I4Life: Intraneural stimulation to restore sensory, motor and autonomic neural functions

Silvestro Micera

Bertarelli Foundation Chair in Translational NeuroEngineering, Center for Neuroprosthetics, EPFL

The BioRobotics Institute, Scuola Superiore Sant'Anna

EPFL

fondation bertarelli

Sant'Anna Scuola Universitaria Superiore Pisa

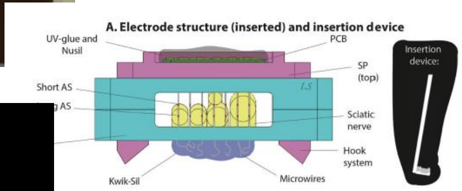
DISCLOSURE: Dr. Micera holds shares of Sensars Neuroprosthetics and Onward, newcos working to commercialize neuroprosthetic devices

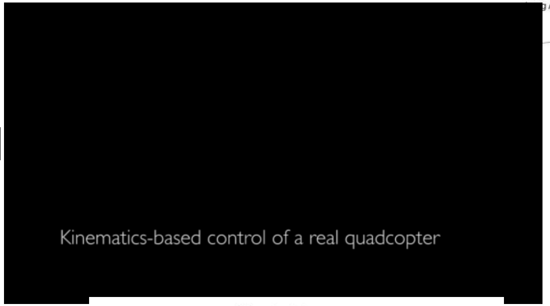
NeuroBionics @TNE

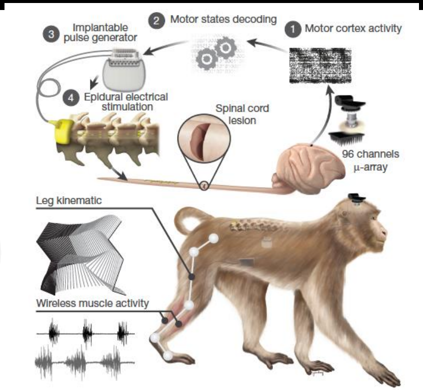
- **Develop personalized neuroprostheses** to improve the quality of life of disabled people exploiting biomedical engineering principles

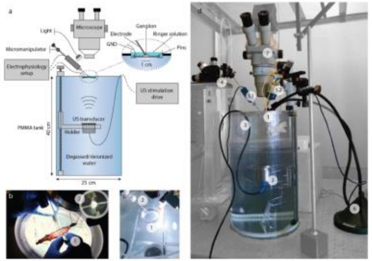
- Speed-up the transfer to clinical trials and real-life environment

- Exploit the potentials of neuroscience-driven approaches





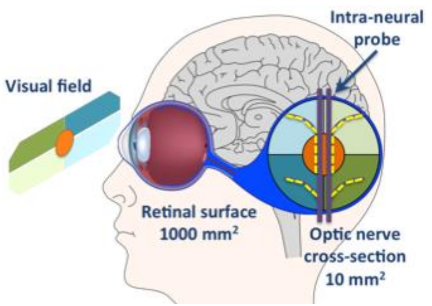


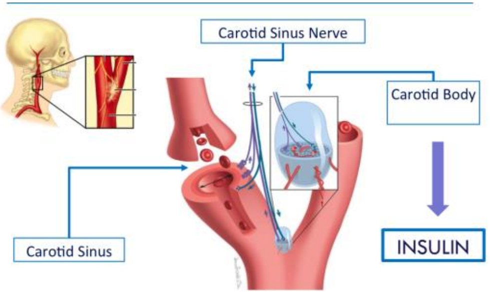


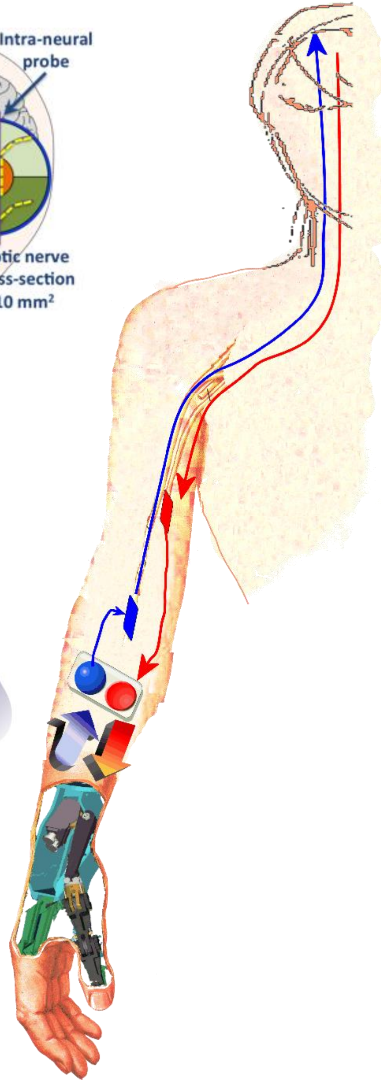
Speaker

Intraneural stimulation for neuromodulation

- Tactile and position feedback in limb amputees
- Vision restoration
- Autonomic nerve closed-loop stimulation
- Grasping restoration

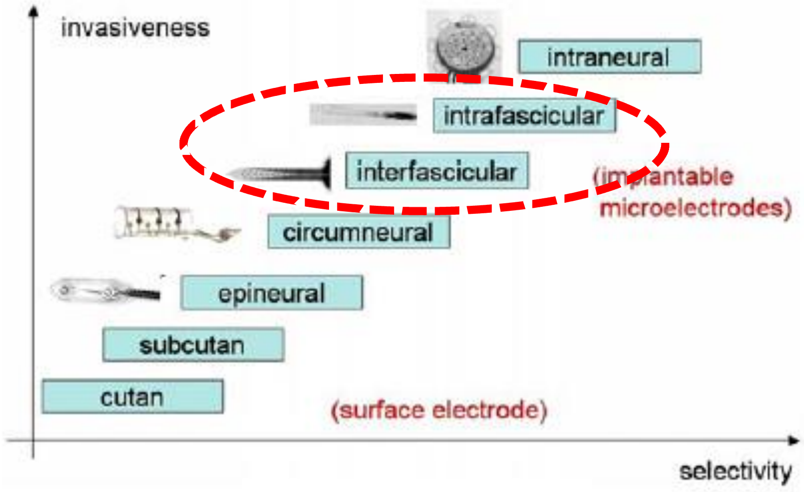




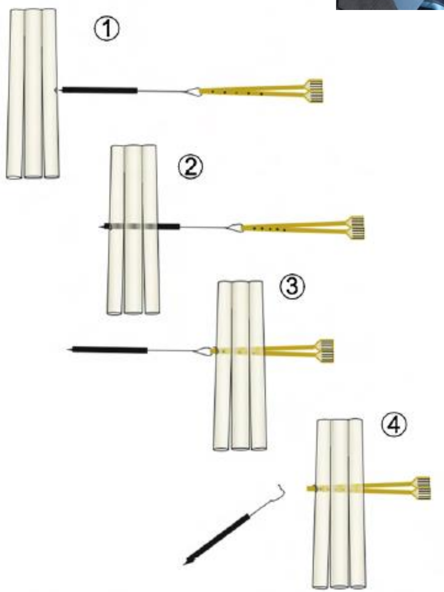


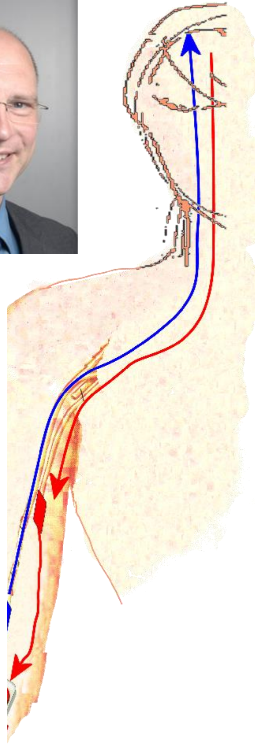
Bidirectional neurocontrolled hand prostheses

- Peripheral direct stimulation can restore the sensory communication with the cortex



TIME Electrodes





Intraneural electrodes seem to represent a good trade-off between high selectivity and reduced invasiveness

Micera, et al., IEEE T-NSRE, 2008

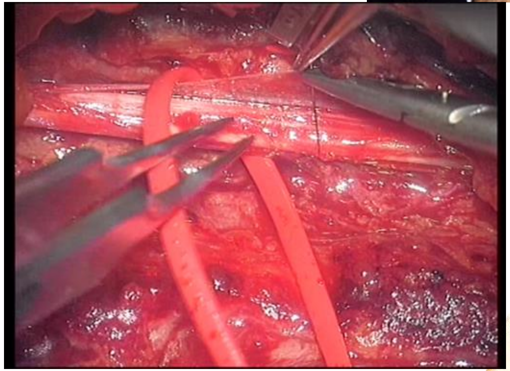
EPFL

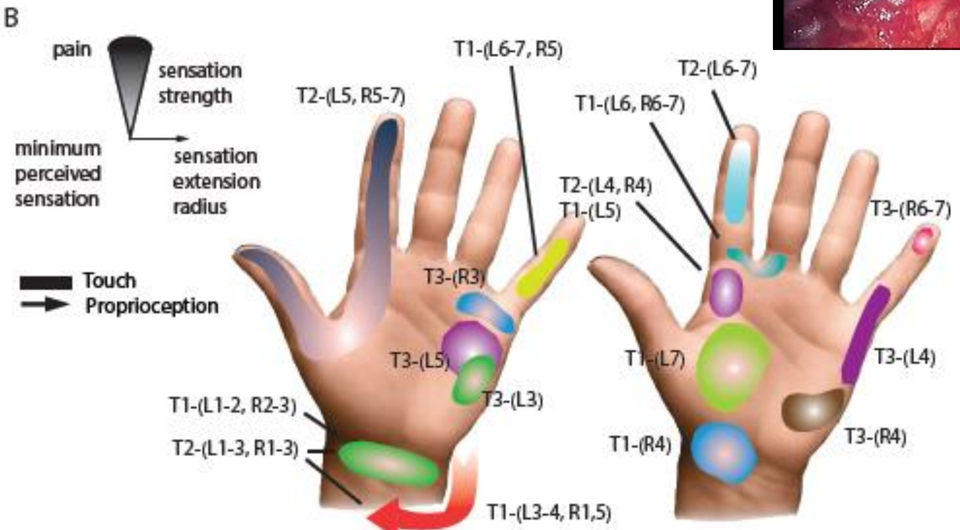
fondation bertarelli

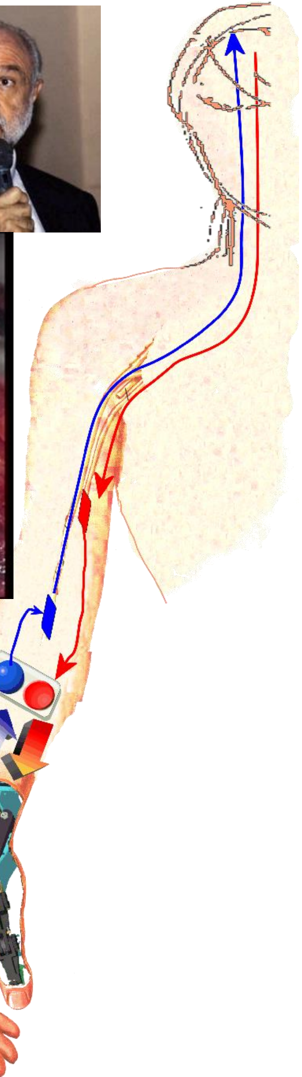
Sant'Anna Scuola Universitaria Superiore Pisa

