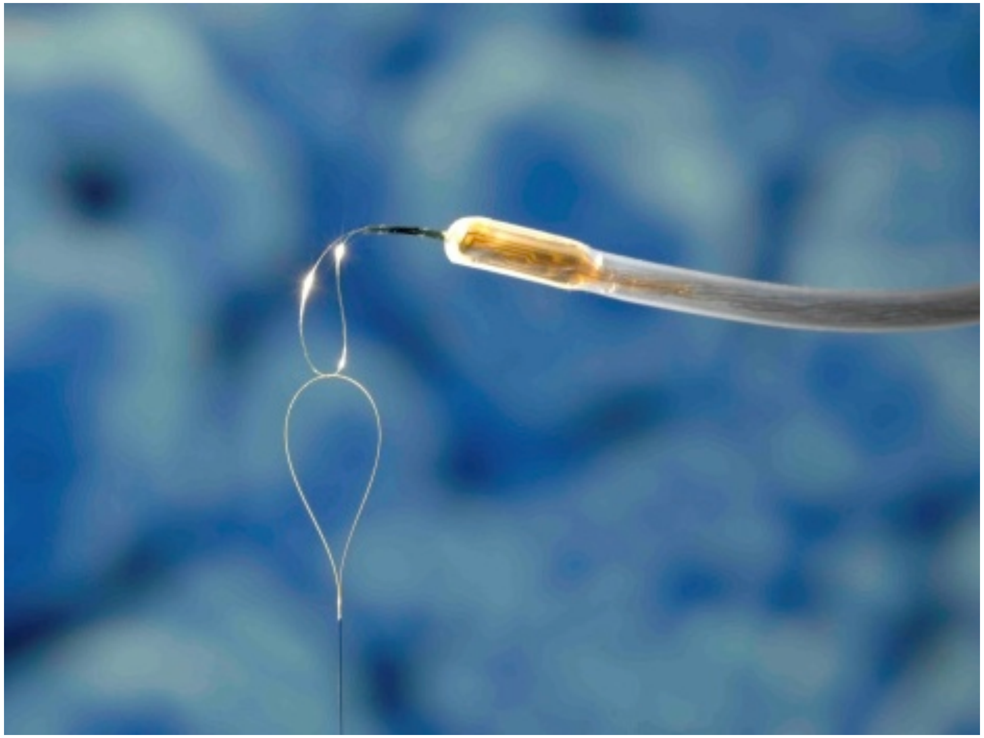
NEUE ENTWICKLUNGEN AUF DEM GEBIET DER NEUROPROTHETIK

Wechselwirkung Zelle/Material – Implantate und Sensoren in der Medizintechnik

Workshop Heraeus Holding GmbH, 21. Januar 2016, Hanau



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Fraunhofer Institute for Biomedical Engineering IBMT

- Largest research and development division in the field of ultrasound within Europe
- World-wide leading developer of cryo technology and biobank design
- Core competences
  - Neuroprosthetics
  - Development of automated in vitro culture systems
  - Molecular and cellular biotechnology
  - Cell-free bioproduction
  - Nanobiotechnology
  - Biochip and point-of-care-technologies
  - (mobile) laboratory
  - Information technology
  - Regulatory affairs of medical systems
- Founded: 1987
- **Headquarter** IBMT: Sulzbach

Fraunhofer Institute for Biomedical Engineering IBMT

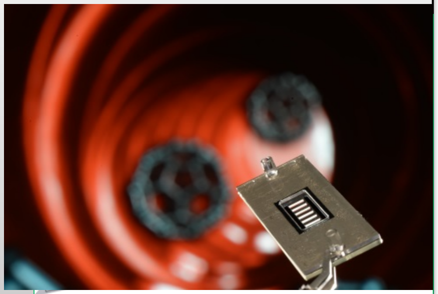
Cryo & Stem Cell Technology

- Pluripotency & Regeneration
- Biomedical Optics
- Automation Processes
- Marine Biopolymers (Coquimbo/Chile)
- Cooperation Laboratory EFPIA (Babraham/UK)

Bioprocessing & Bioanalytics

- Biomonitoring & Cryobanking
- Cellular Bioprocessing
- Preclinical Nanotechnology & Nanotoxicology

MEDICAL BIOTECHNOLOGY



Medical Ultrasound

- Ultrasound Systems/Clinical Applications
- Biomedical Ultrasound Research
- High-Frequency Piezosystems

Technical Ultrasound

- Technical Ultrasound Systems
- Transducer Development
- Manufacturing Technology (ISO 9001 & 13485)
- Simulation

ULTRASOUND

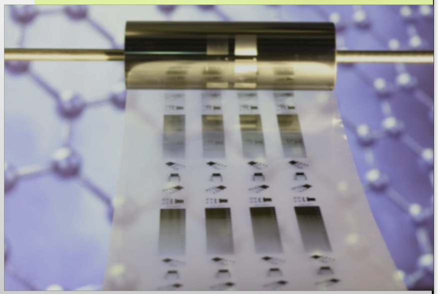
Biomedical Microsystems

- Microsensors & Microfluidics
- Biotelemetry
- Active Implants

Medical Engineering & Neuroprosthetics

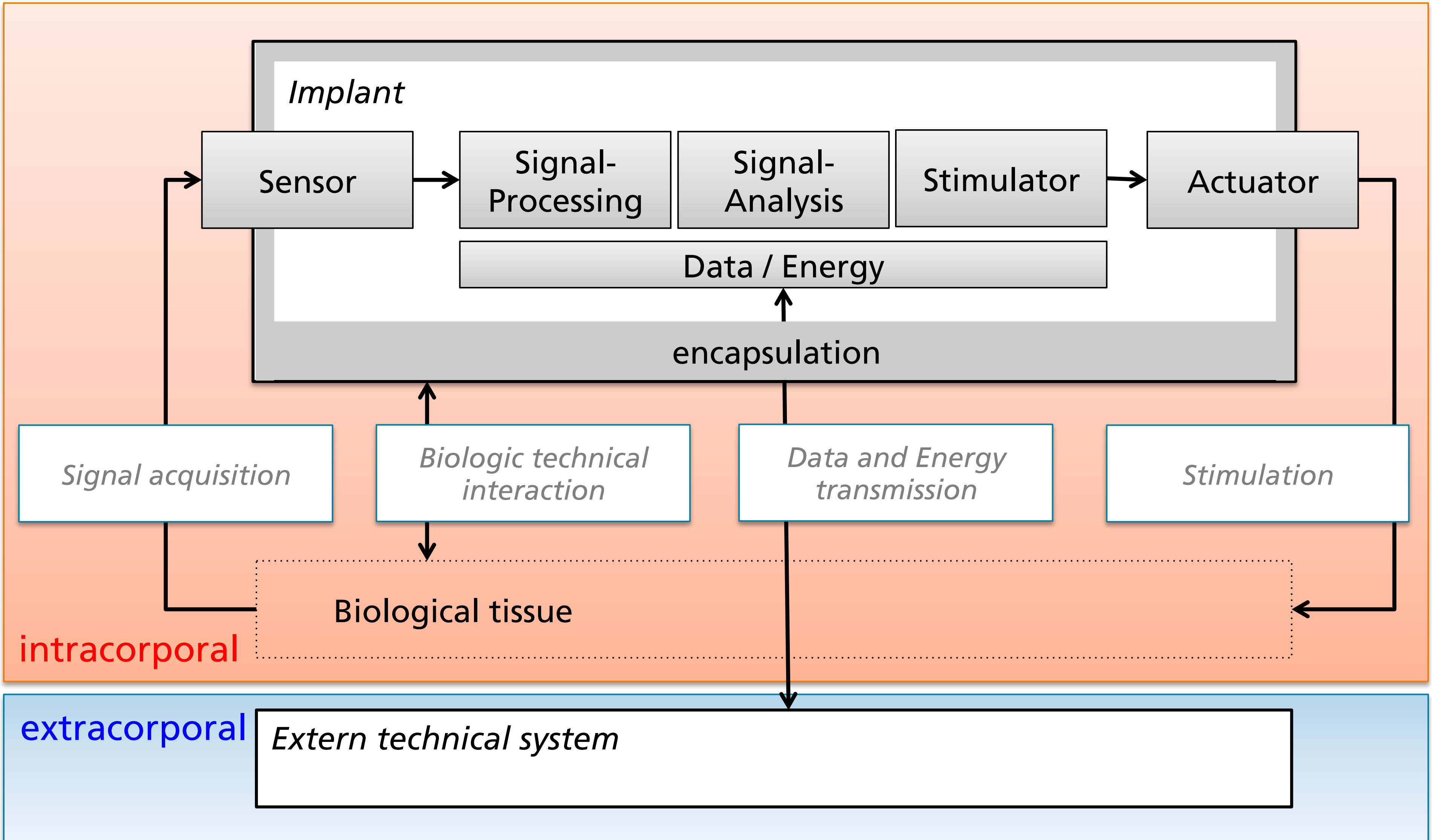
- Neuromonitoring
- Neuroprosthetics
- Silicone Technology
- Health Information Systems

