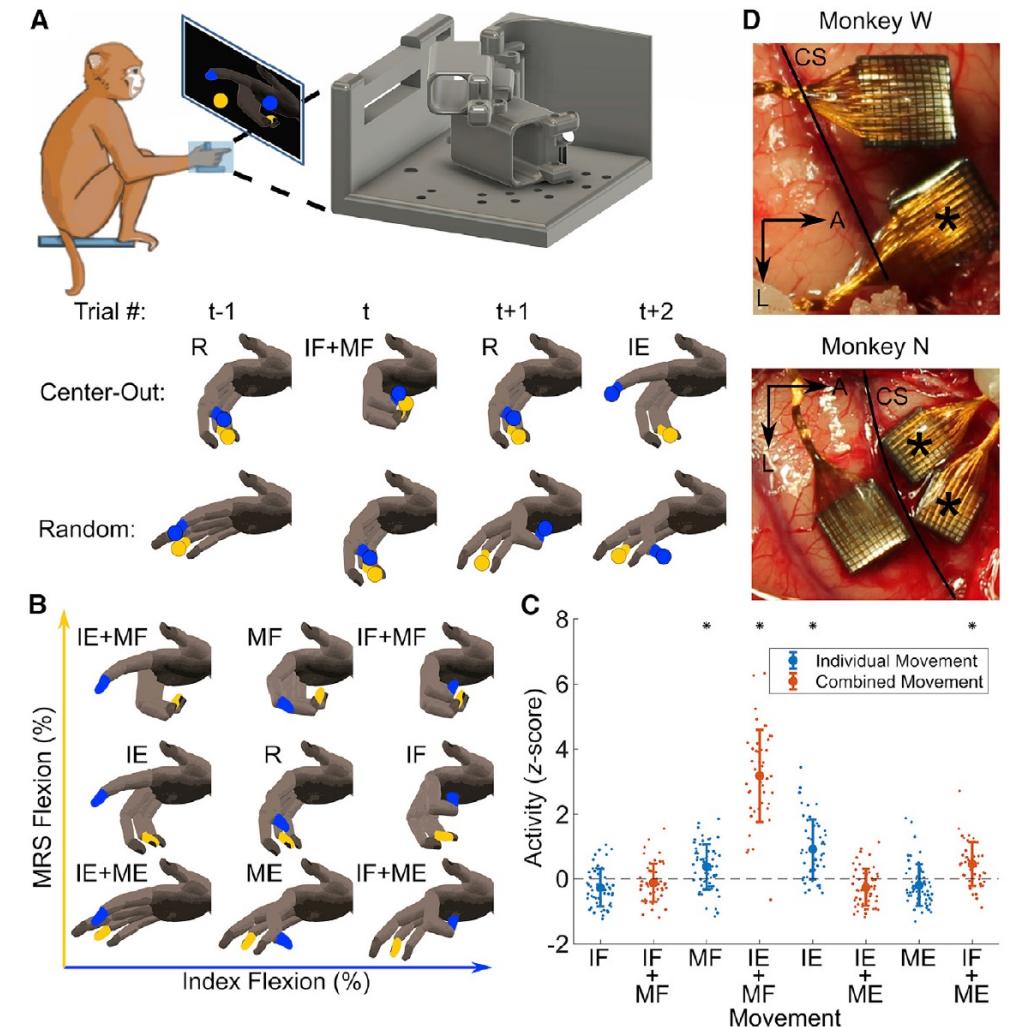
# Brain decoding of finger movements

- 3 -

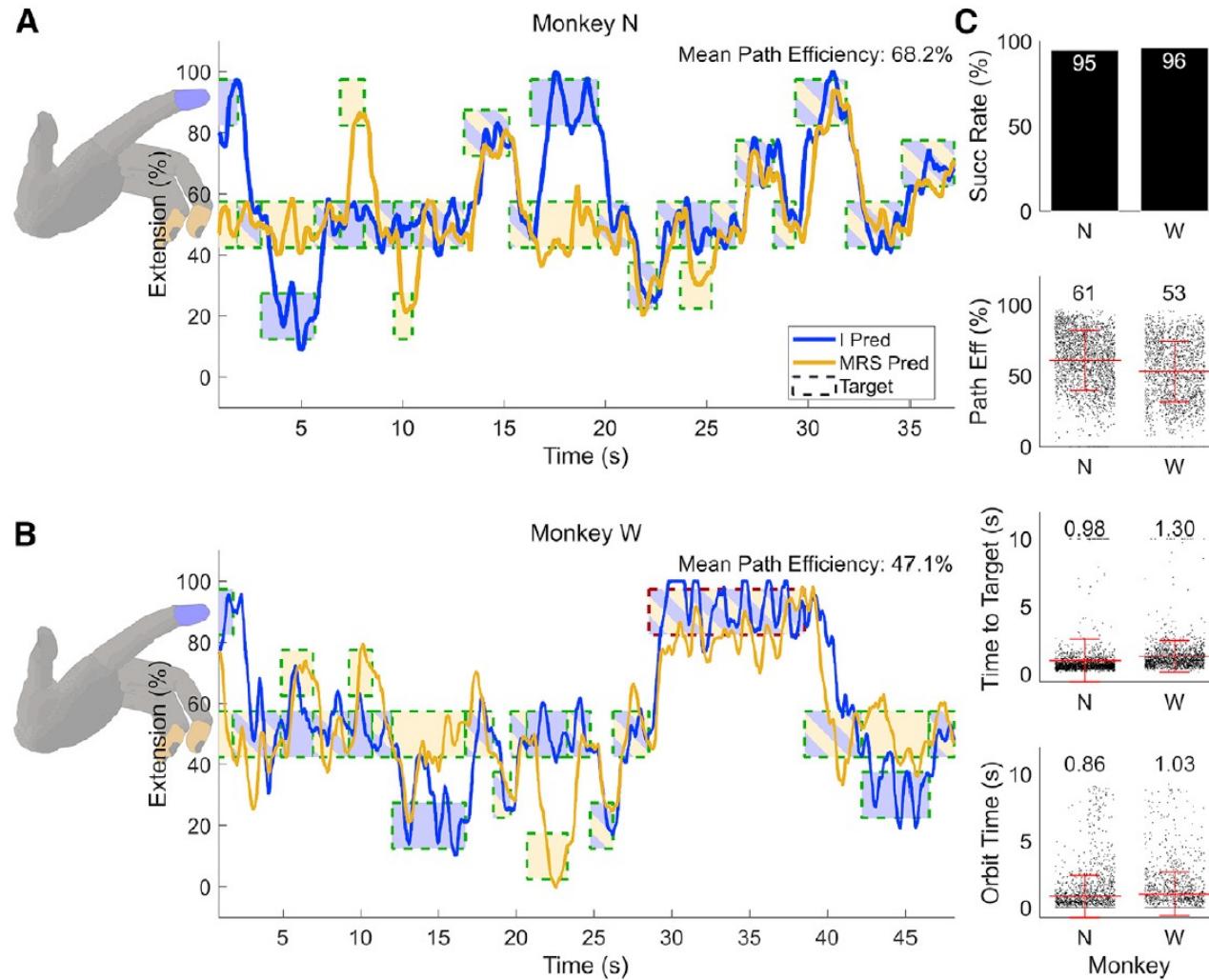
Fine, independent, and simultaneous online control of two systematically individuated groups of fingers within one hand to acquire two targets, one each for the index finger and the middle-ring-small (MRS) fingers, in a non-prehensile task

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

Nason et al., 2021



# Brain decoding of finger movements

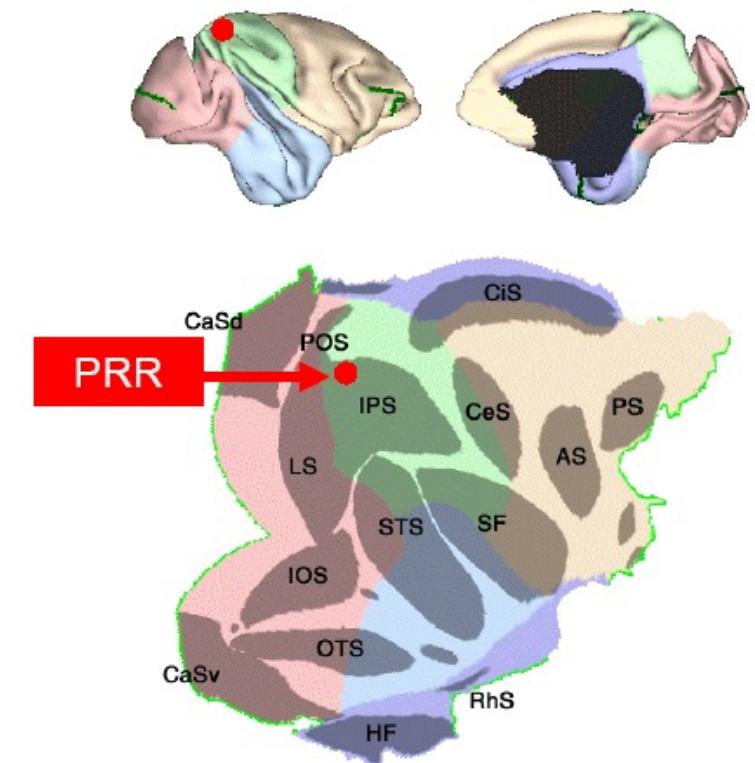


# Brain decoding – High level areas

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

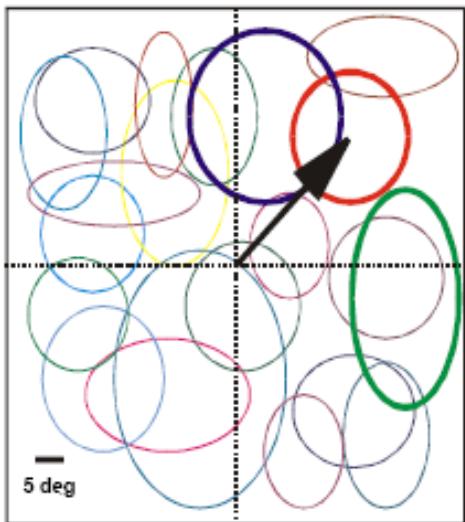


D. Van Essen, H. Drury (1998)

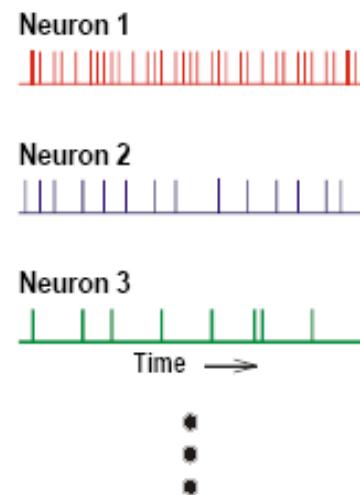
Musallam et al., 2007

# Brain decoding – High level areas

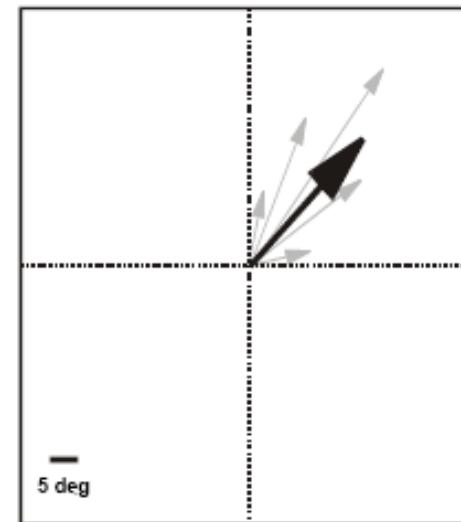
## Estimating the Planned Reach Direction



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

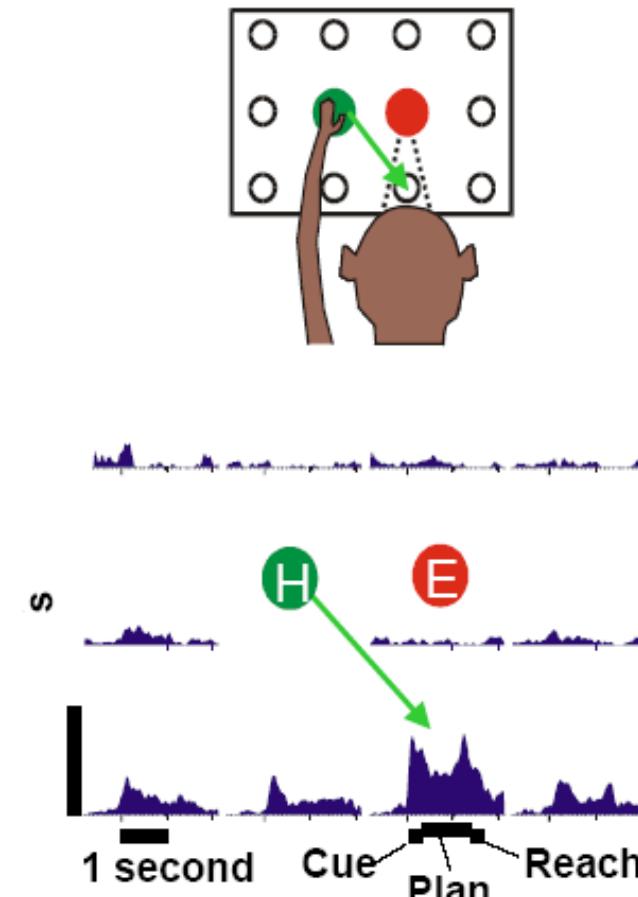
## Potential Advantages of PRR Neurons for Prosthetic Systems

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:

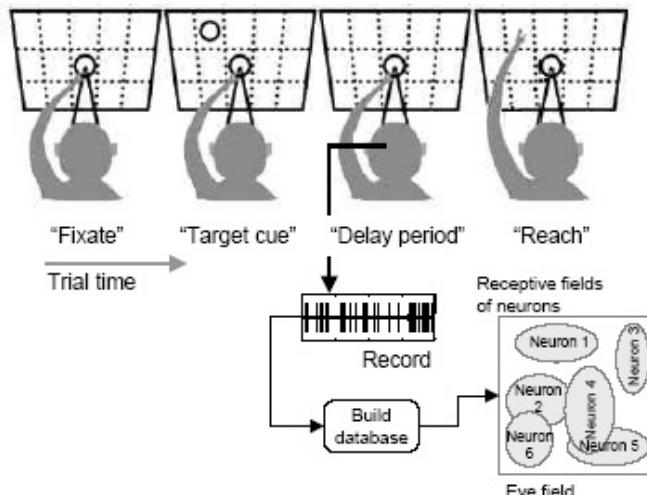
- not encode muscle forces
- reorganize little following injury
- adapt quickly to calibrate the system



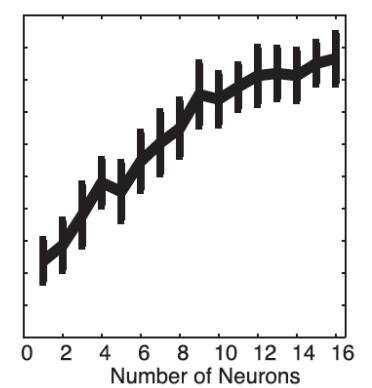
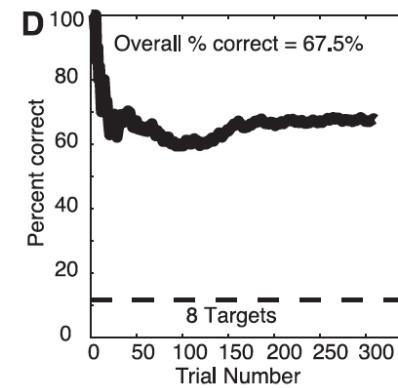
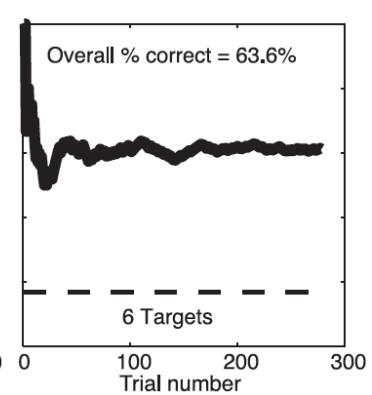
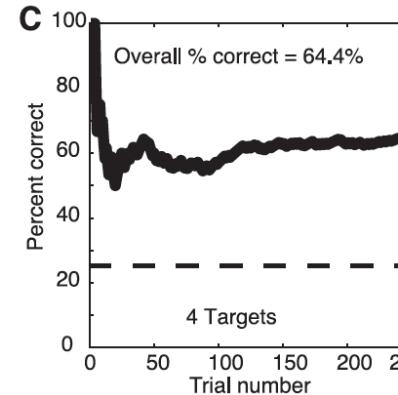
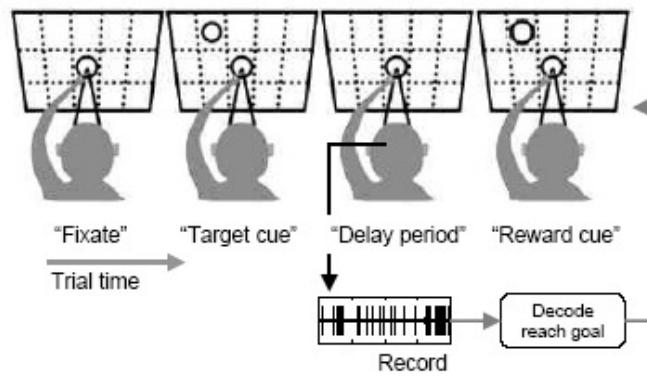
Batista, Buneo, Snyder, Andersen (1999) Science 285.

# Brain decoding – High level areas

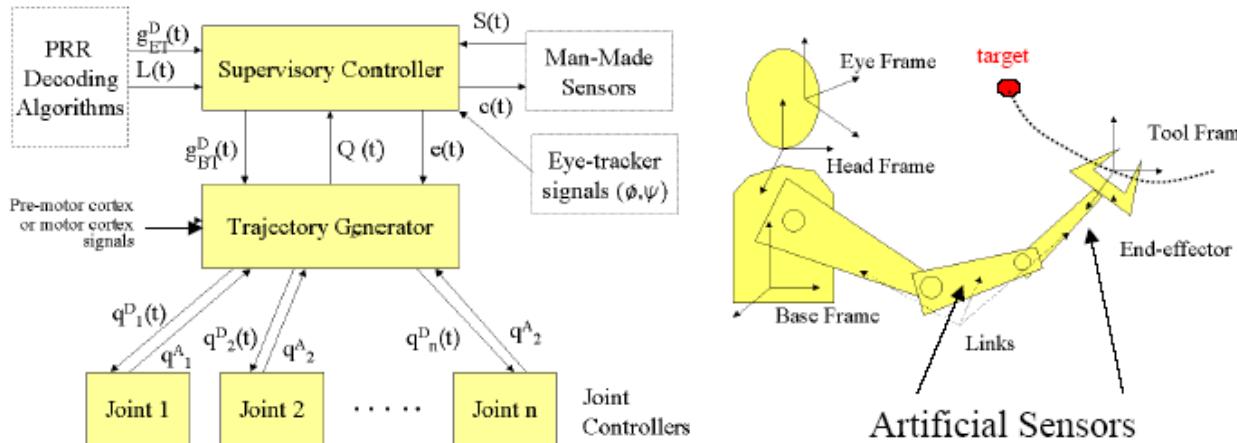
a) Reach Task



b) 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

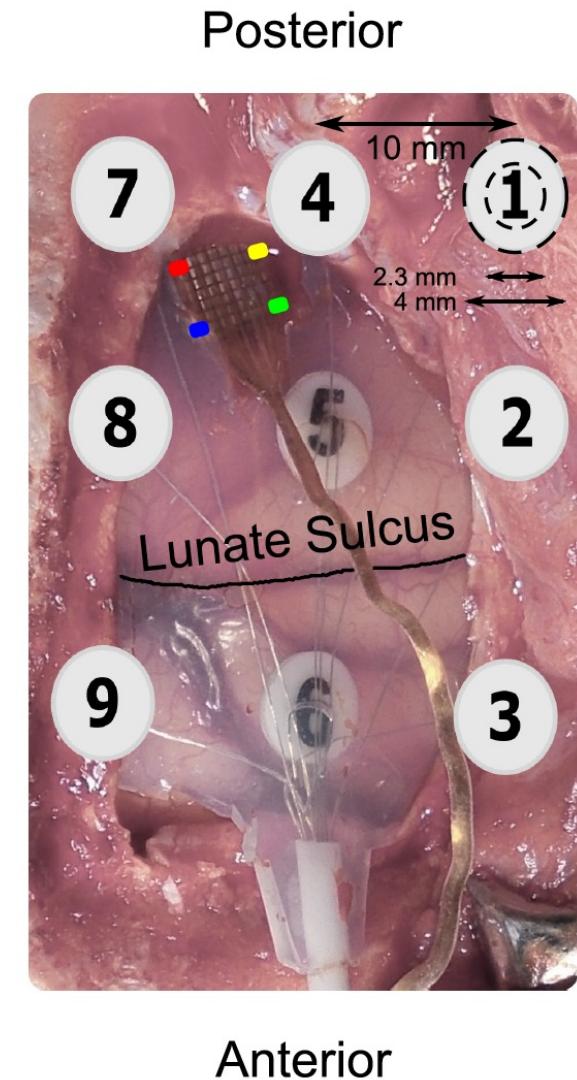
Electrocorticogram (ECoG) refers to the signal obtained from macroelectrodes (typically 2–3 mm in diameter)

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

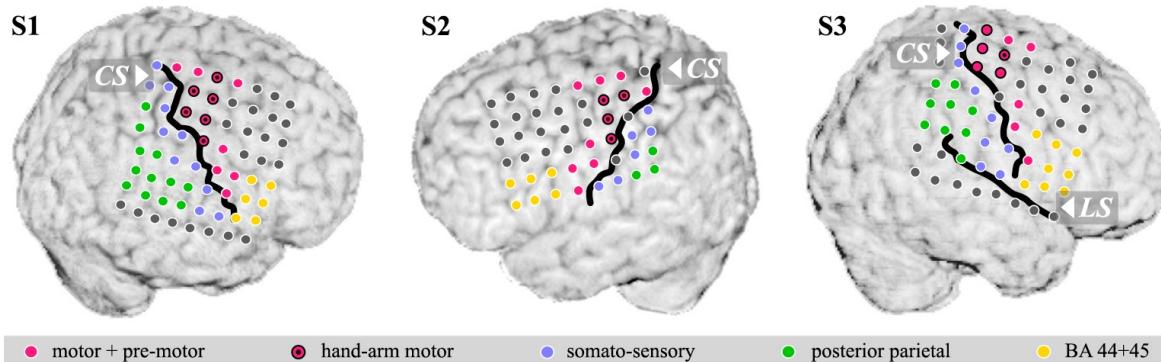
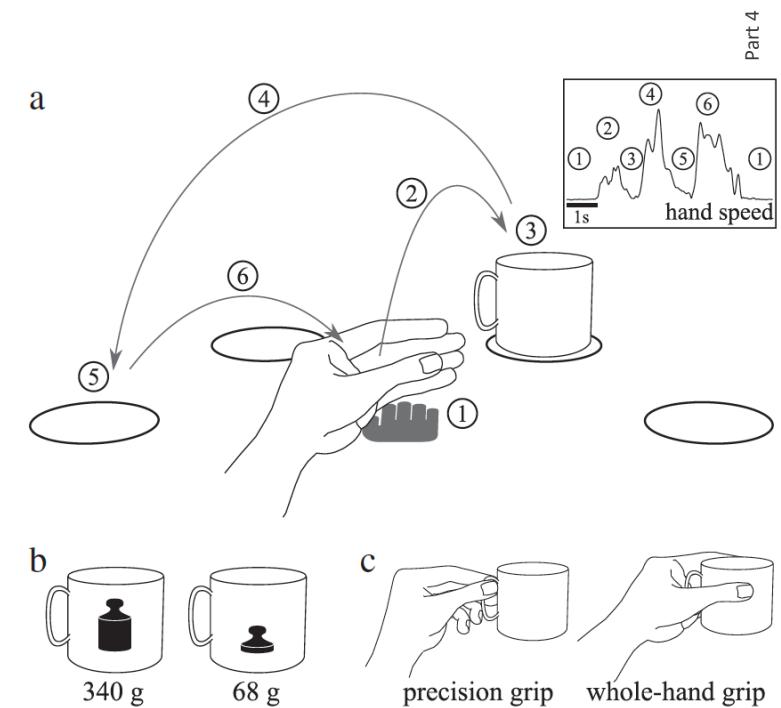
A computational model was used to estimate the spatial spread of LFP and ECoG



