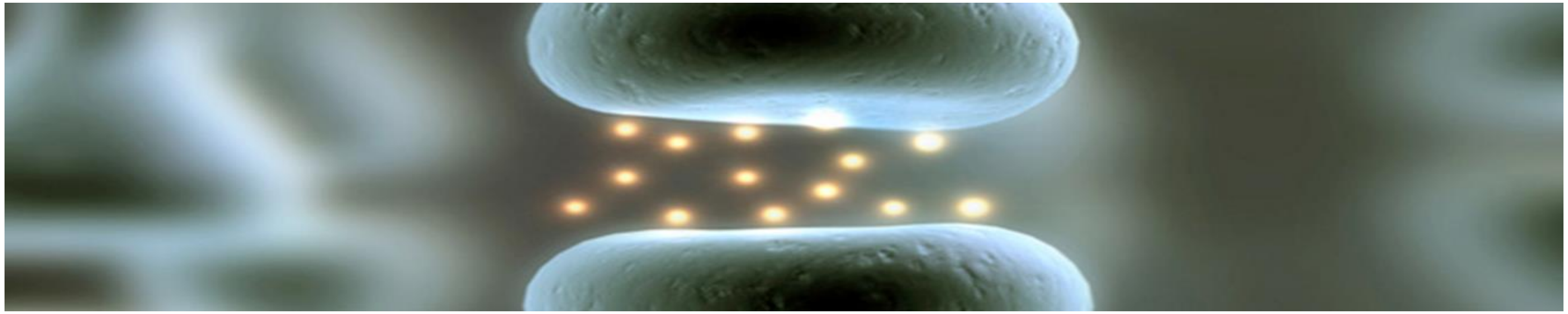
# Implants designed to restore sensorimotor functions



Thomas Guiho – October 6th 2023
M2 – Bionic – Part II
thomas.guiho@inria.fr – CAMIN team (INRIA)

# Implants designed to restore sensorimotor functions


**Introduction – Neuroprotheses?**

Application domains

Marketed technologies

Research perspectives

Beyond stimulation…

# A - CAMIN team ?

**INRIA** : National Institute for Research in Digital Science and Technlogy

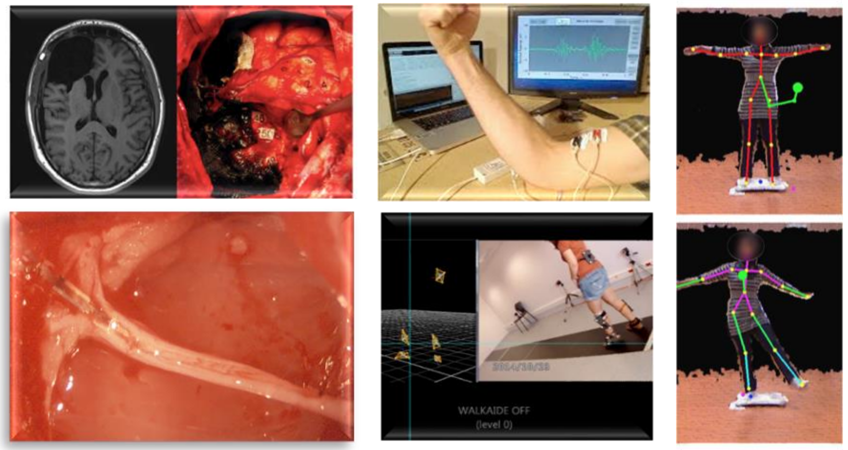
**Based in Montpellier** and attached to the Sophia Antipolis center

**CAMIN :** Dedicated to **Neuroprostheses**

**Axes of research :**

**Exploration & analysis**
- Electrophysiology
- Signal processing
- Sensors
- Technology
- Experimentation

**Assistance & restoration**
- Neuroprosthesis
- Automatic control
- Technology
- Experimentation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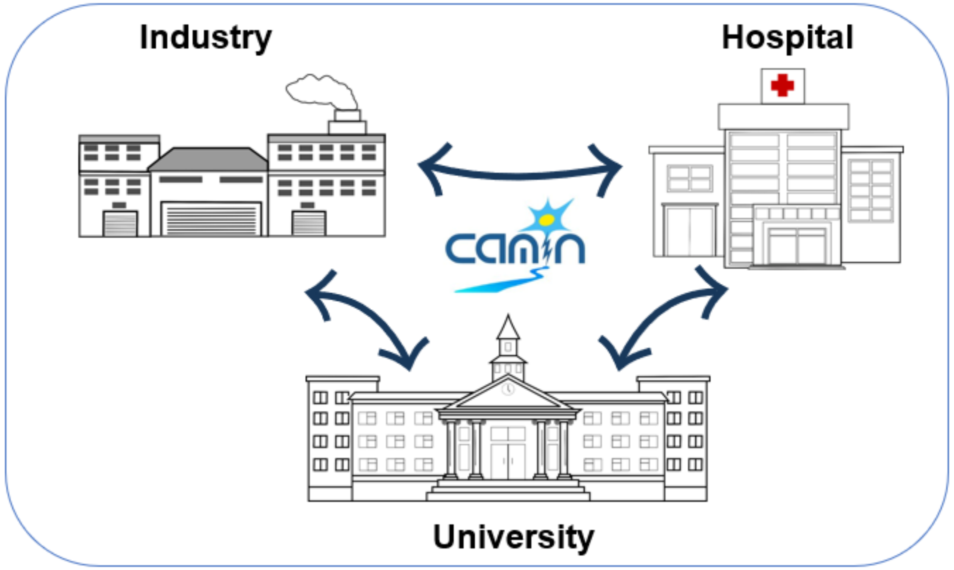
EXLORATION
ANALYSIS
movement
ASSISTANCE
RESTORATION


Industry
Hospital
University


International collaborations
2 associated teams


Keywords:

Sensorimotor disabilities

Nervous system

Biomechanics

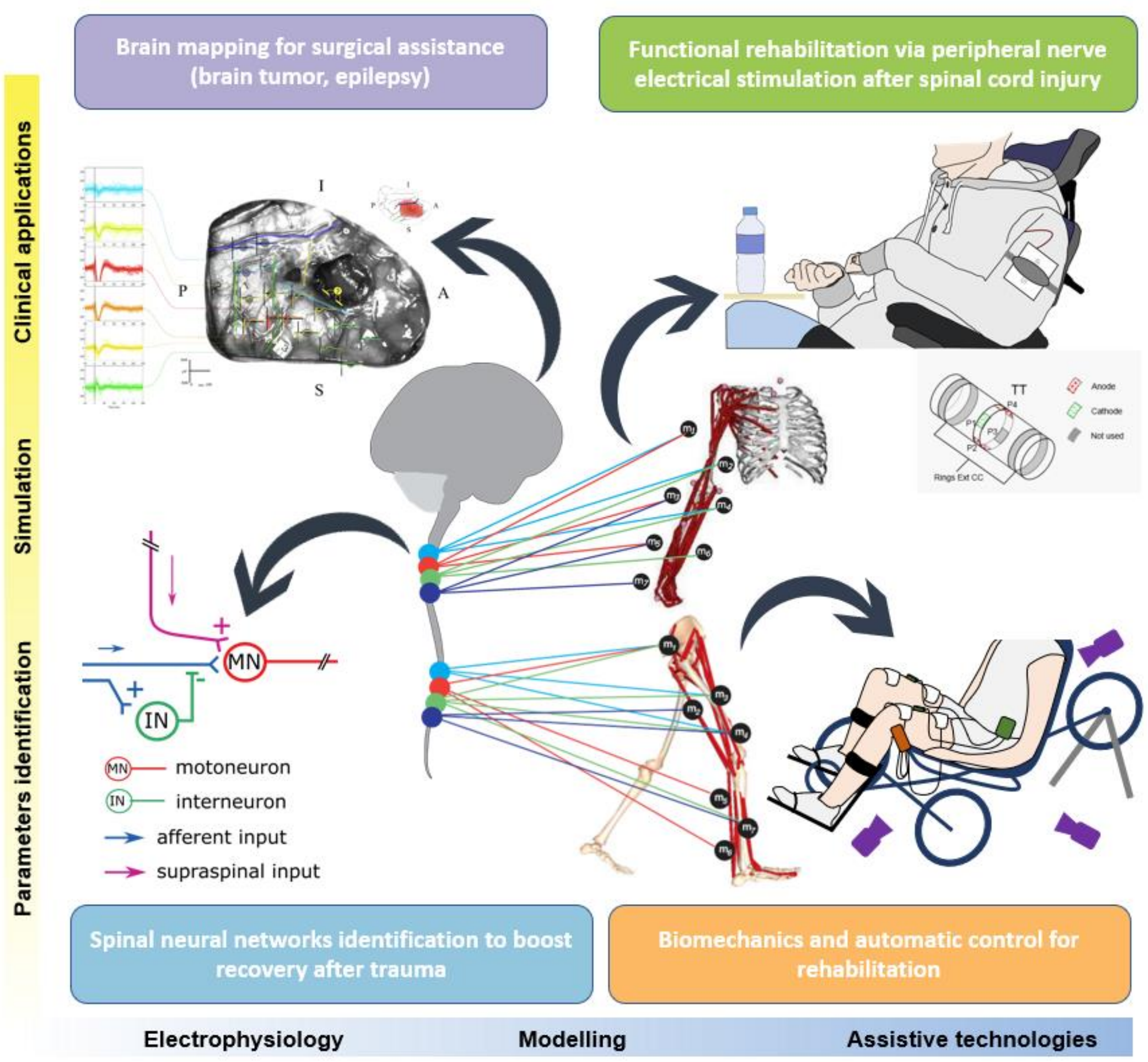
Modeling

Simulation

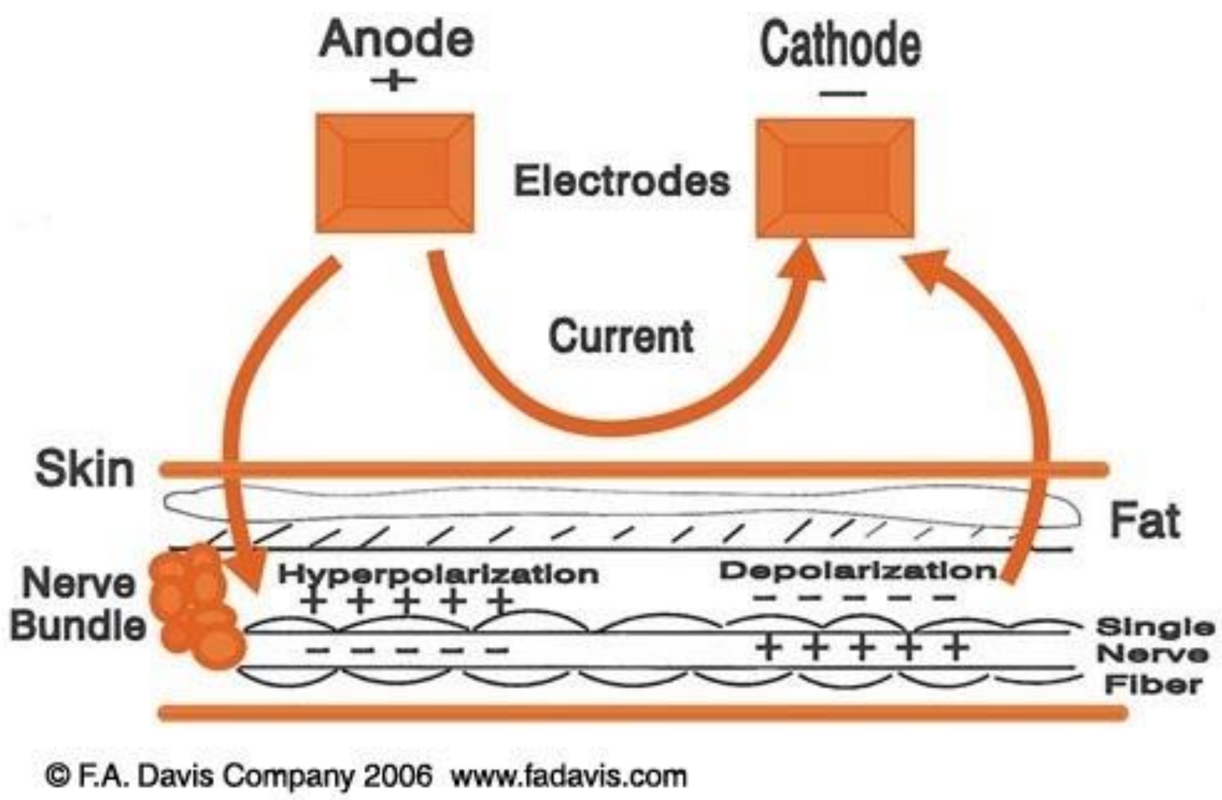
Stimulation

Optimal control

Rehabilitation



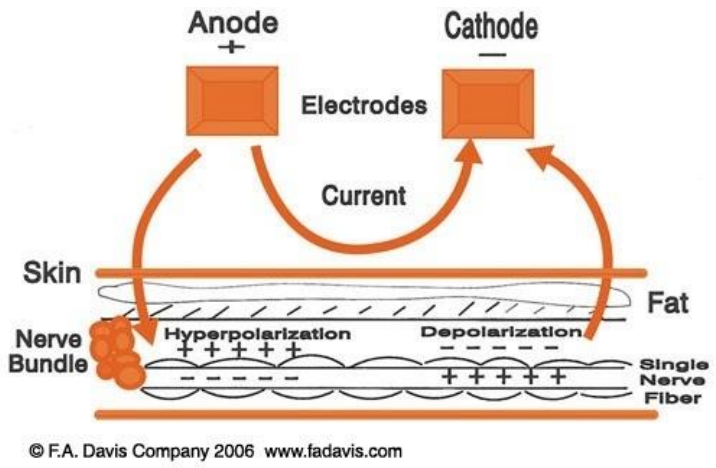
# D - Principle of Electrical Stimulation



# D - Principle of Electrical Stimulation

**Direct Current (DC) – Galvanic**

Continuous unidirectional flow of charged particles with a duration of at least 1 second.
One electrode is always the anode (+) and one is always the cathode (-) for the entire event.




There is a build-up of charge since it is moving in one direction causing a strong chemical effect on the tissue under the electrode

"High Volt", "HVGS", "ESTR", and "Iontophoresis" are clinical examples of direct current forms of stimulation

Note : **Monophasic** also refers to direct current, but it is typically pulsed, so the chemical effect is minimal

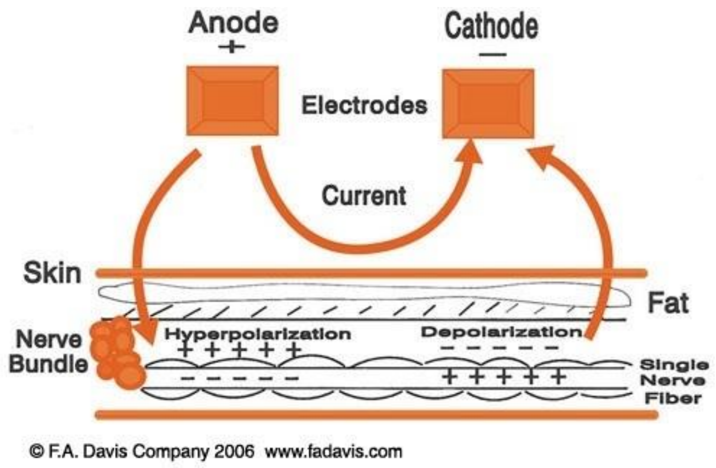
# D - Principle of Electrical Stimulation

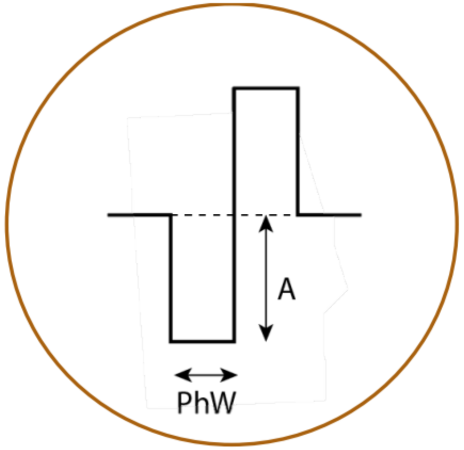
**Alternating Current (AC) – Biphasic**

Continuous changing voltage level and direction; direction changes at least once per second.
Electrodes continuously alternate their polarity each cycle, therefore no build-up of charge under the electrodes