BIOMEDICAL ENGINEERING

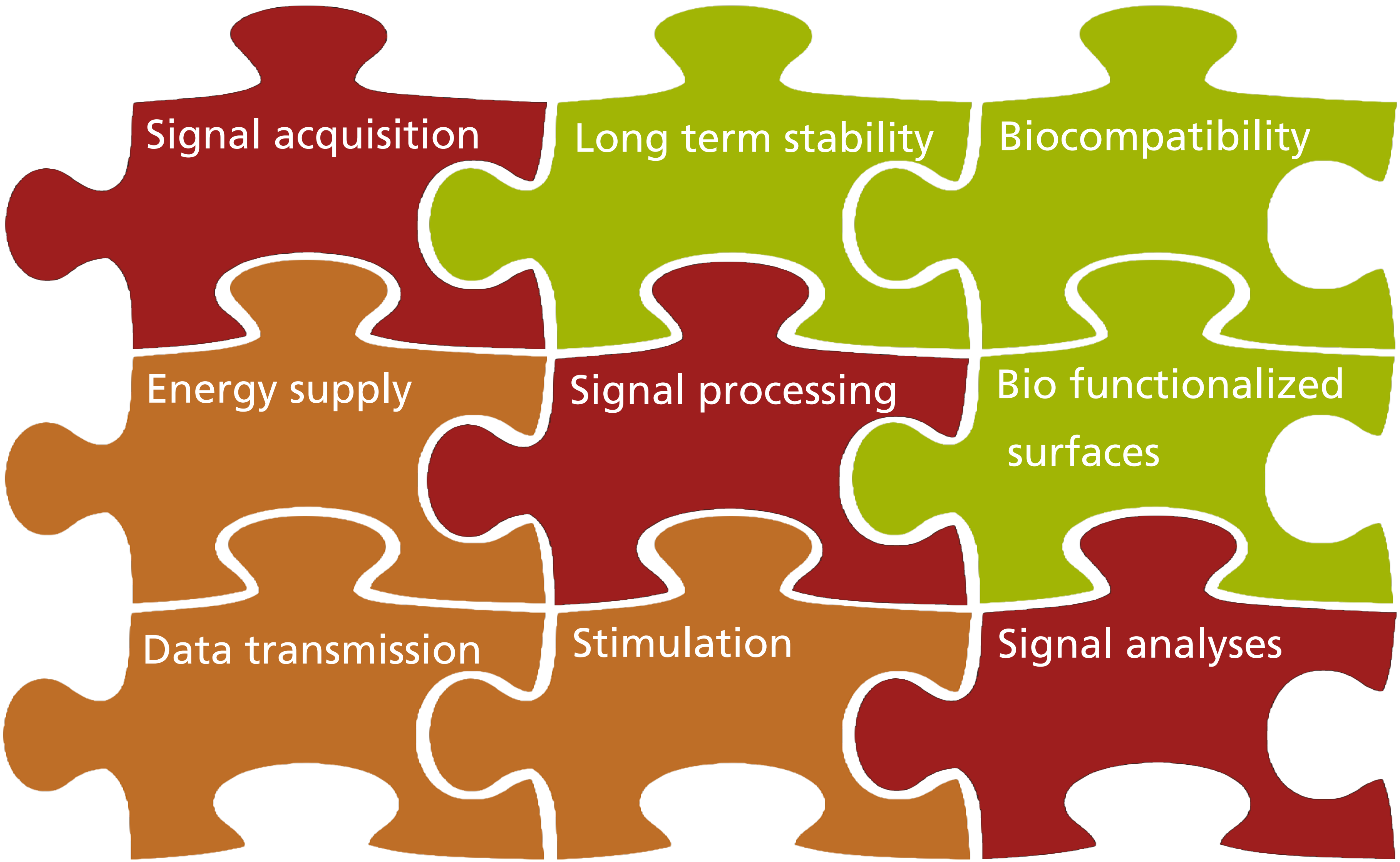


Main Departments

Interfaces


Implant
Sensor
Signal-Processing
Signal-Analysis
Stimulator
Actuator
Data / Energy
encapsulation
Signal acquisition
Biologic technical interaction
Data and Energy transmission
Stimulation
Biological tissue
intracorporal
extracorporal
Extern technical system

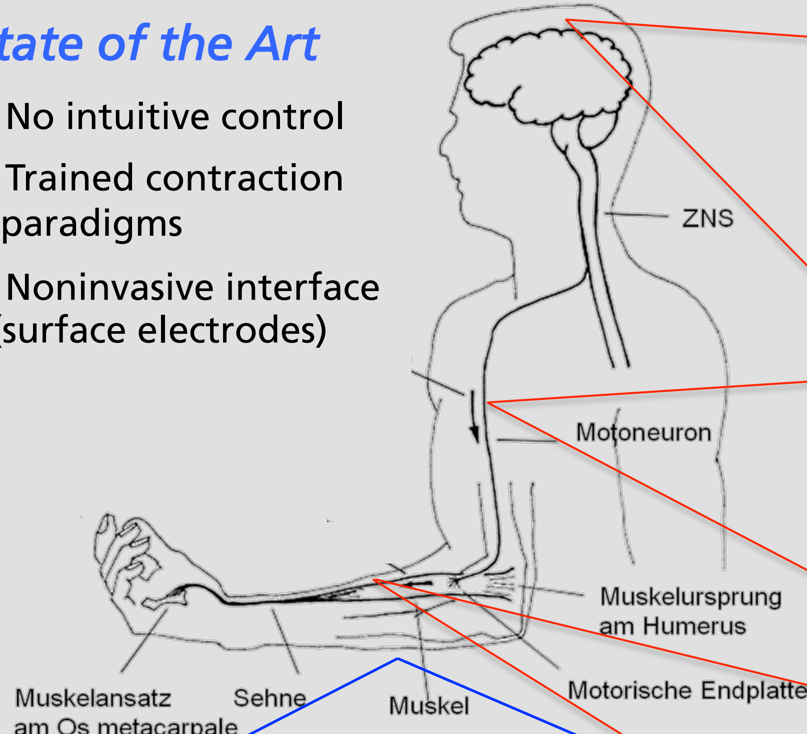
Challenges


Signal acquisition
Long term stability
Biocompatibility
Energy supply
Signal processing
Bio functionalized surfaces
Data transmission
Stimulation
Signal analyses

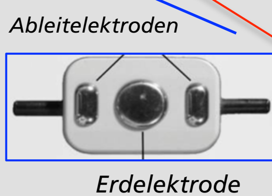
(Mind) Controlled Hand Prostheses

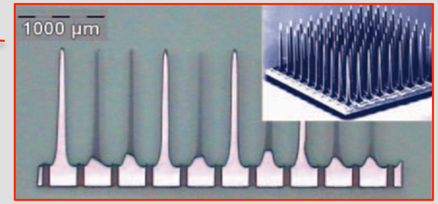
State of the Art

- No intuitive control
- Trained contraction paradigms
- Noninvasive interface (surface electrodes)

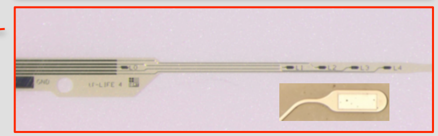


Otto Bock - State of the Art
surface electrodes
arm

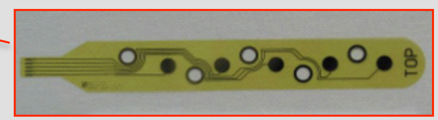




Utah State Universit (USA)
Electrode array
Motor cortex



Project Neurobotics (EU)
intrafascicular electrode
Peripheral nervous system



Project Myoplant (BMBF)
Epimysial electrode
muscle

Research

- Mind controlled
- Association of a movement
- Invasive interface (implantable electrodes)

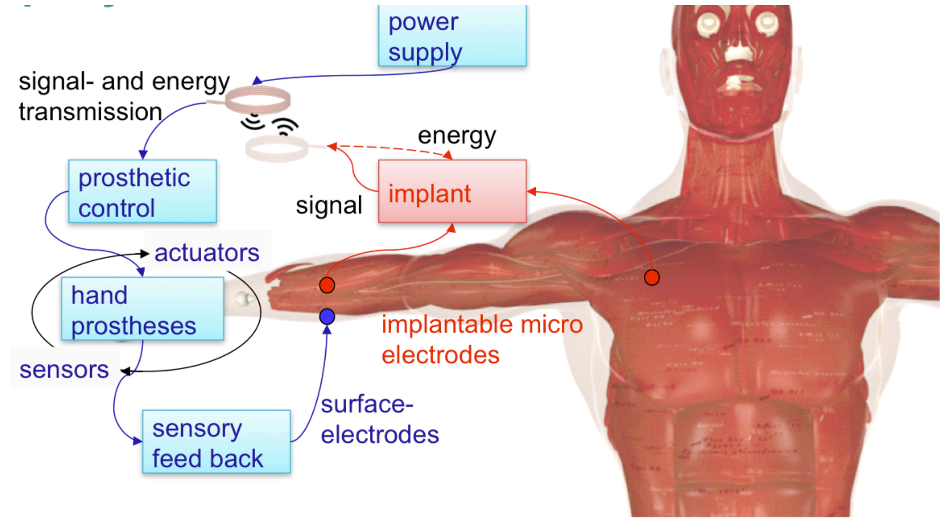
Neurobotics IBMT

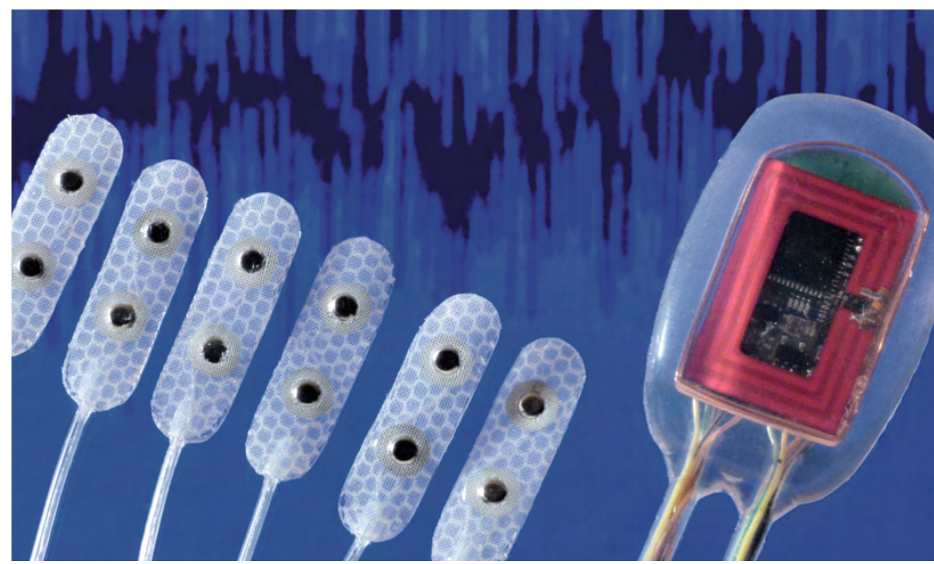
Myoplant IBMT

[1] Hochberg, L.R. et al.: Neuronal ensemble control of prosthetic devices by a human with tetraplegia, nature Vol 442, 13 July 2006, pp 164-171 (2006).
[2] Hoffmann, K.-P., H. Dietl: „Handprothesen: Nach dem Vorbild der Natur“ Deutsches Ärzteblatt 04/10 2010: 11-14