Bidirectional neurocontrolled hand prostheses

- Four week implant in a 35 year old man, from Denmark with a trans-radial amputation in 2004 (fireworks accident during family celebration)
- Two TIMEs in the median and two in the ulnar nerve

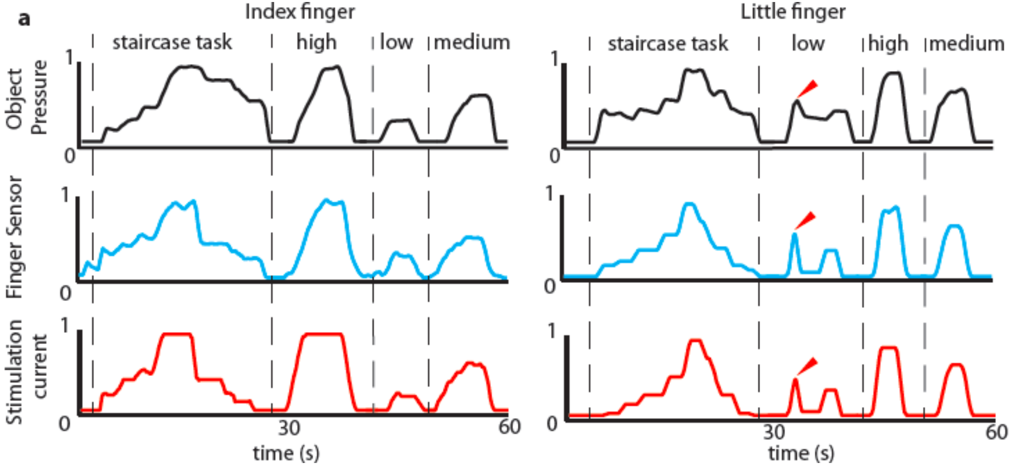


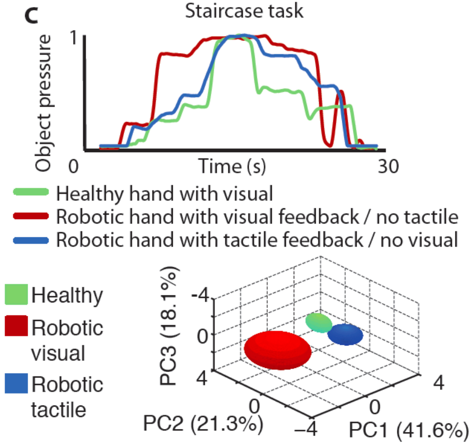




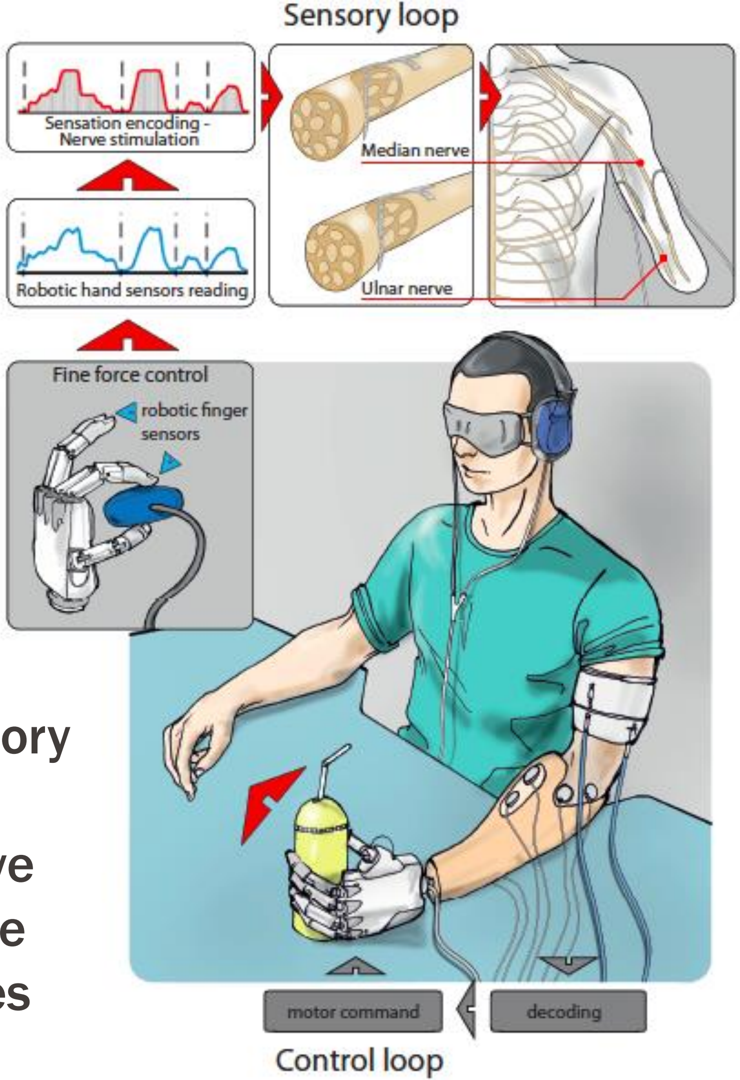
S.Micera

Bidirectional neurocontrolled hand



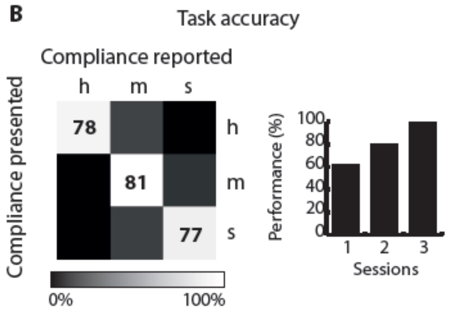


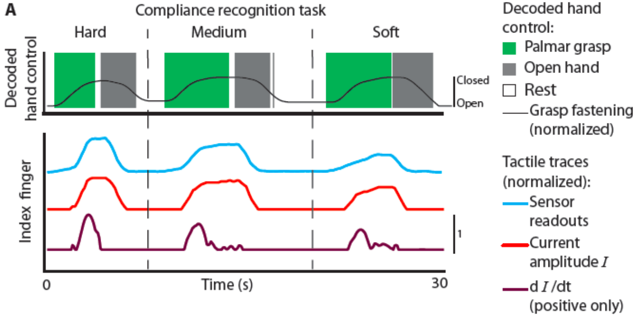
The artificial sensory feedback allowed the user to achieve performance close to the natural ones



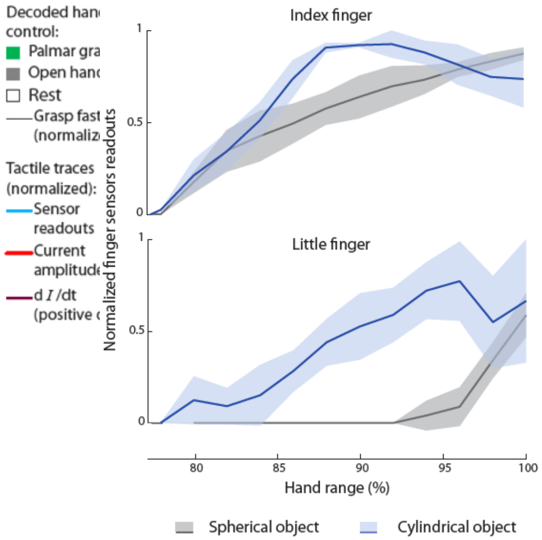
i4LIFE – Intraneural stimulation

Bidirectional neurocontrolled hand

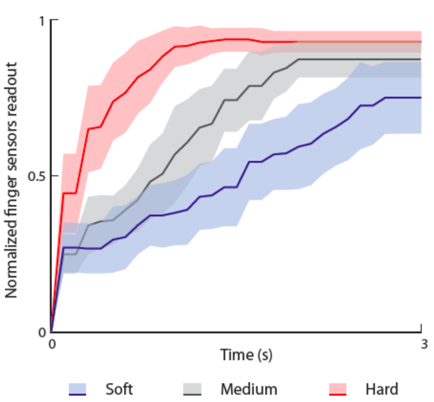


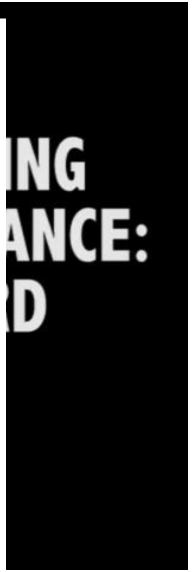


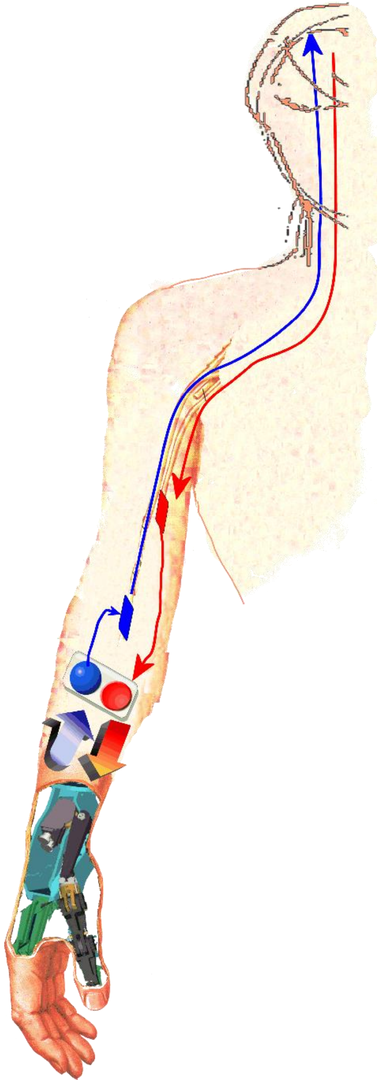
Shape recognition



Compliance recognition







S.Micera

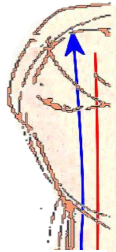
i4LIFE – Intraneural stimulation

EPFL

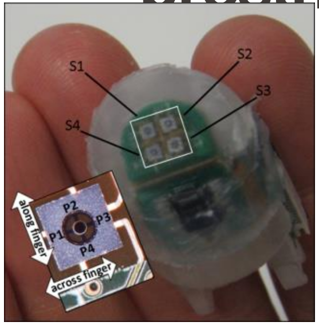
fondation bertarelli

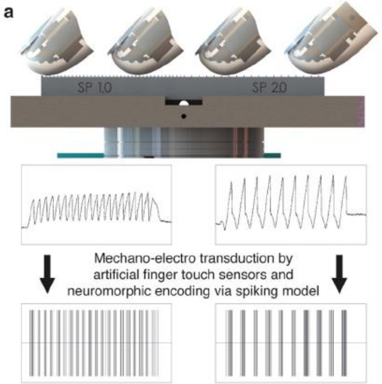
Sant'Anna Scuola Universitaria Superiore Pisa