Alternative current "waves" can be symmetrical or asymmetrical

"Russian", "NMES", "FES", and "TENS" are clinical examples of alternating current forms of stimulation



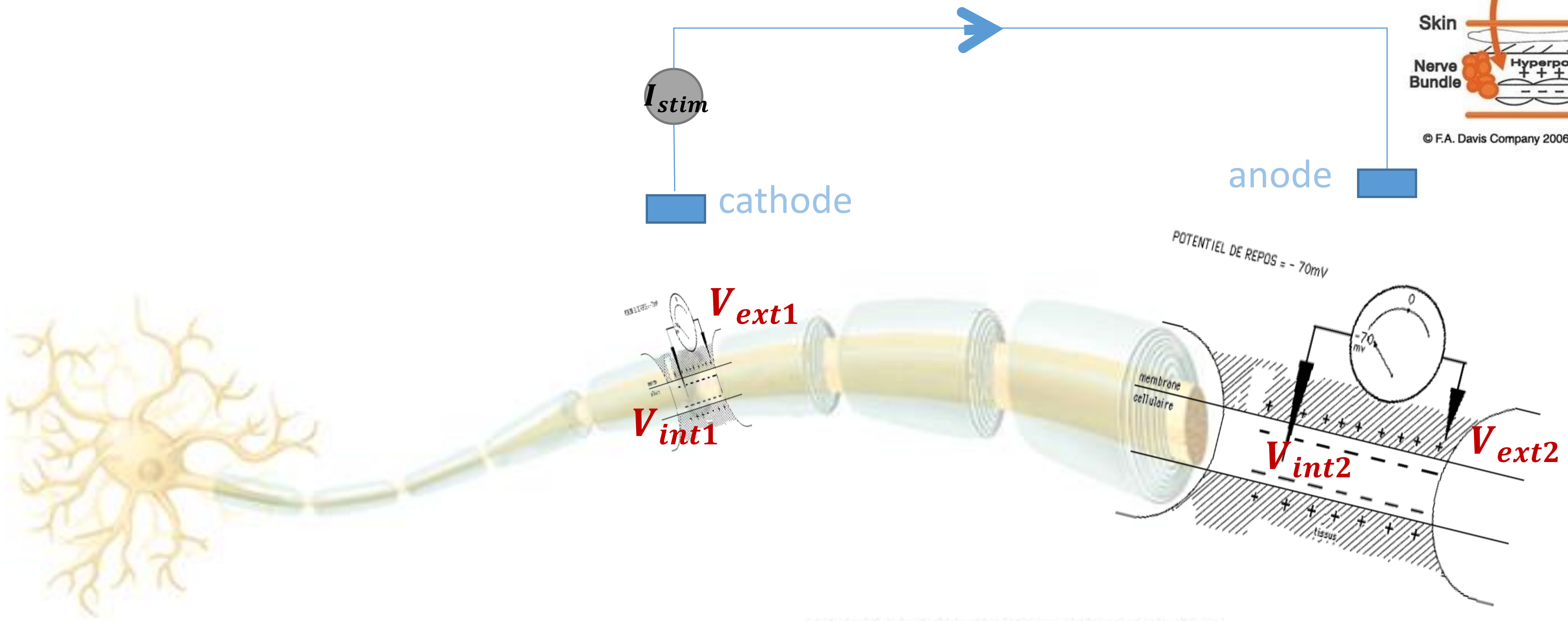

**Most modern stimulators use**

- Current controlled stimulation
- Biphasic charge balanced pulses

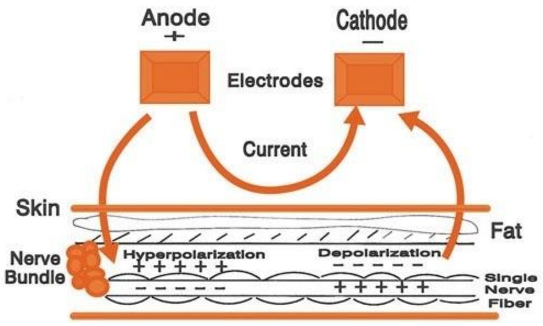
| | |
|---|---|
| A | Current amplitude |
| PhW | Phasewidth |
| F | Frequency |

# D - Principle of Electrical Stimulation

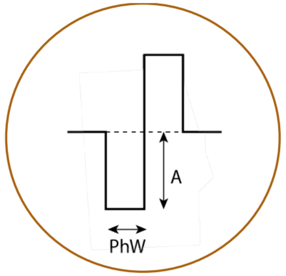
## Alternating Current (AC) – Biphasic








**Most modern stimulators use**

- Current controlled stimulation
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| | |
|---|---|
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# D - Principle of Electrical Stimulation