Epimysial Electrode

- Control of upper extremity prostheses by a new type of permanently implanted EMG electrodes
- Implantable telemetric link for signal and energy
- Evaluation of the entire implant system in the animal model
  - Electrodes
  - Data processing
  - Telemetric link (energy and data)

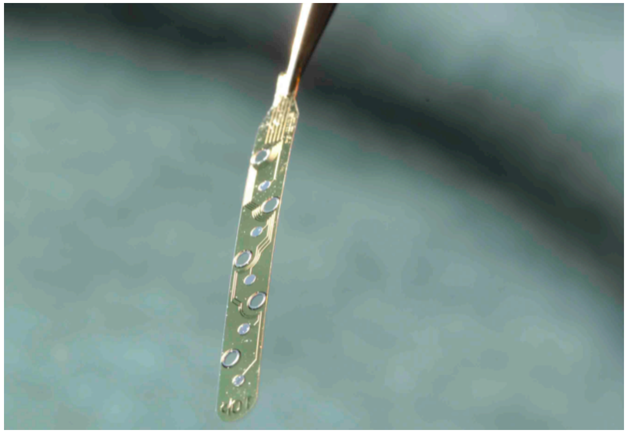




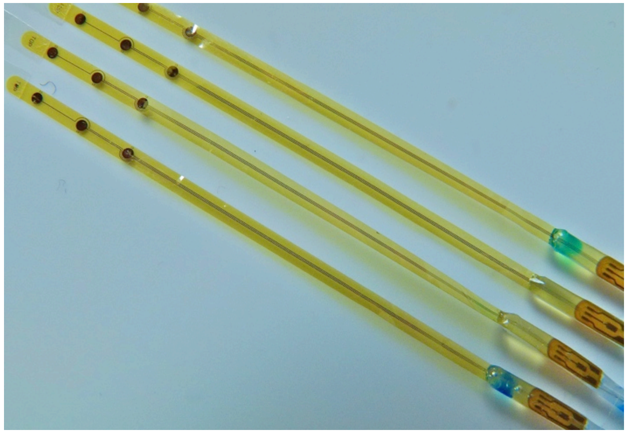
Epimysial Electrode

- Typical muscle length contraction ~ 5%
- Mechanical longtime stability
- Optimization of the Electrode design
- Changes in the design, Different materials
- Additional mechanical characterization

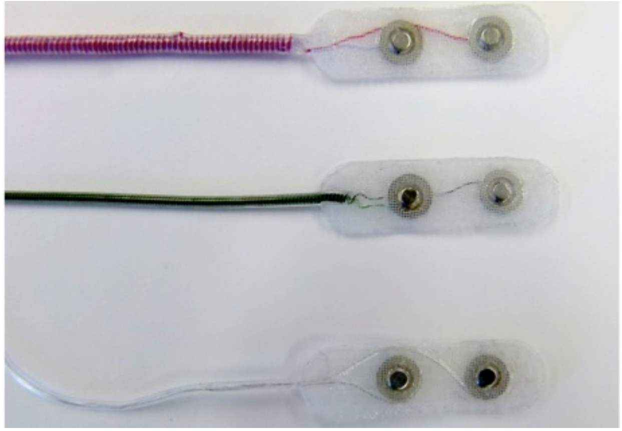
Polyimide



Polyimide

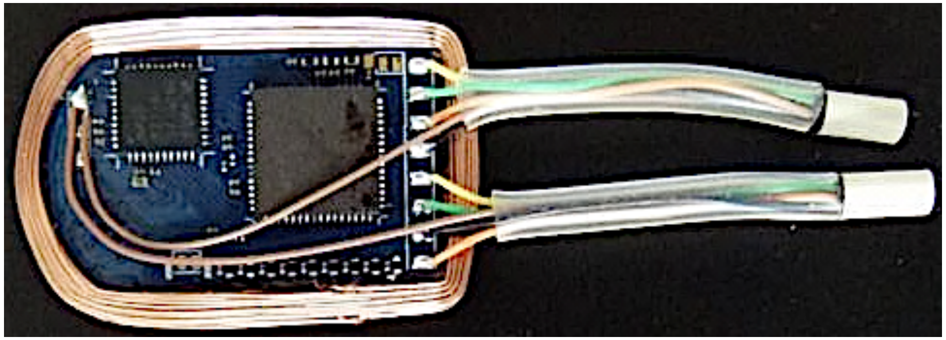


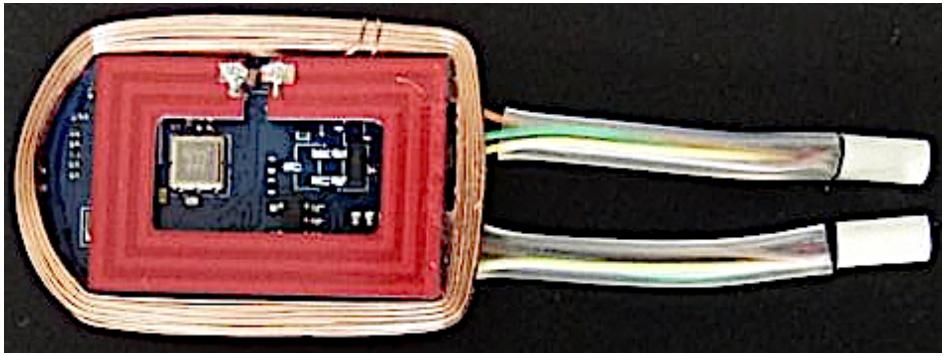
PDMS



Implant (1)

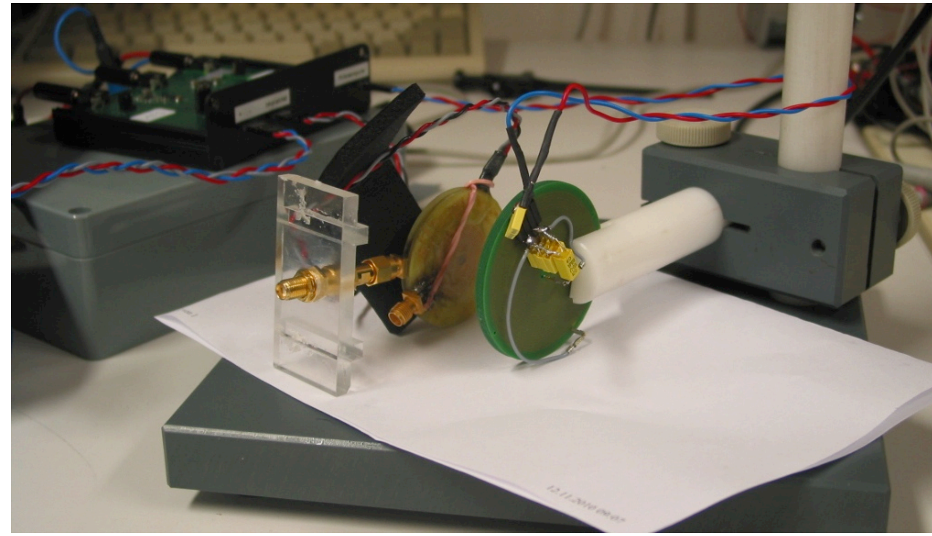
- Electronics capsuled in silicone (Size 38×25×8 mm)
- Application specific integrated circuit (ASIC)
  - Two stage differential amplifier with adjustable gain
  - Band-pass 6 – 1500 Hz
- Microcontroller (Texas Instruments MSP430)
- Signal transmission with RF transceiver: Zarlink ZL70101
  - Nearly real-time transmission up to a rate ~70kBit/s
  - MICS band between 402 and 405 MHz
- Inductive coupled energy supply

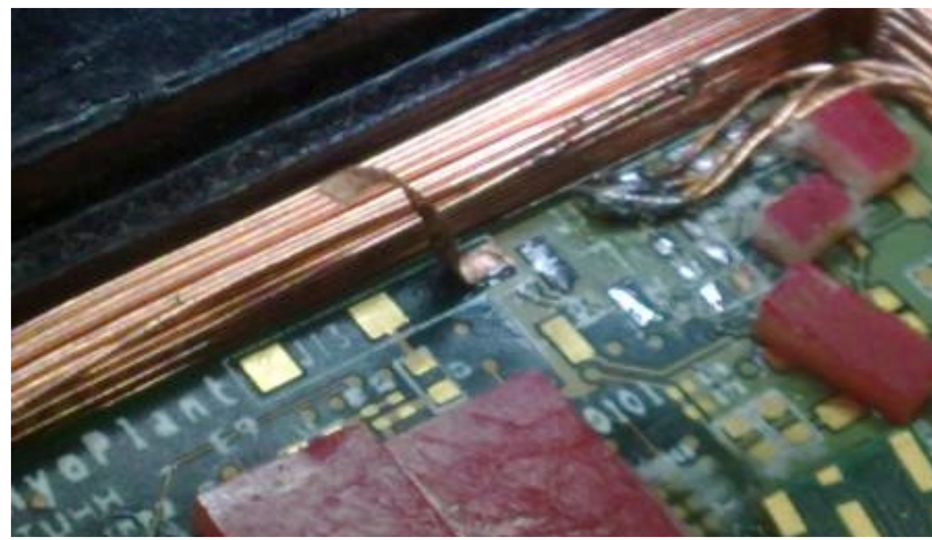




Implant (2)