# 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.



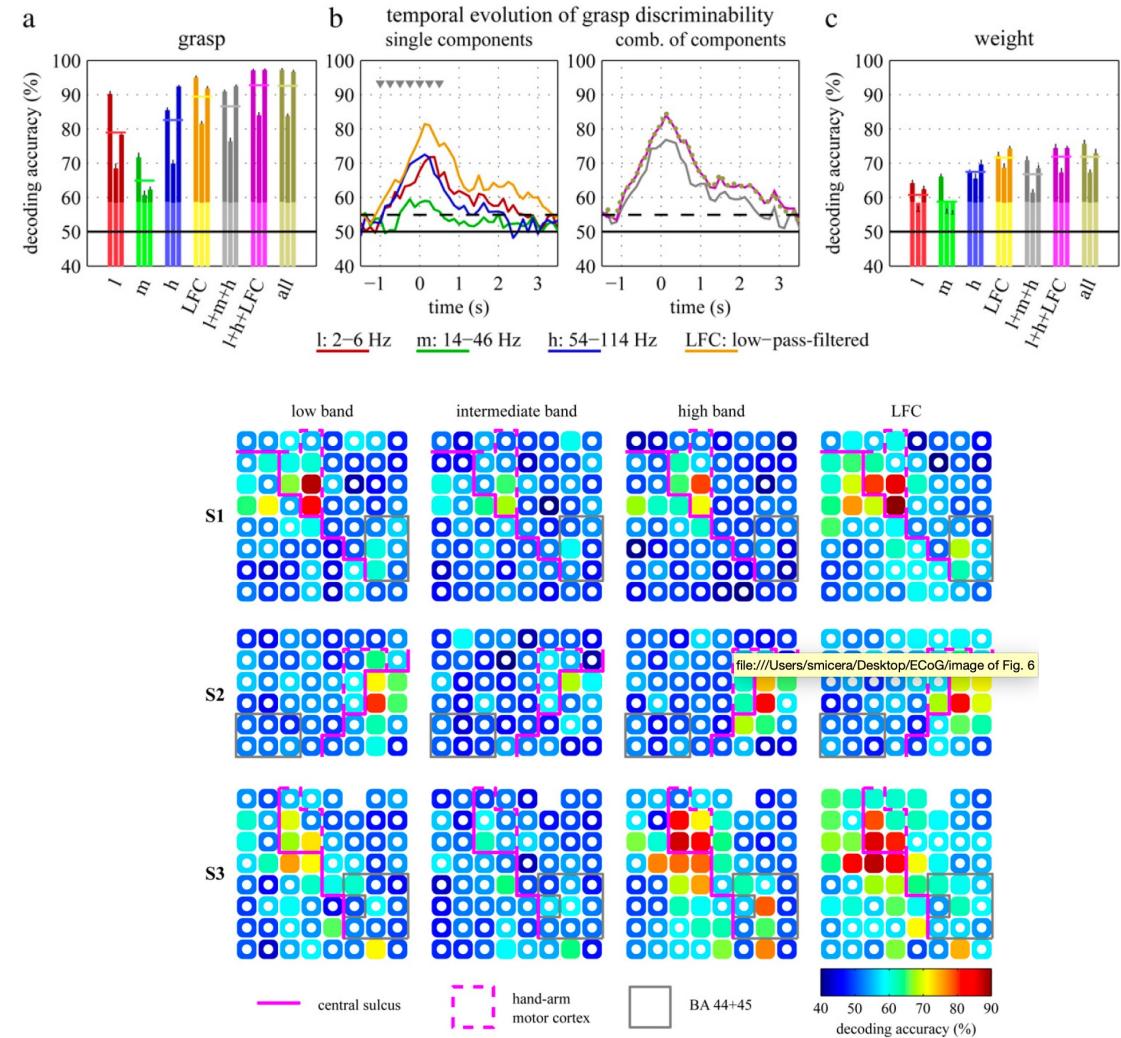
# ECoG-based grasping decoding

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

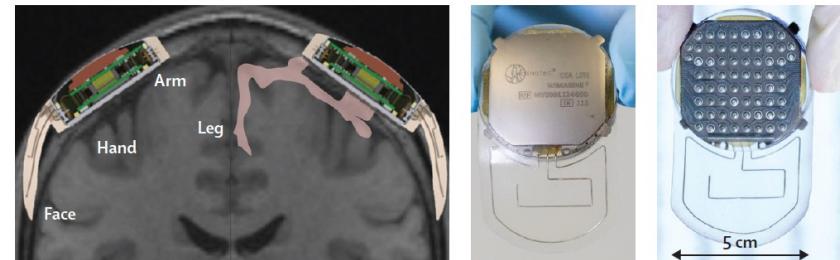
The researchers recruited a 28-year-old man, who had tetraplegia following a C4–C5 spinal cord injury

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

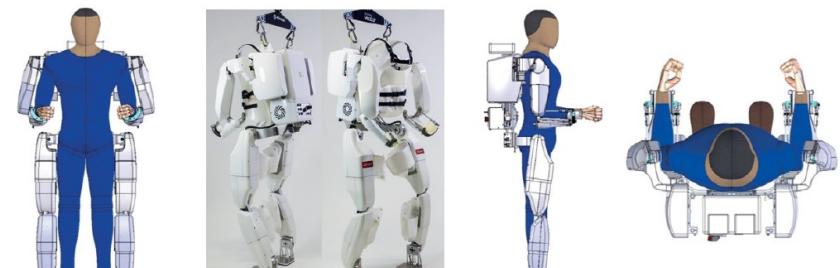
Epidural electrocorticographic (ECoG) signals were processed online by an adaptive decoding algorithm to send commands to effectors (virtual avatar or exoskeleton)

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

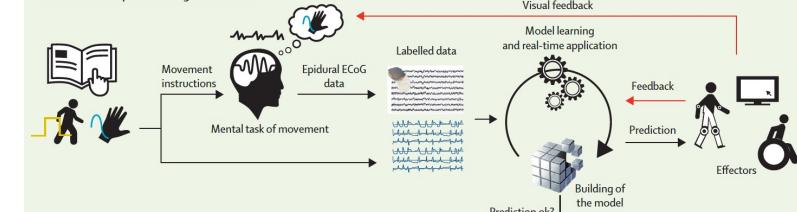
B WIMAGINE wireless recorder



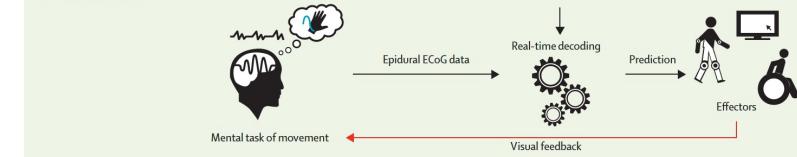
C EMY exoskeleton



A Real-time adaptive learning of the model



B Usage of the model



**EPFL** ECoG-based exoskeleton control

L

# EPFL EMG interface for robotic systems

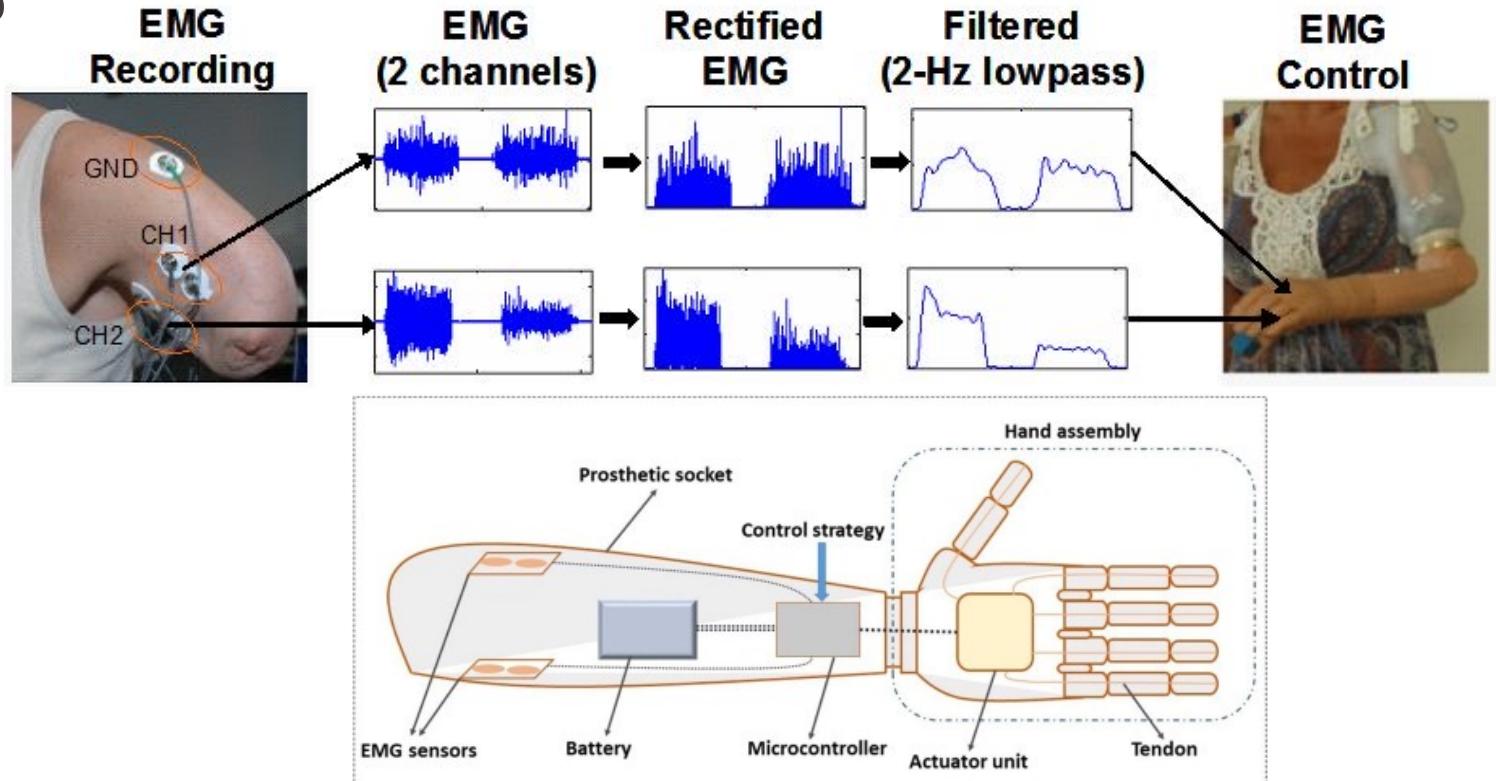
How to use EMG signals for this goal

- 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)

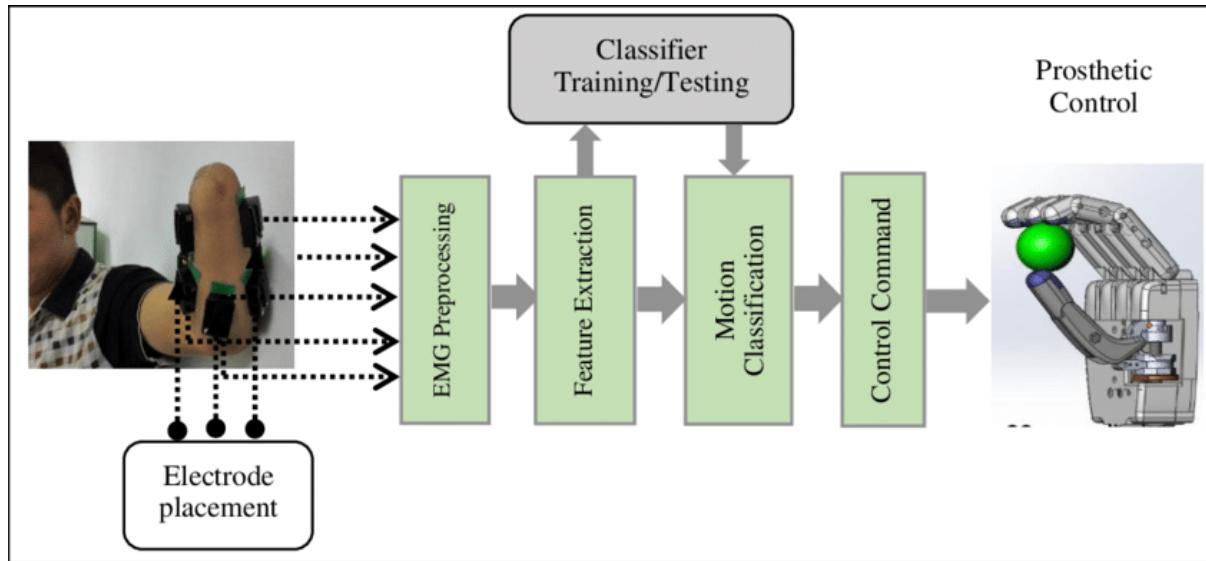
# Hand prosthesis – Proportional control

$N$  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 approach



# 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

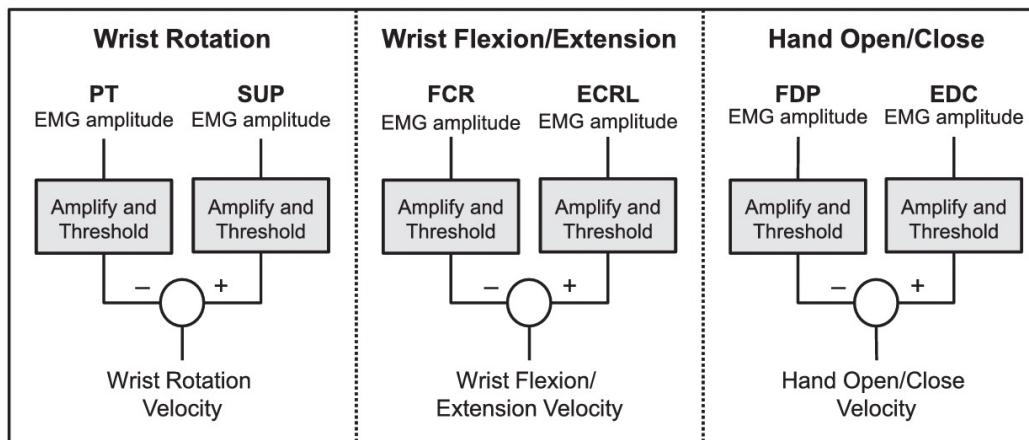
# EPFL Intramuscular EMG (iEMG) control

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

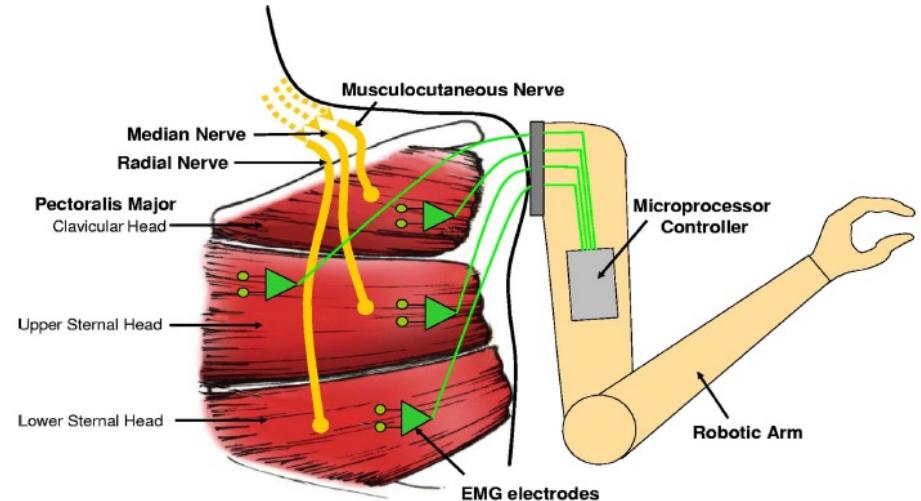
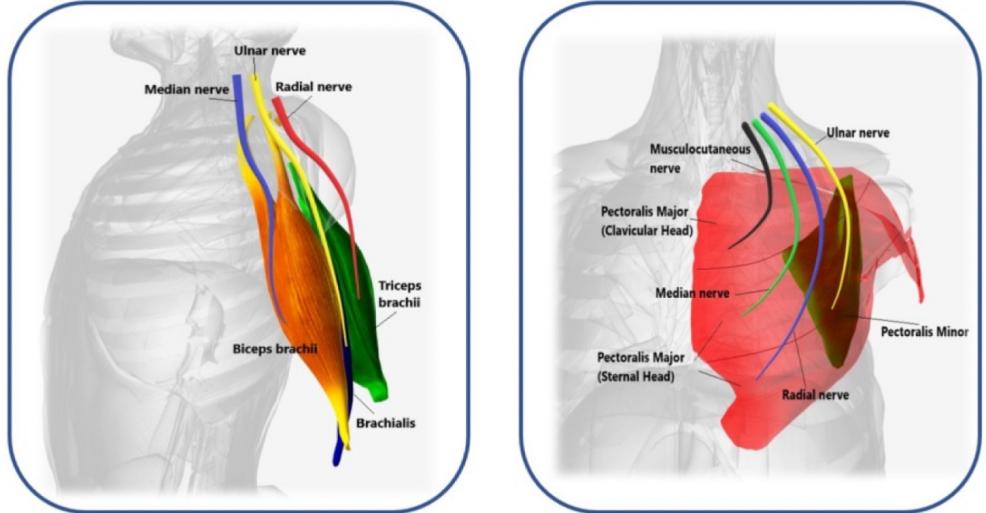
Intramuscular EMG signals can be recorded using percutaneous fine wire electrodes inserted using needles

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



# EPFL Targeted muscle reinnervation (TMR)

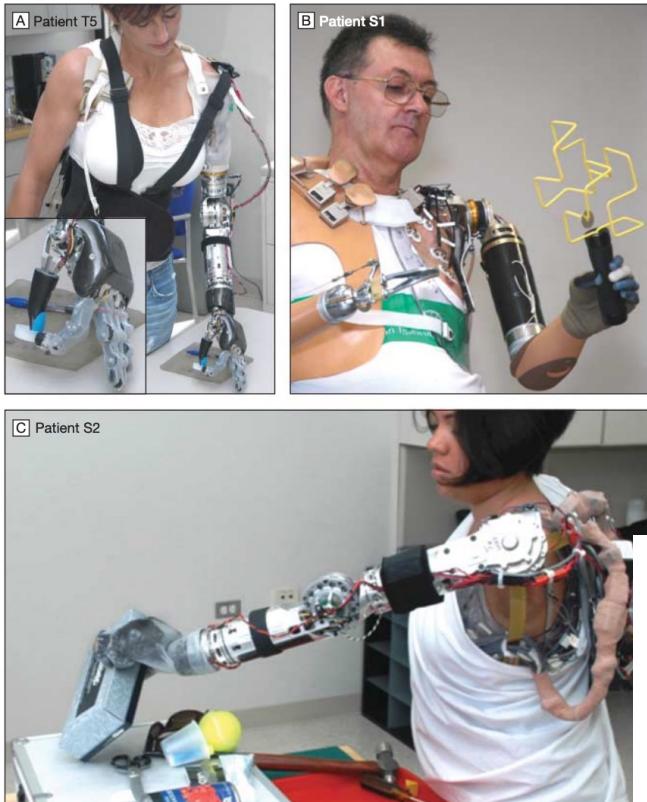
Part 4



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

# Targeted muscle reinnervation (TMR)



Hargrove et al., 2017

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

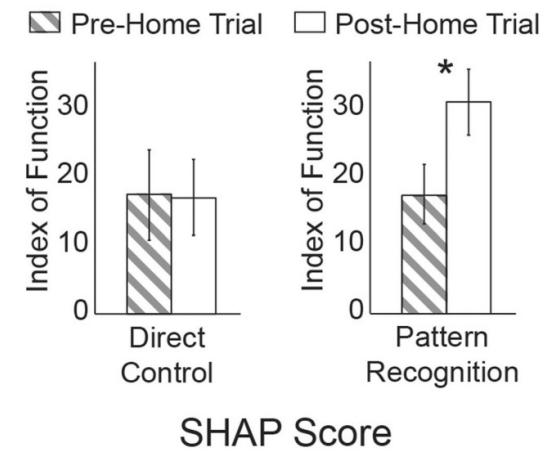
Notably, these tests required movements along 3 degrees of freedom.

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.

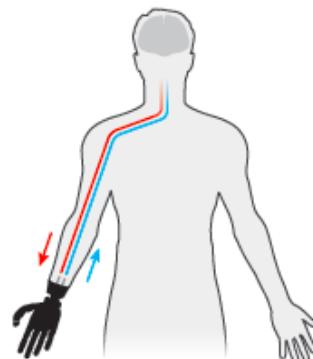
Subject	Direct Control Wear Time (hrs)	Pattern Recognition Wear time (hrs)	Number of Recalibrations	Preference of Control
S1	41	15	7	PR
S2	280.1	301.6	39	PR
S3	196.8	183.6	73	PR
S4	254.6	366.9	56	PR
S5	91.4	85.1	10	PR
S6	54.9	27.9	20	DC
S7	157.7	128.5	18	PR
S8	33.2	73.0	38	PR

Table 2. Wear time, recalibration and control preference.



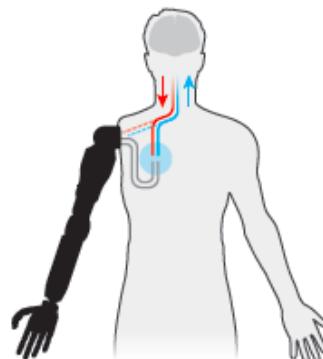
# Sensory feedback

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



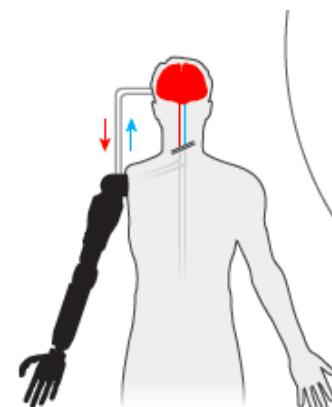
## *Use the remaining nerves*

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.

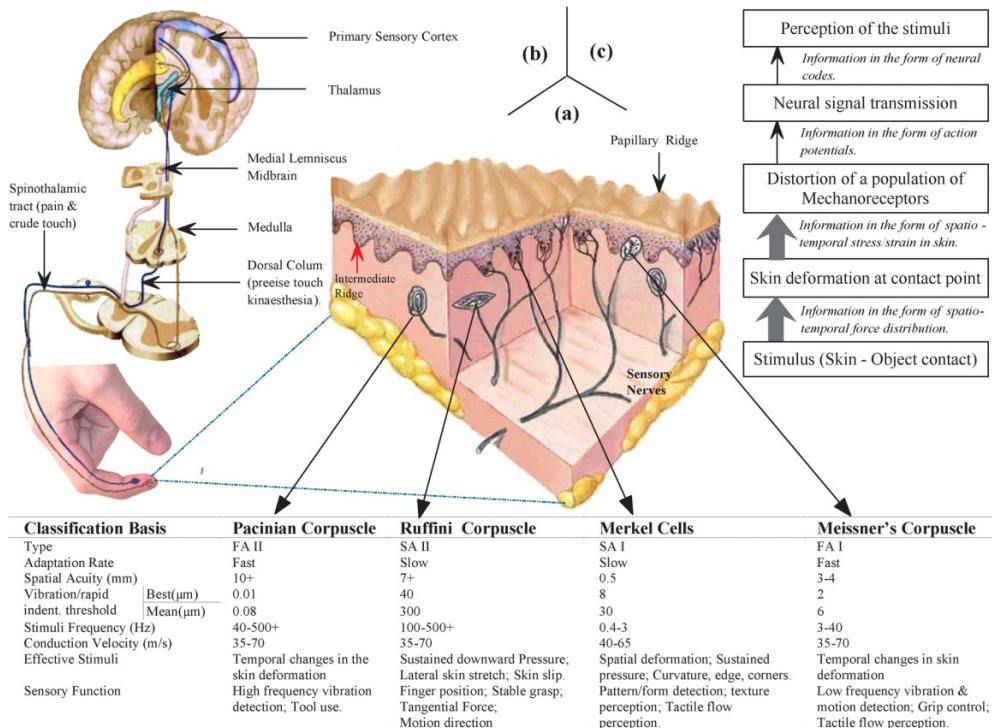


## *Stimulate the brain*

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

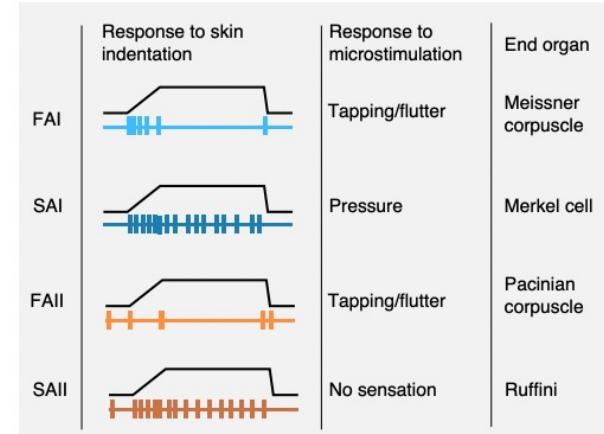
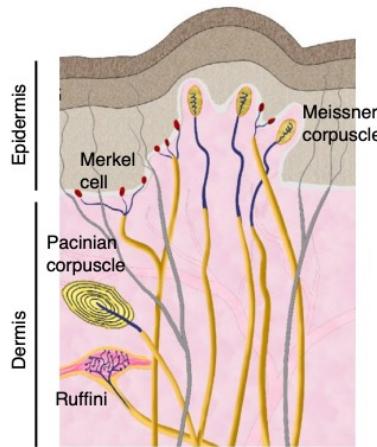
# Human touch system



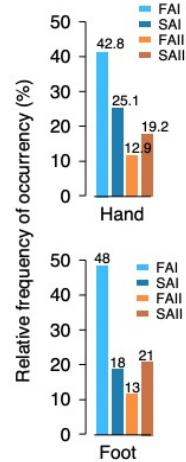
- During object manipulation and tactile exploration, the glabrous skin of the hand undergoes complex spatiotemporal mechanical deformations, which in turn, drive very precise spiking responses in individual afferents
- Coarse object features, such as edges and corners, are reflected in spatial patterns 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