**Direct Current (DC) VS Alternating Current (AC)**

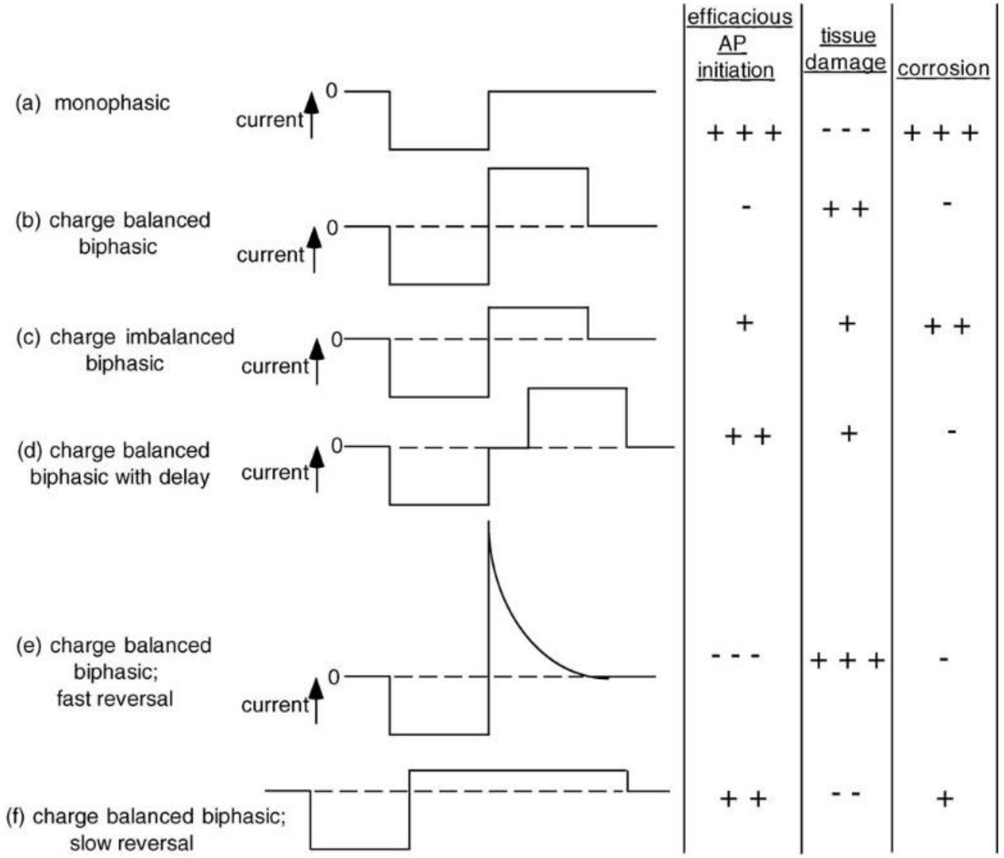
Efficiency

VS

Tissue damage

VS

Corrosion




*From Merrill et al., Journal of Neuroscience Methods. 2004.*

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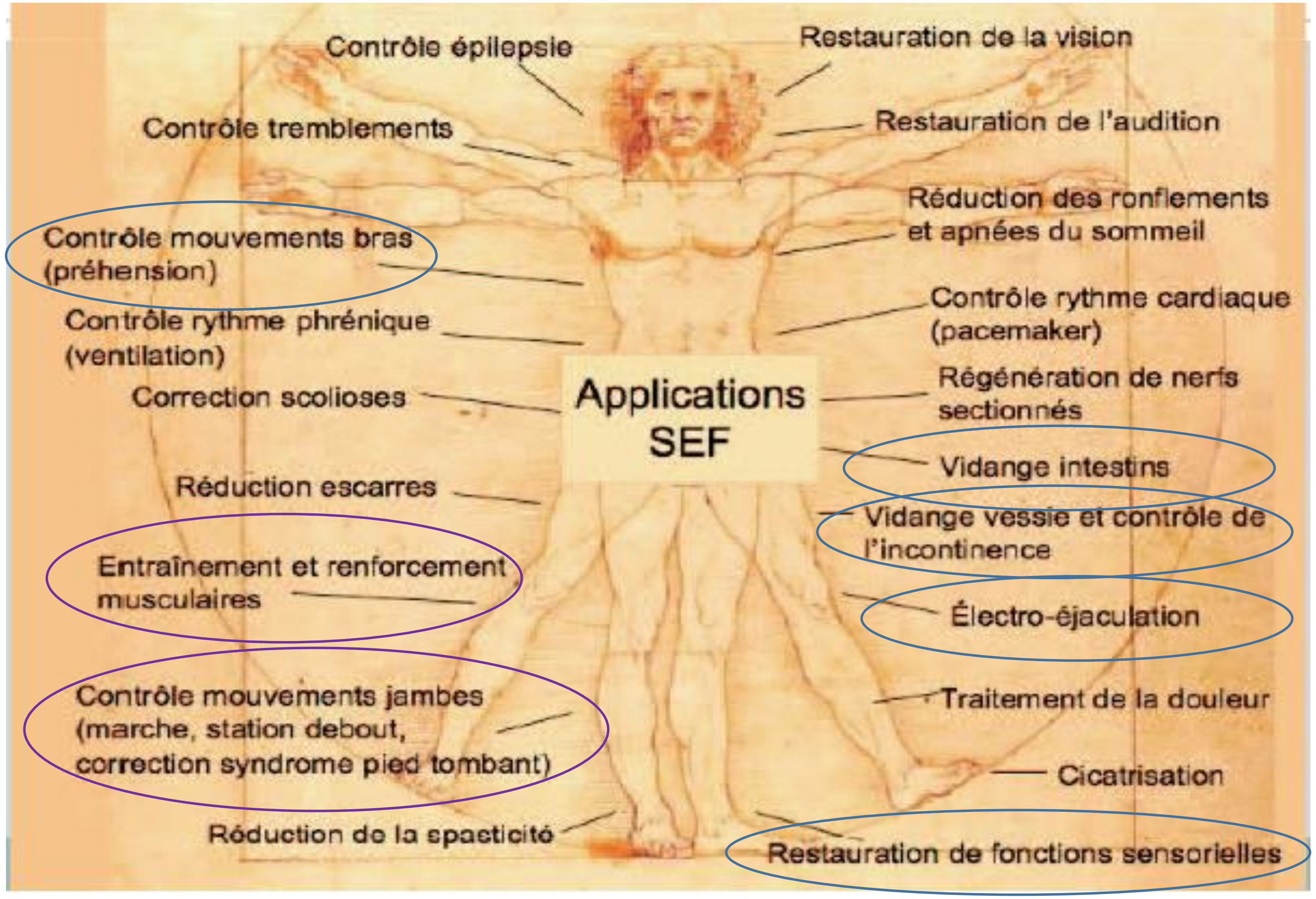
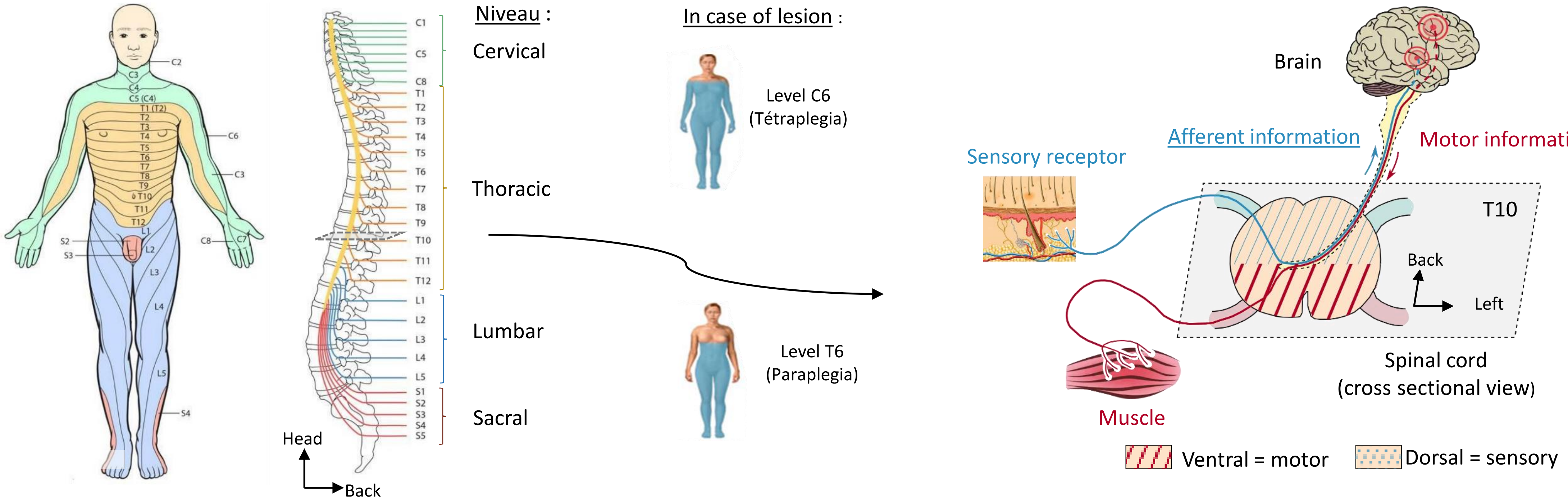
Beyond stimulation…

# Areas of application



# In a context of spinal cord injuries (SCI)



# Implants designed to restore sensorimotor functions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# Electrical Stimulation and SCI

## Target <-> Selectivity

### Periphery:

**Spinal cord injury**

Muscle paralysis due to damages of the neural tissue

Strategy #1: Direct action on the effector

Strategy #2: Overcoming motor control failure

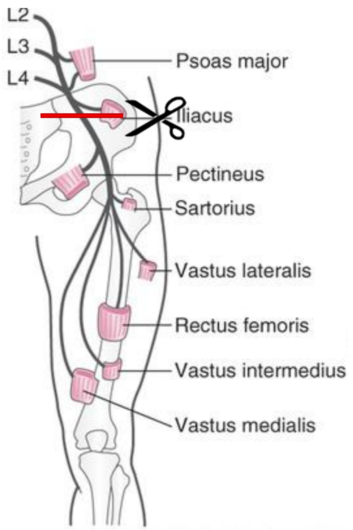
-> Muscle stimulation

-> Peripheral nerve stimulation

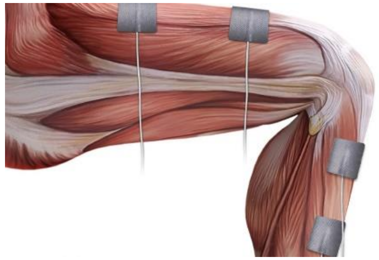
-> Spinal cord stimulation

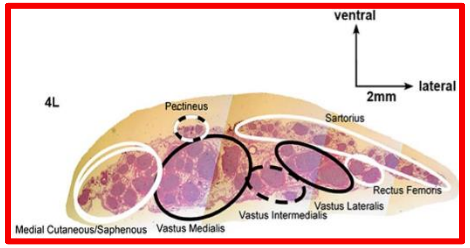
Expertise of CAMIN team

New axis of research



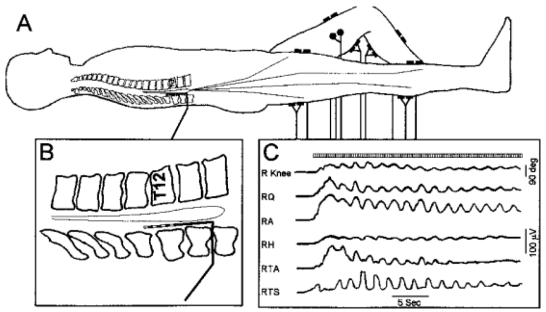

[1]