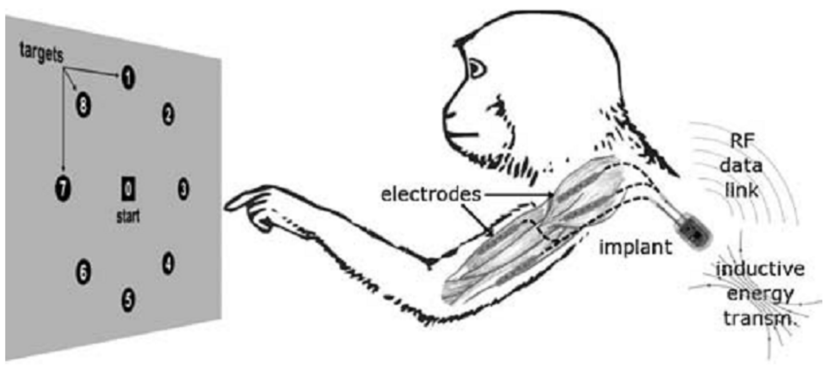
- Two multipolar connectors (NCP-06, Omnetics Connector Corporation)
- Intra-operatively sealed with silicone (MED2000, Nusil)
- IBMT Configuration for data transfer
  - Transfer rate: ~260 kBit/s
  - Error rate: ~1% (optimal link)
  - Latency (Signal acquisition, conditioning and transmission): ~23 ms ±7ms
  - Up to 10 channels digitized with 10 bit resolution





Experimental Setup

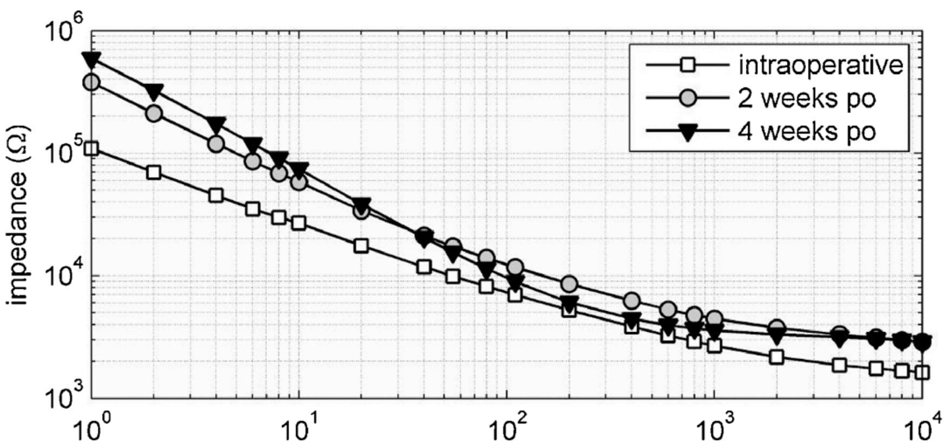
- Rhesus macaque (7 years old)
- Implantation into the musculus deltoideus
- Electrode placement
  - (sub-) epimysial
  - Longitudinal
- The animal was trained to touch the visual cues
- Moving its hand to the respective peripheral target position (from the central to one of the eight peripheral positions and back to the central)



[1] Ruff, R., et. al: Acquisition of Myoelectric Signals to Control a Hand Prosthesis with Implantable Epimysial Electrodes, Poceedings 32nd Annual IEEE EMBS Conference, 31.08.-04.09.2010, Buenos Aires (Argentinien).
[2] Lewis, S. et al.: Impedance of implanted myo-electrodes. Impedance of implanted myo-electrodes 10th Vienna International Workshop on FES and 15th IFESS Annual Conference, 08.09.-12.09.2010, Wien (Österreich).

Electrode impedance

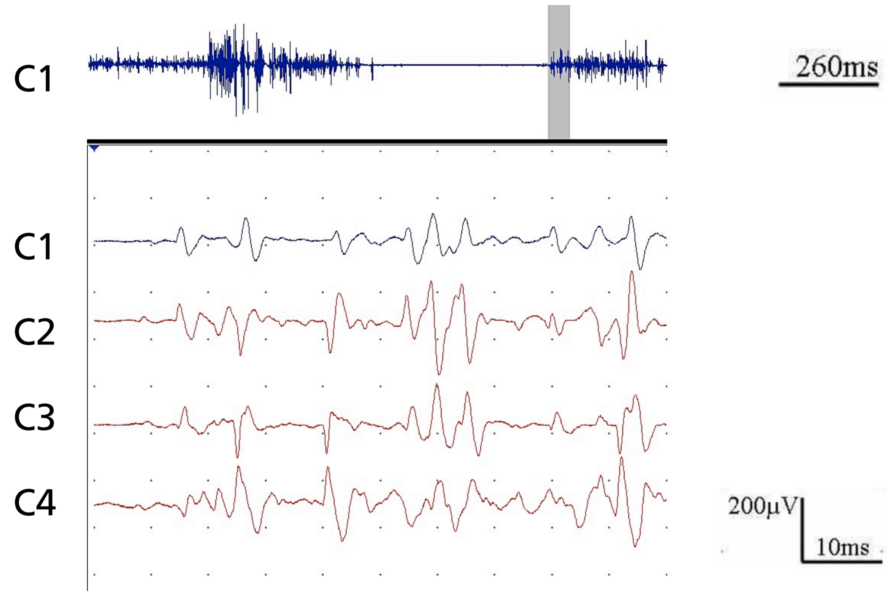
- Bode plot of electrode impedance at three time periods after implantation
  - After implantation: very similar to measurements in physiologic saline
  - After two weeks: increase over the whole frequency range
  - After four weeks: further increase for frequencies below 35Hz and slightly reduced for higher frequencies
  - Later: no further changes
  - Encapsulation has reached a steady state after four weeks.

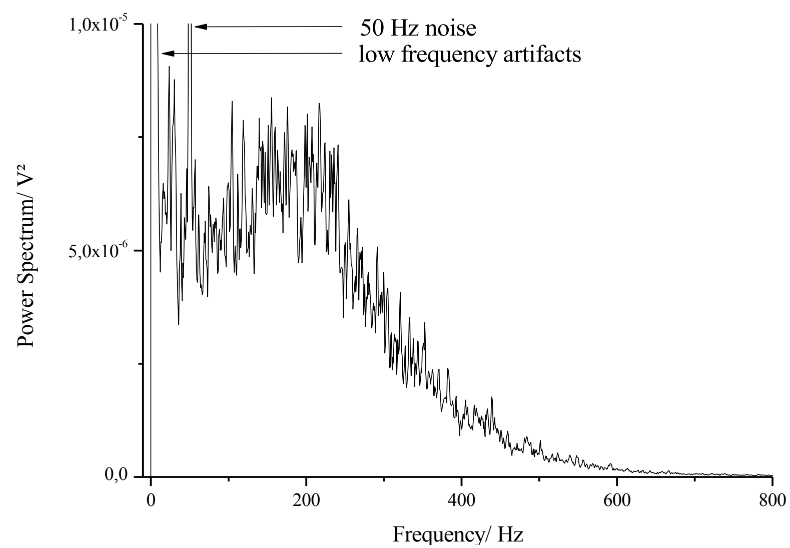


[1] Lewis, S. et al.: Impedance of implanted myo-electrodes. Impedance of implanted myo-electrodes 10th Vienna International Workshop on FES and 15th IFESS Annual Conference, 08.09.-12.09.2010, Wien (Österreich).

Epimysial Electrode

- First results
- Frequency range: 100 Hz to 10 kHz
- Sampling rate: 20 kHz
- Two different movements:
  - From the central to the peripheral position
  - Back to the central position
- Frequency spectrum
  - Filter: 1 Hz – 10 kHz
  - Sampling rate: 20 kHz
  - Two main signal components in the power spectrum
    - Lower frequency: 10 - 40Hz
    - Higher frequency: 100 - 500Hz





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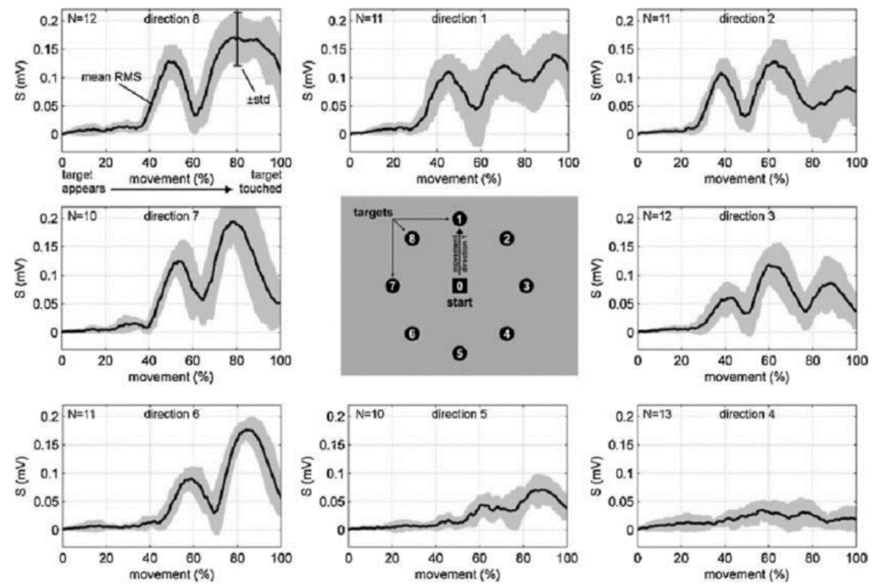
Myoplant

Results

- 4 weeks after implantation
- Recording system is triggered by visual cue.
- Strong correlation between recorded signals and goal directed arm movement
- Intuition of movement could be detected by signal analysis
- Six classifiers and seven time and frequency domain features were investigated
- Signals could be clustered
- All experimental procedures were conducted in accordance with German laws governing animal care.