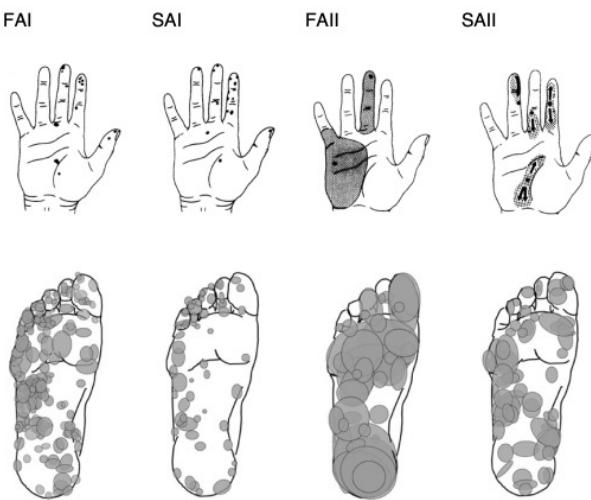
b



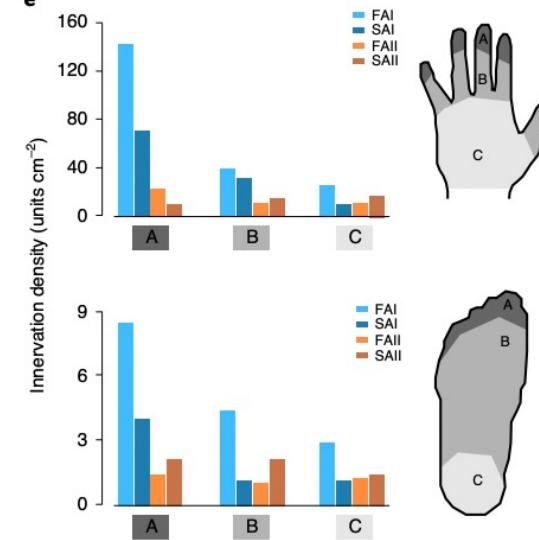
c



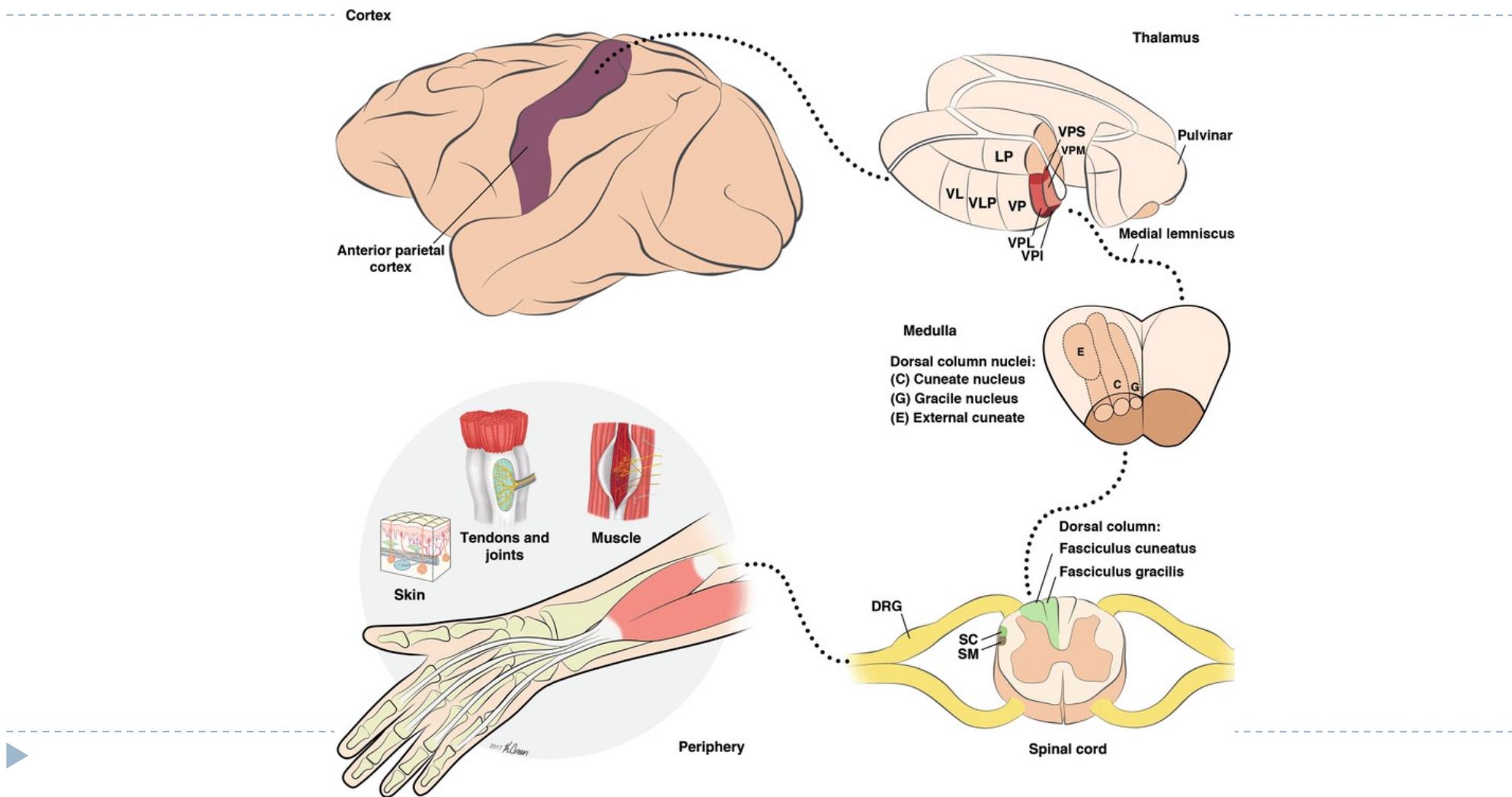
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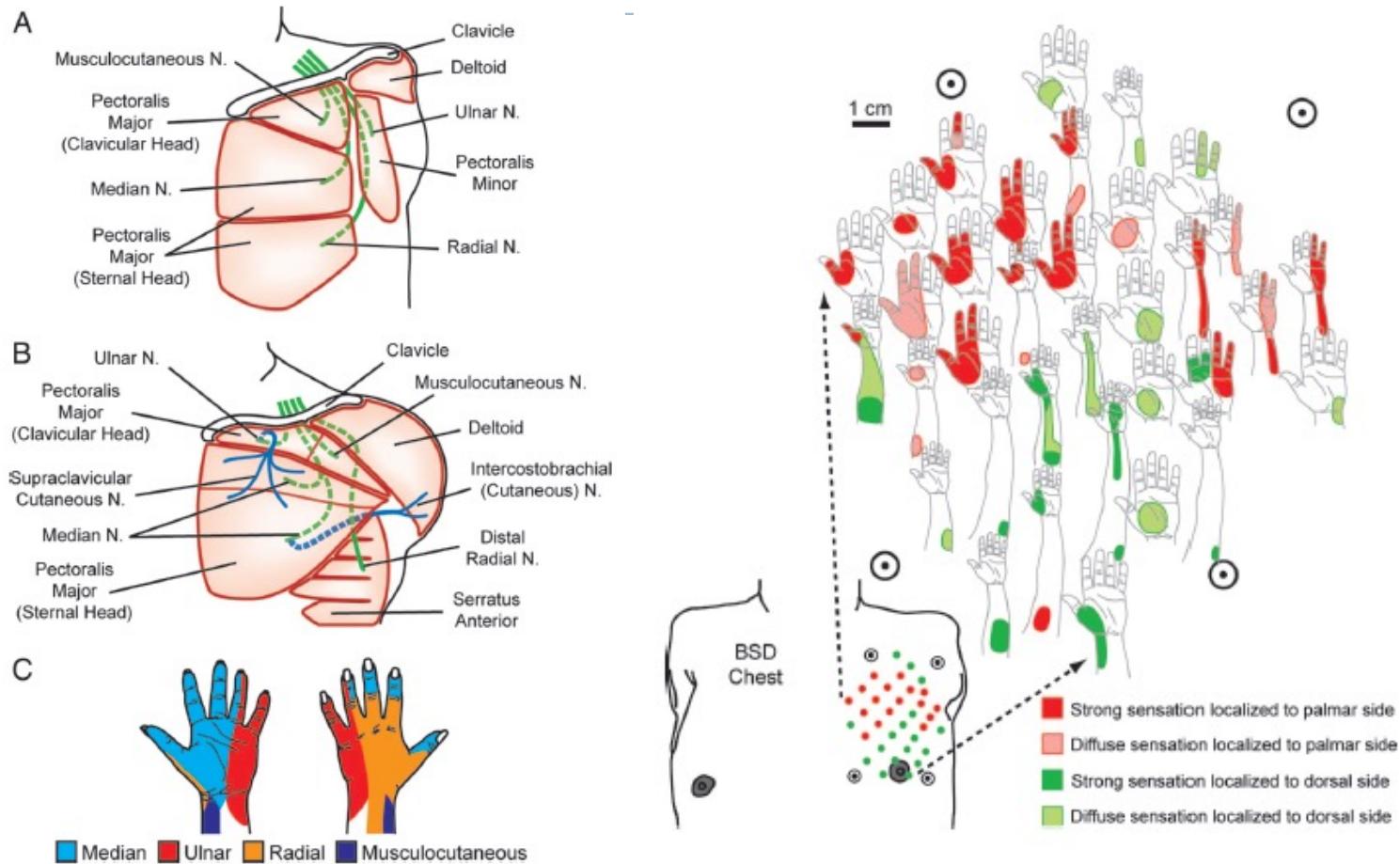
e



# Human touch system

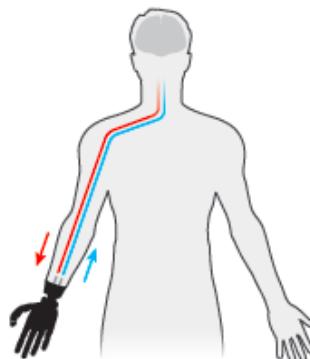


# Targeted Muscle Reinnervation



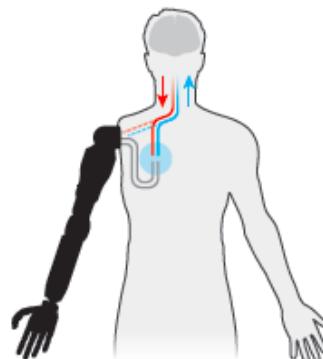
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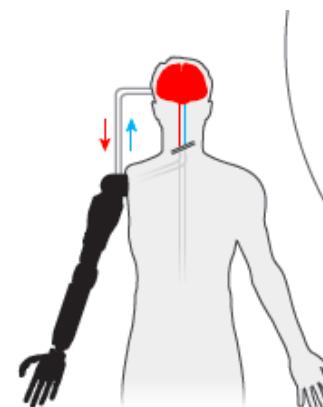
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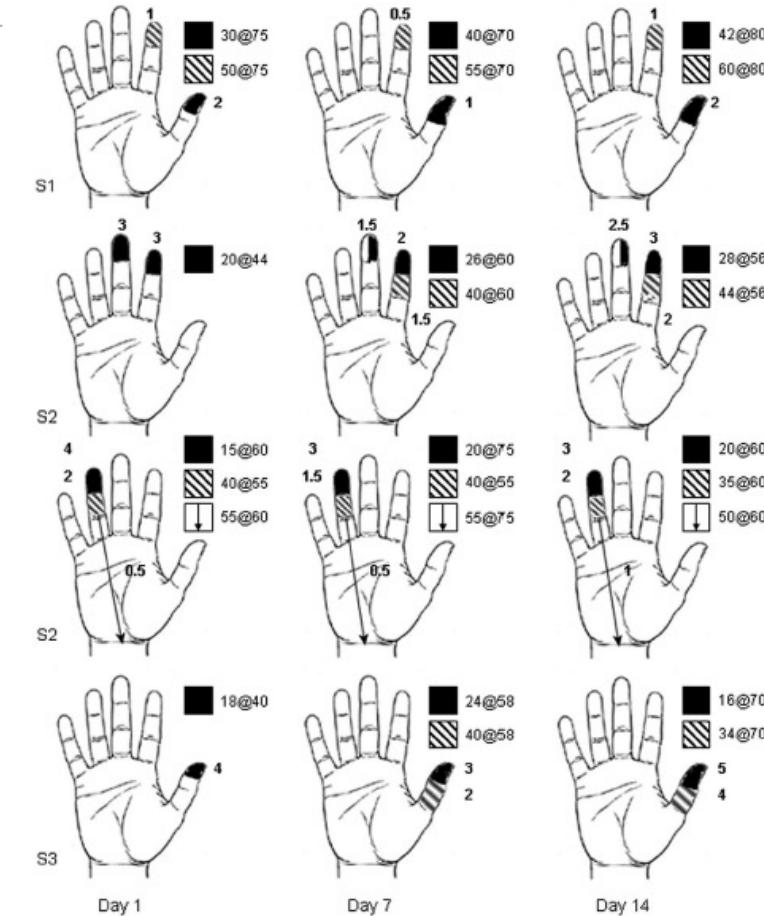
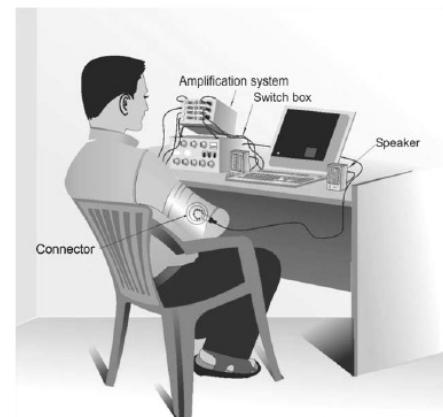
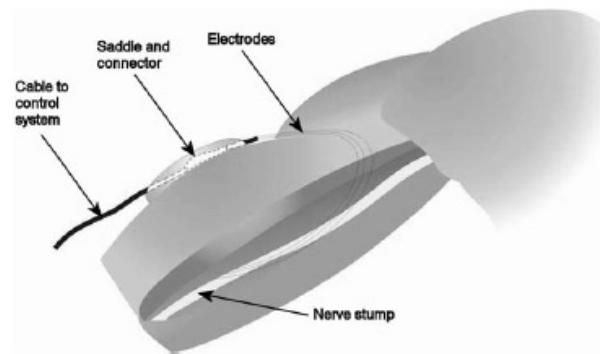


## *Stimulate the brain*

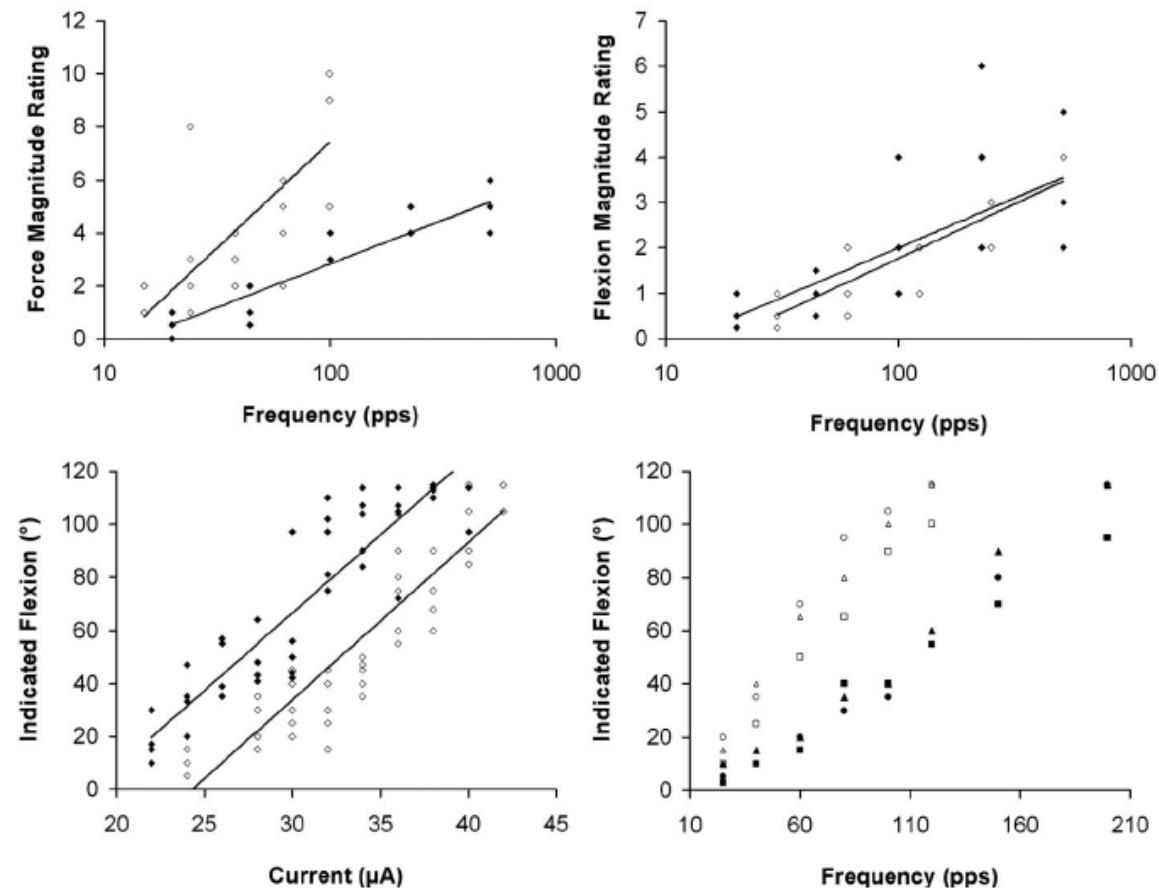
Sensory signals are routed around a severed spinal cord and into the brain, where they produce sensations by direct stimulation of the cortex.

Kwok, Nature, 2013

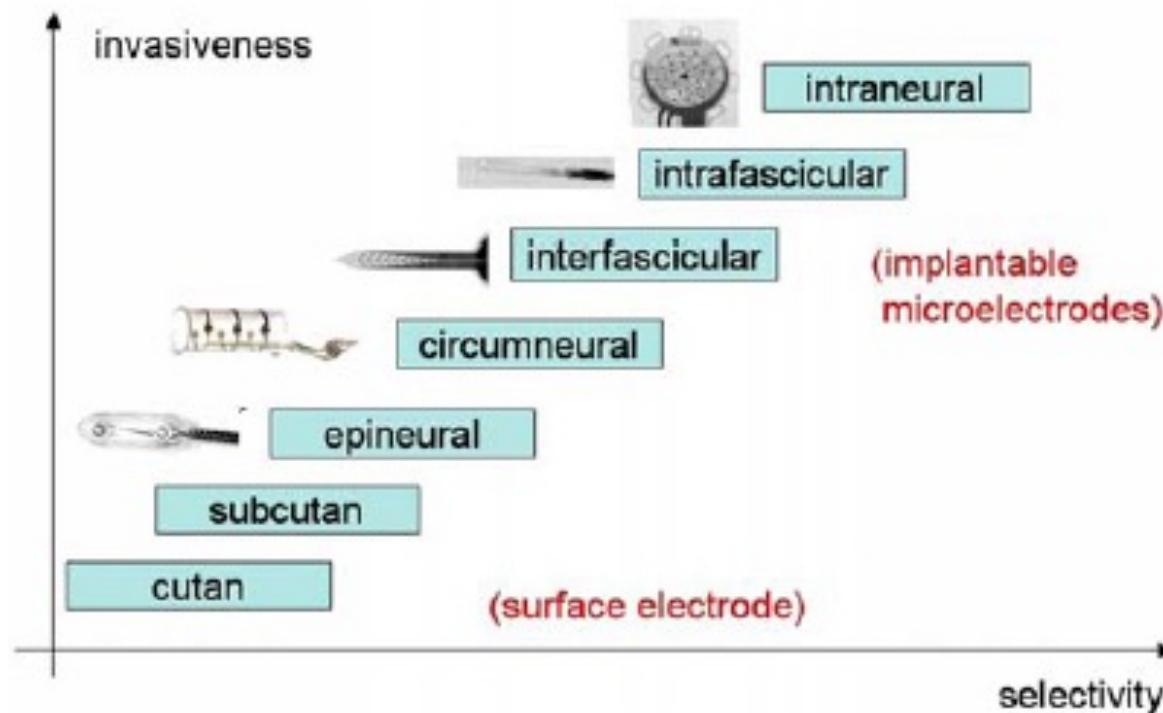
# First intraneuronal experiment



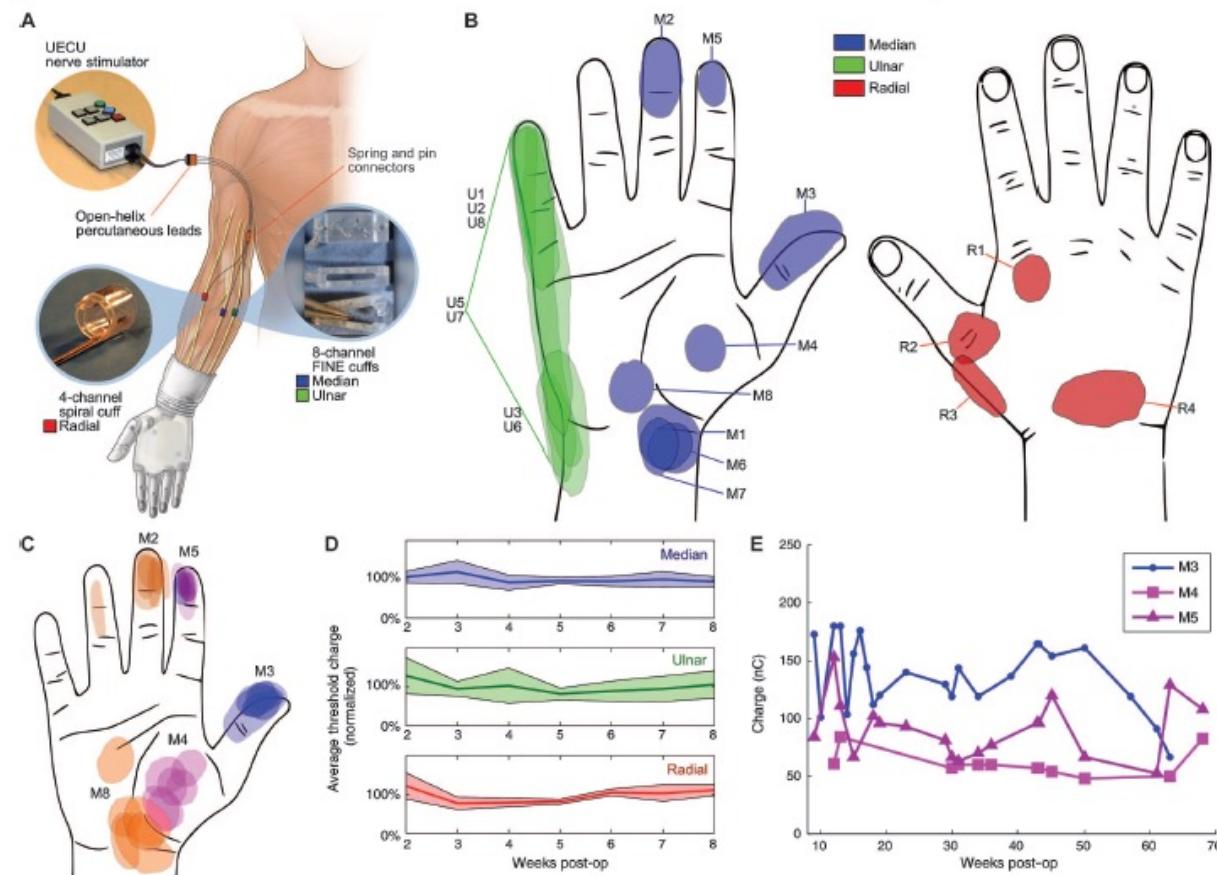
# First intraneural experiment



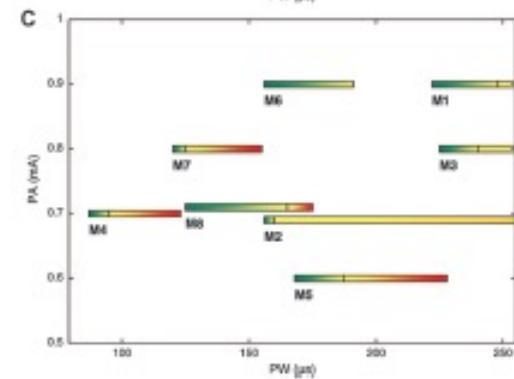
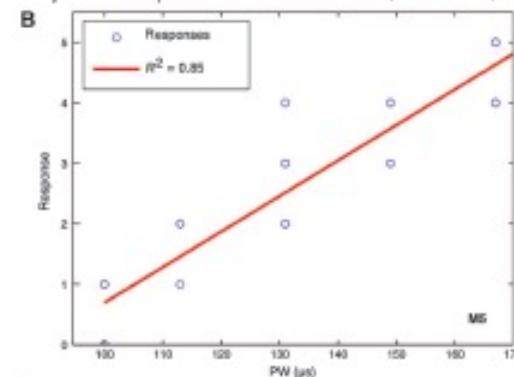
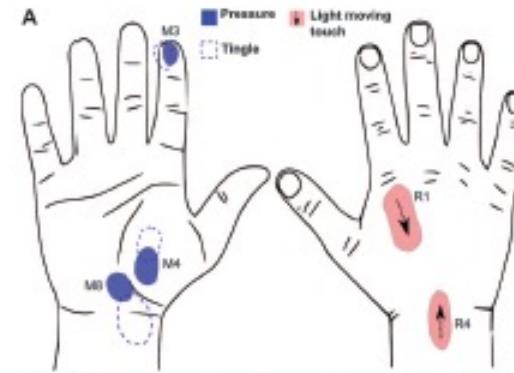
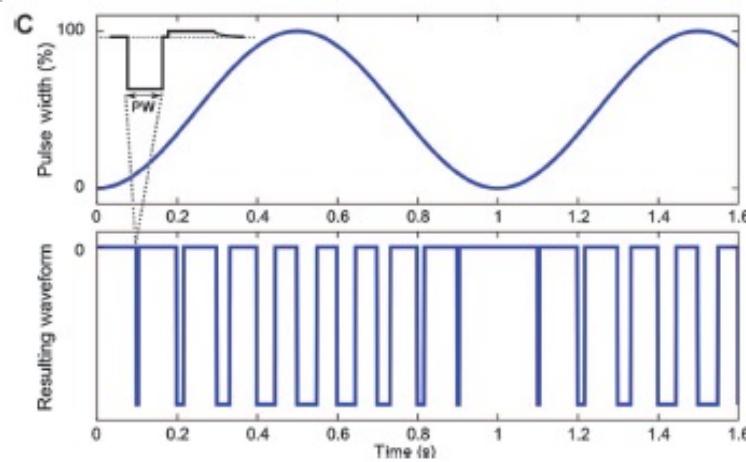
# Peripheral implantable electrodes