### Central Nervous System:

[2]




Strategy #2: Spinal cord stimulation -> Direct action on the motor command

Complexity:

1) Less Biomechanical issues
-> Intraspinal networks promoting selectivity

2) Many Biomedical challenges
-Identifying neural networks
- Improving stimulation selctivity

Neuroscience + Automatic control + Computational model + signal processing

*PNS - Promising but selectivity issues*

# Peripheral Nerve Stimulation

Cuff Electrodes in a context of SCI

# Electrical Stimulation and SCI

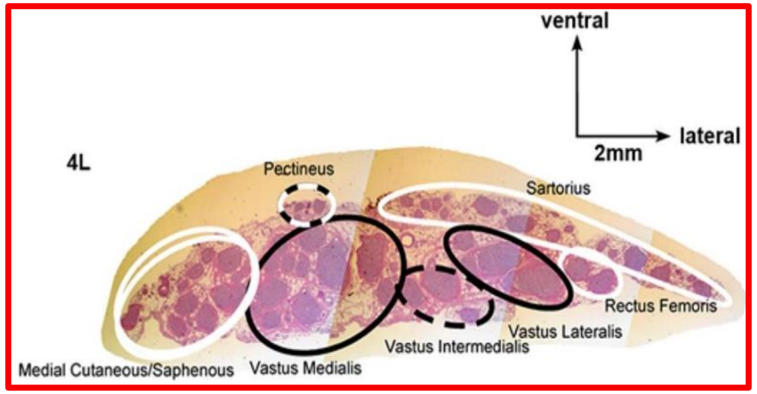
**Approach developped in the team – Peripheral Nerve Stimulation**

Ability to activate specific fibres within the nerve to target specific functions

**Spatial selectivity**

**Selectivity to direction of propagation**

**Selectivity to fibre diameter**




Femoral nerve cross-section.
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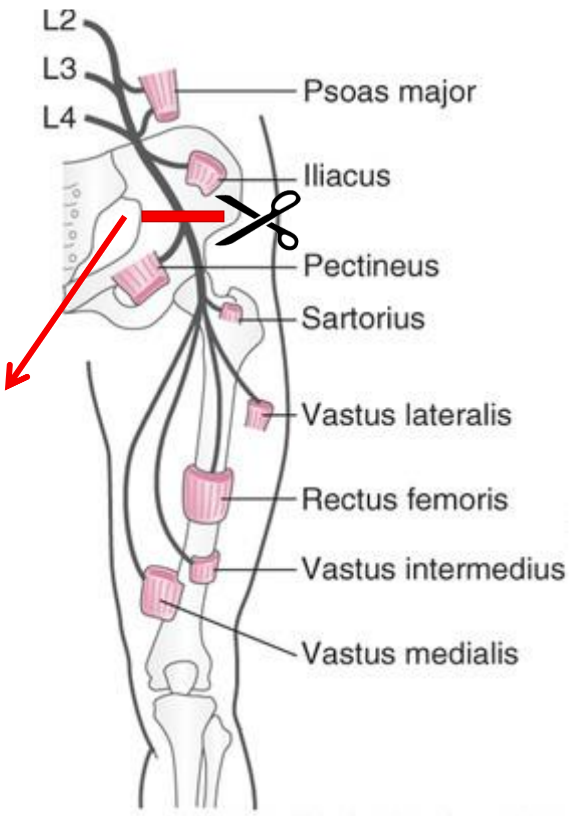



Muscular distribution of the femoral nerve
Moore& Roy, Rapid Review Gross and Developpement Anatomy © Elsevier

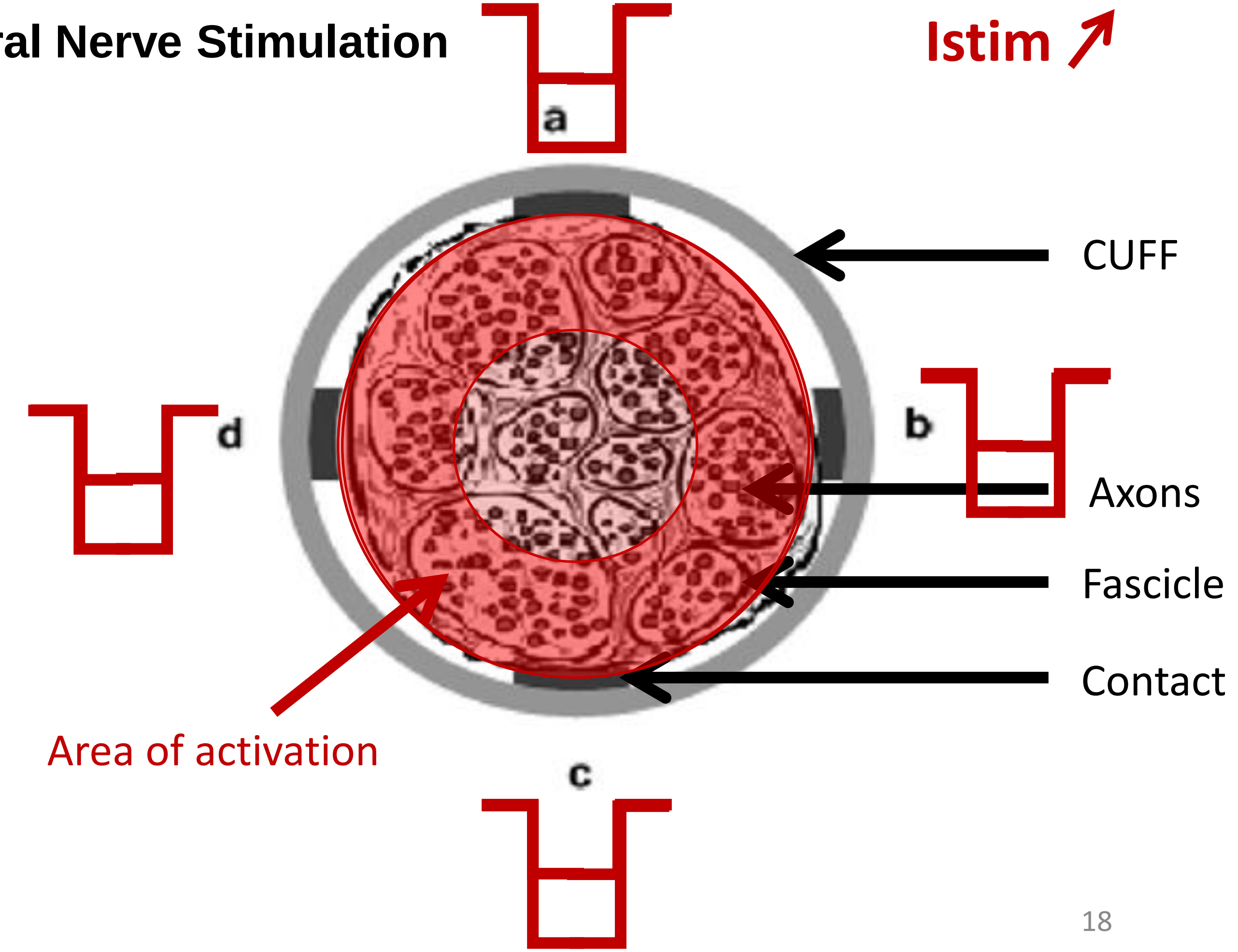
=> Avoid activating undesirable afferent or efferent functions