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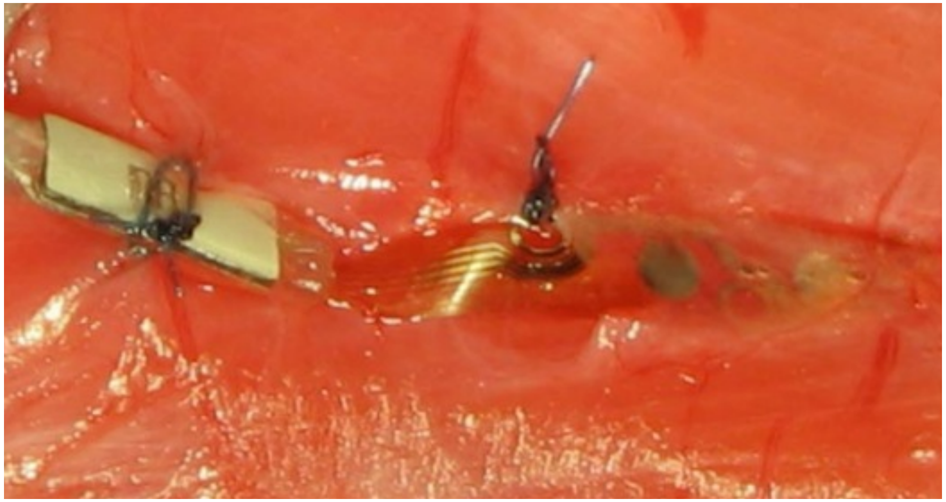
Myoplant

Advantages of Signal Acquisition

- Electrodes are placed at the epimysium of the muscle
- Fixed electrode position (epimysial)
- More selective compared with surface electrodes
- Less invasive compared with nerve electrodes
- Muscles as "biological amplifier" for nerve signals
- High amplitude (approx. 200 µV)
- Low frequency range (up to 600 Hz)
- Small transfer rate
- Less artefacts, high signal-to-noise ratio (approx. 80 dB at 200 Hz)
- Application longer than 8 month

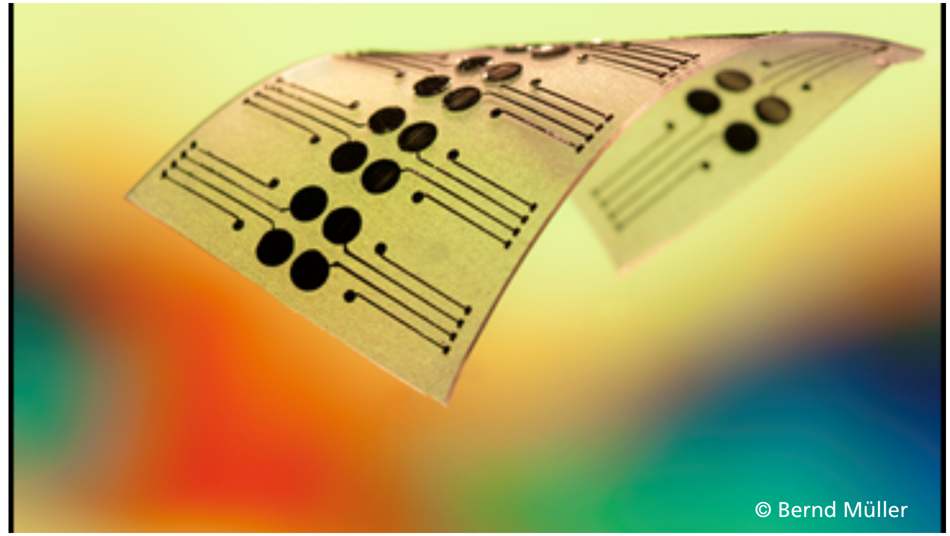


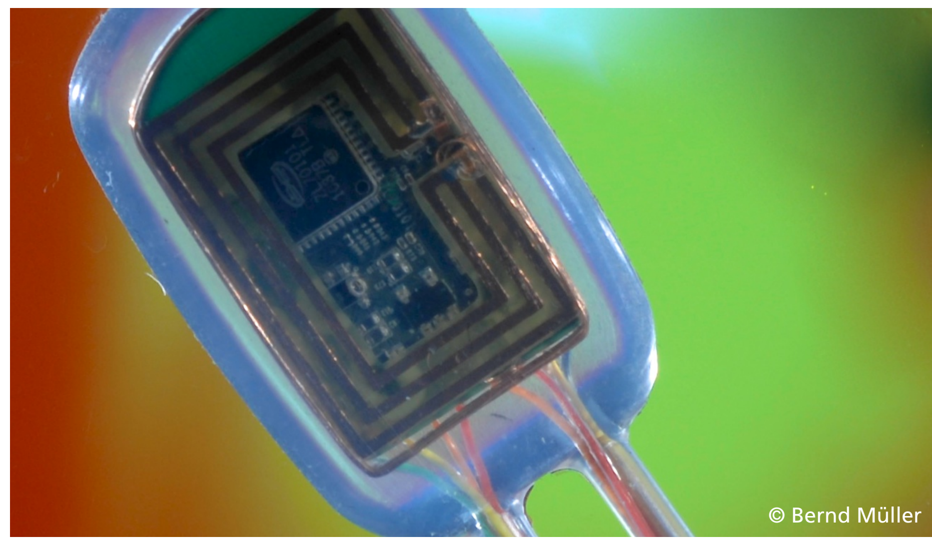
Summary

- Key components of the fully implantable system
  - Implantable flexible micro electrode for the invasive acquisition of muscle activities.
  - Signal conditioning, signal pre-processing.
  - Telemetry module for inductive energy and signal transmission.
  - Pattern recognition and classification of the signals.
  - Signal processing and detection of the desired hand movement.
  - Artificial limb control.
  - Hand prosthesis including actuators and sensors.
  - External charging unit for energy supply of the implant, the artificial limb, and sensory feedback.
  - Regulatory affairs including quality and risk management.

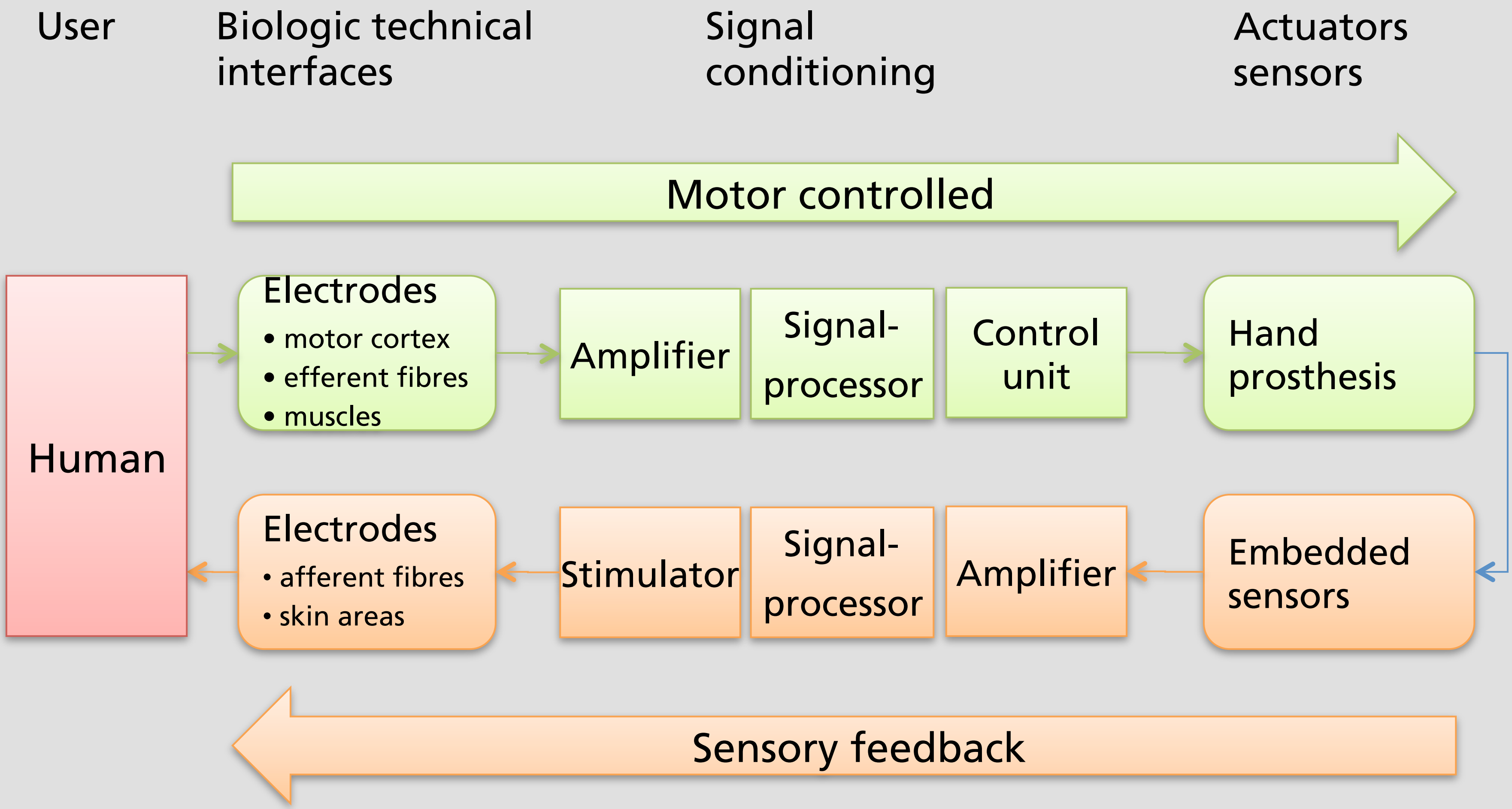
Next steps

- Further miniaturization of the system.
- Improving long-term stability by evaluating different encapsulation and housing technologies.
- Optimizing power management.
- Including sensory feedback for the patients using neural stimulation electrodes.
- New electrode materials and new microfabrication technologies (All Polymer Electrodes).
    - High mechanical stability combined with optimized electrochemical characteristics.