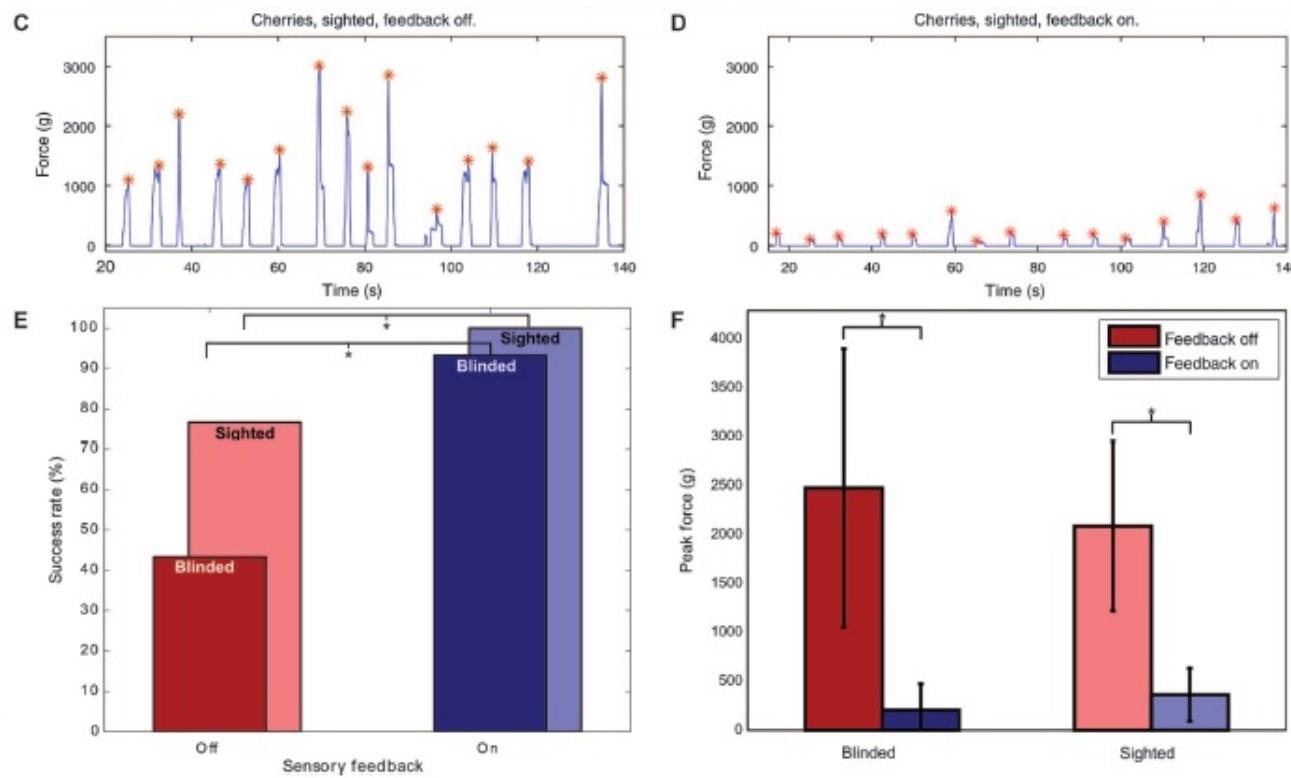
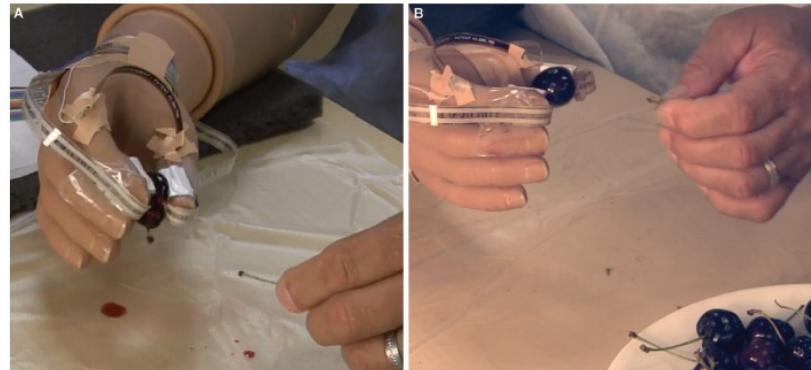
# Sensory feedback using FINE electrodes



# Sensory feedback using FINE electrodes



# Sensory feedback



# Short-term implant of TIMEs in an amputee



P.M. Rossini

- 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



S. Raspopovic



M. Capogrosso

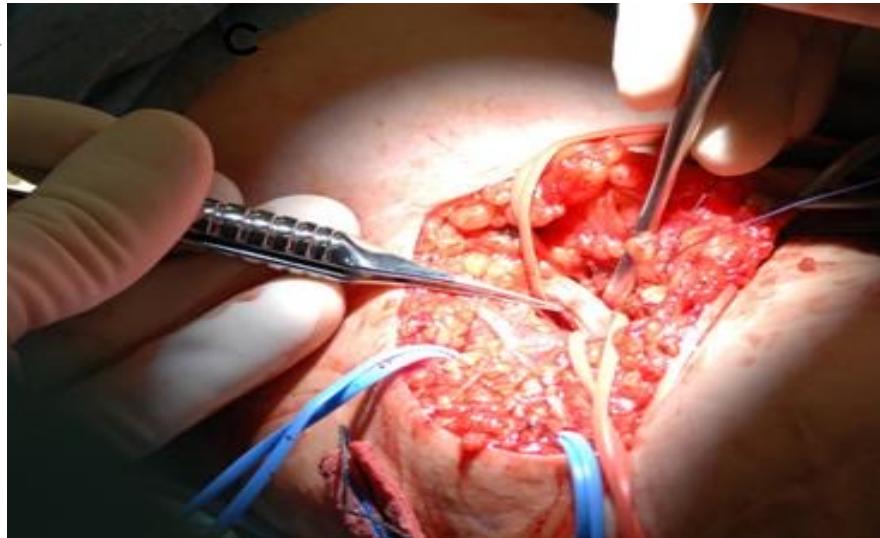
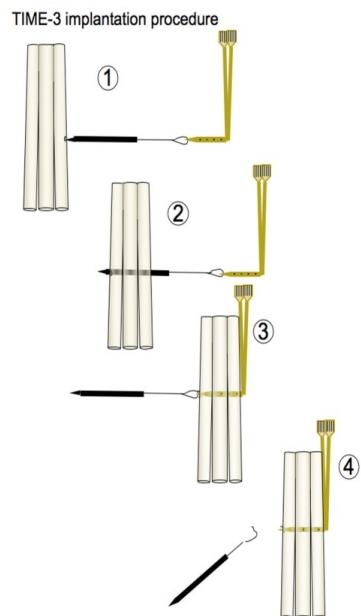


M. Bonizzato



# TIME implant

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

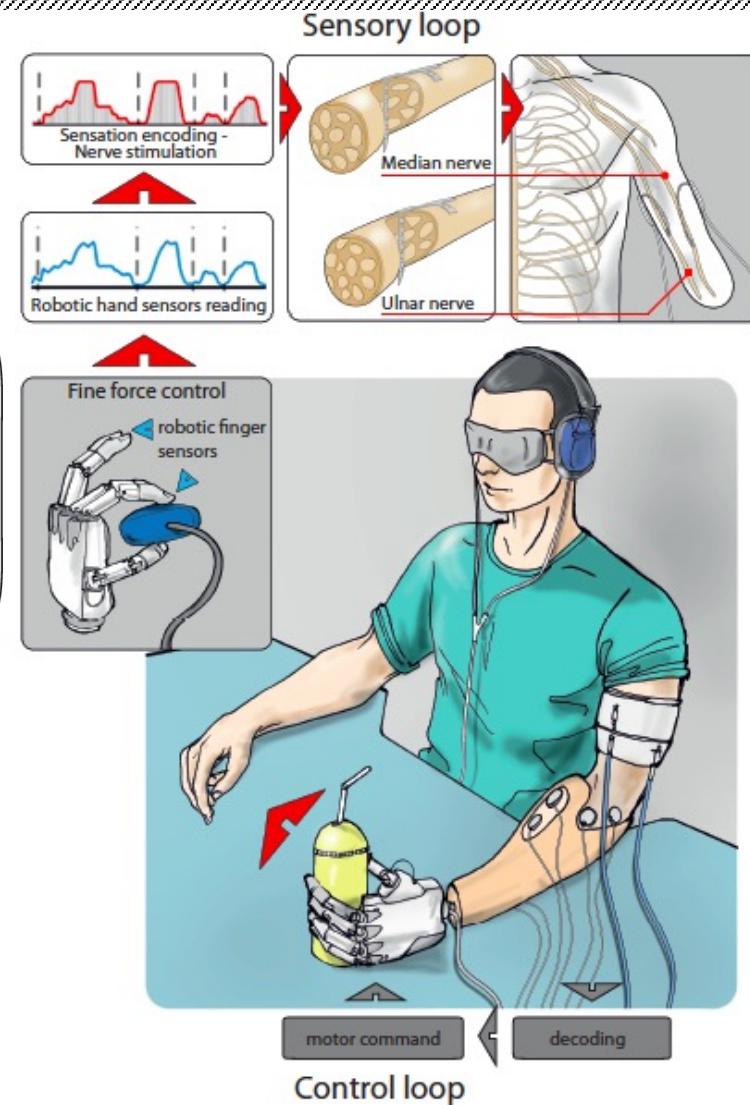


## ▪ Surgical technique:

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

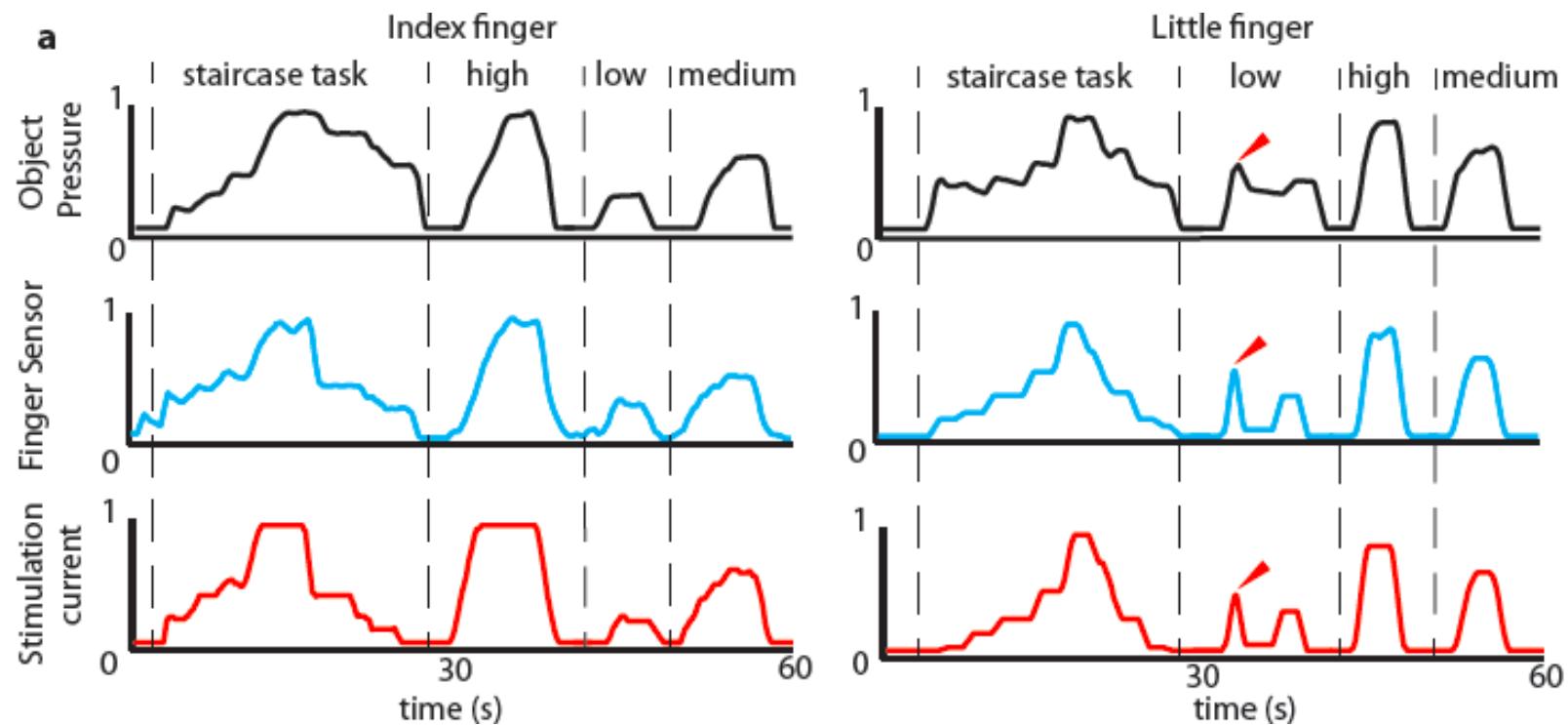
# Closed-loop control based on sensory feedback

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

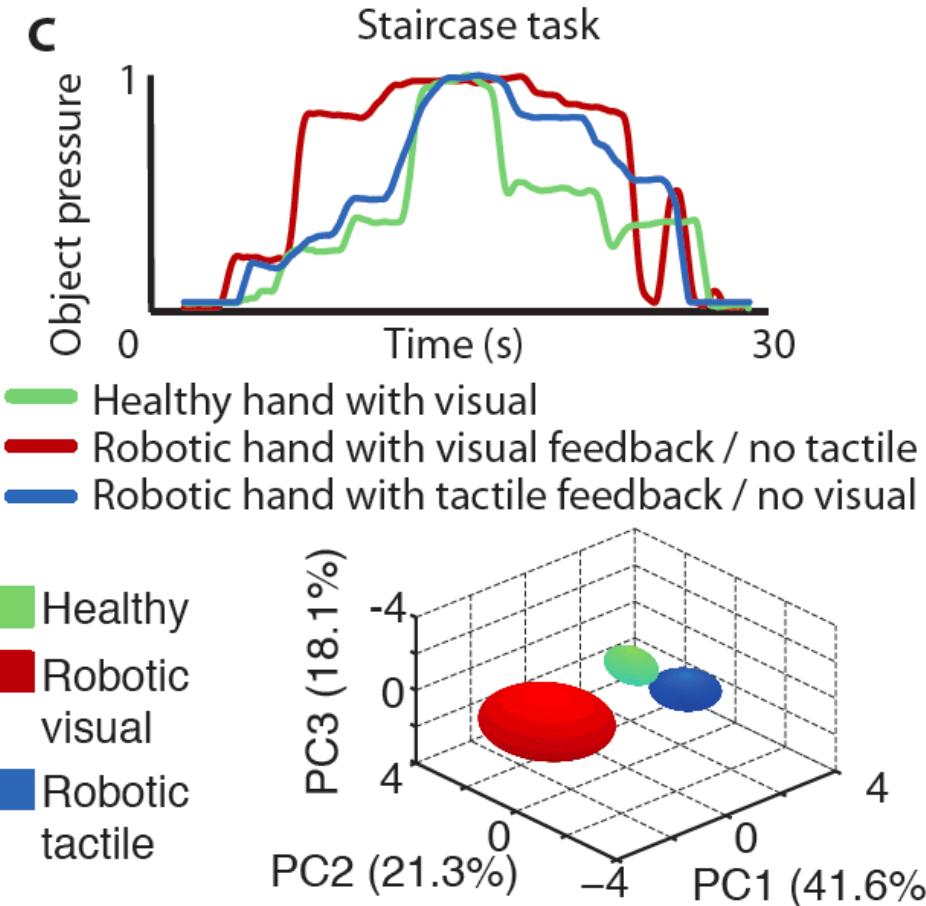


Azzurra dexterous hand  
(Prensilia srl)

# Selection of grasping force levels

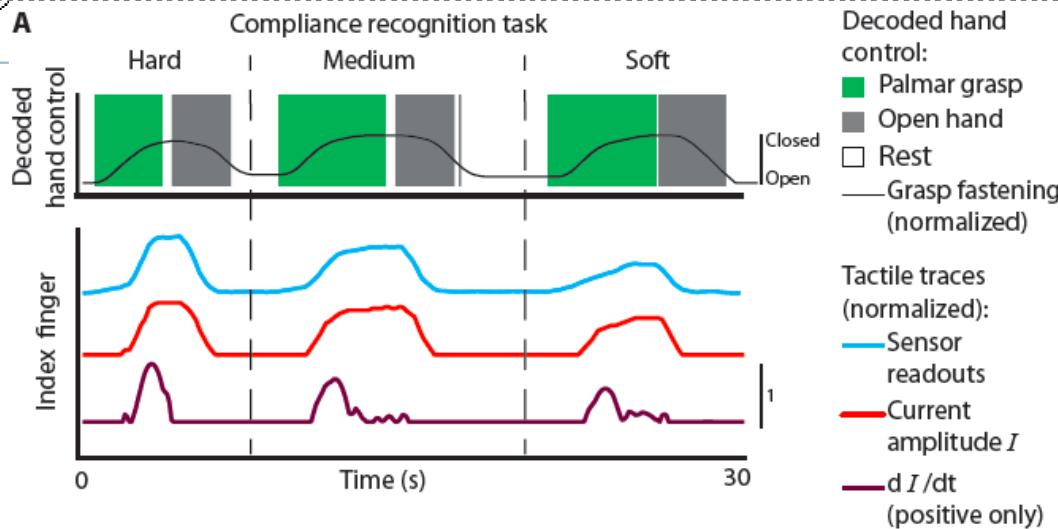


## Modulation of grasping force



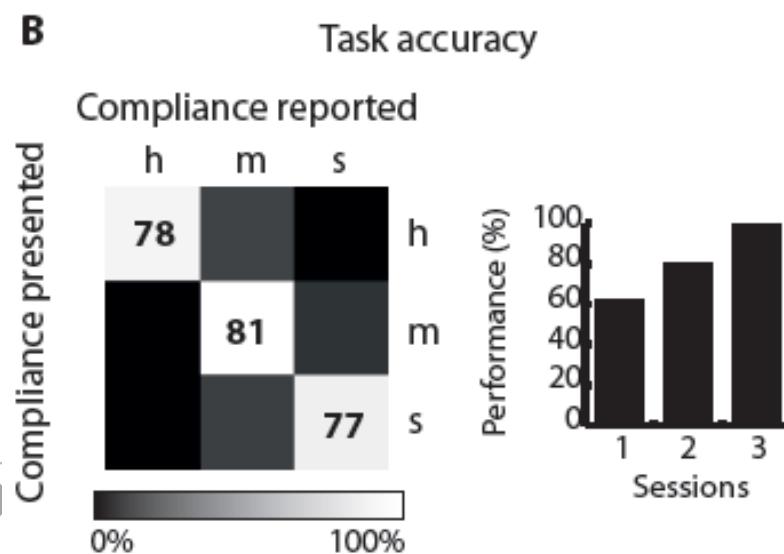
The artificial sensory feedback allowed the user to achieve performance close to the natural ones

# Compliance recognition



Three objects with different stiffness properties

Quite good performance and interesting learning ability



# Shape recognition

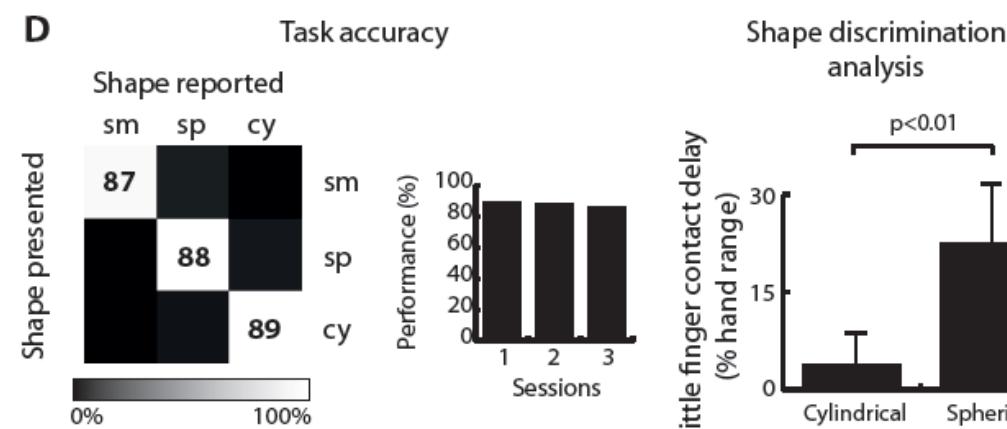
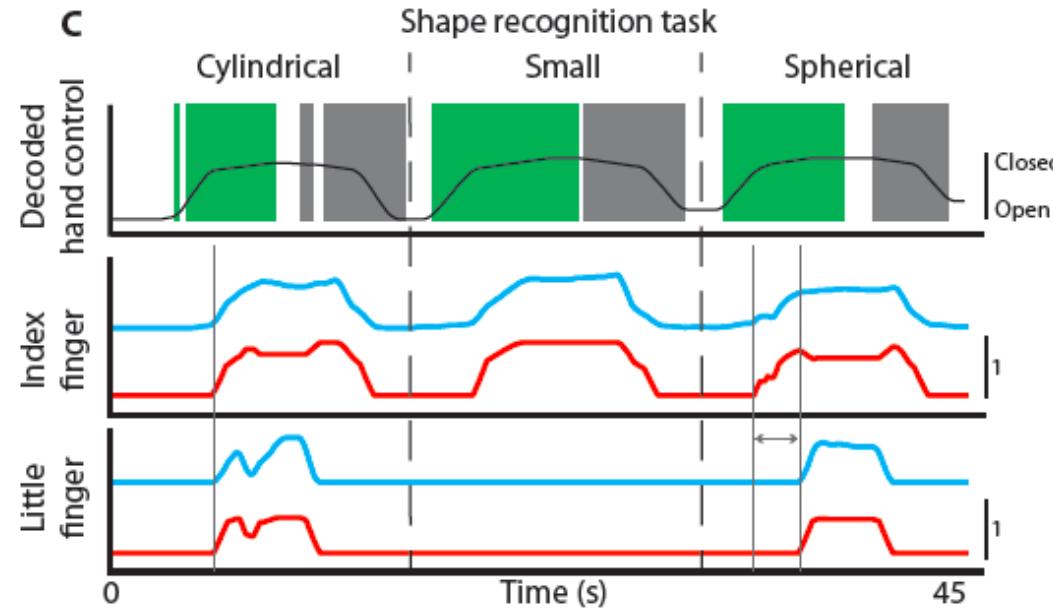
Decoded hand control:

- Palmar grasp
- Open hand
- Rest

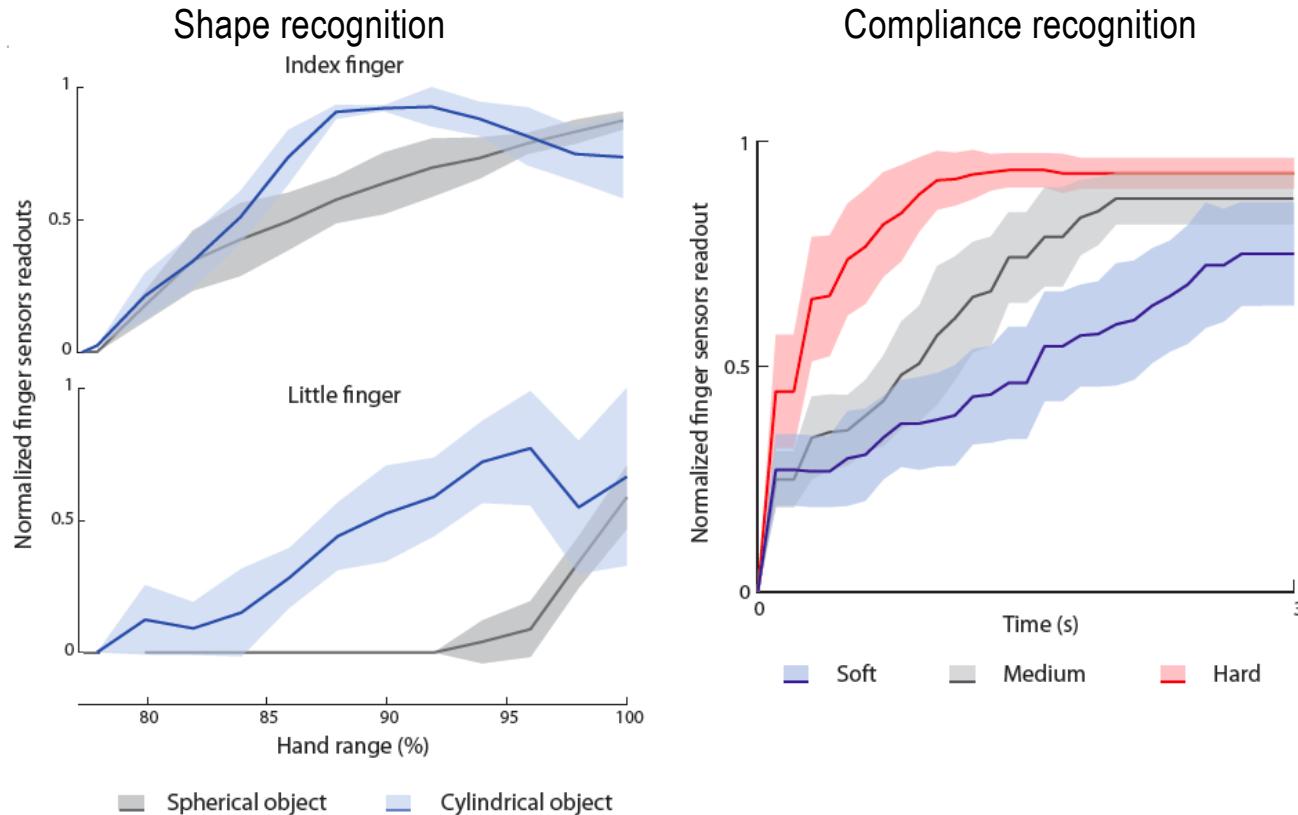
Grasp fastening (normalized)

Tactile traces (normalized):