# Electrical Stimulation and SCI

**Approach developped in the team – Peripheral Nerve Stimulation**

**Spatial selectivity -> Case of a cuff electrode**

*Ring configuration*

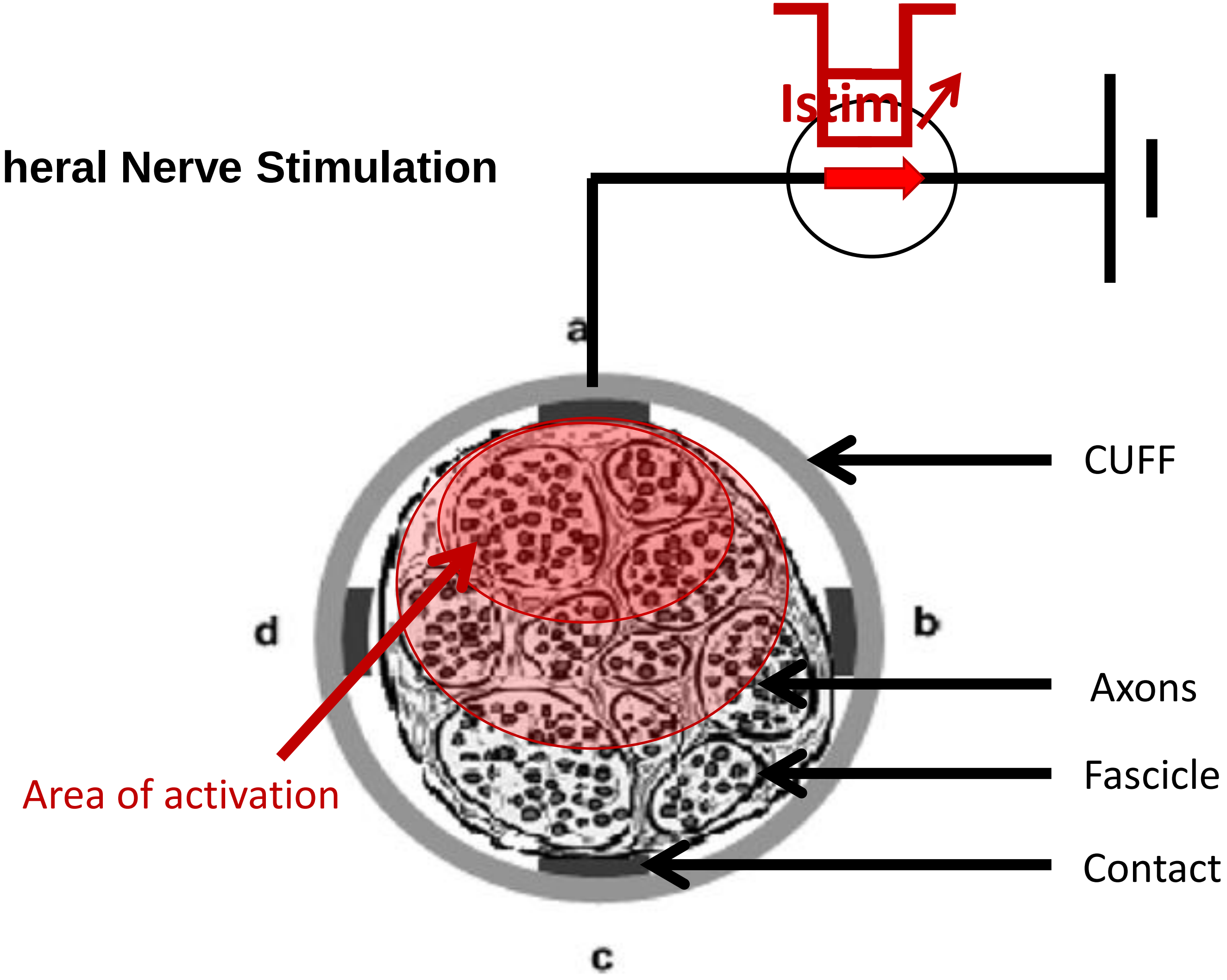


# Electrical Stimulation and SCI

**Approach developped in the team – Peripheral Nerve Stimulation**

**Spatial selectivity**

*Single Cathode configuration*

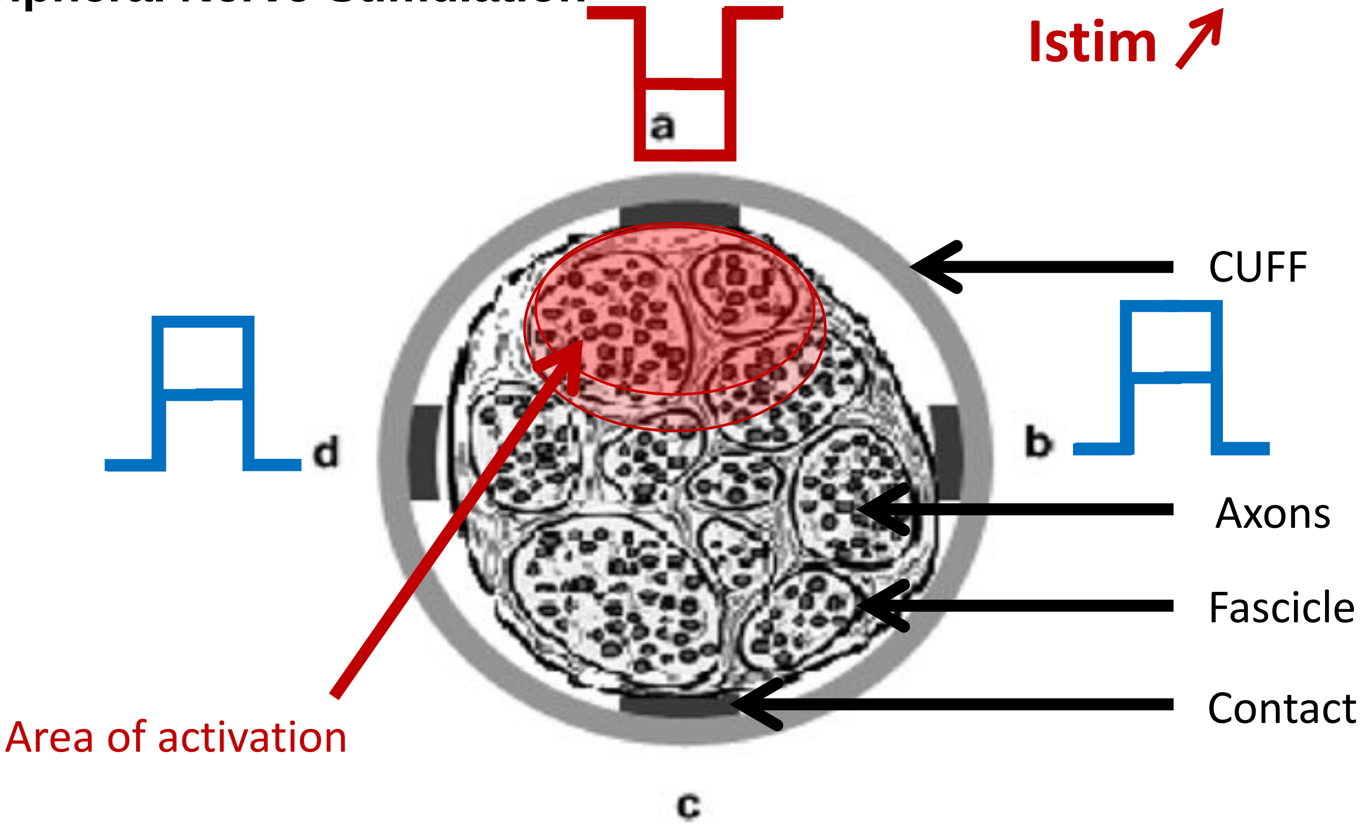