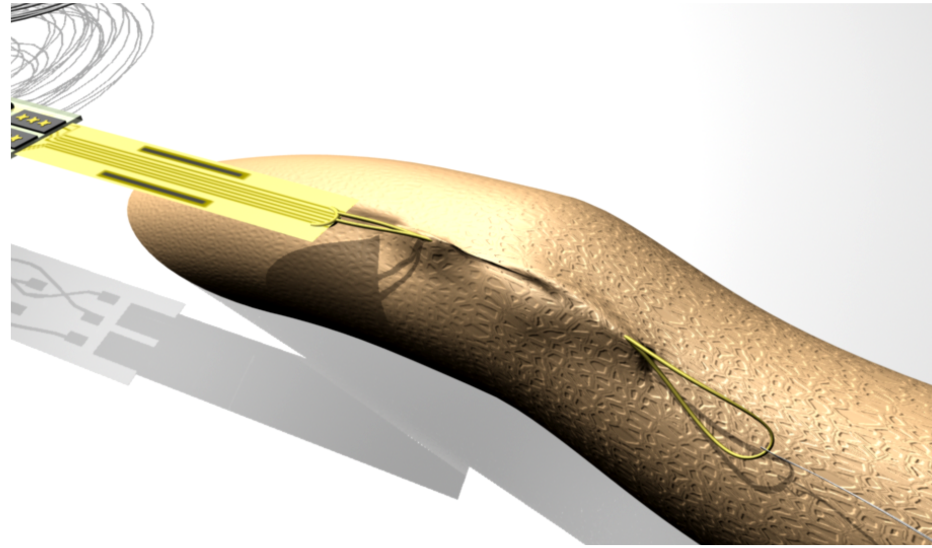
Bidirectional Interfaces for Hand Prostheses

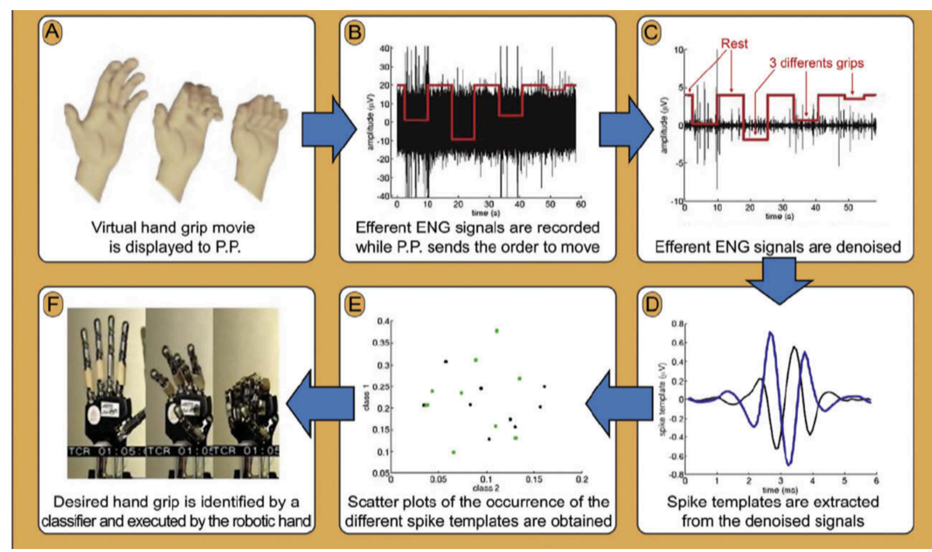


[1] Hoffmann, K.-P., H. Dietl: „Handprothesen: Nach dem Vorbild der Natur“ Deutsches Ärzteblatt 04/10 2010: 11-14

Intrafascicular Electrode (tf-LIFE)

- tf-LIFE („thin-film longitudinal intrafascicular electrode“)
- Combination of a loop-shaped thin-film multi-channel electrode and a second loop with a thin needle
- Using the needle, the electrode can be pulled longitudinally through the nerve
- Only the thin-film electrode remains inside the nerve
- High selectivity can be achieved (depending on the placement of the electrode)

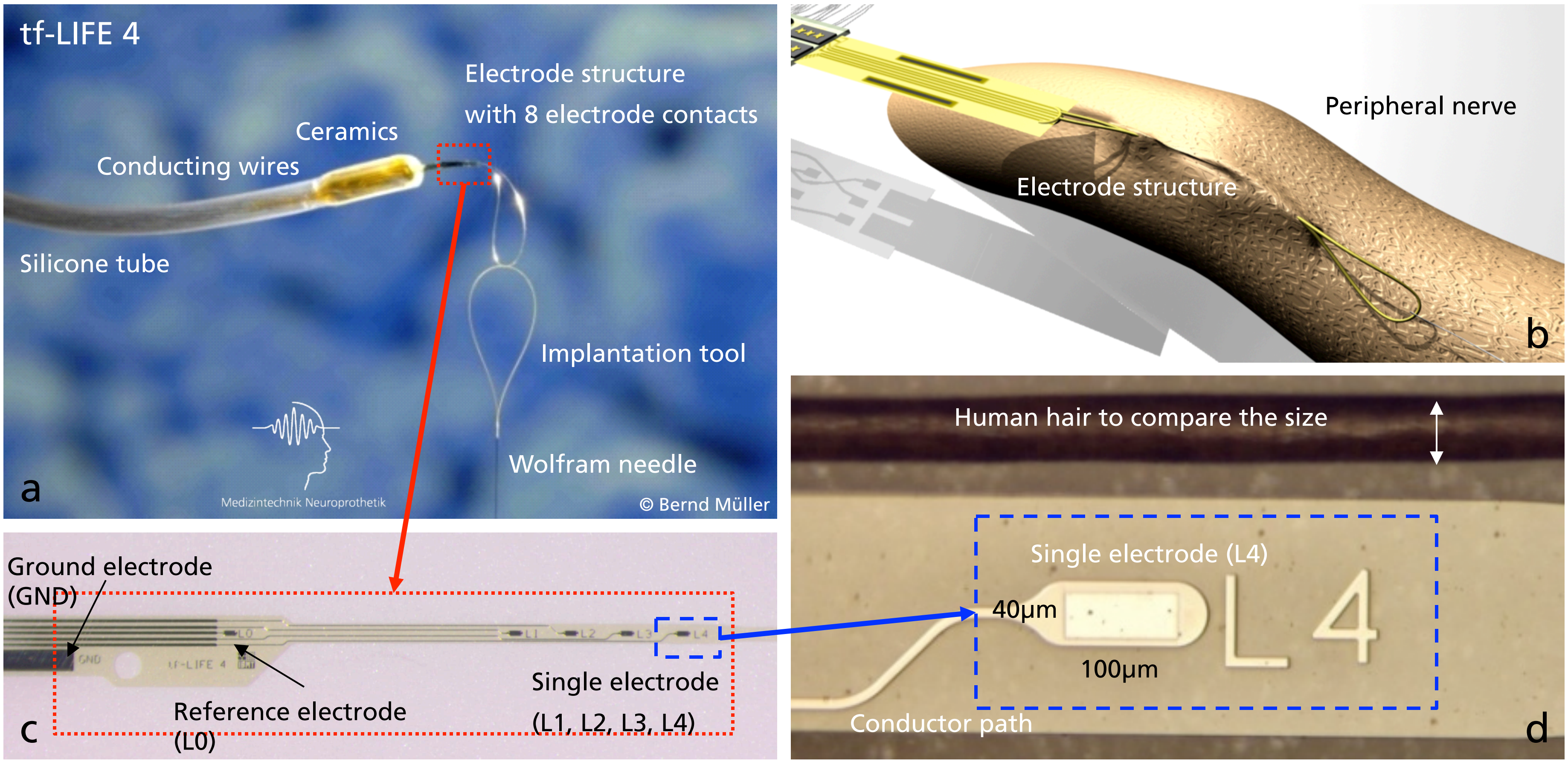




[1] Rossini, P.M., et al.:Double Nerve Intraneural Interface Implant on a Human Amputee for Robotic Hand Control“ Clin Neurophysiol. 121, 5 2010: 777-783.