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

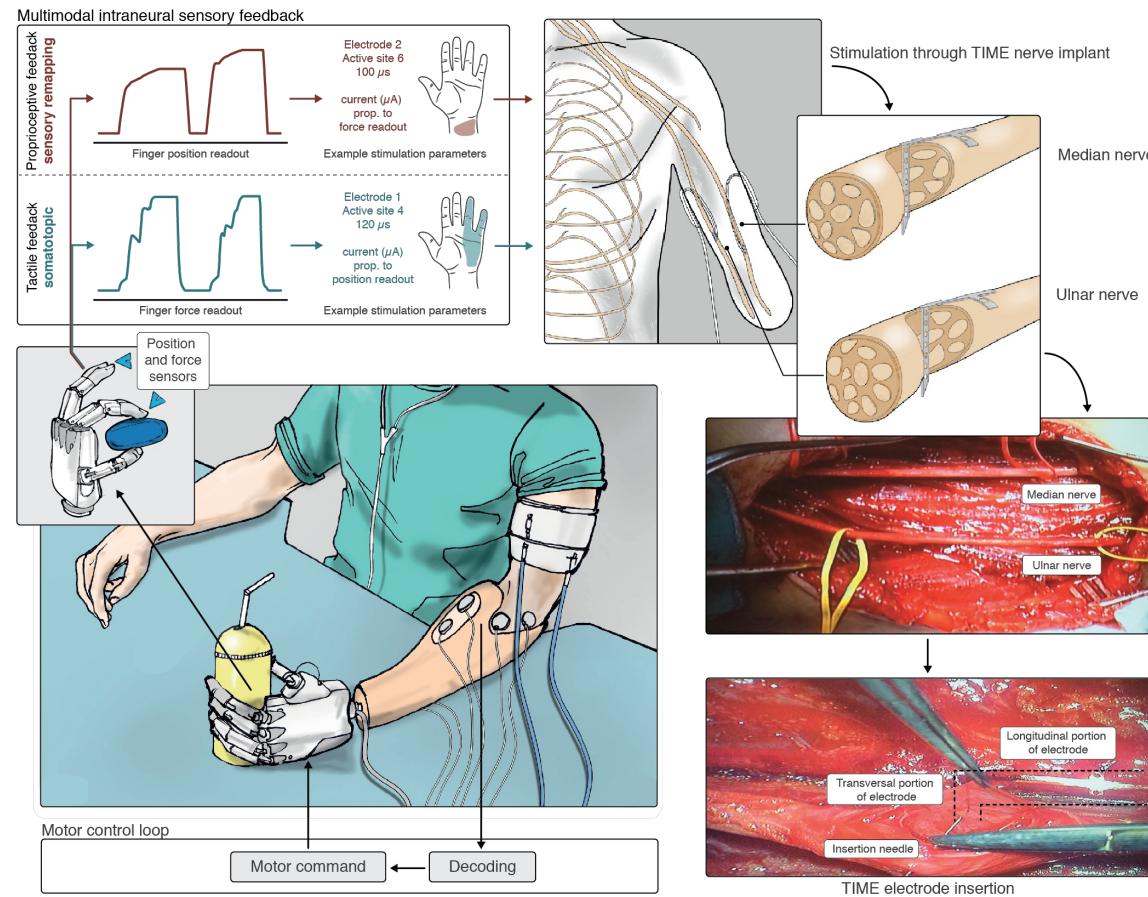


# Why this is possible?

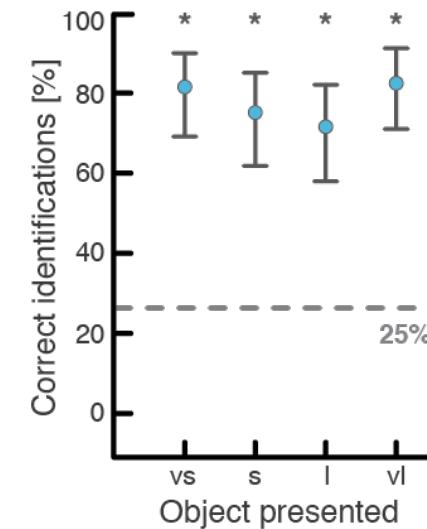
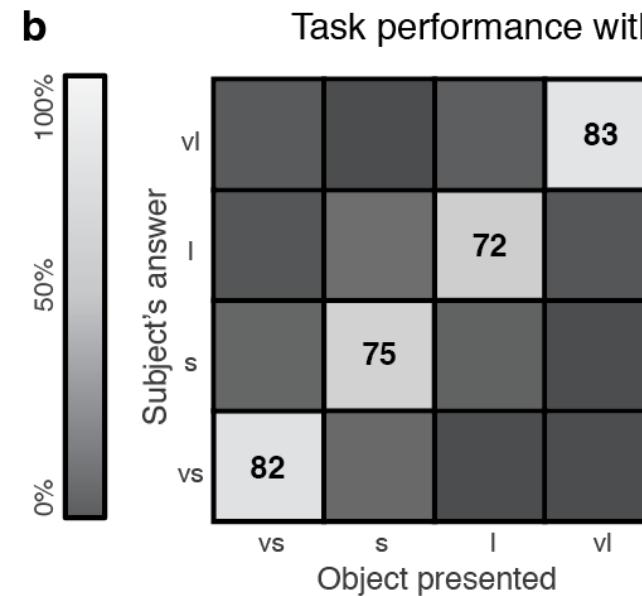
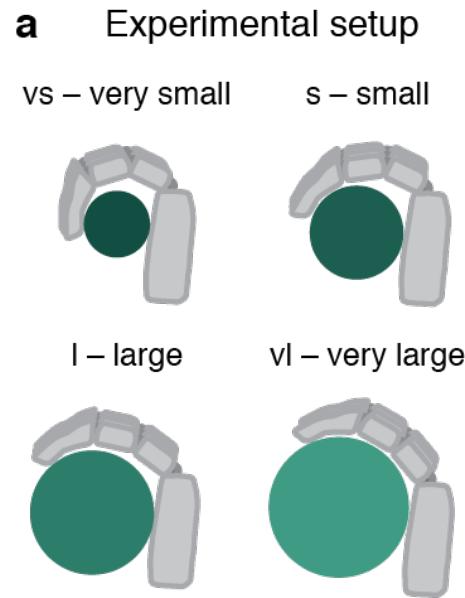


Different force profiles were provided to the users using the afferent stimulation  
→ this is **NOT** on-off sensation!

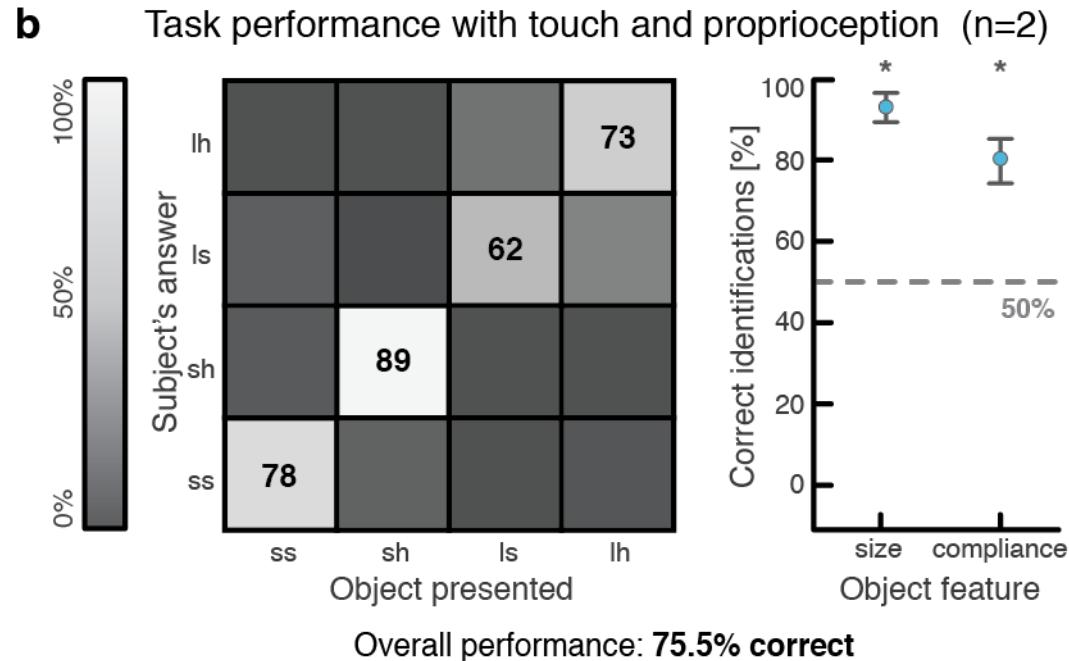
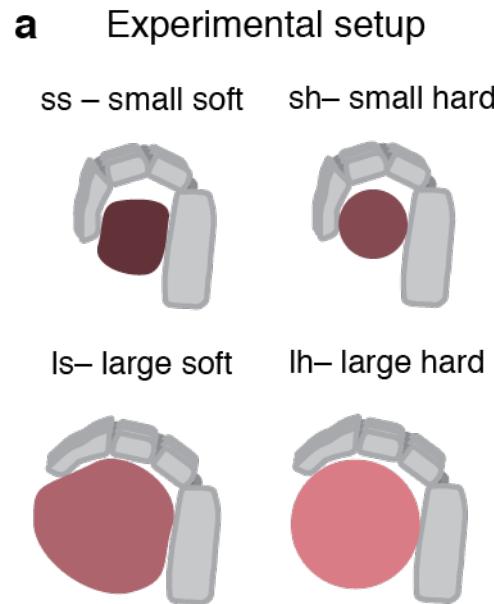
# Restoration of proprioception and tactile feedback



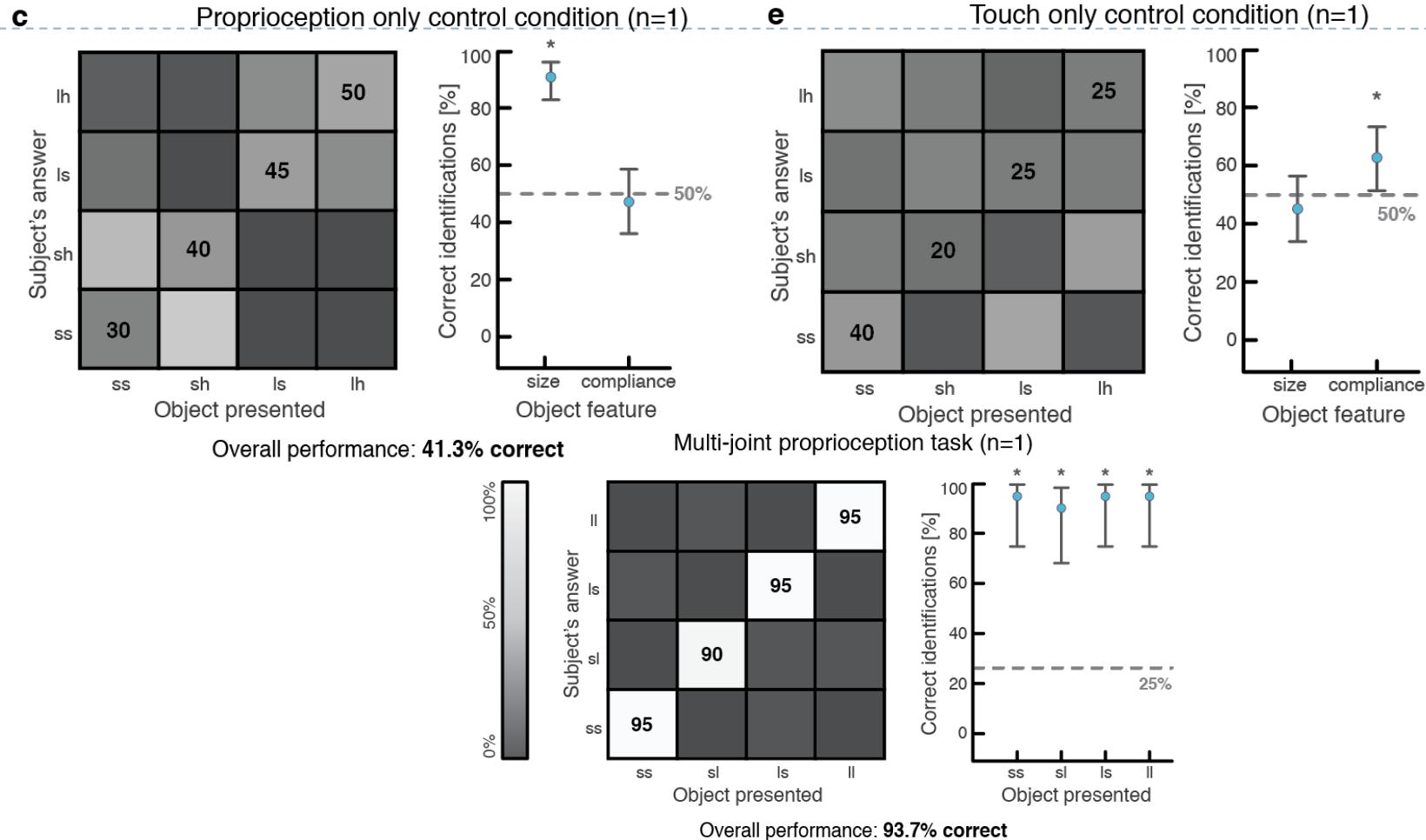
# Restoration of proprioception and tactile feedback



# Restoration of proprioception and tactile feedback



# Restoration of proprioception and tactile feedback

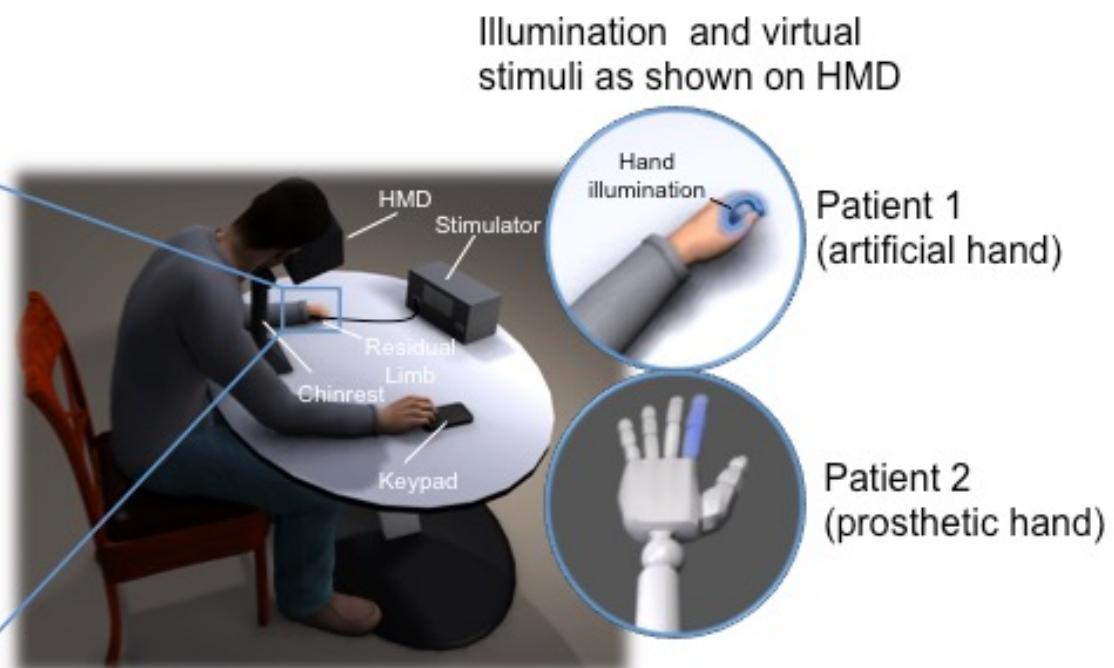
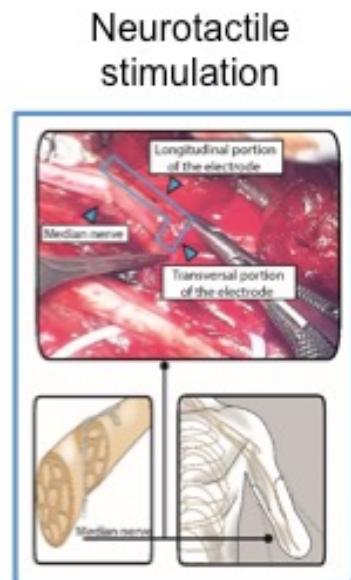


# Embodiment



O. Blanke

G. Rognini

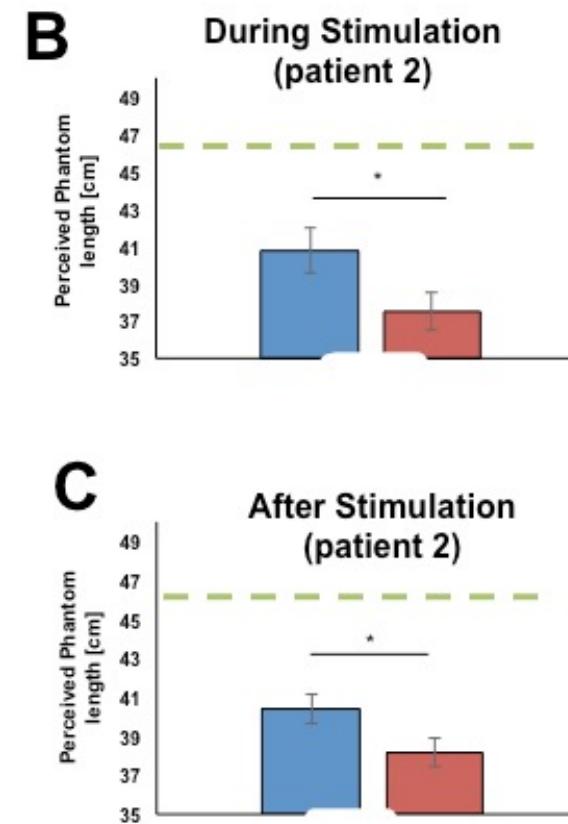
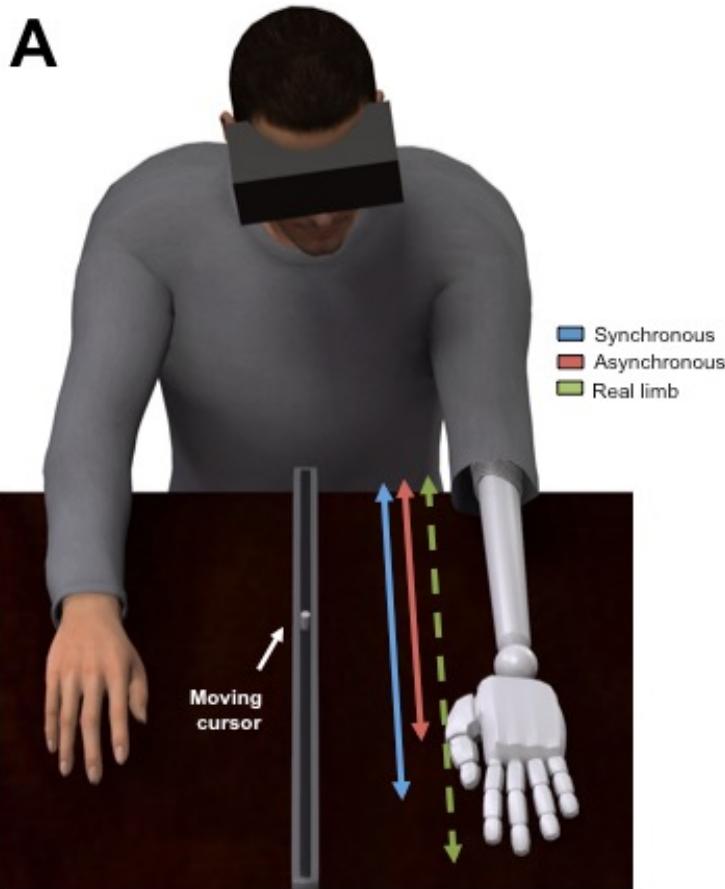


Illumination and virtual stimuli as shown on HMD

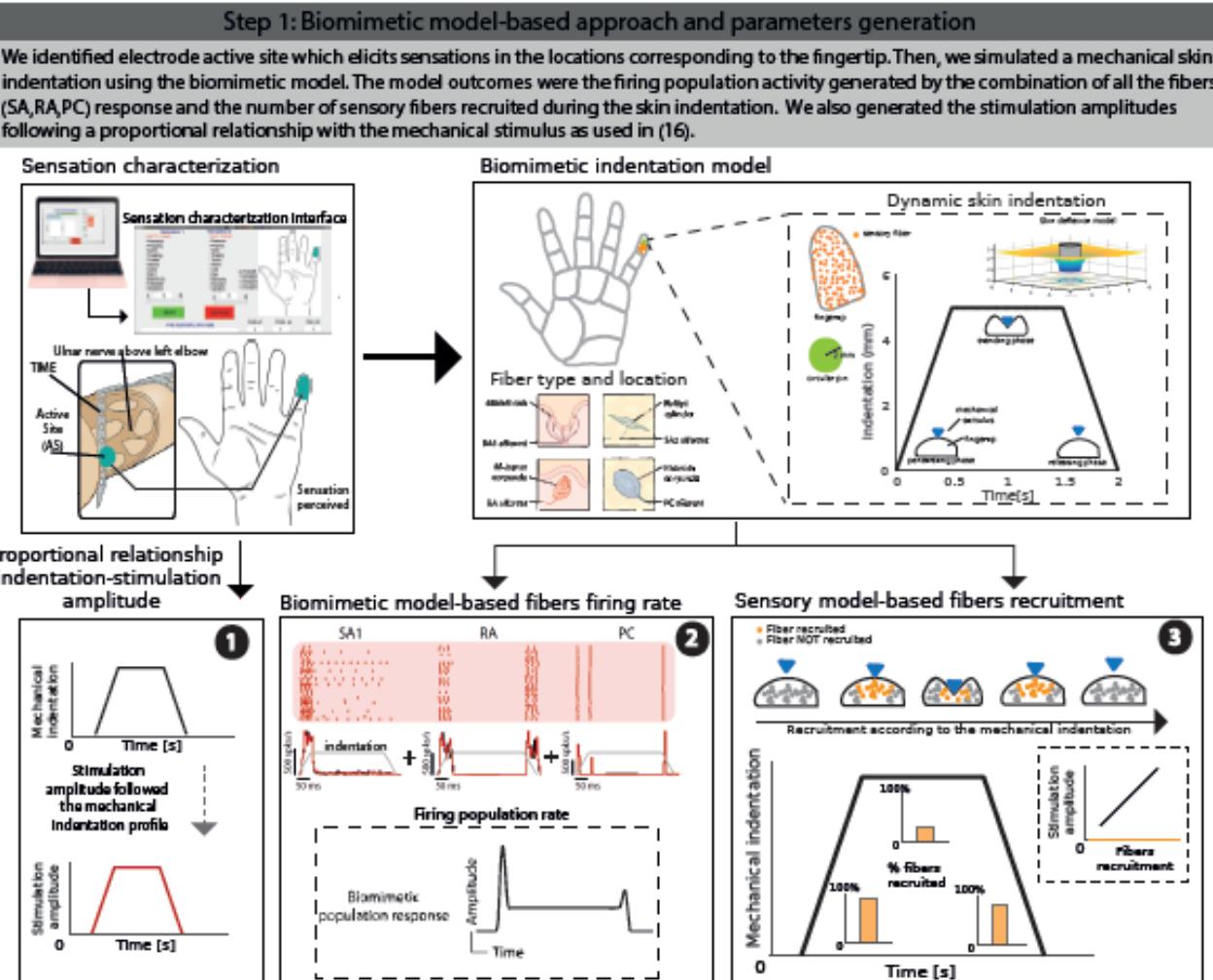
Patient 1  
(artificial hand)

Patient 2  
(prosthetic hand)

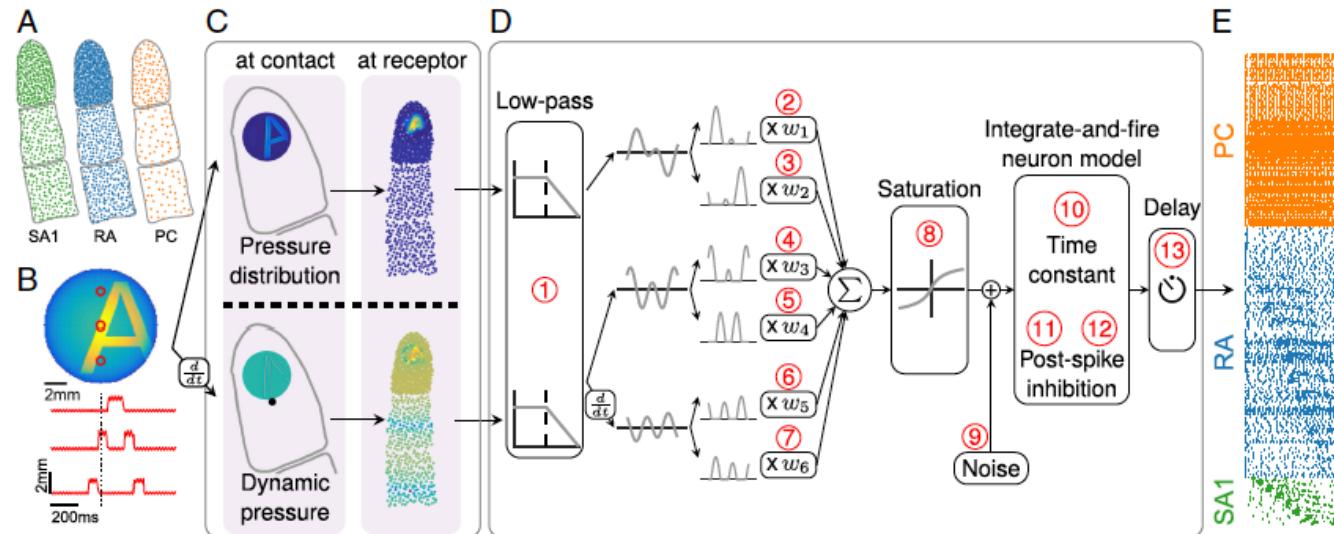
# Embodiment



# Biomimetic encoding strategy



# Biomimetic encoding strategy

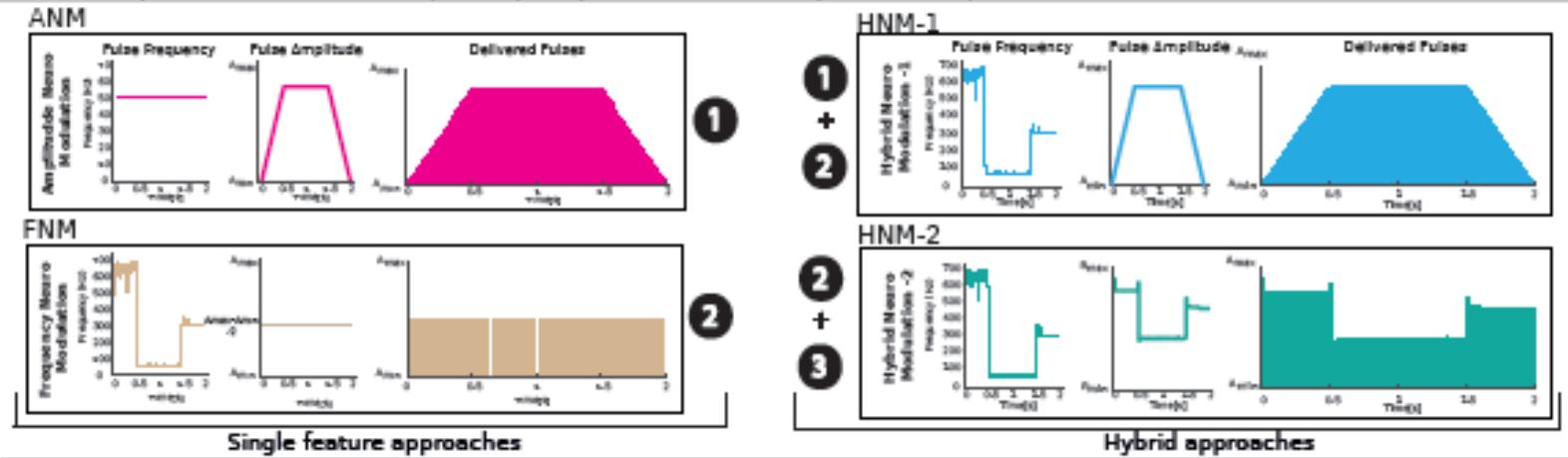


**Fig. 1.** Overview of the model. (A) Receptors are distributed across the skin given the known innervation densities of SA1, RA, and PC afferents. (B) The stimulus—in this case, a vibrating embossed letter A scanned across the skin—is defined as the time-varying depth at which each small patch of skin (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 RAs show mixed spatial and vibration responses.