# Electrical Stimulation and SCI

**Approach developped in the team – Peripheral Nerve Stimulation**

**Spatial selectivity**

*Tripolar Transverse configuration*



# Electrical Stimulation and SCI

**Approach developped in the team – Peripheral Nerve Stimulation**

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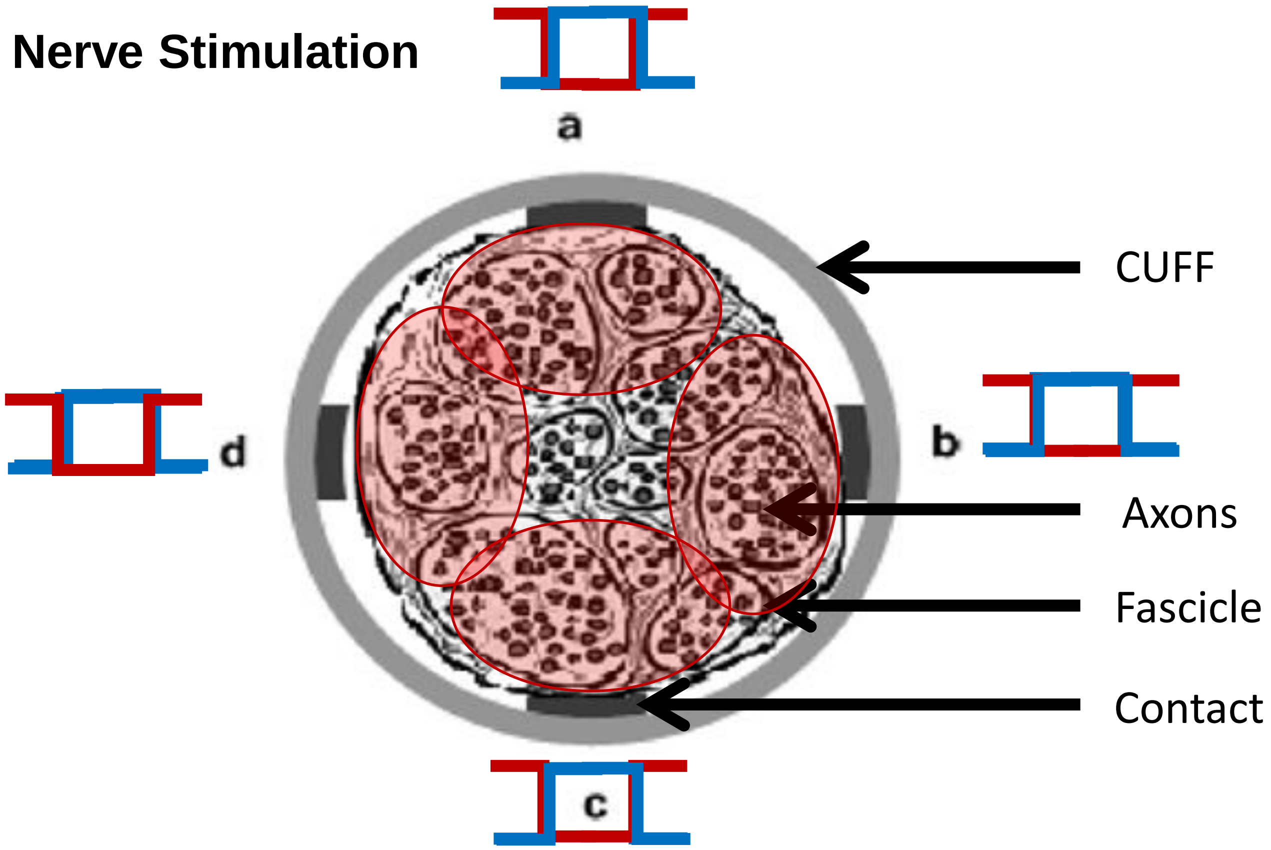
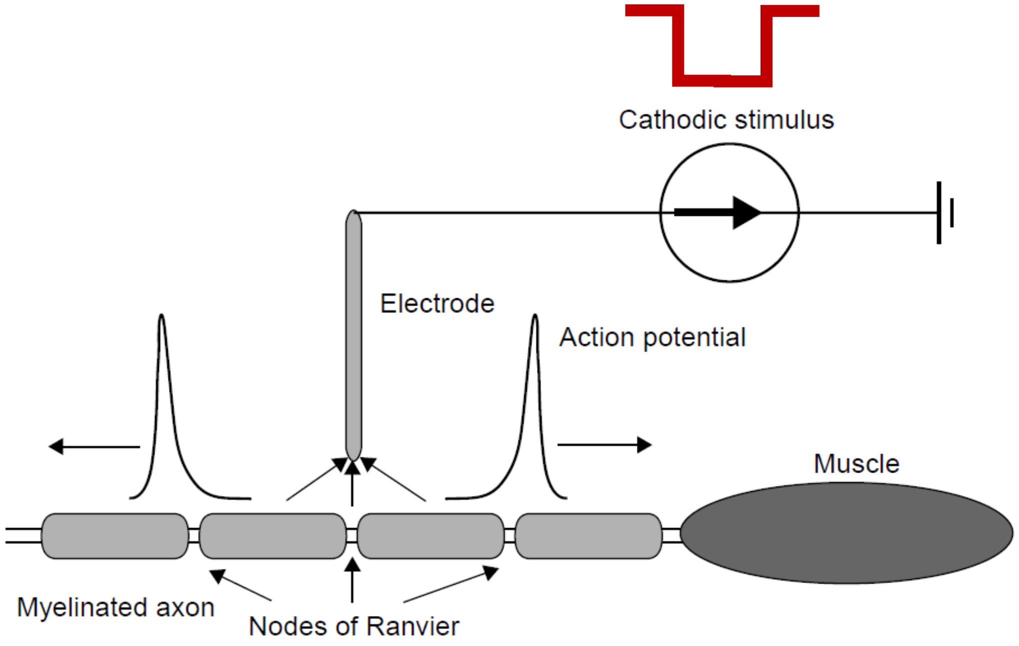