Bidirectional Interface

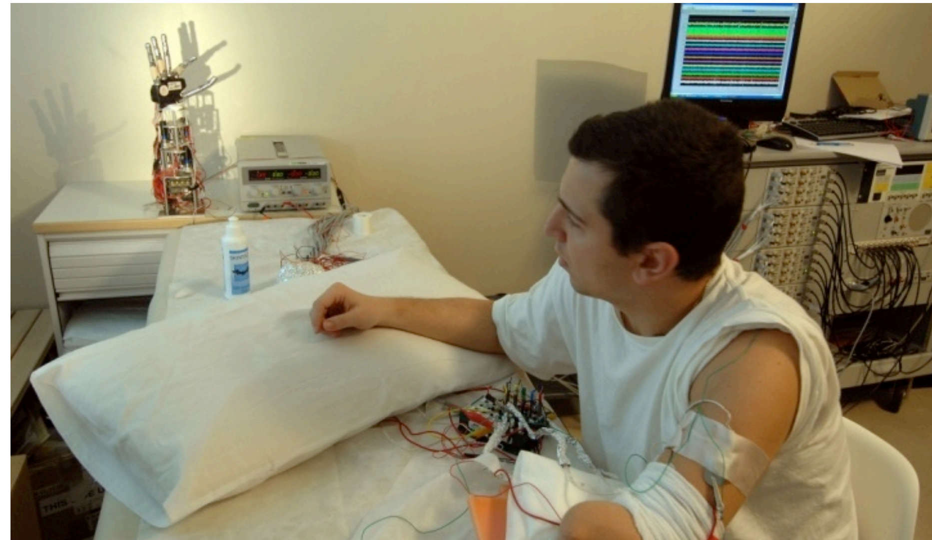
- tf-LIFE 4 (thin film - Longitudinal IntraFascicular Electrode)

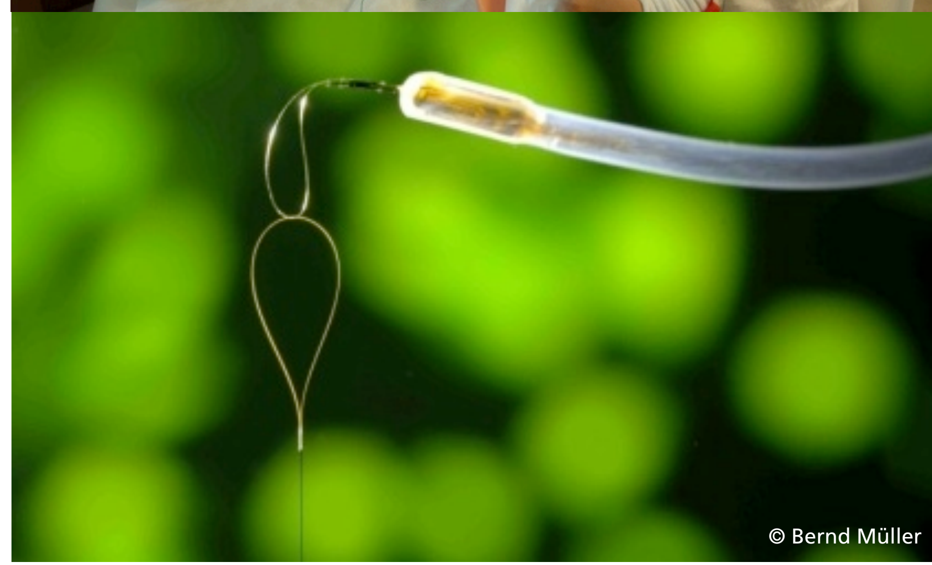


Fraunhofer
IBMT

Results

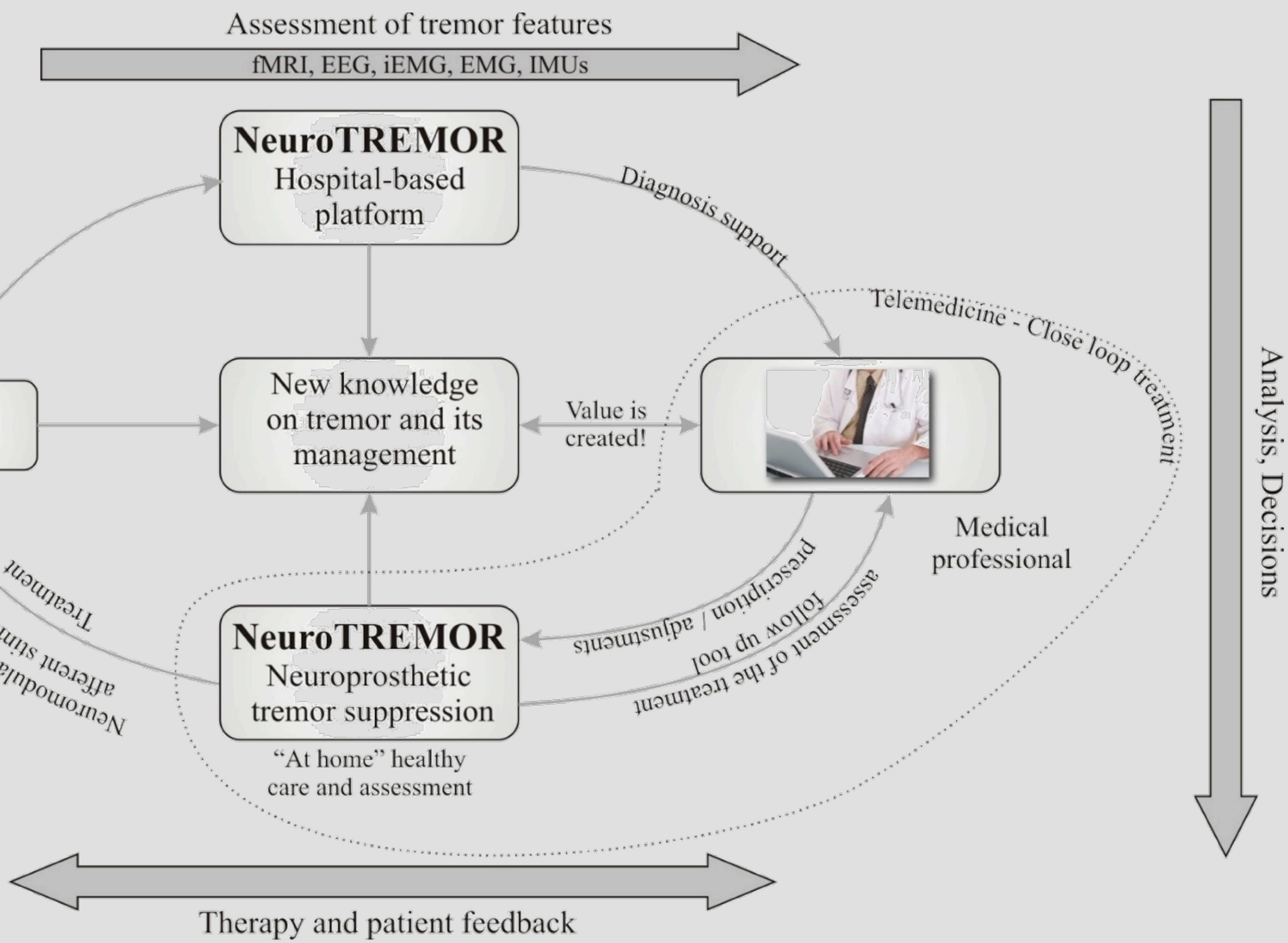
- 24 days experiment
- Bidirectional implanted interface
  - tf-LIFE 4
- Application
  - N. medianus
  - N. ulnaris
- Signal acquisition (32 channels)
  - Intuitive motor control
  - Precision grip
- Stimulation (32 channels)
  - Sensory feedback
  - Perceive the amputated hand





[1] Rossini, P.M., et al.:Double Nerve Intraneural Interface Implant on a Human Amputee for Robotic Hand Control" Clin Neurophysiol. 121, 5 2010: 777-783.
[2] Benvenuto, A. et al.: Intrafascicular thin film multichannel electrodes for sensory feed-back: evidences on a human amputee. Proceedings 32nd Annual IEEE EMBS Conference, 31.08.-04.09.2010, Buenos Aires

A novel concept for support to diagnosis and remote management of tremor



EU Project NeuroTREMOR: FP7-ICT-2011-7-287739

Background of the project

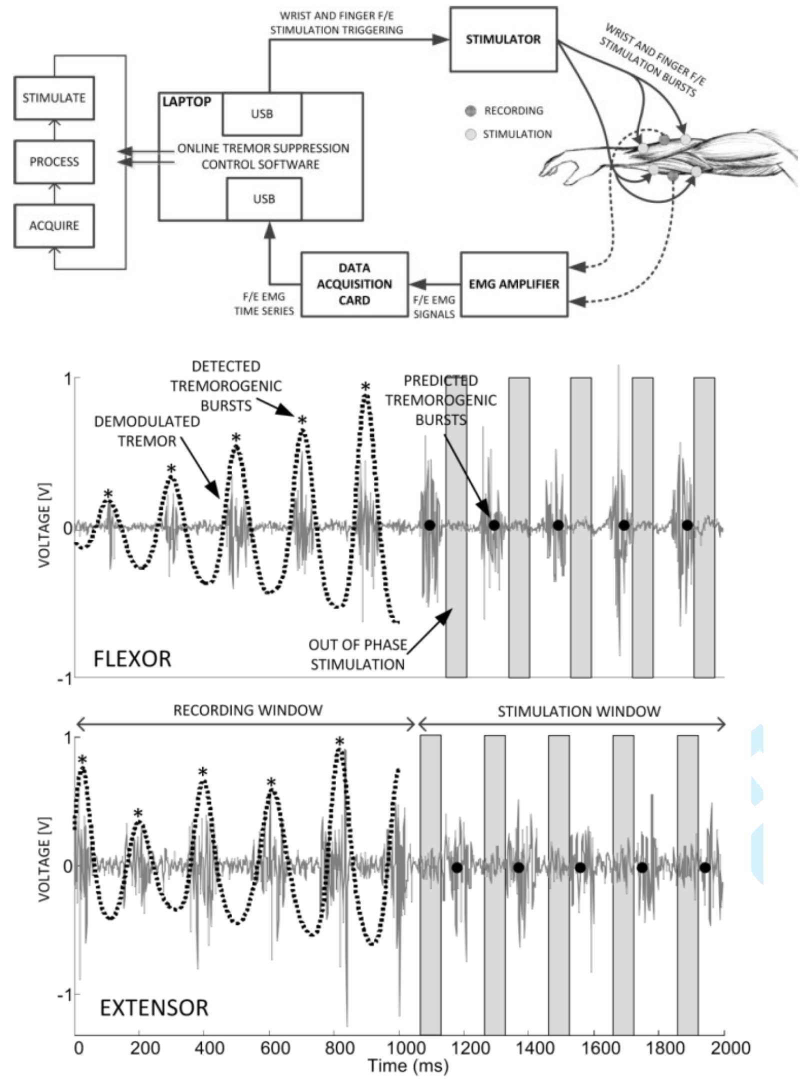
- Pathological tremor:
  - Involuntary rhythmic contraction of counteractive muscle groups
  - Most frequent movement disorder (up to 15% of people >50)
- Various conditions and diseases may cause pathological tremor
  - E. g. Parkinson‘s Disease (PD), Essential Tremor (ET)
  - Misdiagnosis quite common: 30-50% of ET patients do not have ET (Benito-León et al., 2006)
  - Treatment of tremor is disease-specific

https://mmcneuro.files.wordpress.com/2013/01/essential-tremor-is-characterized-by-sporadic-and-postural-tremor-on-hands.jpg