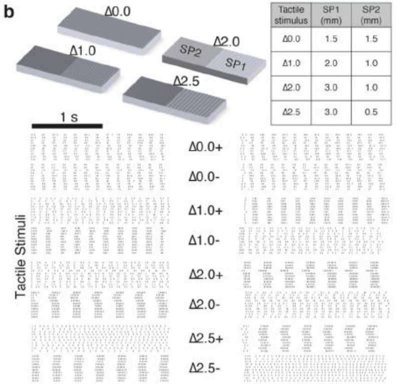
Bidirectional neurocontrolled hand prostheses



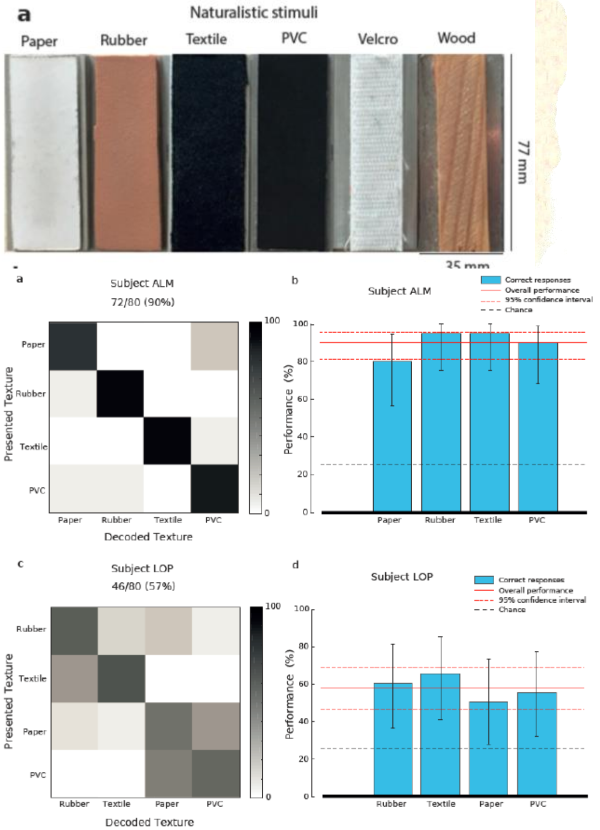
S.Micera

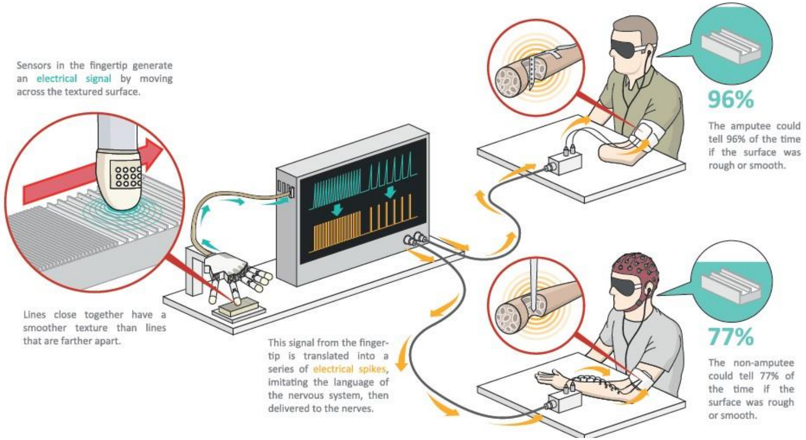






Tactile stimulus	SP1 (mm)	SP2 (mm)
Δ0.0	1.5	1.5
Δ1.0	2.0	1.0
Δ2.0	3.0	1.0
Δ2.5	3.0	0.5





i4LIFE – Intraneural stimulation

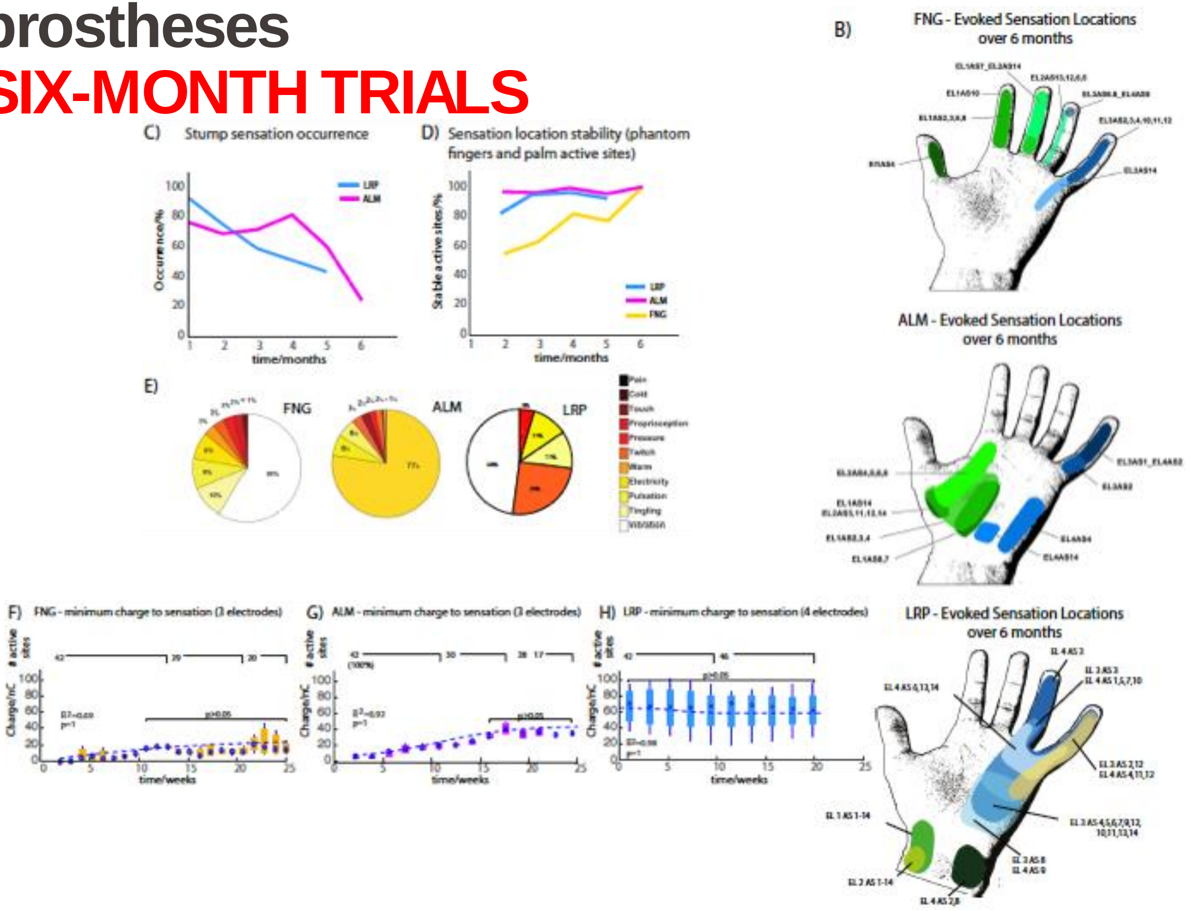
Bidirectional neurocontrolled hand prostheses
SIX-MONTH TRIALS

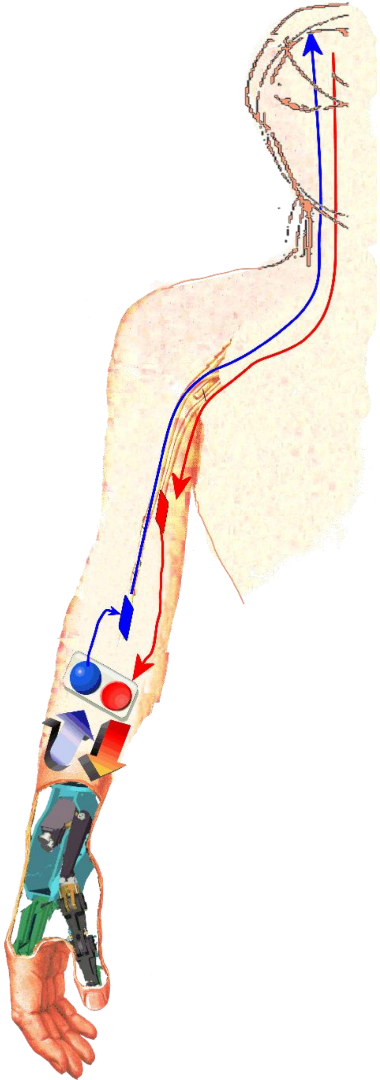
- Three new patients enrolled for a long term study to confirm and extend previous results
- Subject 2 implanted from Nov 2015 to May 2016
- Subject 3 implanted from June 2016 to Dec 2016
- Subject 4 implanted from June 2017 to Dec 2017