# Biomimetic encoding strategy

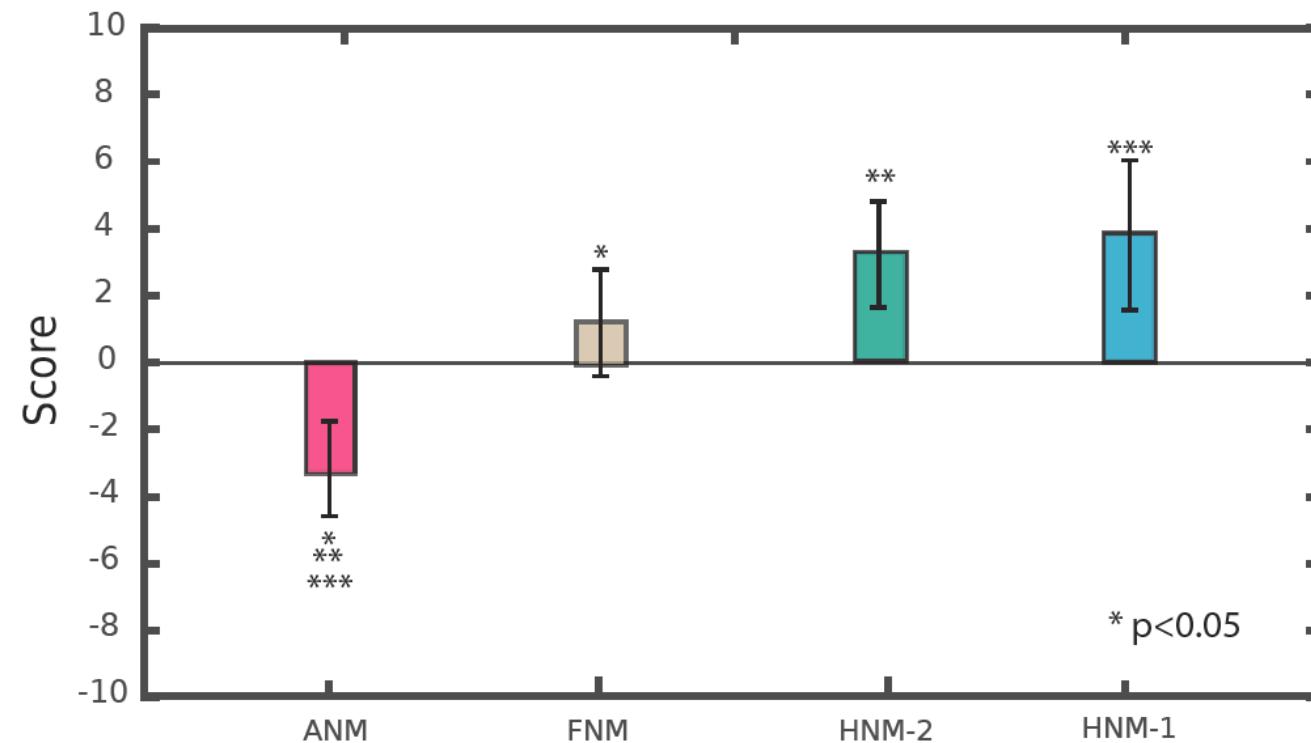
## Step 2: Sensory encoding strategies

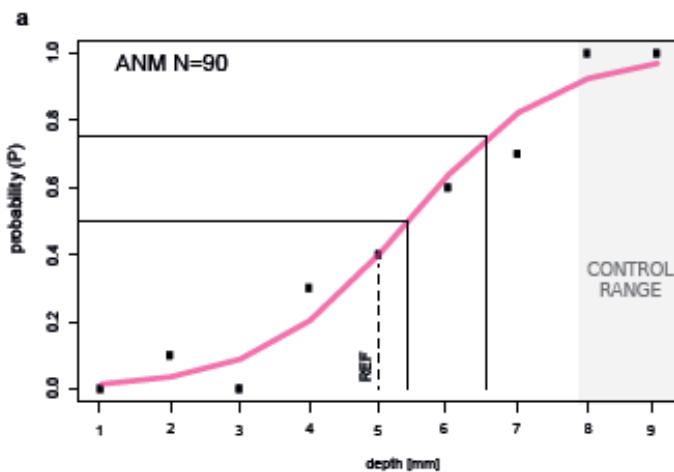
Different encoding strategies in which only one stimulation feature is modulated (Single feature) or both frequency and amplitude of the stimuli are simultaneously modulated (Hybrid). We converted the firing population rate generated by the biomimetic model in the frequency of the intraneuronal stimulation (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  $\mu$ s.



# Biomimetic encoding strategy

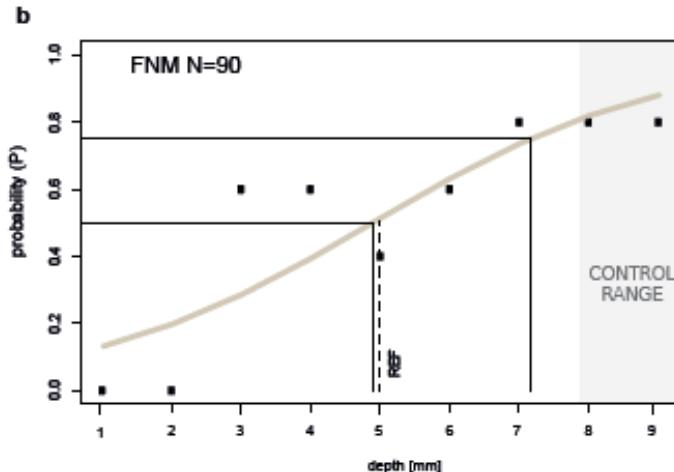
**b** Perceived naturalness among different encoding strategies N=16





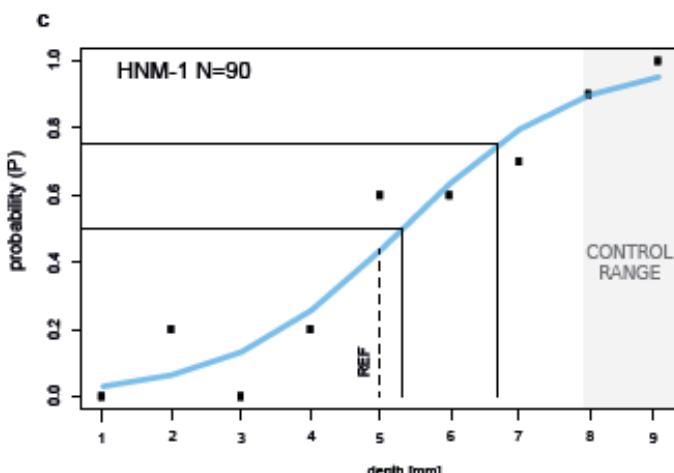
Point of Subjective Equality (PSE): 5.51 mm

Just-Noticeable Difference (JND): 1.01 mm



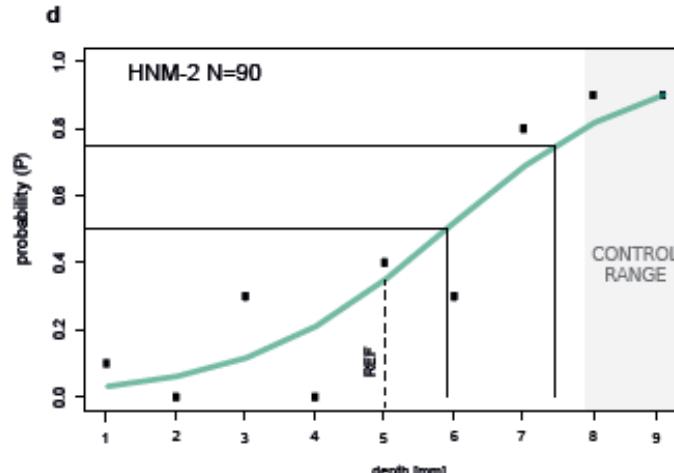
Point of Subjective Equality (PSE): 4.87 mm

Just-Noticeable Difference (JND): 2.26 mm



Point of Subjective Equality (PSE): 5.31 mm

Just-Noticeable Difference (JND): 1.35 mm

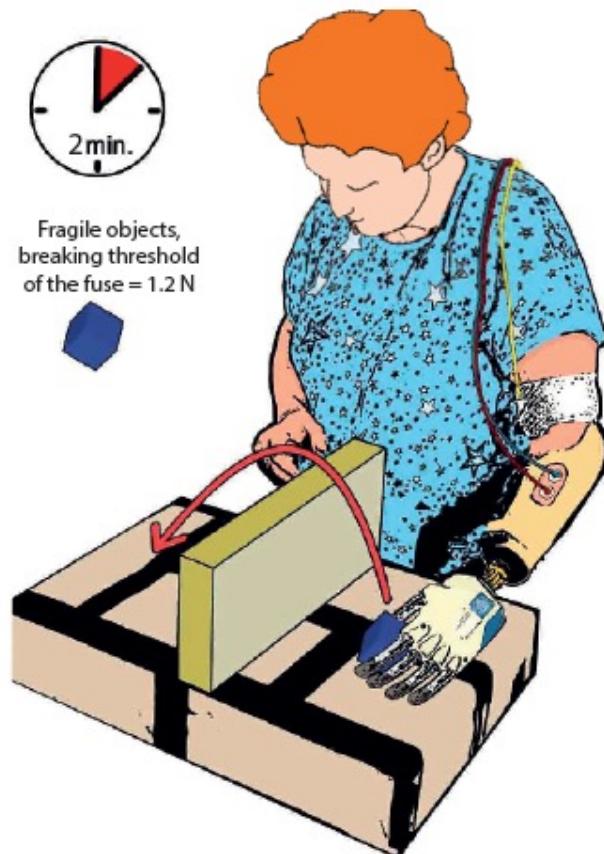


Point of Subjective Equality (PSE): 5.87 mm

Just-Noticeable Difference (JND): 1.55 mm

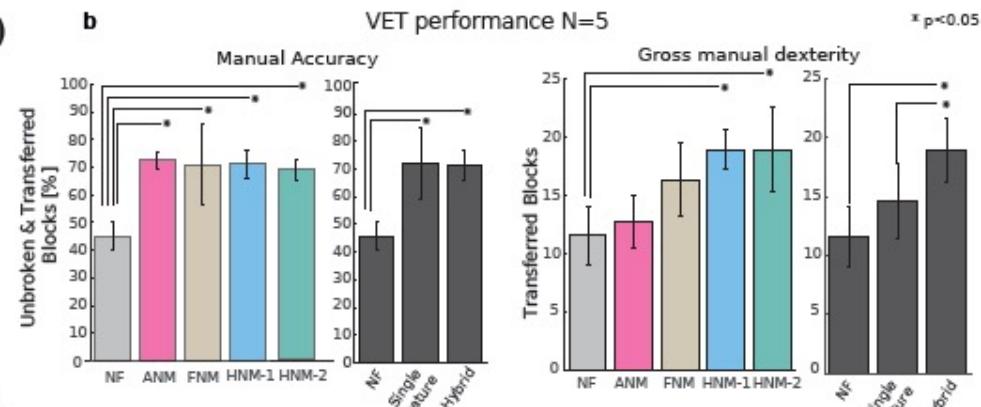


### a Setup - Virtual Eggs Test (VET)

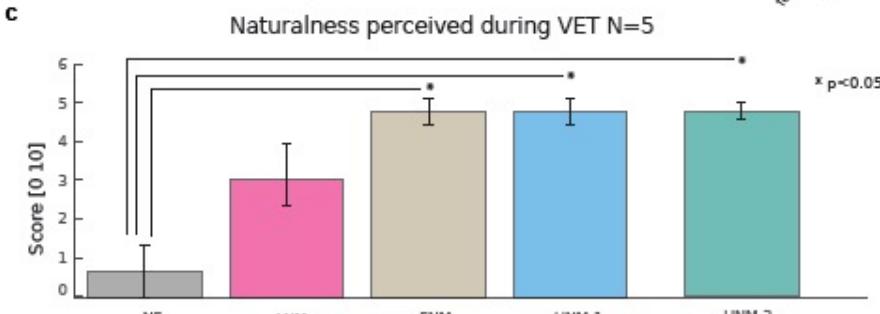


Q1) It seemed like I was grasping a real object  
 Q2) I felt the intensity of the grasping force applied by the robotic hand on the object

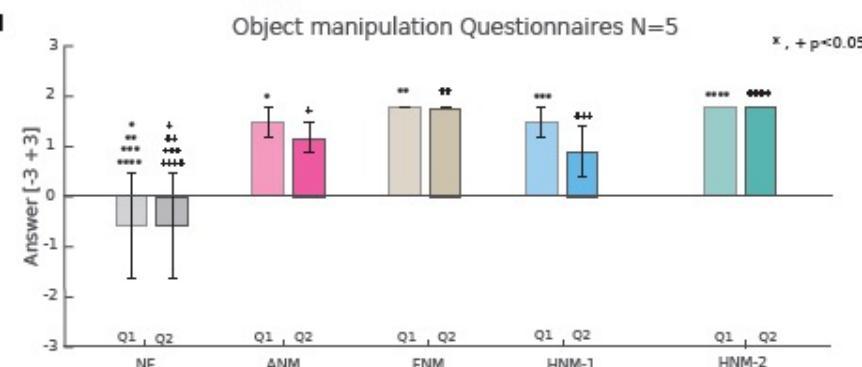
b



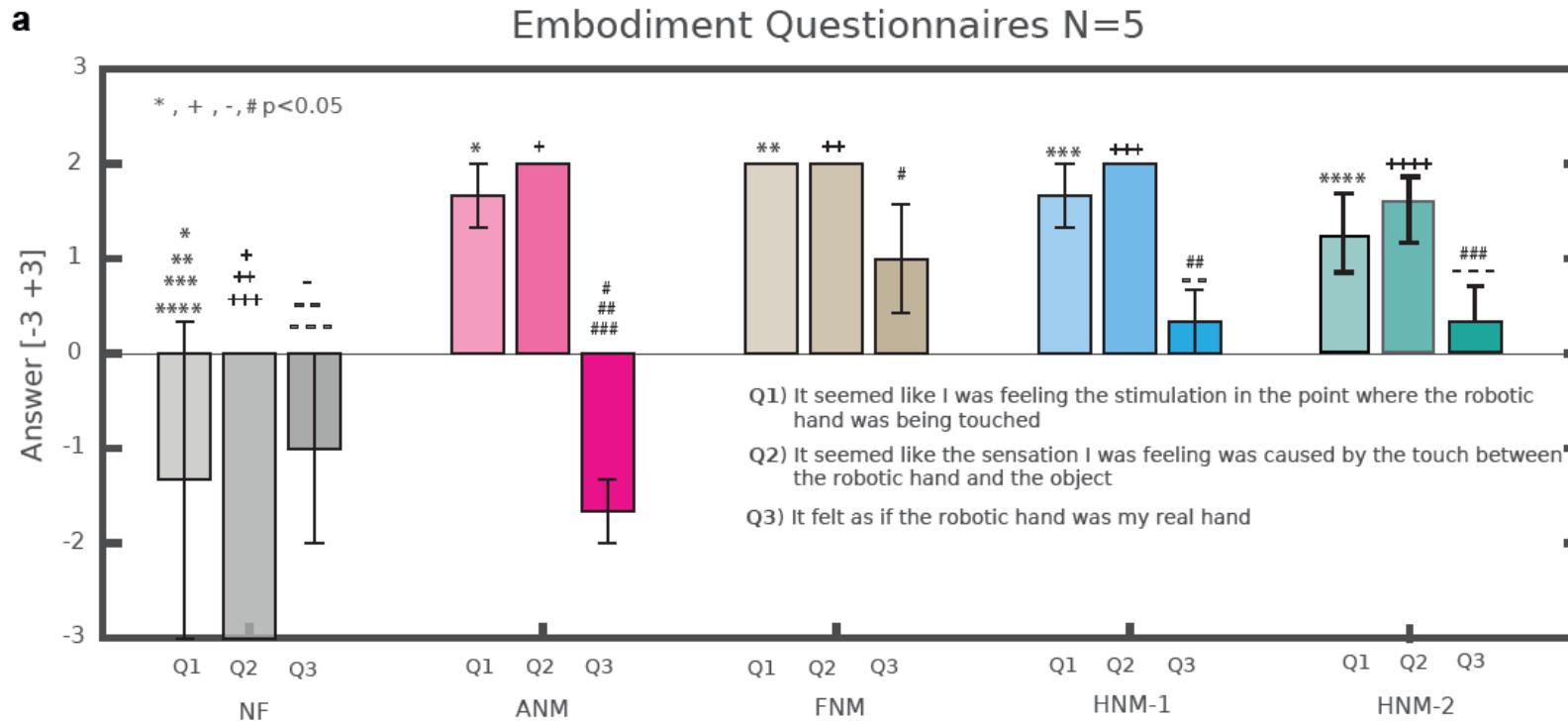
c



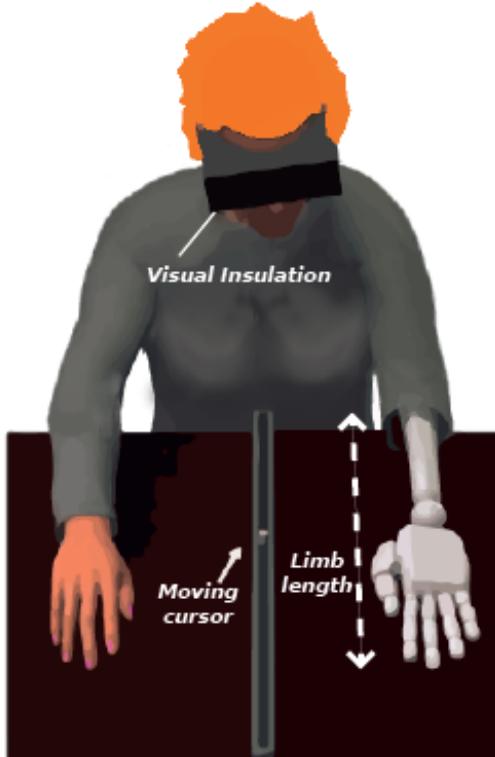
d



# Biomimetic encoding strategy

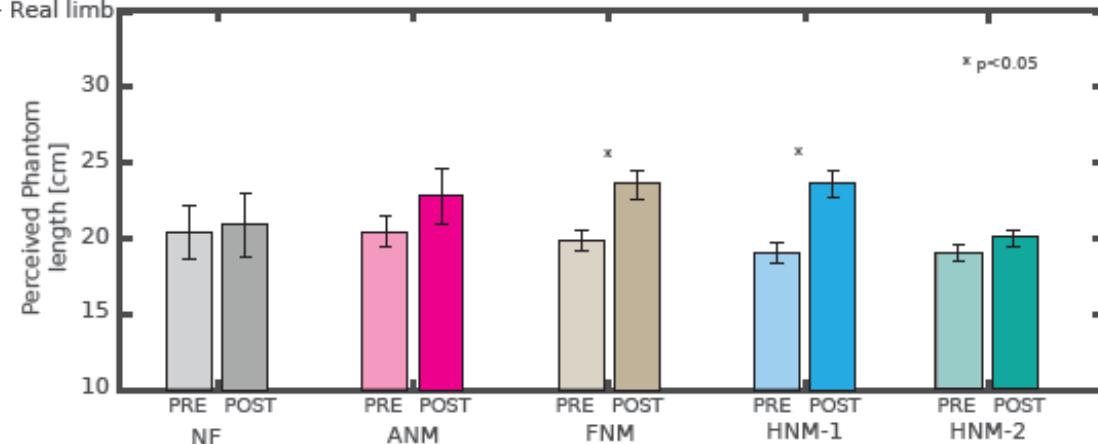


**a** Telescoping task setup

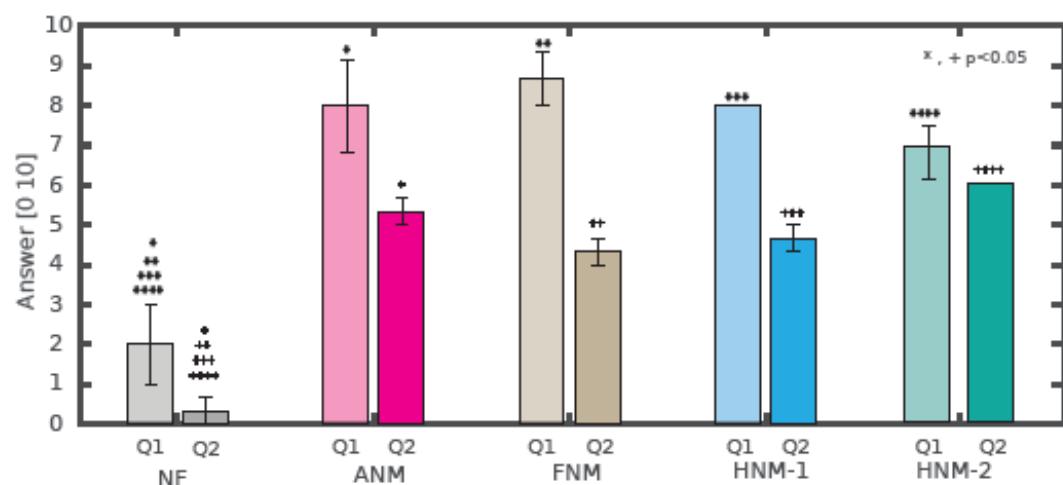


Q1) It seemed like the phantom hand had changed orientation as the robotic hand  
Q2) I felt my phantom arm longer

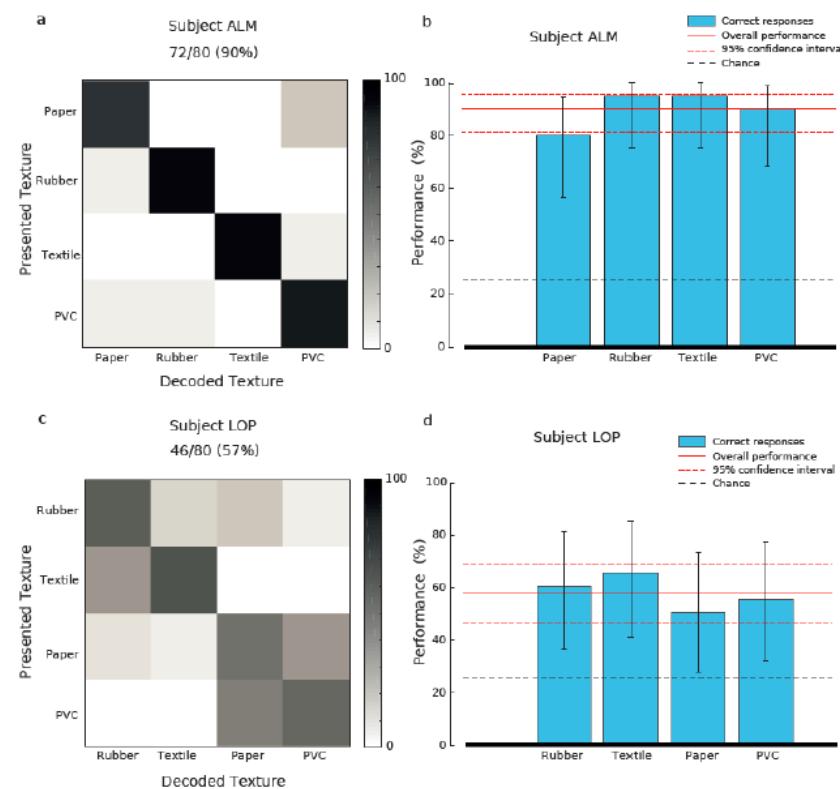
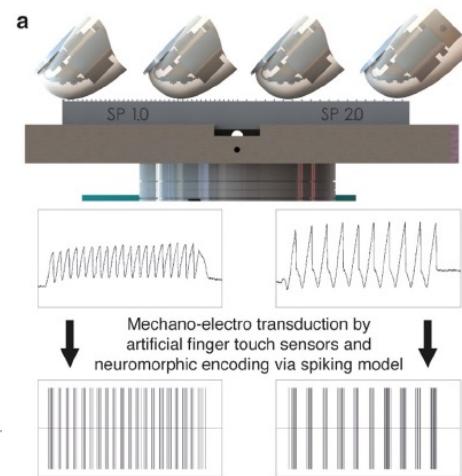
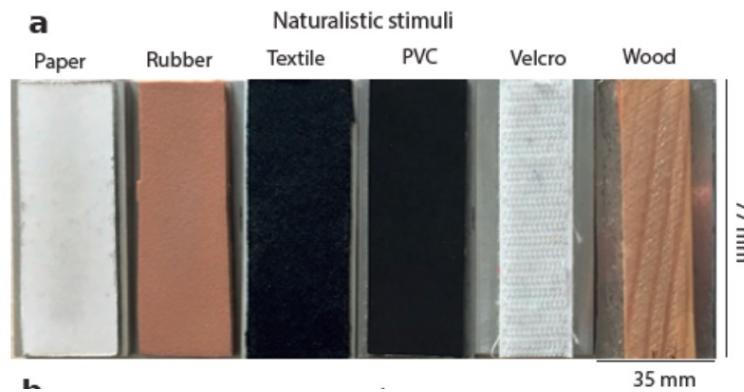
**b** Telescoping pre-post VET N=5