J. Benito-León et al., “Essential tremor: emerging views of a common disorder,” Nat Clin Pract Neurol, vol. 2, pp. 666–678, 2006.

Strategy

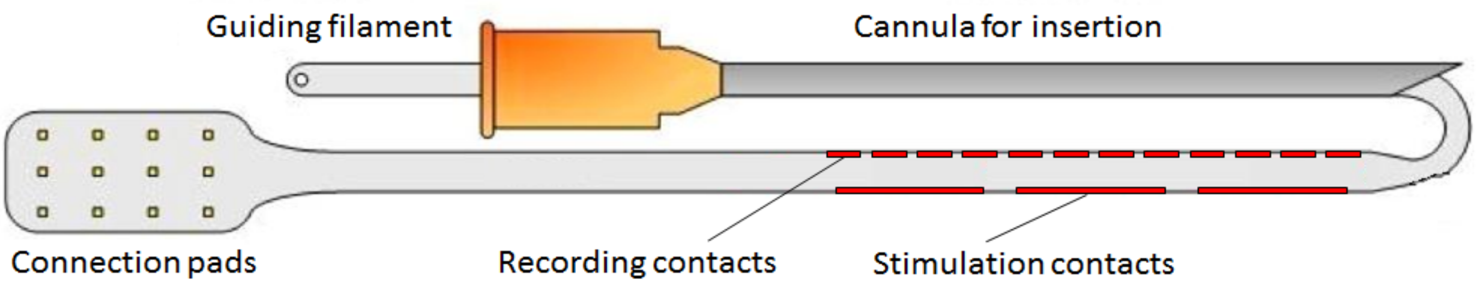
- Tremor detection using EMG recording of the respective muscles
- Counteractivng by electrically stimulating the antagonist in an out-of-phase manner
- Tremor suppression even possible with sub-motor threshold stimulation
  - Less side effects such as muscle fatigue and discomfort for the patients
- Suitable, highly selective interfaces are required



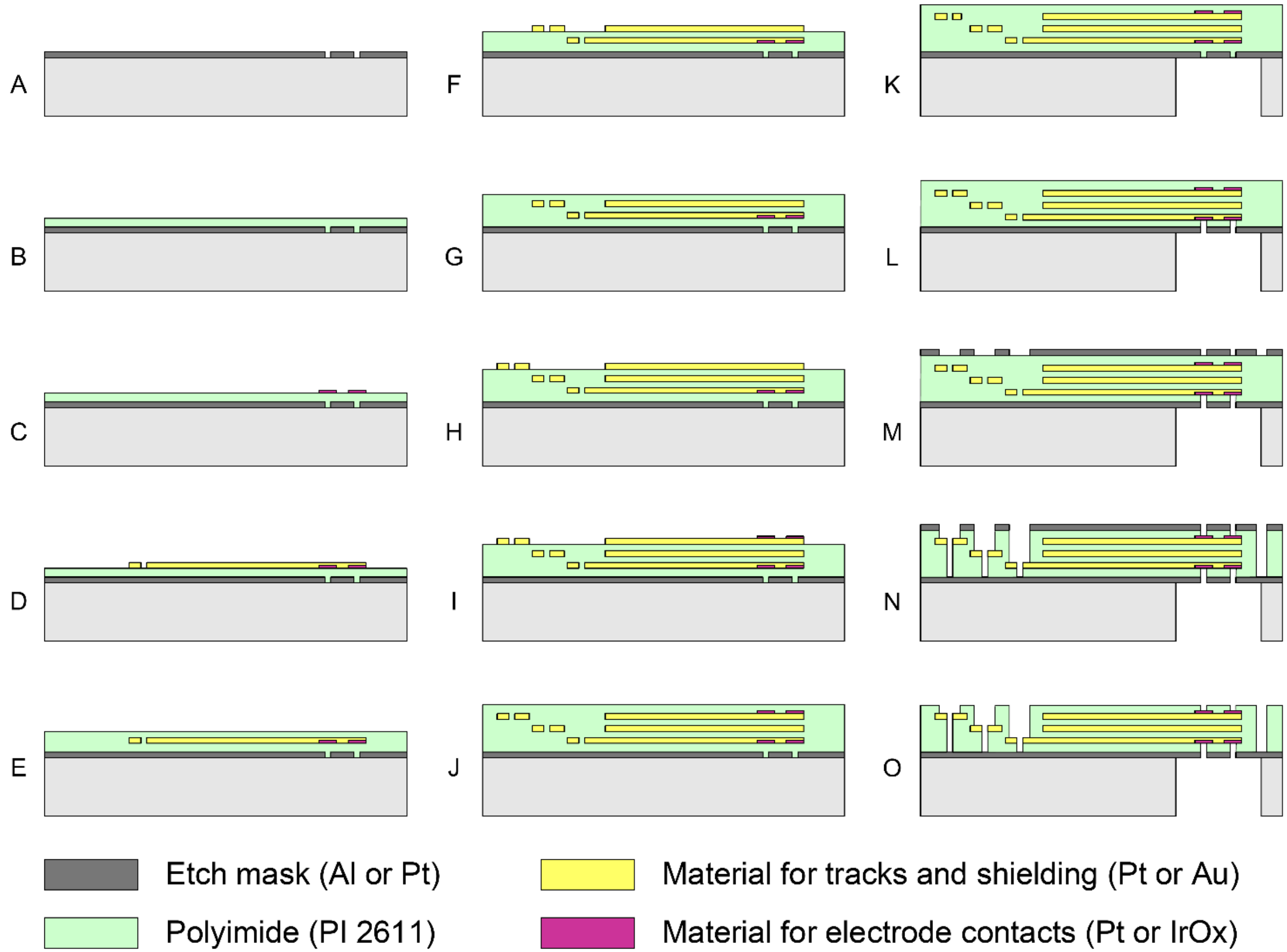
Dosen et al.: „Online tremor suppression using electromyography and low level electrical stimulation“, IEEE Trans Neural Syst Rehabil Eng (2014)

Electrode design

- Insertion with the help of a cannula (25 G)
- Total length: 6.8 cm; foil thickness: 20 µm
- Width of the filament including the electrode contacts: 420 µm
- 12 recording contacts (area 5,257 µm^2)
- 3 stimulation contacts (area 1.1 mm^2)
- Optional: integration of a shielding layer for suppression of stimulation artefacts

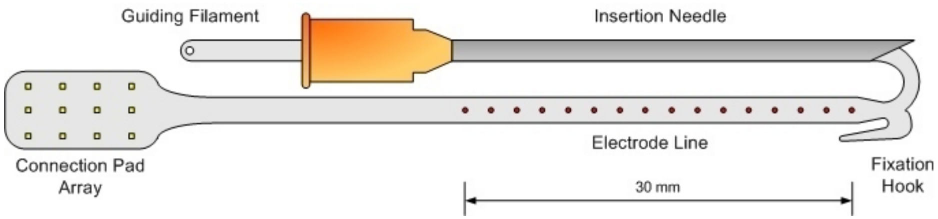


Double-sided polyimide process



Muscle: Intramuscular electrode

- Intramuscular EMG recording
- Electrode is inserted with the help of a needle
- 16 channels for high-resolution EMG
- Recording of high-resolution intramuscular EMG
- Decoding the neural code of human movements
- Development of new human-machine interfaces
- Demove: Decoding the neural drive to muscles for advanced assistive technologies



[1] Poppendieck, W., S. Muceli, C. Welsch, M.-O. Krob, A. Sossalla, K. Yoshida, D. Farina, K.-P. Hoffmann: „Development of multi-channel intramuscular EMG recording electrodes“ Proceedings of 3-Ländertagung D-A-CH (BMT) 2013, Graz (Österreich) 2013

Discussion and next steps

- Successful tests of the double-sided multi-channel electrode for recording and stimulation in patients
- Reduction of tremor by electrical stimulation
- Next steps:
  - Expansion of the system for other muscle groups
  - Development of a fully implantable system for treatment of tremor including implantable electronics, energy supply and wireless data transmission

Outlook, Vision and Ideas

- Alternative Stimulation
- New materials, new technologies (PDMS), all Polymer electrodes
- Multimodal flexible implantable sensors, moveable structures
- Mechanical, optical and biochemical functionalization of different materials
- Drug delivery systems
- Closed loop systems with different sensors and actuators including signal and energy transmission
- Complete implantable interactive systems for functional assistance