- Results confirmed the long-term usabilty of our approach

Bidirectional neurocontrolled hand prostheses

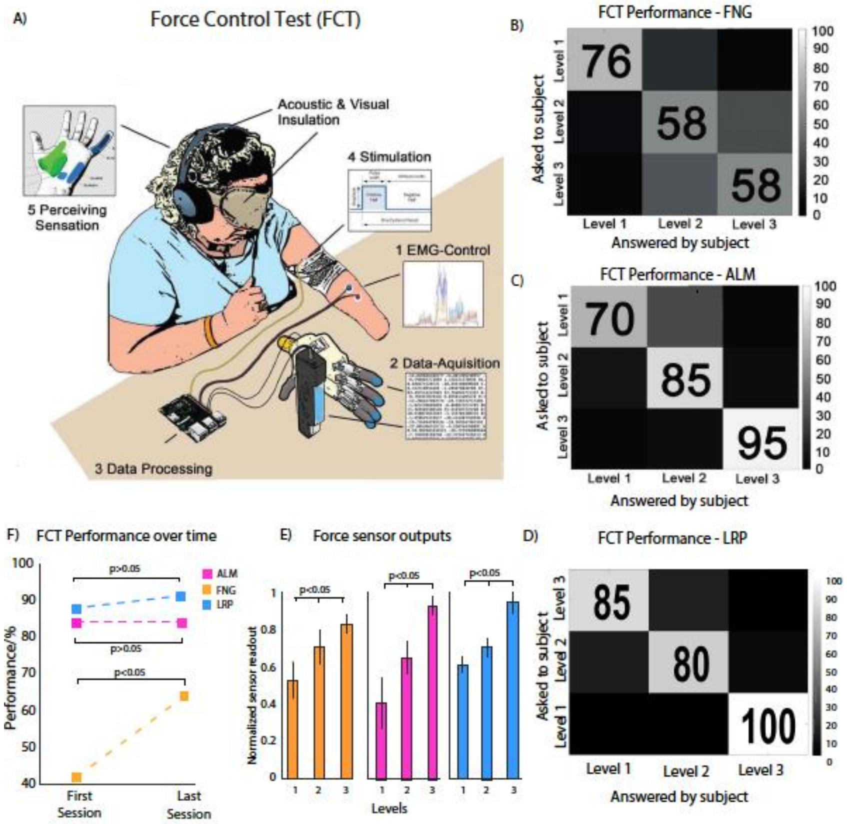
SIX-MONTH TRIALS

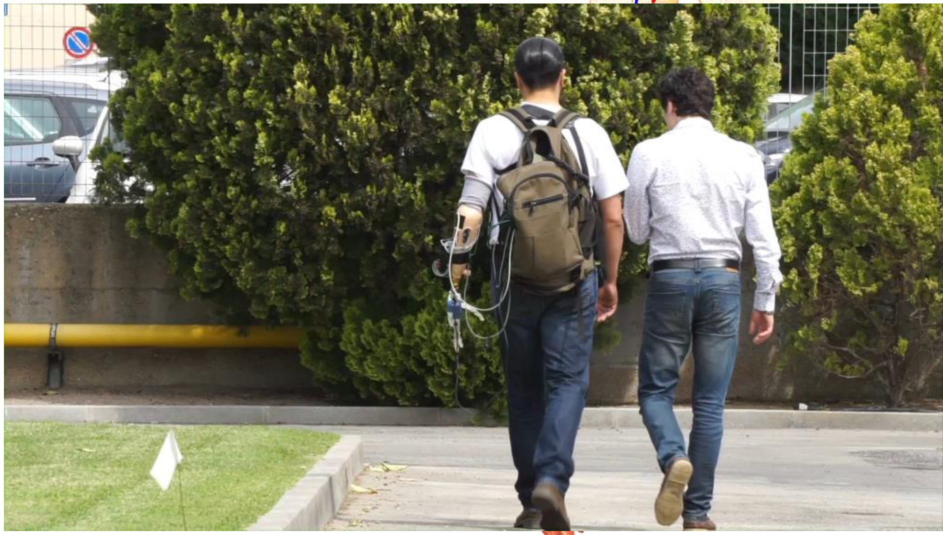




S.Micera

Bidirectional neurocontrolled hand prostheses



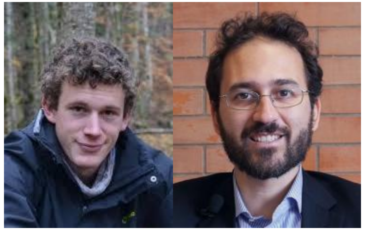


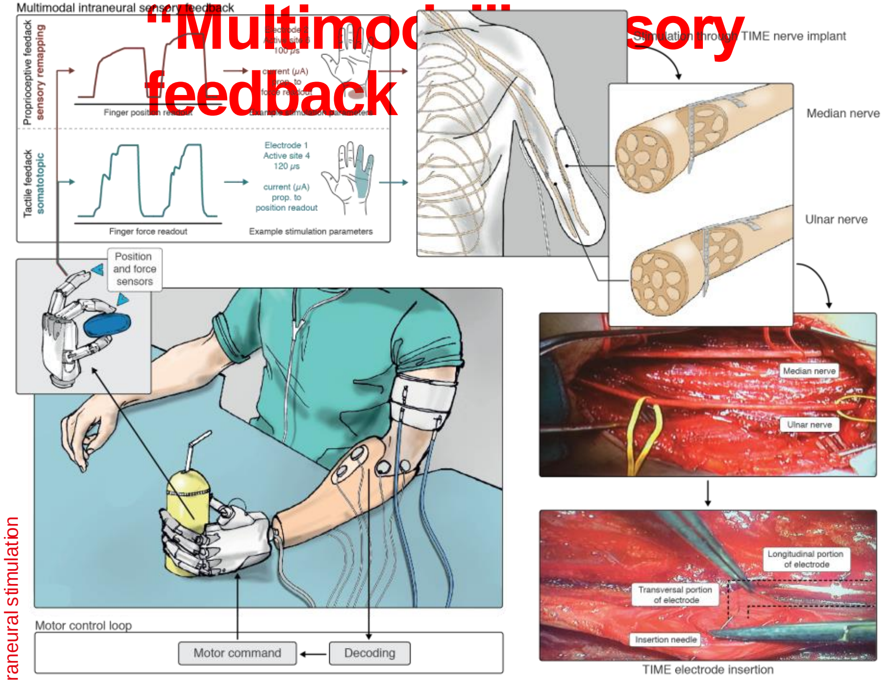
i4LIFE – Intraneural stimulation

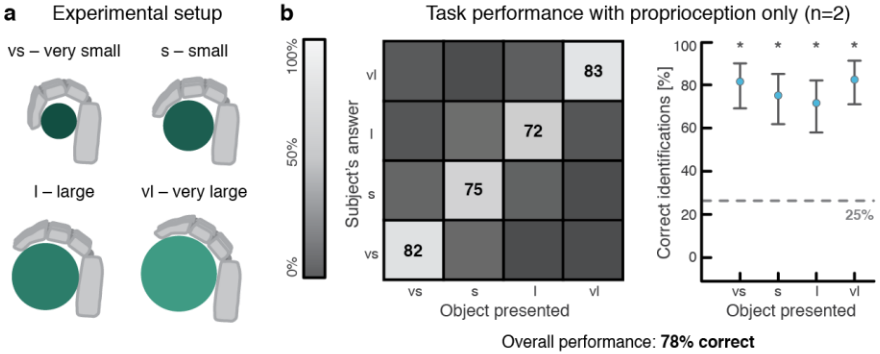
Bidirectional neurocontrolled hand prostheses

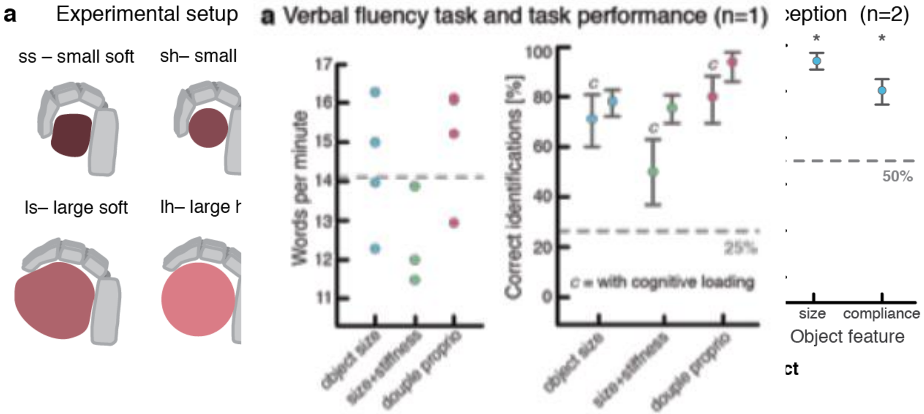
“Multimod sory feedback

S.Micera









i4LIFE – Intraneural stimulation

Bidirectional neurocontrolled hand prostheses

B

fe

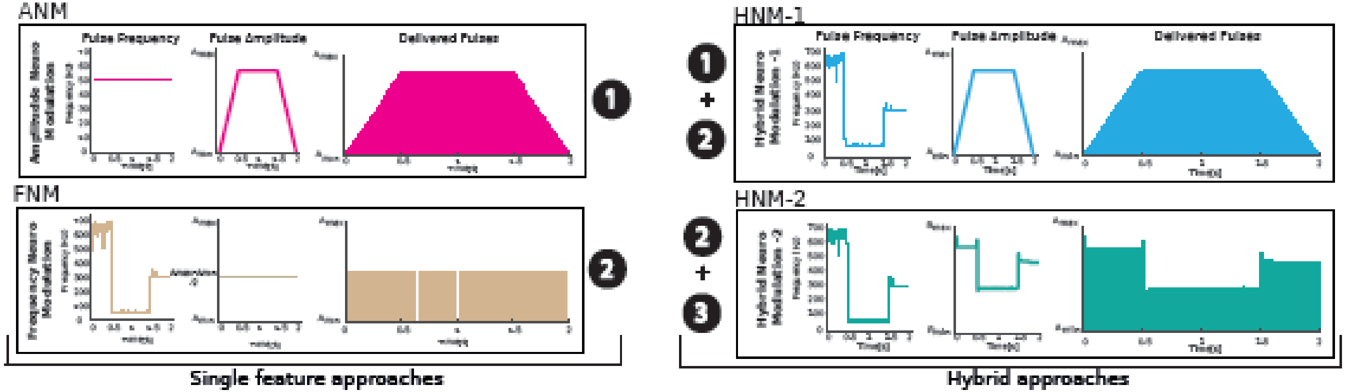
Step 1: Biomimetic model-based approach and parameters generation

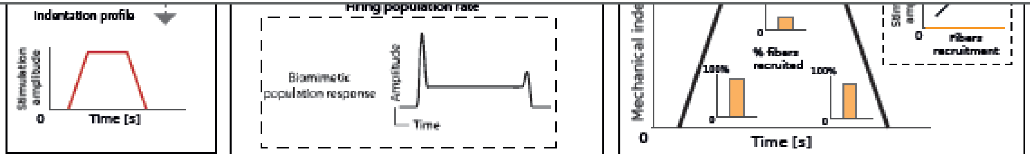
We identified electrode active site which elicits sensations in the locations corresponding to the fingertip. Then, we simulated a mechanical skin indentation using the biomimetic model. The model outcomes were the firing population activity generated by the combination of all the fibers (SA,RA,PC) response 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).