**c** Phantom limb dimension perceptions Questionnaires N=5



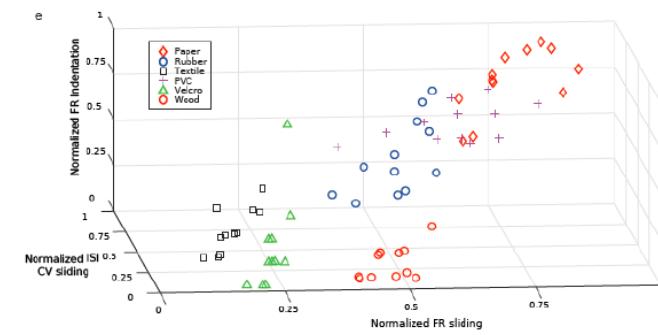
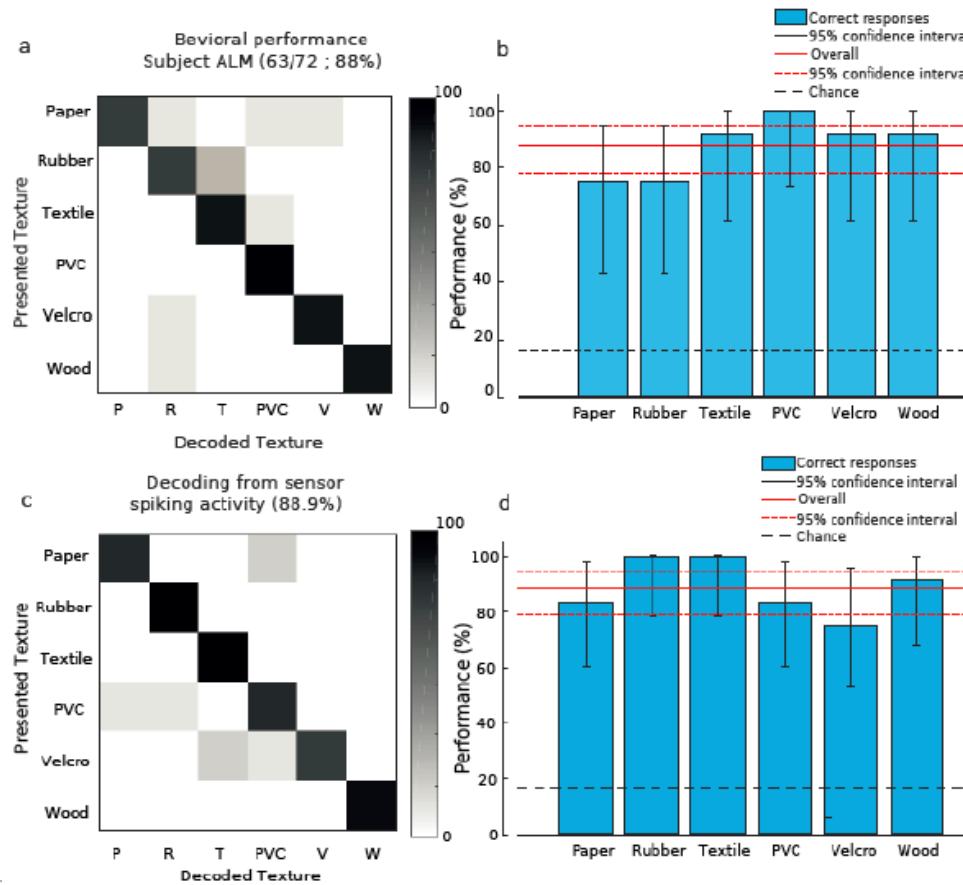
# Restoring perception of real textures



Ondo et al., eLIFE, 2016

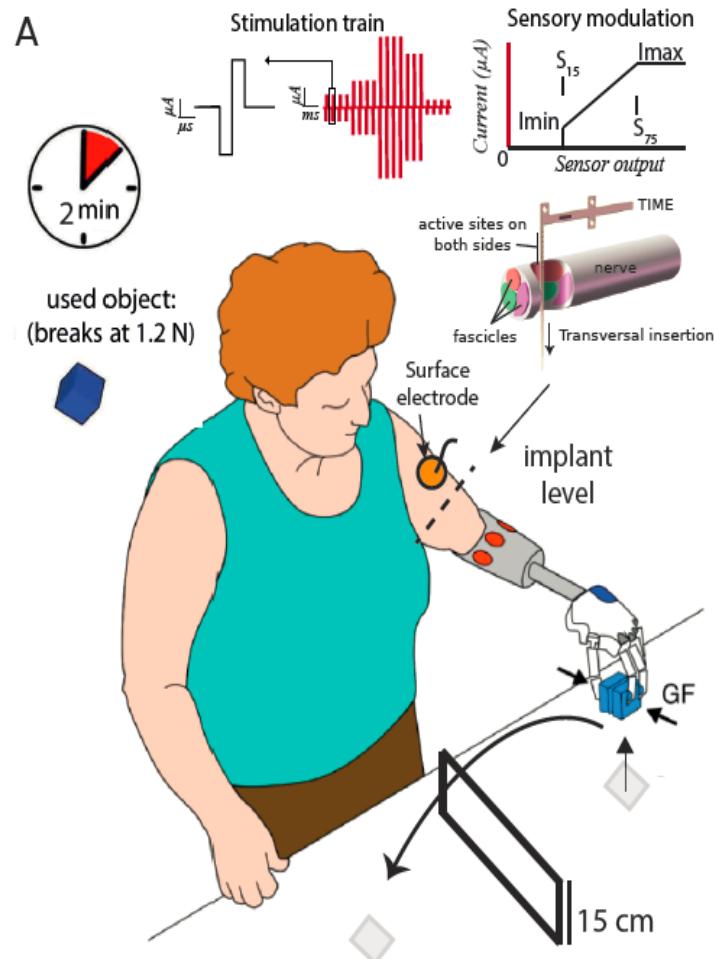
Mazzoni et al., Sci Rep, 2019

# Restoring perception of real textures



Implanted interfaces  
can also be used to  
understand basic  
principles

# Effects of cognitive load



## B Induced sensations & stimulation parameters

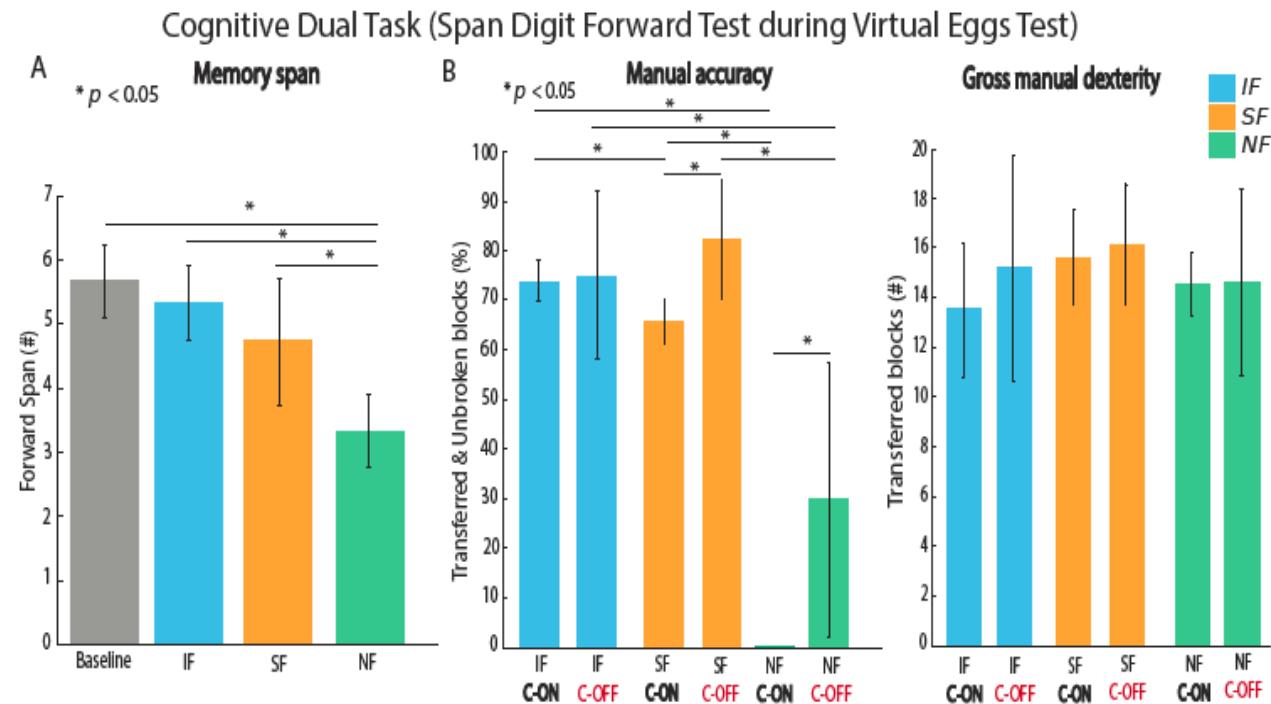
### Intraneuronal sensory Feedback (IF)

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 $\mu$ s
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 $\mu$ s
frequency	50 Hz

# Effects of cognitive load



# Bidirectional neurocontrolled leg prostheses



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

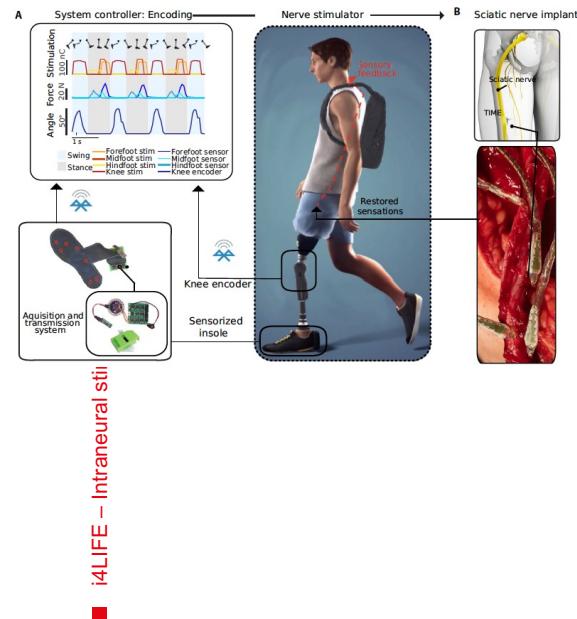
**Carbon Fiber Foot Case**  
 A lightweight, high strength carbon fiber foot shell contains the electromechanical actuation system

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

# Bidirectional neurocontrolled leg prostheses

## Sensory feedback

Enhancing functional abilities and cognitive integration  
of the lower limb prosthesis



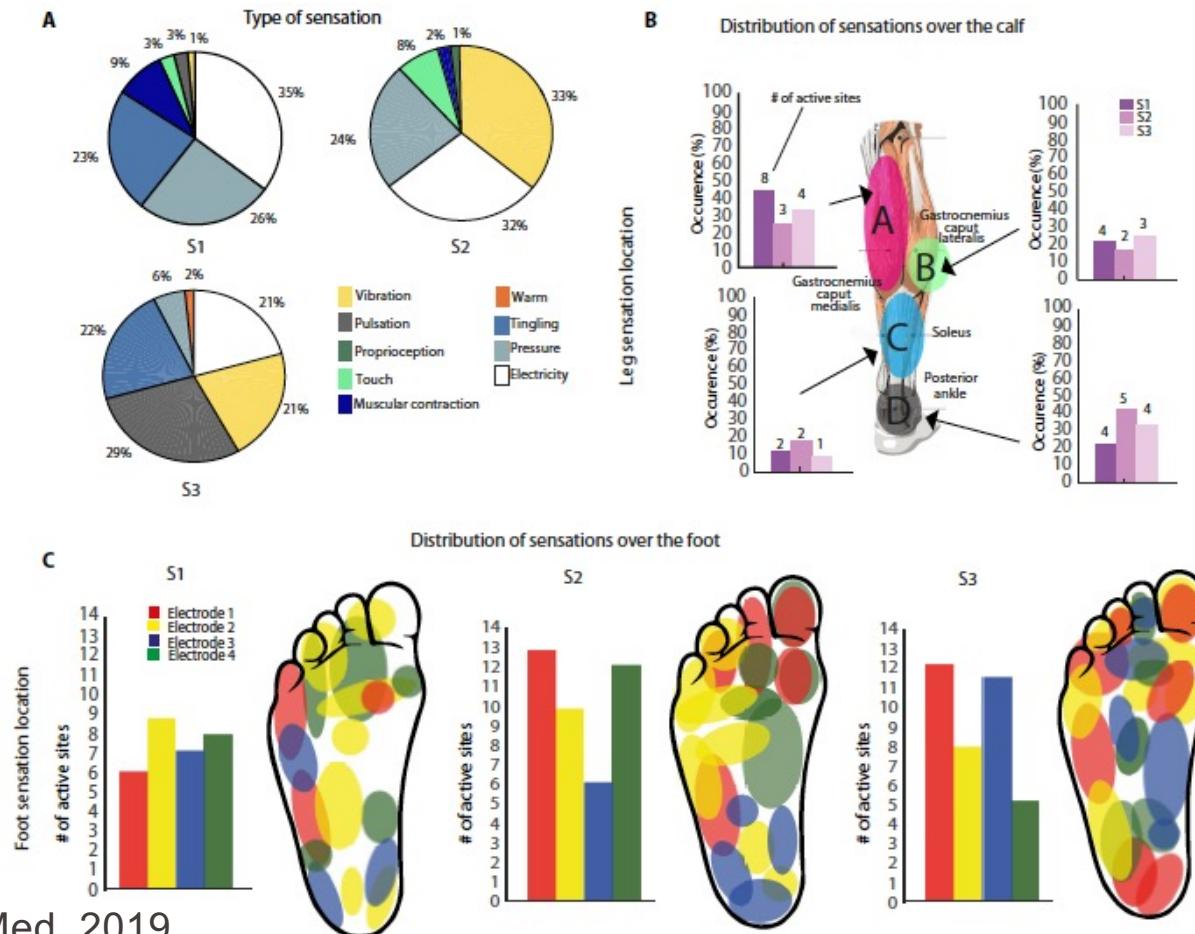
Movie S2:  
Neuroprosthesis working principle and active tasks

Caution: Investigational device

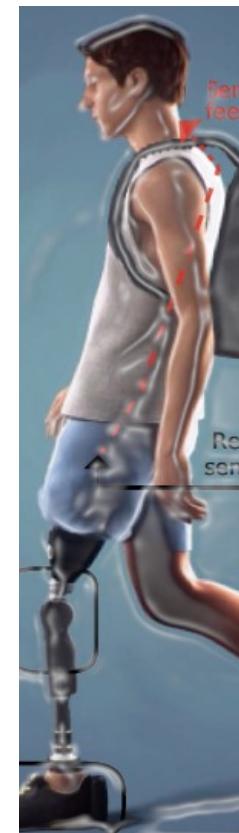
# Bidirectional neurocontrolled leg prostheses

## Sensory feedback

Petrini et al.,  
Science Trans Med, 2019

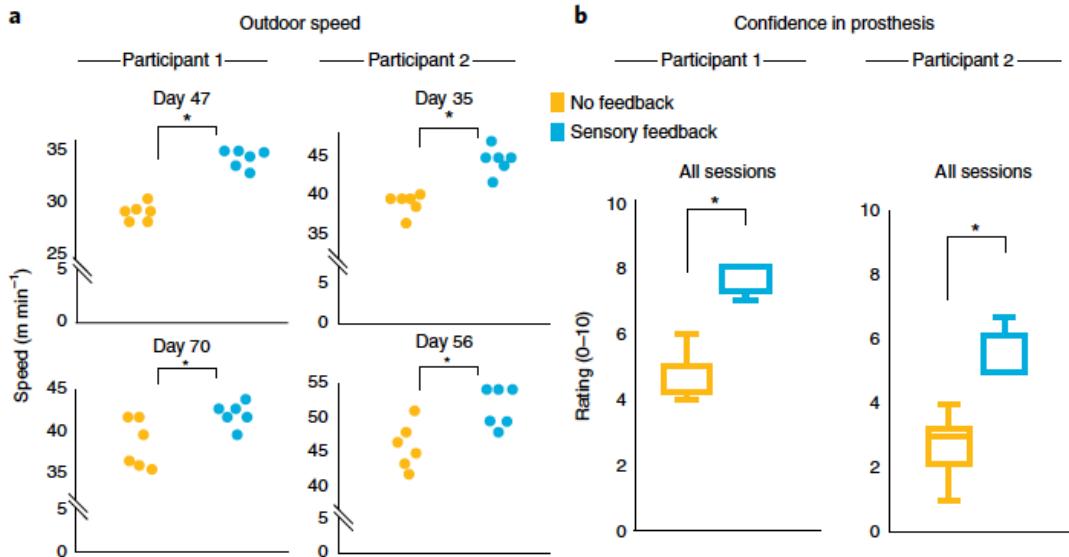


S.Micera



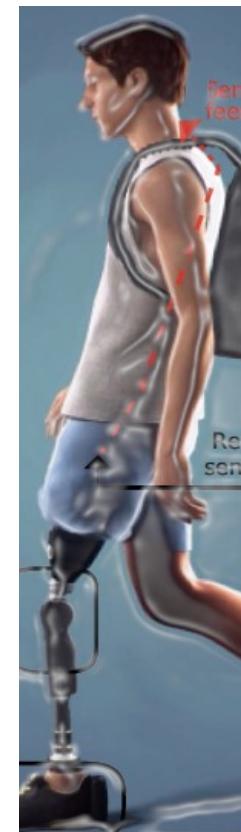
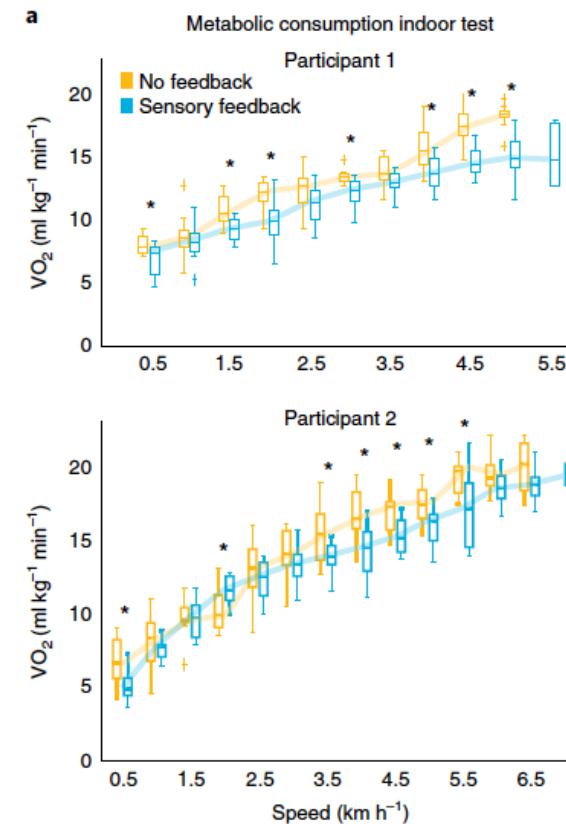
# Bidirectional neurocontrolled leg prostheses

## Sensory feedback



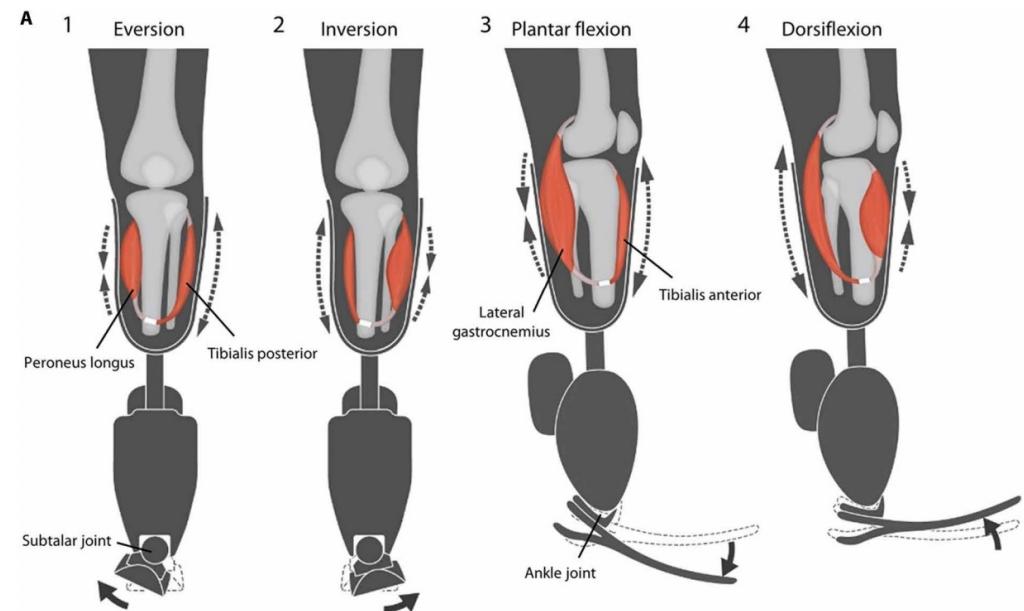
Walking speed and self-reported confidence increased while mental and physical fatigue decreased for both participants

Participants exhibited reduced phantom limb pain with neural sensory feedback.



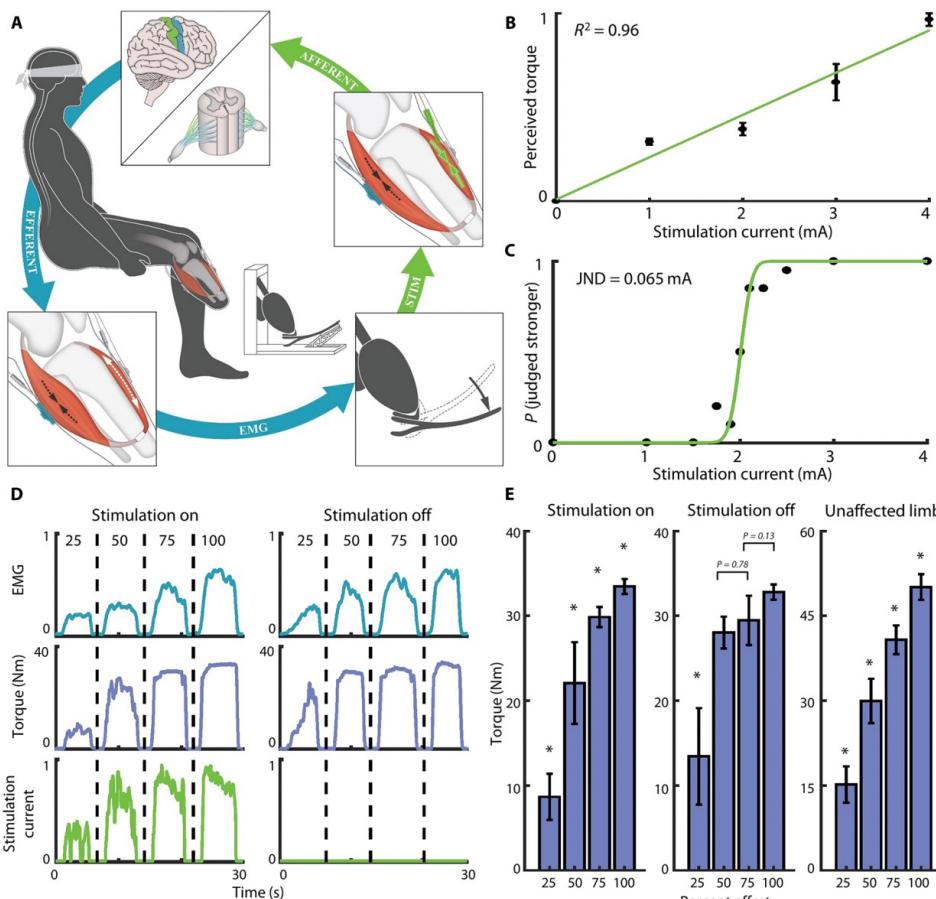
# Agonist-antagonist myoneural interface

- 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

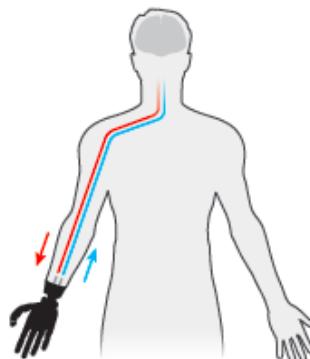


- (A) Schematic of the prosthesis-in-the-loop control architecture, in which afferent feedback of prosthetic joint torque is provided via FES of the antagonist muscle. The patient perceives this stimulation as a natural sensation of ankle torque
- (B) Magnitude estimation of perceived dorsiflexion torque 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

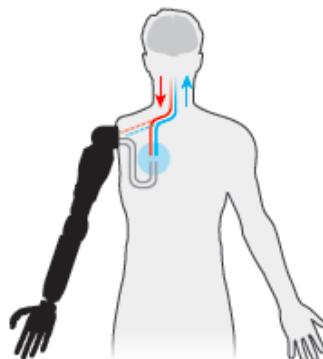
# Sensory feedback

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



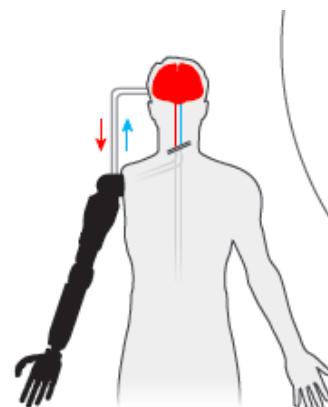
## *Use the remaining nerves*

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.