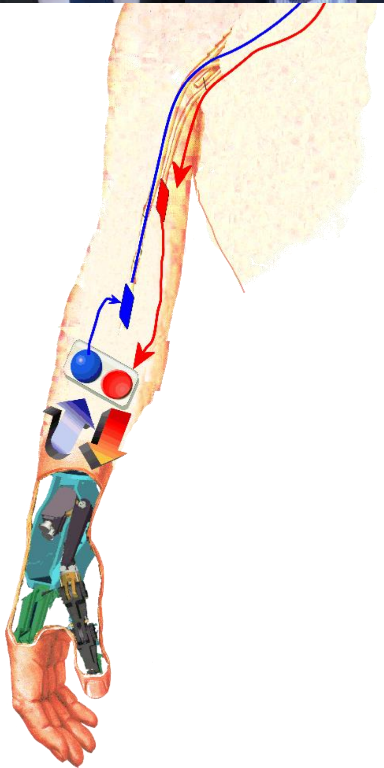
Sensation characterization Biomimetic indentation model

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 simultaneuosly 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 µs.

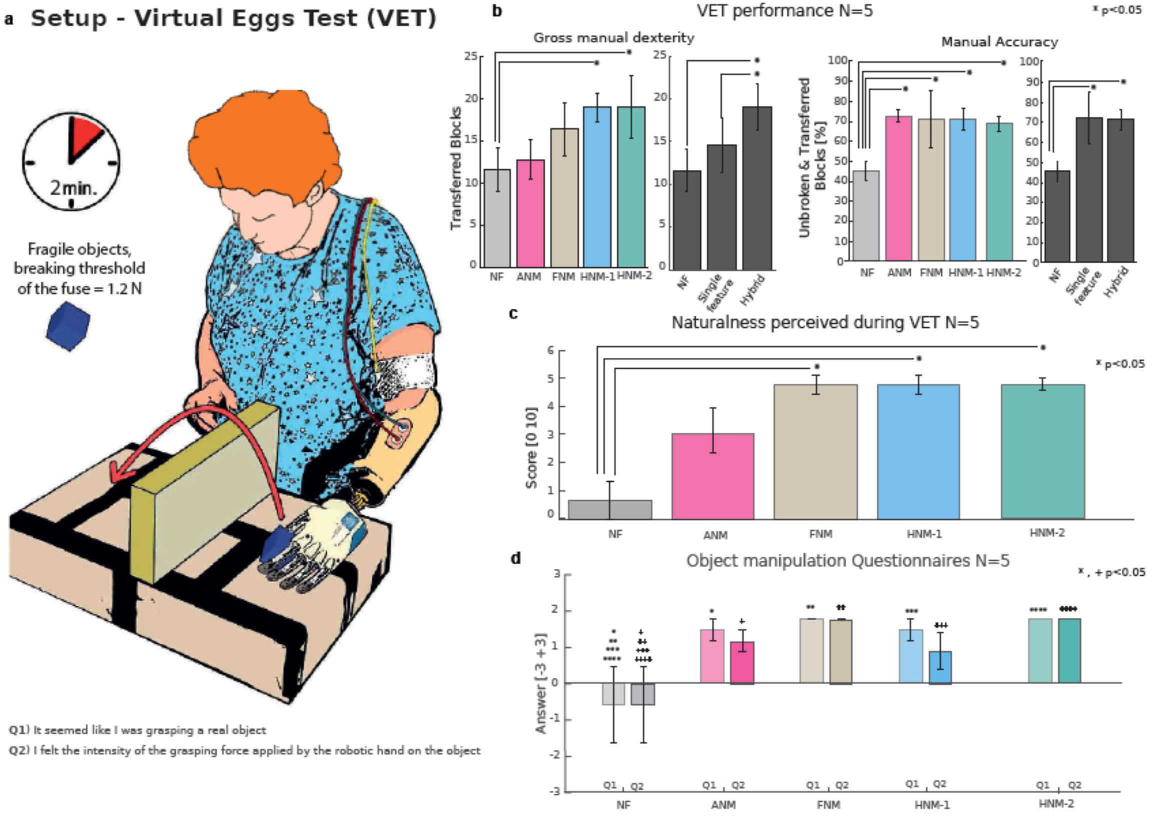


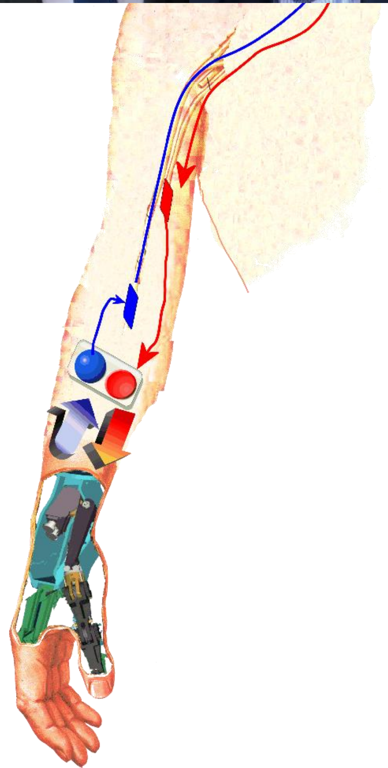




i4LIFE –

Bidirectional neurocontrolled hand prostheses





i4LIFE – Intraneural stimulation

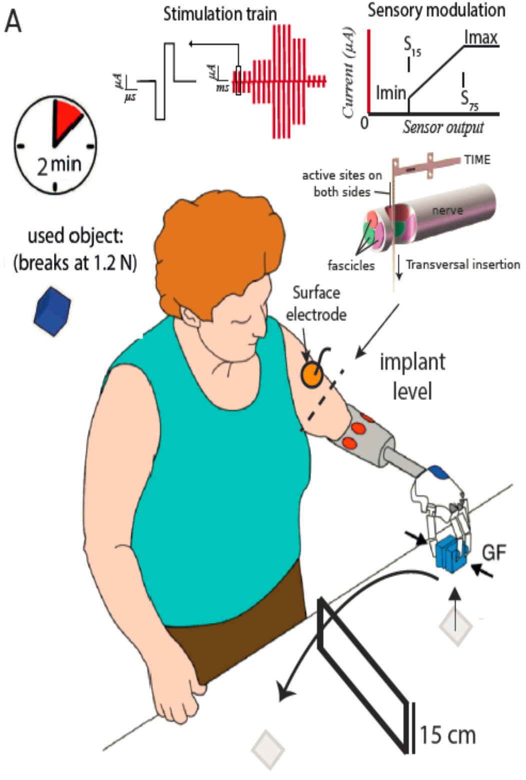
EPFL

fondation bertarelli

Sant'Anna Scuola Universitaria Superiore Pisa

Bidirectional neurocontrolled hand prostheses

Cognitive load



B

Induced sensations & stimulation parameters

Intraneural sensory Feedback (IF)

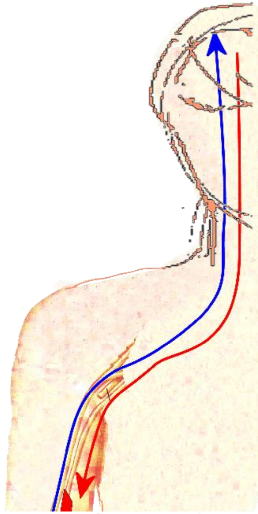
sensation type	vibration
sensation intensity	$S_{min}=1$, $S_{max}=8$
electrode position	proximal part of ulnar nerve above elbow
amplitude	A_{min}=200 μA , A_{max}= 300 μA
pulse-width	80 μs
frequency	50 Hz

Superficial sensory Feedback (SF)

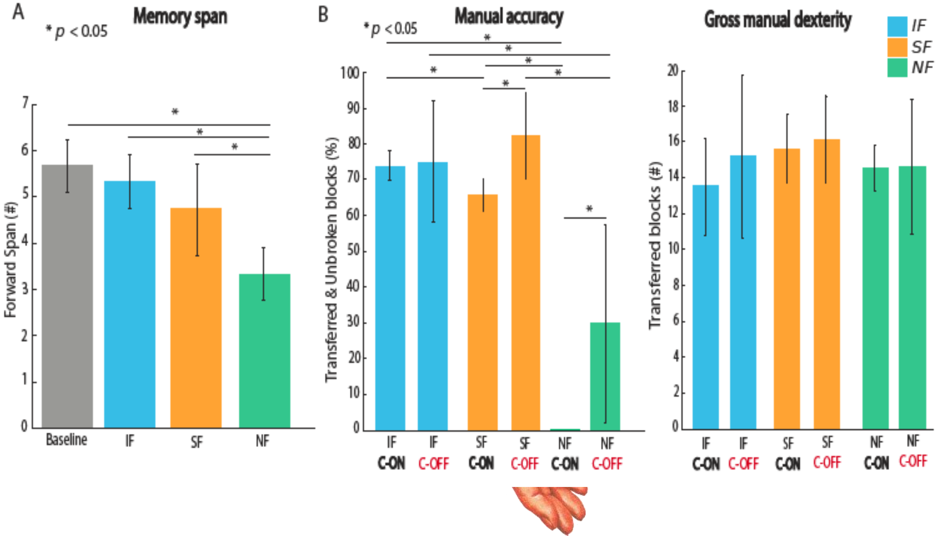
sensation type	electricity
sensation intensity	$S_{min}=1$, $S_{max}=8$
electrode position	on the skin of the left arm
amplitude	A_{min}=100 μA , A_{max}= 500 μA
pulse-width	200 μs
frequency	50 Hz

NEXT STEPS

- Longer term implants also in ecological settings
- Additional testing on multimodal stimulation
- Embodiment and peripersonal space



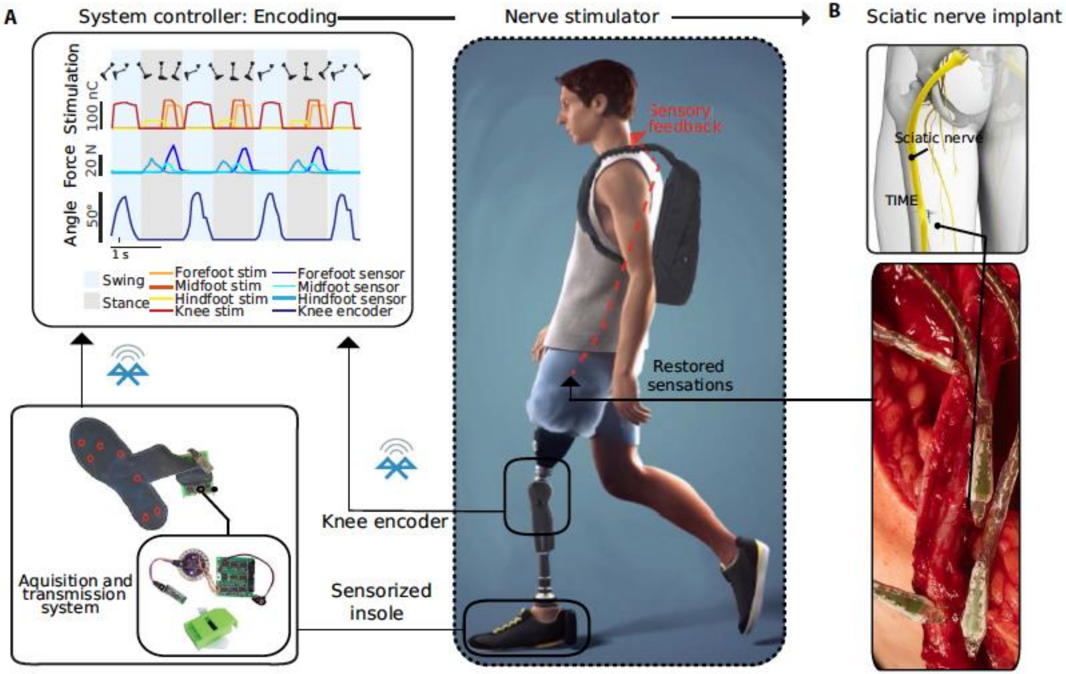
Cognitive Dual Task (Span Digit Forward Test during Virtual Eggs Test)

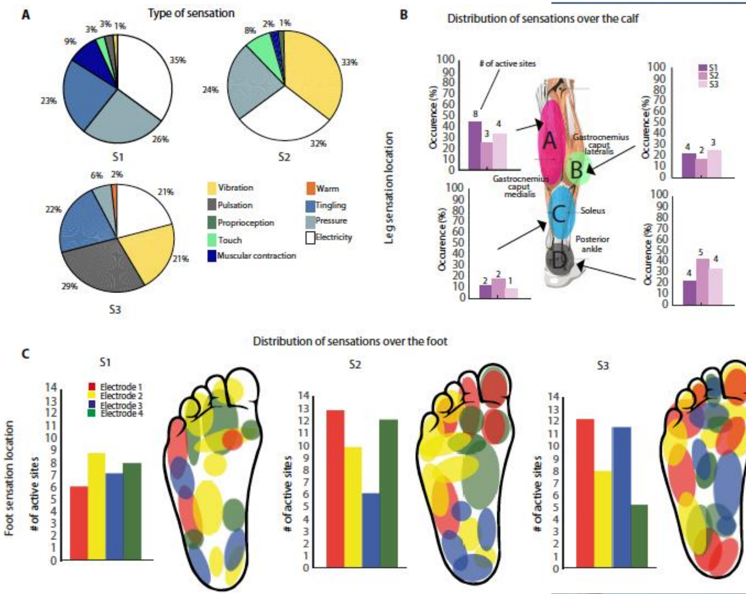


Bidirectional neurocontrolled leg prostheses

Sensory feedback

S.Micera

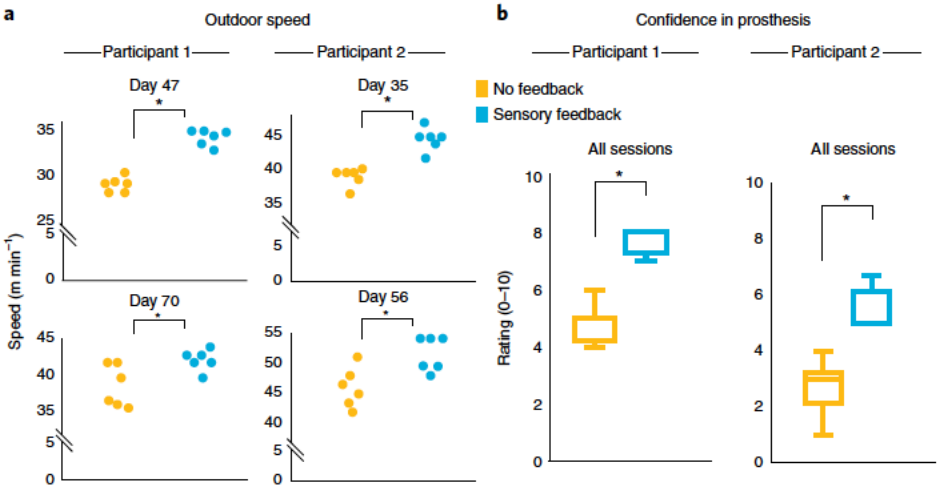


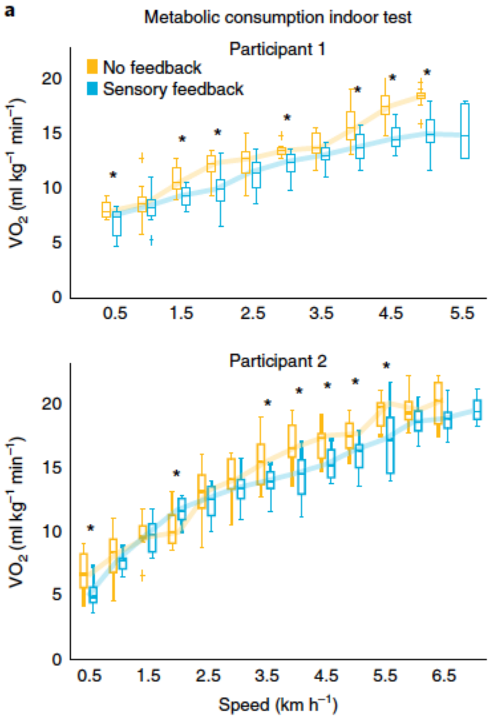


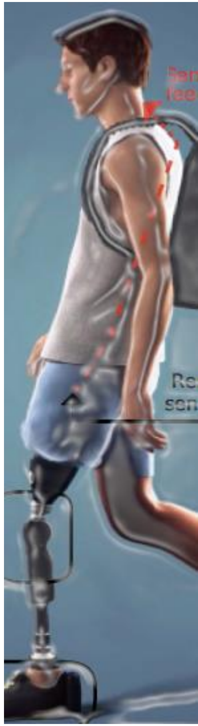
EPFL
fondation bertarelli
Sant'Anna Scuola Universitaria Superiore Pisa

Bidirectional neurocontrolled leg prostheses

Sensory feedback







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

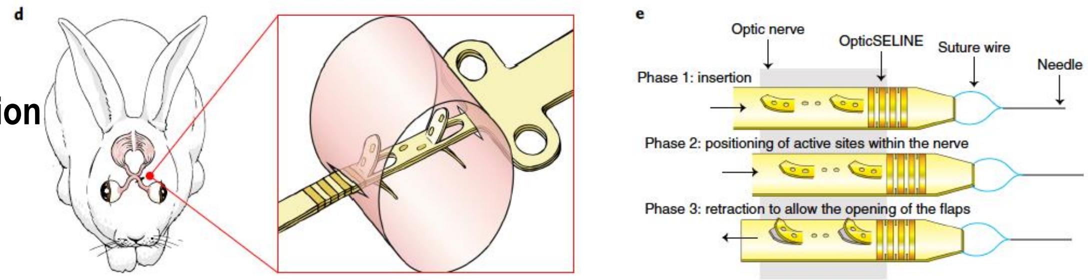
Participants exhibited reduced phantom limb pain with neural sensory feedback.