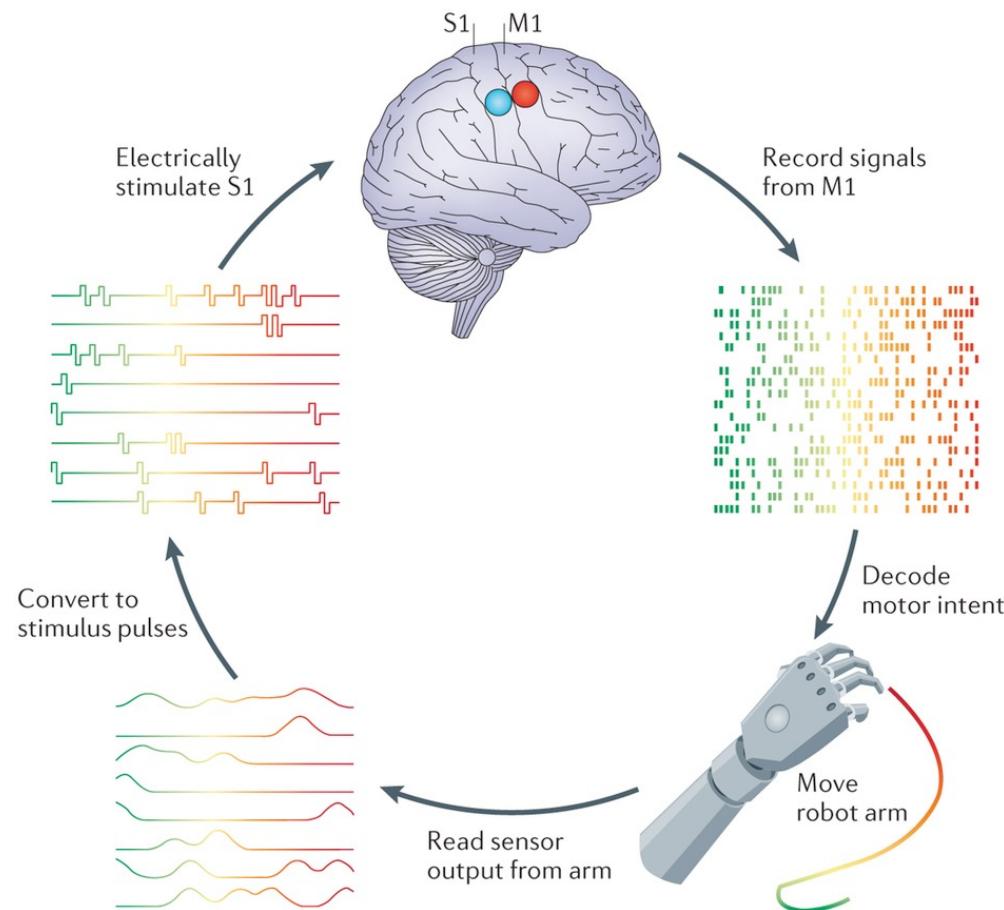


## *Stimulate the brain*

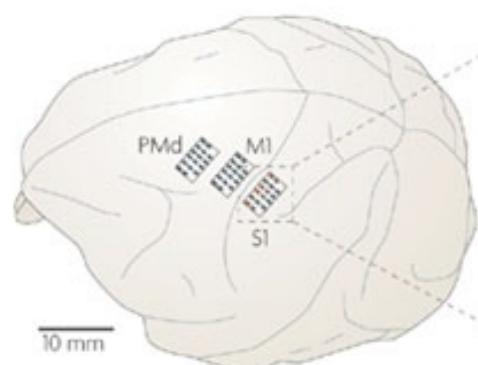
Sensory signals are routed around a severed spinal cord and into the brain, where they produce sensations by direct stimulation of the cortex.

Kwok, Nature, 2013

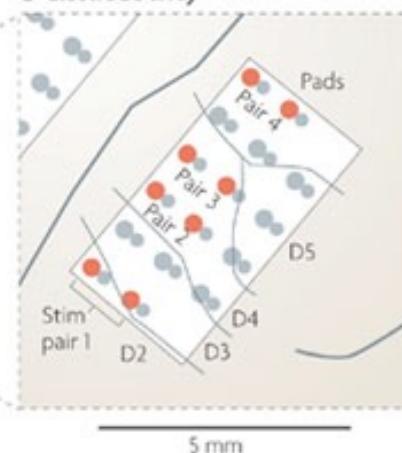
# Brain-to-machine-to-brain interface



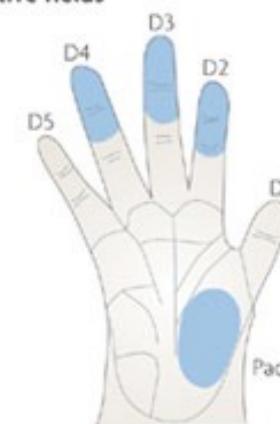
**a** Implantation sites



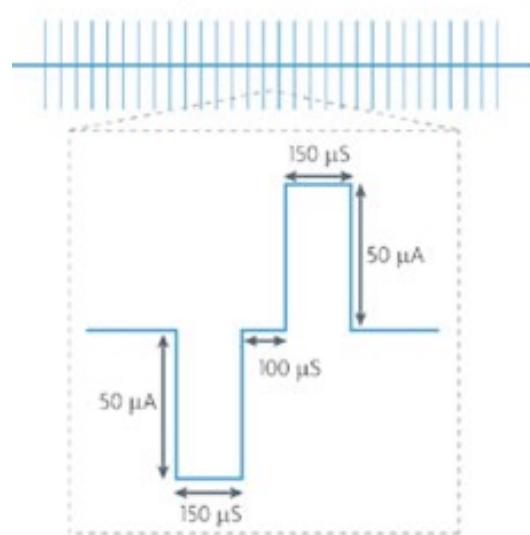
**b** Electrode array



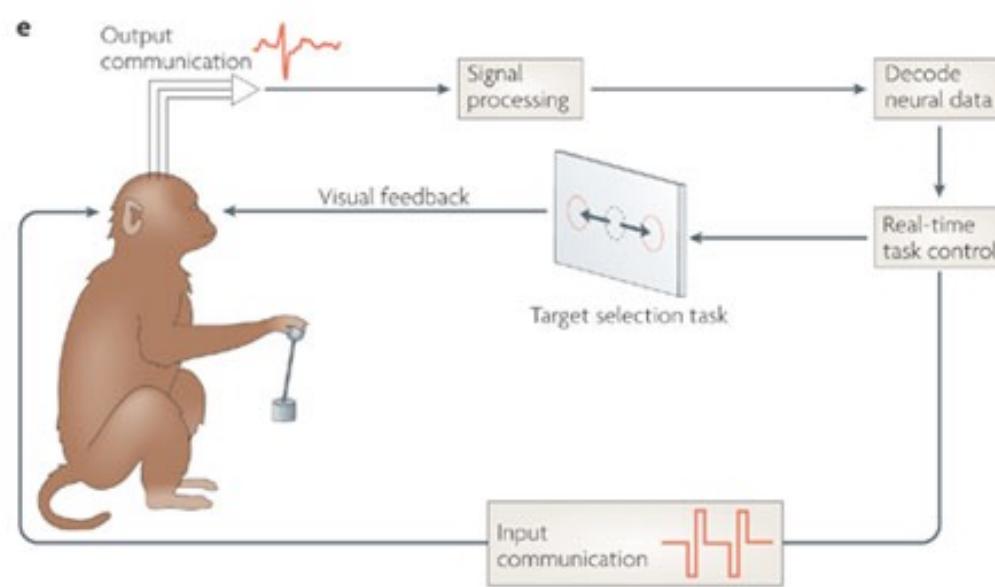
**c** Receptive fields



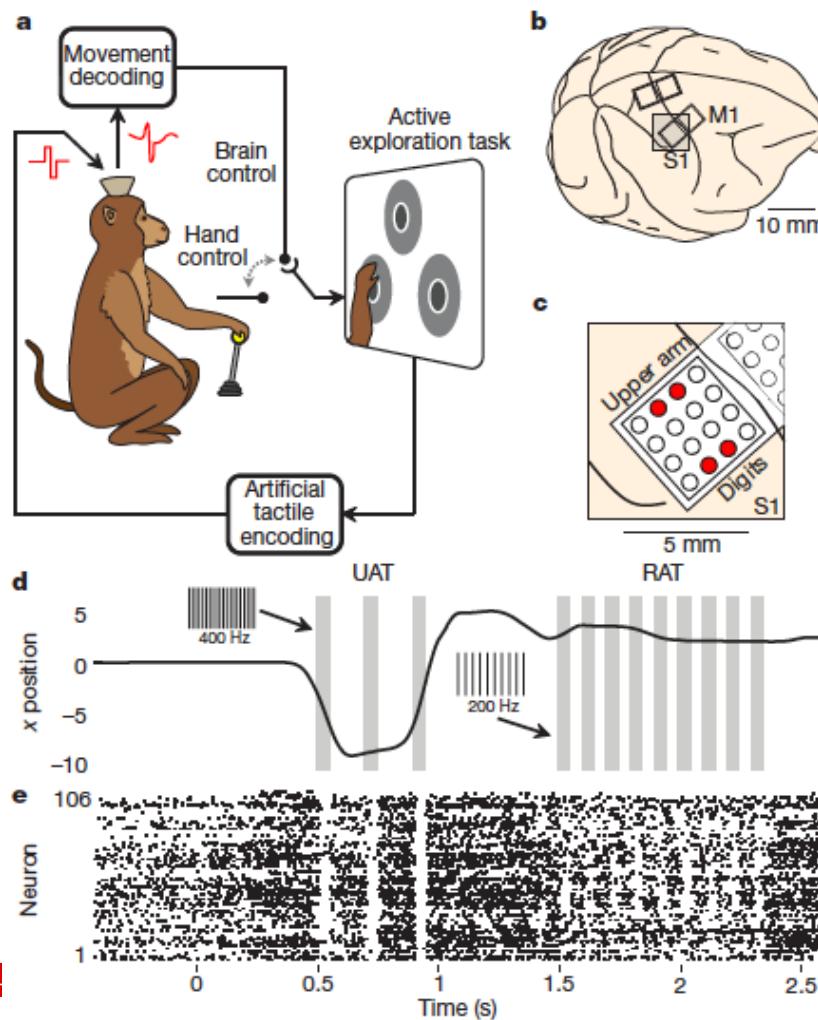
**d** Stimulation pattern



**e**



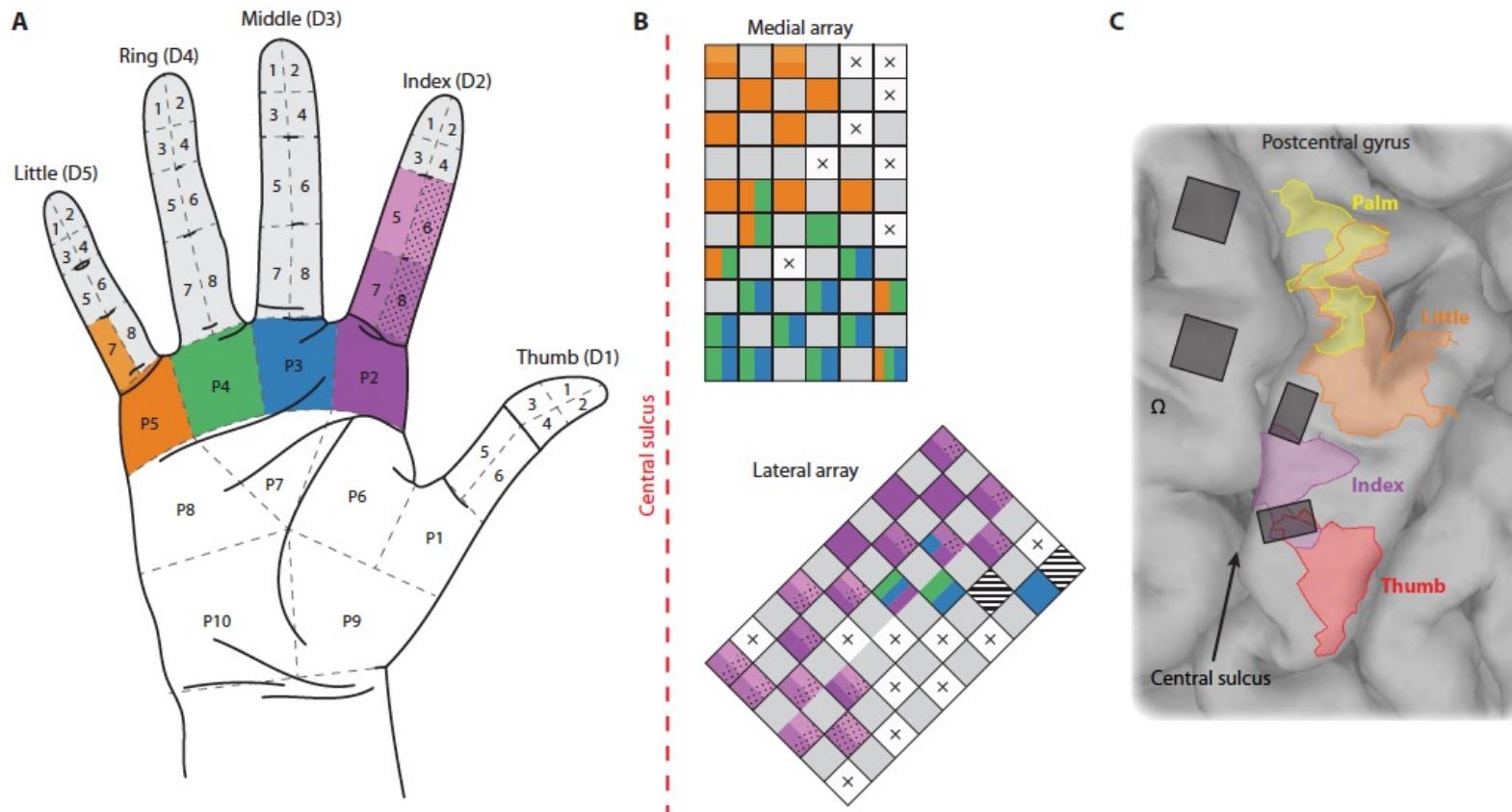
# **Intracortical sensory feedback**



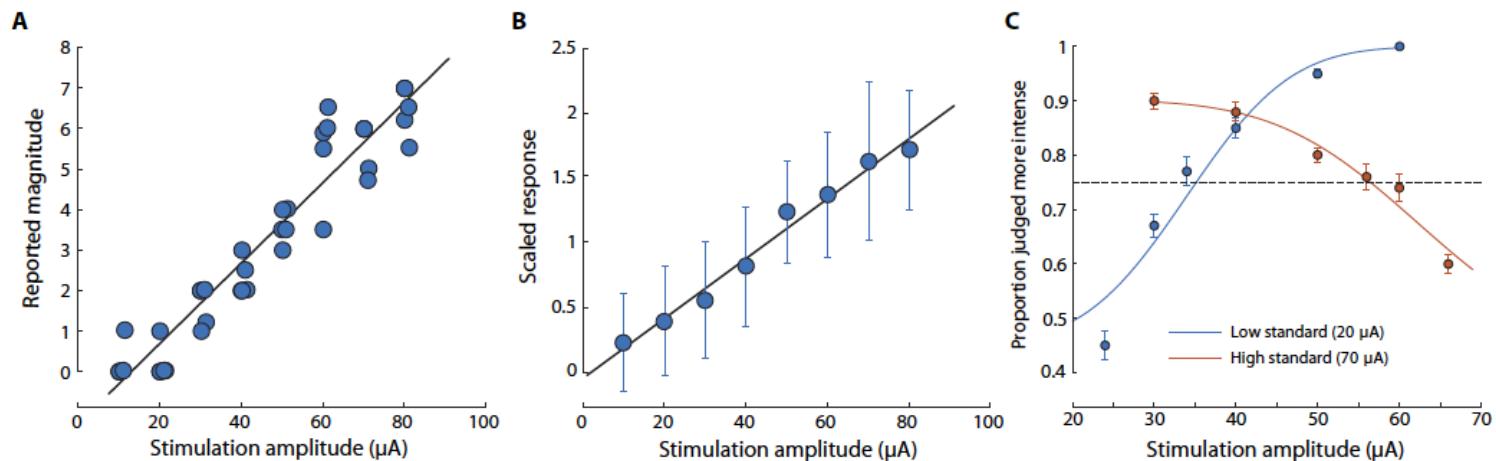
Intracortical sensory feedback is possible but the performance are still limited

O'Doherty et al., 2011

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



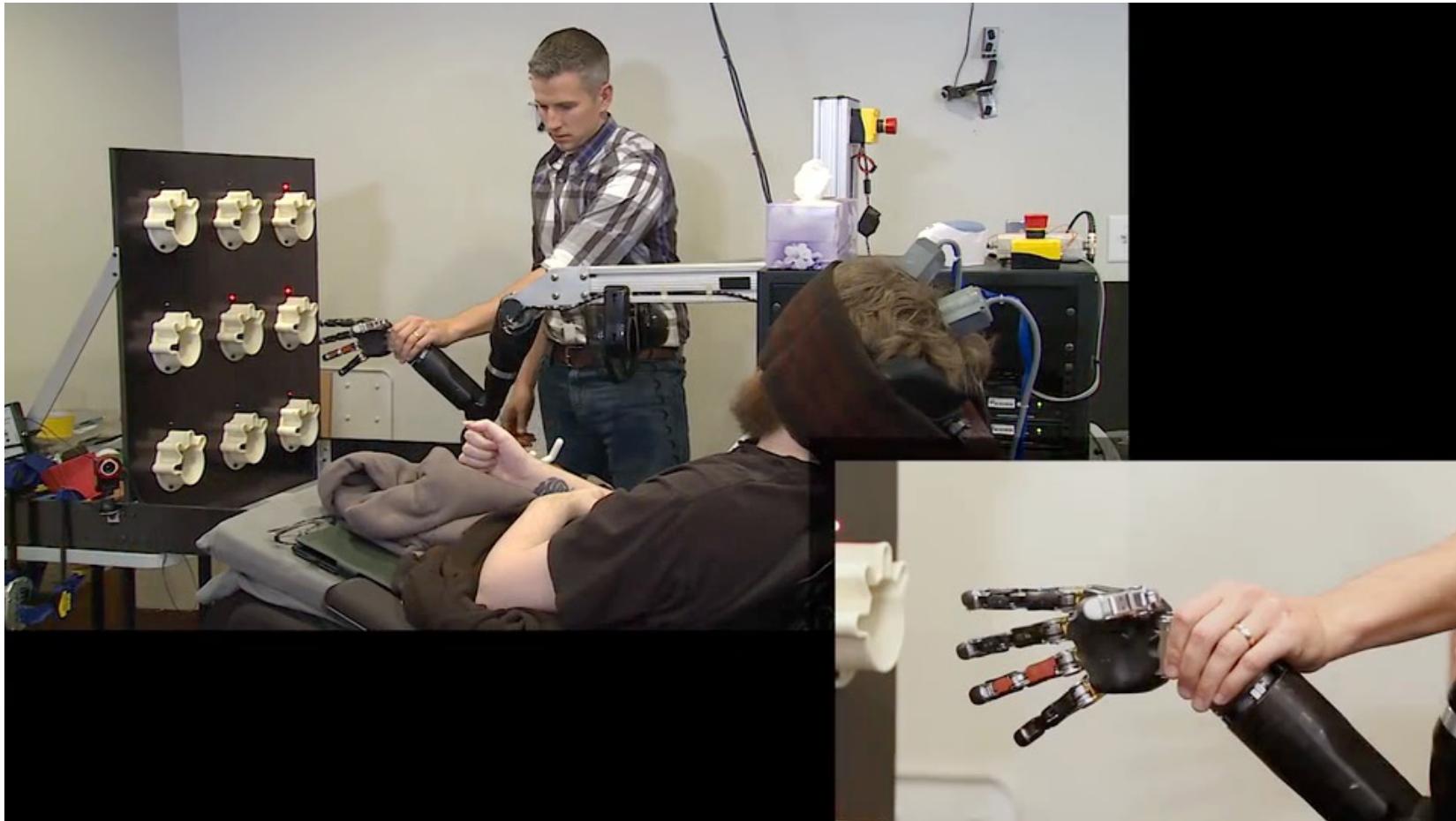
# Brain-to-machine-to-brain interface in a quadriplegic subject



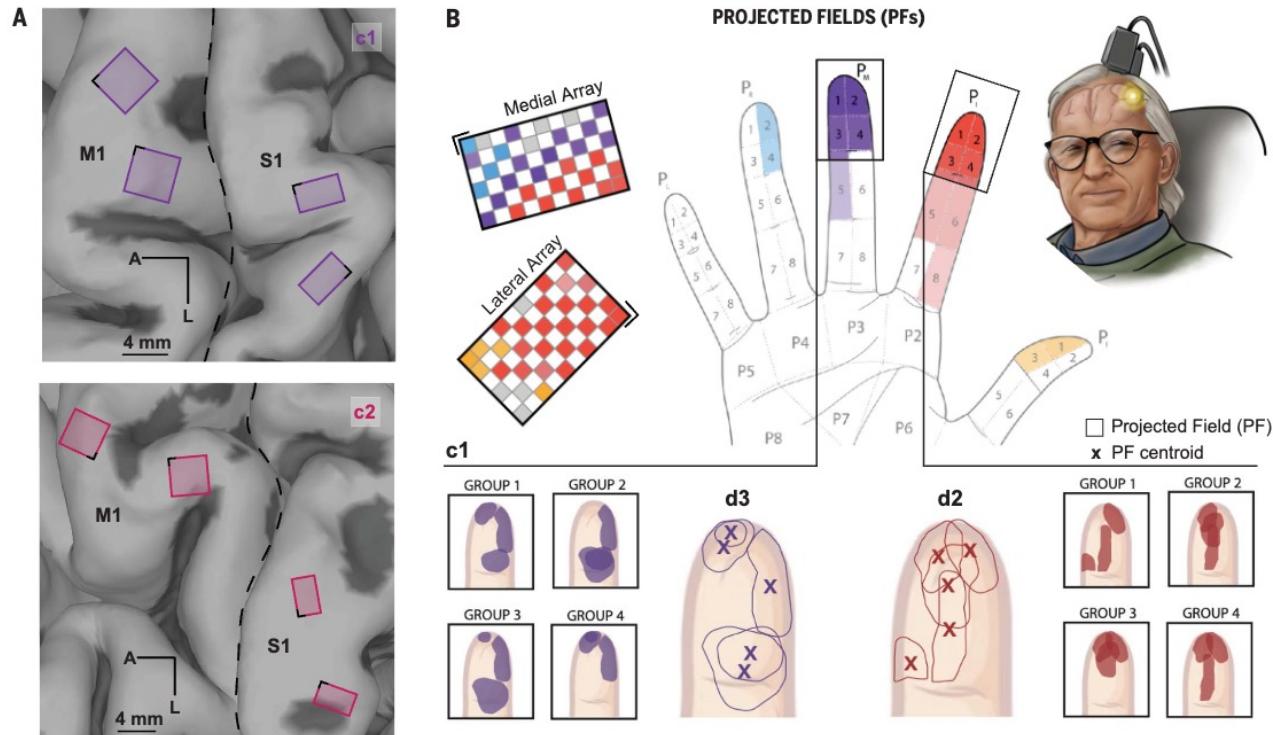
**Table 2. Accuracy of prosthetic finger discrimination.** The percentage of times that sensations were reported to originate from a specific finger (columns) when each prosthetic finger was touched (rows).

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

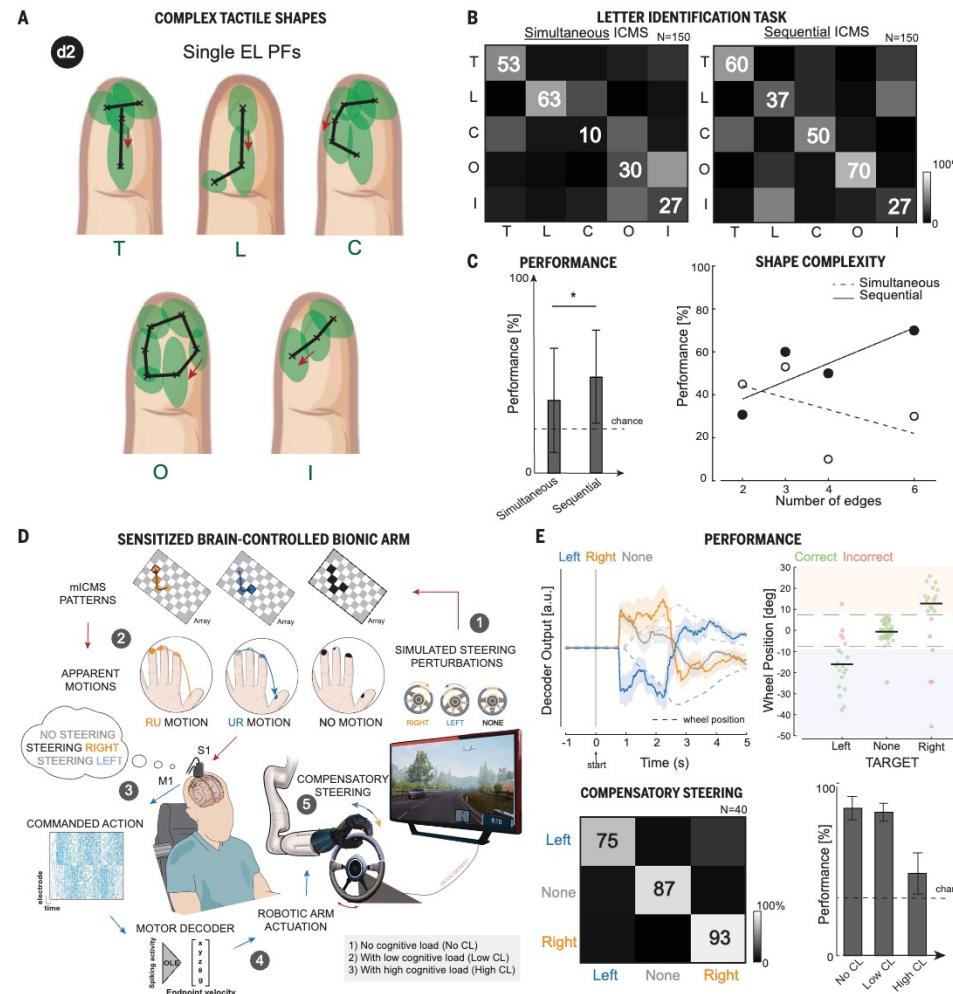
# Brain-to-machine-to-brain interface in a quadriplegic subject



# 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