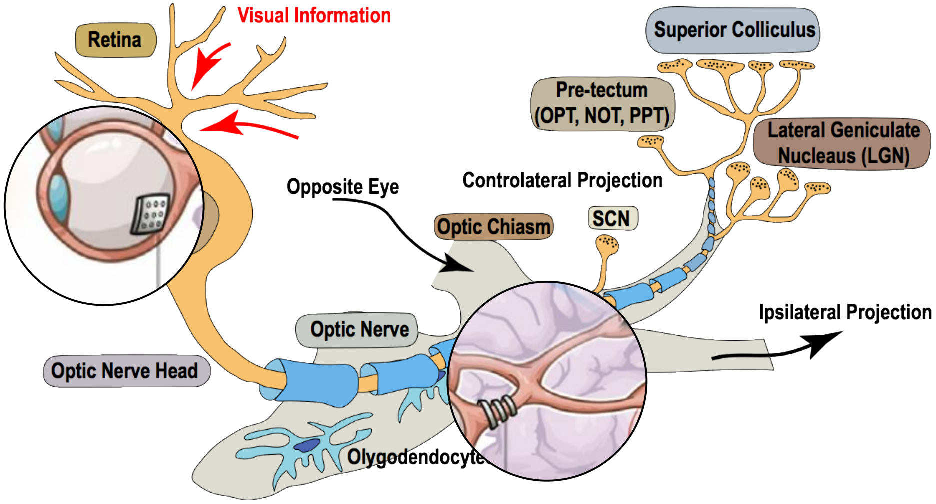
S.Micera

Optic nerve stimulation for vision neuroprostheses

S.Micera

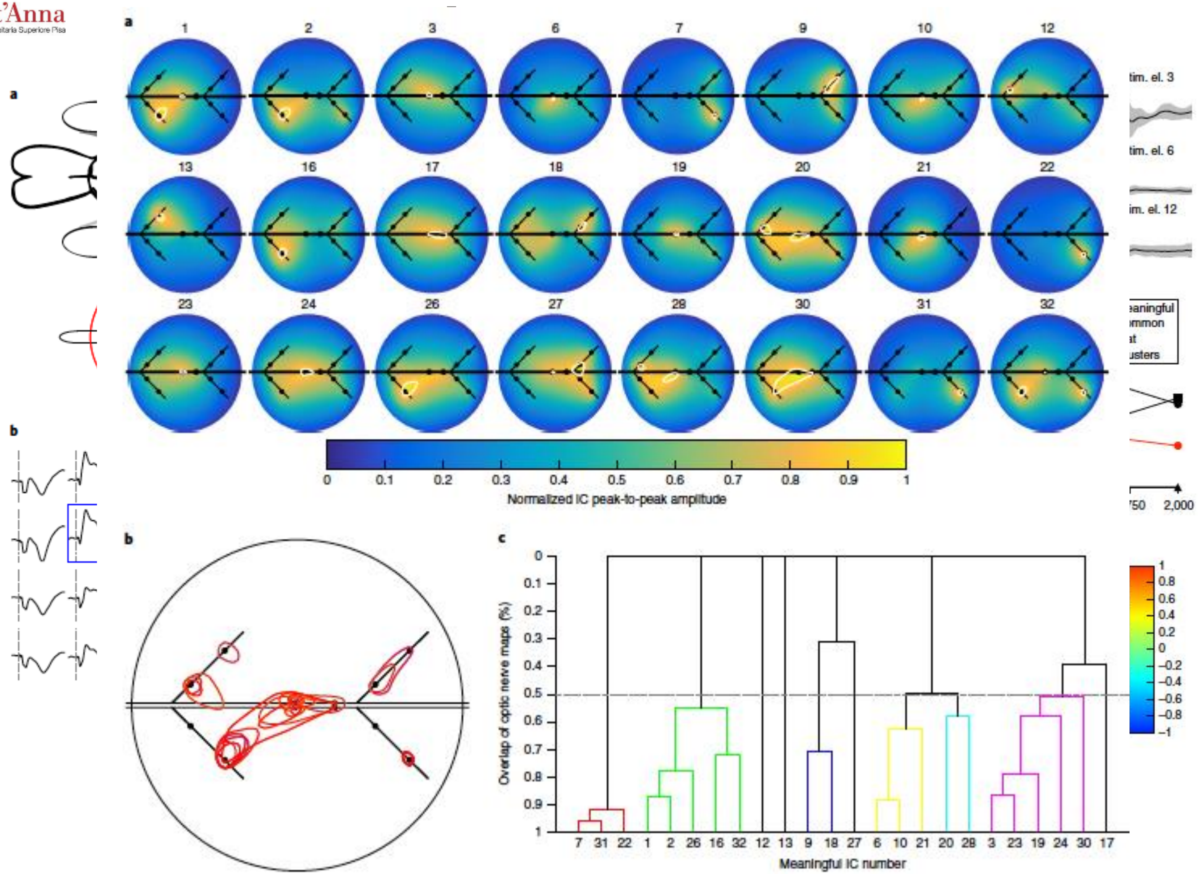
- Mechanical stability
- Mechanical mis/match
- Threshold of activation
- Space compression
- Synaptic circuits





The 3D arrangement of electrodes allows the targeting with a single shank both the central part and the four surrounding quadrants; thus covering the entire visual field

Optic nerve stimulation for vision



Intraneural optic nerve stimulation seems to show a promising selectivity in terms of cortical activation

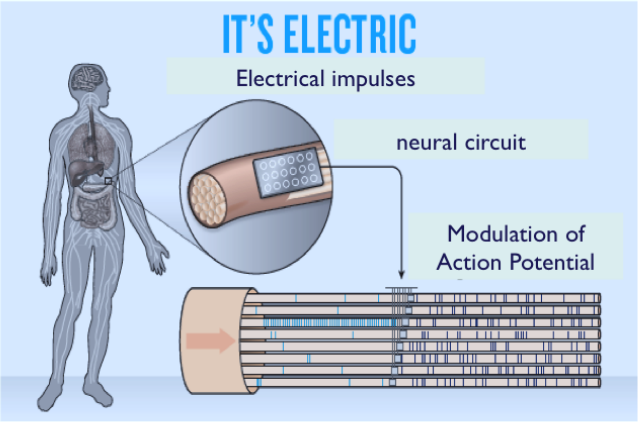
NEXT STEPS

- Further tests in animal models
- Development of machine learning appraoches to optimize stimulation effects

Electroceutical (autonomic nerve stimulation)

Electroceuticals

Medical treatments for chronic diseases based on electrical impulses



Advantages

- Real-time
- Precision
- No drugs side-effect
- Personalized treatment

A NEW AREA OF MEDICINE

A NEW CLASS OF MEDICINES

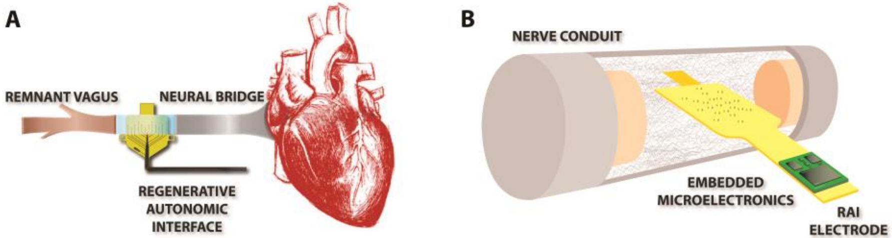
EPFL

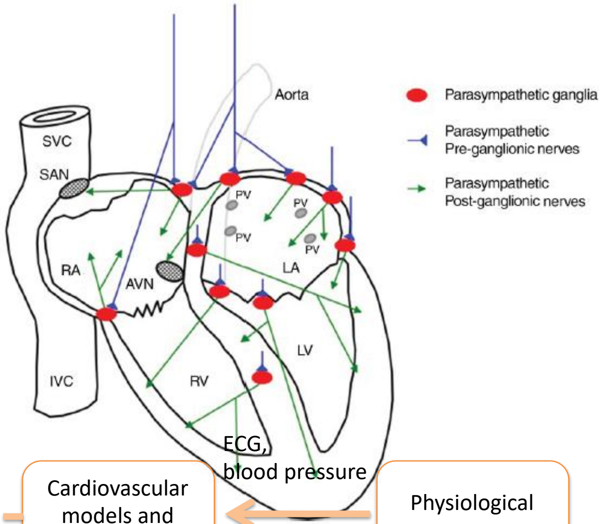
fondation bertarelli

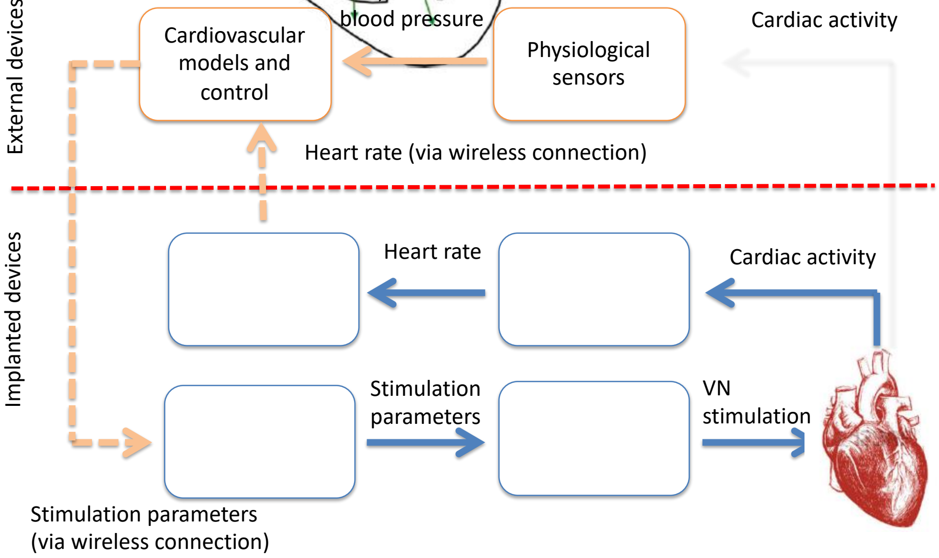
Sant'Anna Scuola Universitaria Superiore Pisa

Electroceutical (autonomic nerve stimulation)

- Heart transplantation can involve the complete explantation of the native heart making surgical denervation inevitable
- The lost of efferent and afferent sympathetic cardiac fibers leaves the endogenous electro-mechanical cardiac coupling under the slow metabolic control



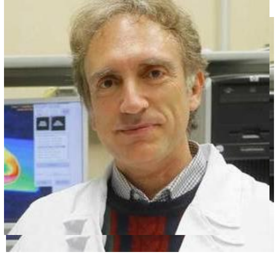




S.Micera

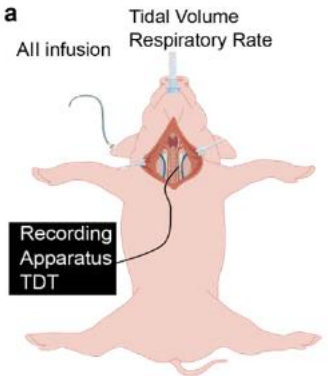
EPFL
fondation bertarelli
Sant'Anna Scuola Universitaria Superiore Pisa

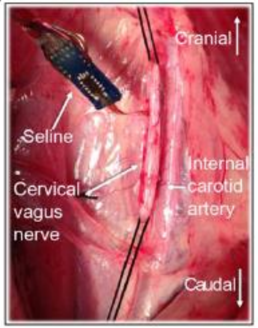
Electroceutical
Decoding from Vagus Nerve activities



S.Micera

Experimental setup

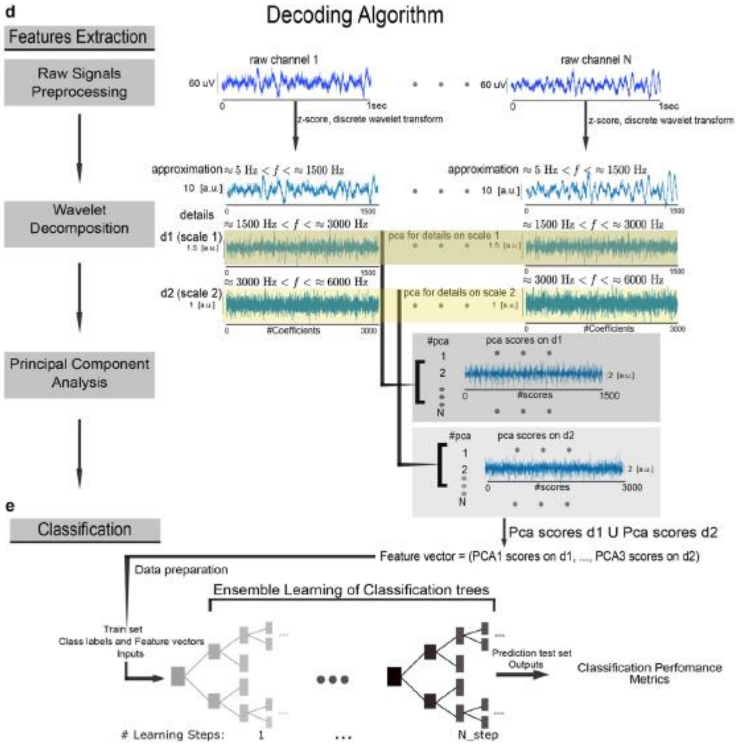




c

Parameter	Challenge	Target
Blood pressure	AngII infusion (80 ng/Kg/min) 7-10 min	150% baseline BP
Tidal Volume	2 min increase	500-800 ml
Respiratory Rate	2 min increase	15-20 br/min

# conditions	Baseline vs challenges: comparisons		
2	vs BPC	vs RRC	vs TVC
3	vs BPC vs RRC	vs BPC vs TVC	vs TVC vs RRC
4	vs BPC vs RRC vs TVC		



We performed the first comprehensive study testing intraneural VN recording to identify physiological (arterial and respiratory) changes

We recorded VN activity through intraneural multi-channel electrodes in anaesthetized pigs at baseline and during alterations in blood pressure and respiratory parameters

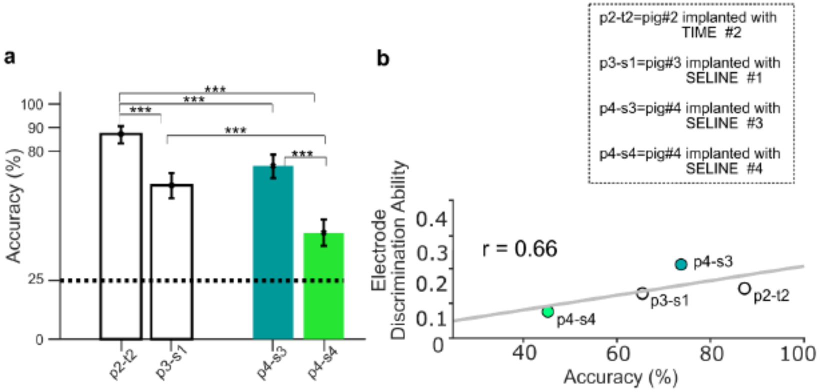
EPFL

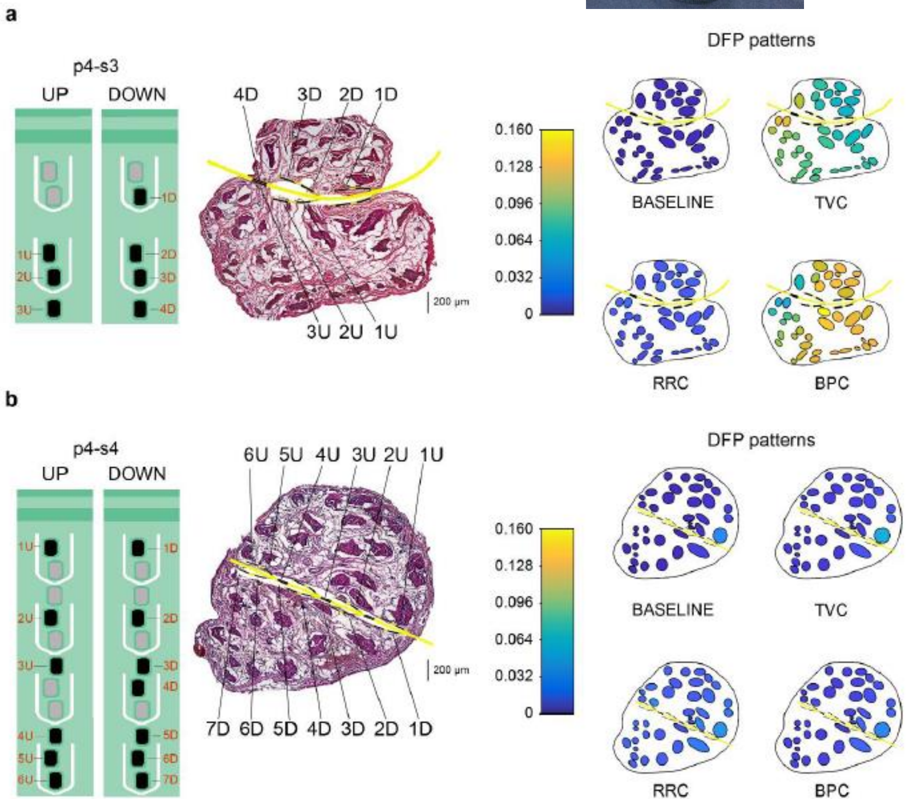
fondation bertarelli

Sant'Anna Scuola Universitaria Superiore Pisa

Electroceutical
Decoding from Vagus Nerve activities

Decoding Baseline vs. Three Challenges

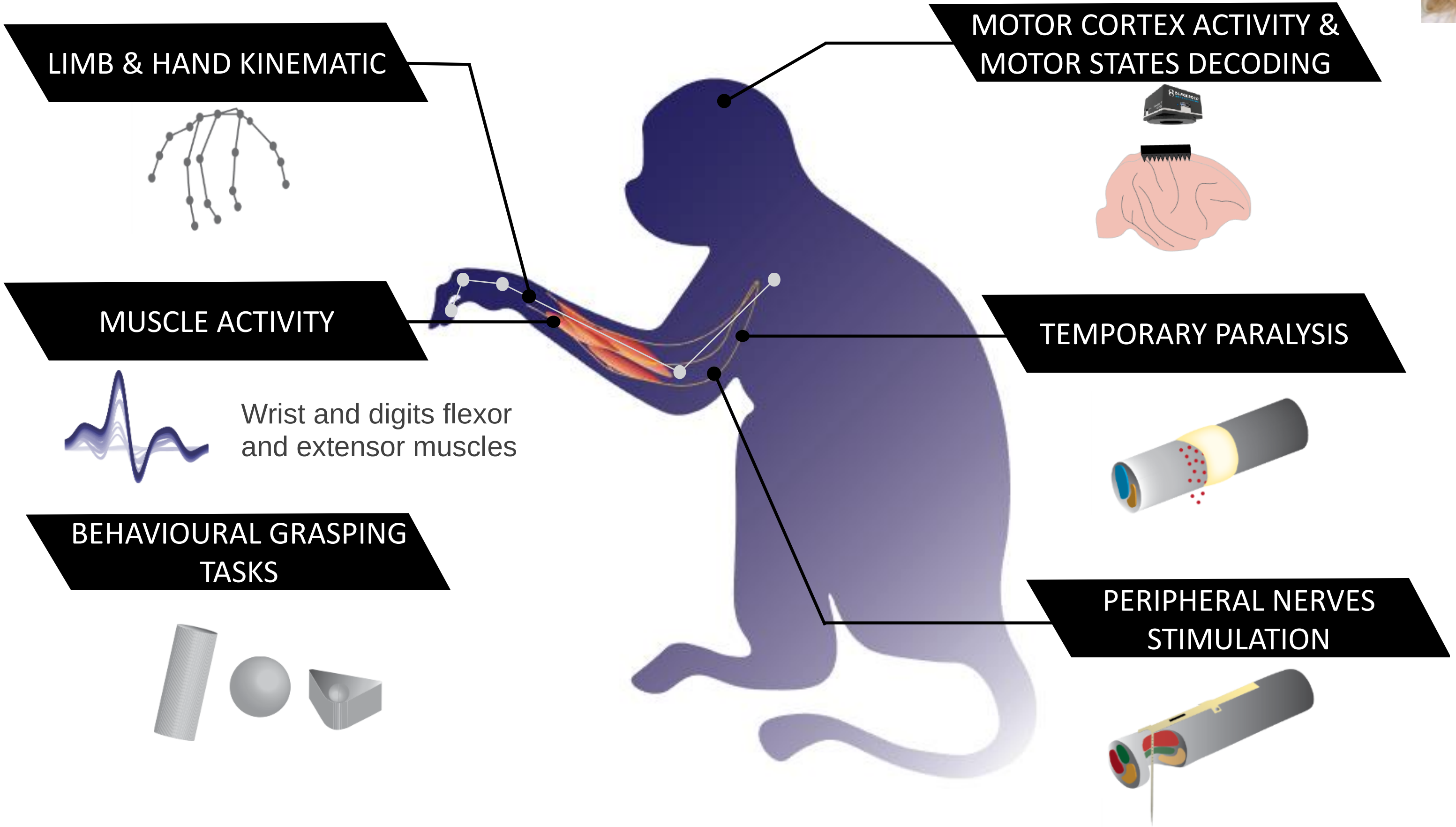




Our algorithm robustly achieved high accuracy levels in identifying different functional changes and discriminating among them

By combining an anatomically validated hybrid neural model and discrimination analysis, we provided new evidence suggesting a functional topographical organization of VN fascicles.

Intraneural stimulation to restore grasping functions



Conclusion

- Intraneural stimulation proved to be a very promising tool to restore neural function
- Our next steps are:
  - To clinically validate the fully implanted bionic limbs
  - To validate in animal models (and later patients) the i4LIFE concept
  - Long-term exploitation for other electroceutical applications

If you can play with the nervous system you have **UNLIMITED** possibilities

Tom Mortimer
Case Western

Acknowledgements

- Prof. Diego Ghezzi
- Prof. Stéphanie Lacour
- Dr. Fiorenzo Artoni
- Vivian Gaillet
- Ilaria Scarpato
- Evgenia Roussinova
- Dr. Sophie Wurth
- Florian Fallegger

- Prof. Fabio Recchia
- Prof. Vincenzo Lionetti
- Dr. Alberto Mazzoni
- Dr. Calogero Oddo
- Dr. Giacomo Valle
- Dr. Fabio Vallone
- Federica Barberi
- Elena Lonsanno

- Prof. Paolo M. Rossini
- Dr. Giuseppe Granata
- Dr. Riccardo Di Iorio
- Dr. Francesco Iodice
- …

- Prof. Eric Rouiller
- Dr. Marco Capogrosso
- Maude Delacombaz
- Dr. Eric Schmidlin
- Simon Borgognon
- Dr. Florian Lanz
- Beatrice Barra
- Dr. Andrew Bogaard

- Prof. Thomas Stieglitz
- Paul Cvancara
- …

- Dr. David Su
- Prof. Eberhard Fetz

- Prof. Stanisa Raspopovic
- Dr. Francesco Petrini