# Electrical Stimulation and SCI

**Approach developped in the team – Peripheral Nerve Stimulation**

**Selectivity to direction of propagation**

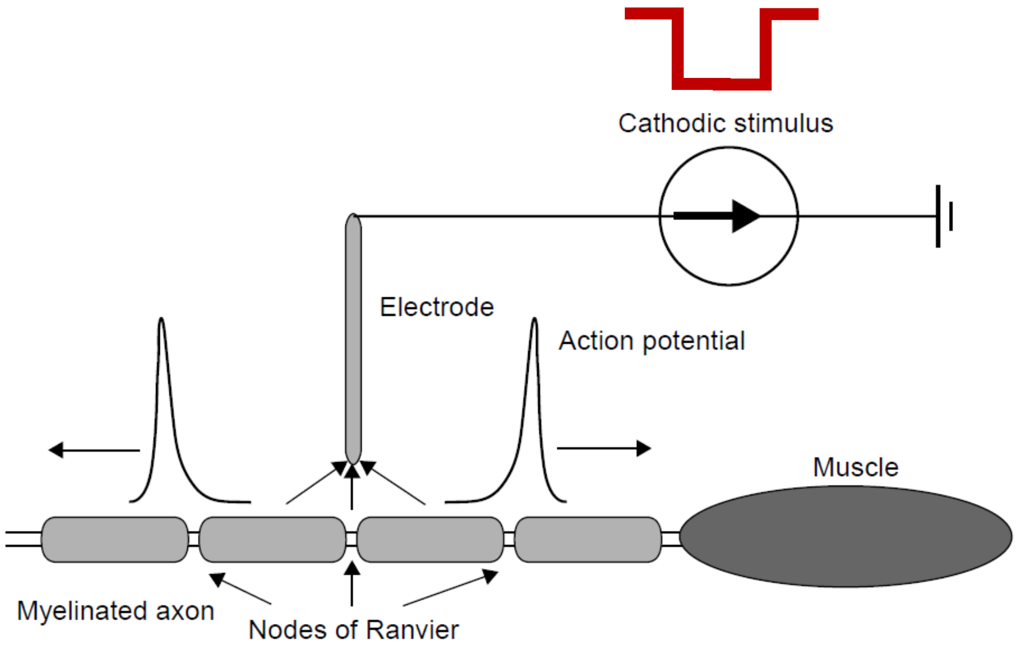



Orthodromic and antidromic propagation

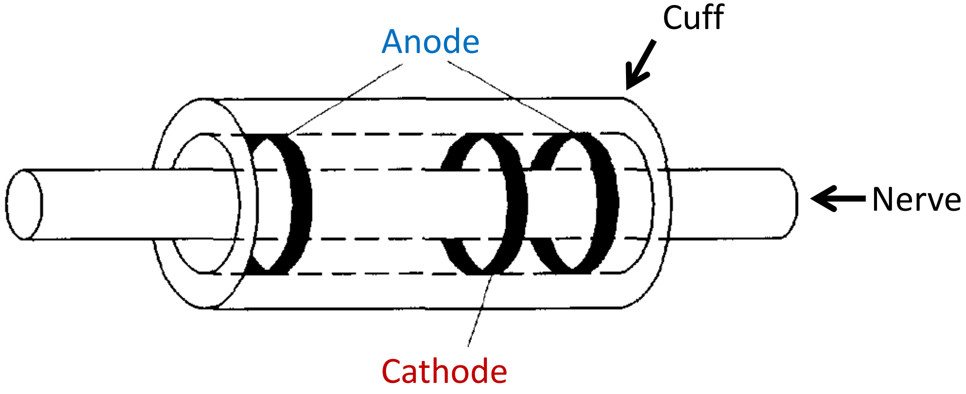
# Electrical Stimulation and SCI

**Approach developped in the team – Peripheral Nerve Stimulation**

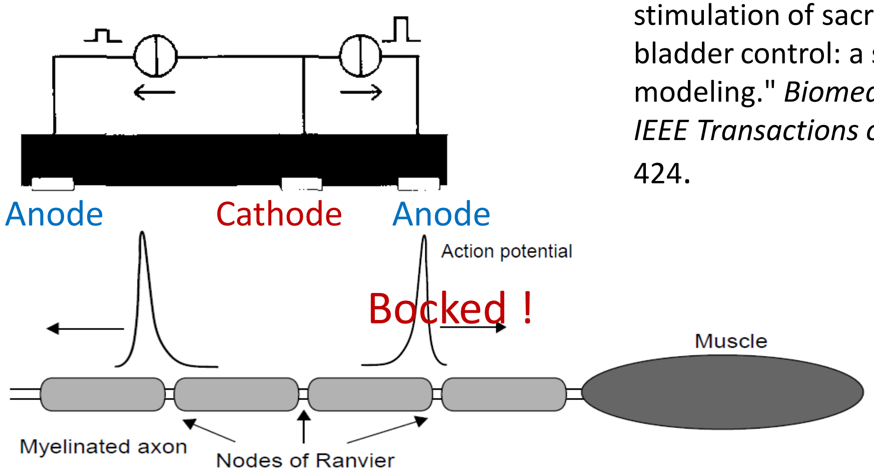
**Selectivity to direction of propagation**




Orthodromic and antidromic propagation




(a)




Rijkhoff, Nico JM, et al. "Selective stimulation of sacral nerve roots for bladder control: a study by computer modeling." *Biomedical Engineering, IEEE Transactions on* 41.5 (1994): 413-424.

# Electrical Stimulation and SCI

**Approach developped in the team – Peripheral Nerve Stimulation**

**Selectivity to fibre diameter**

*Properties of motor units*

| | | | |
|---|---|---|---|
| **Muscle Fibers** | | | |
| Twitch properties | Slow | Fast | |
| Metabolic properties | Oxidative | Oxidative/ glycolytic | Glycolytic |
| Name based on twitch and metabolic properties | SO | FOG | FG |
| Other nomenclature | ST, Type I | FTa, FTA, Type IIA | FTb, FTB, Type IIB |
| **Motor Neurons** | | | |
| Neuron type | $\alpha_2$ | $\alpha_1$ | $\alpha_1$ |
| Neuron size | Small | Large | Large |
| Conduction velocity | Slow | Fast | Fast |
| Recruitment threshold | Low | High | High |

# Electrical Stimulation and SCI

## Approach developped in the team – Peripheral Nerve Stimulation

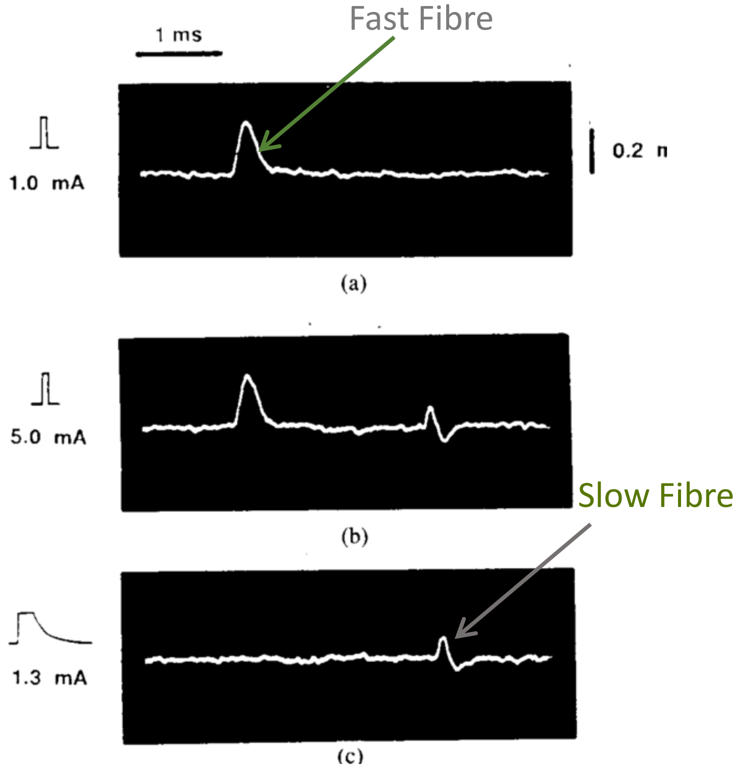
### Selectivity to fibre diameter

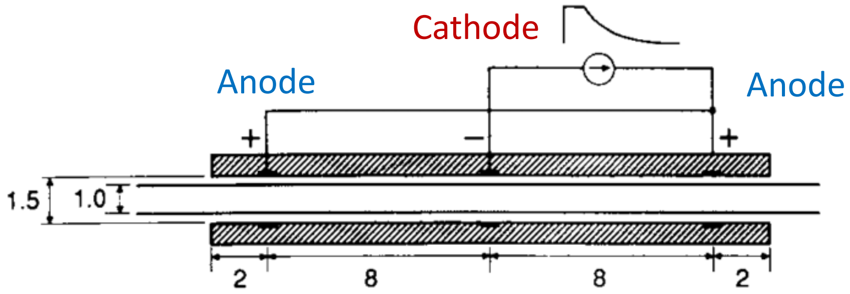
Action potentials of two fibres: fast (120 m/s) and slow (40 m/s).

1mA rectangular pulse: activation of the fast fibre

5mA rectangular pulse: activation of both fibres

Quasitrapezoidal pulse: activation of the slow fibre




Longitudinal section of the CUFF electrode, longitudinal tripolar configuration

Fang, Z. P., & Mortimer, J. T. (1991). Selective activation of small motor axons by quasitrapezoidal current pulses. *Biomedical Engineering, IEEE Transactions on*, *38*(2), 168-174.

# Electrical Stimulation and SCI

**Approach developped in the team – Peripheral Nerve Stimulation**

Ability to activate specific fibres within the nerve to target specific functions

**Spatial selectivity**

**Selectivity to direction of propagation**

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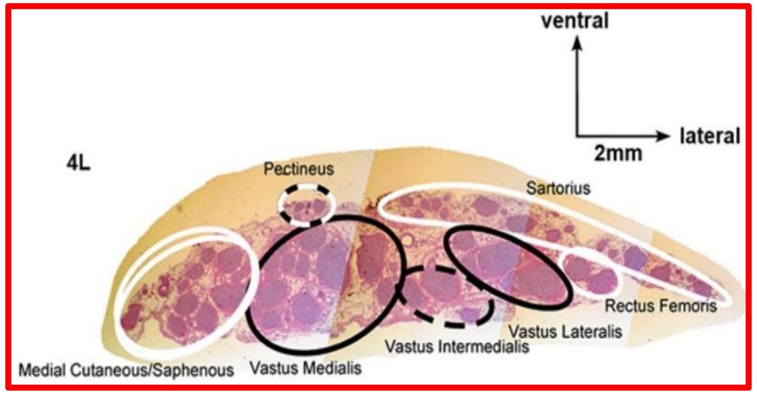


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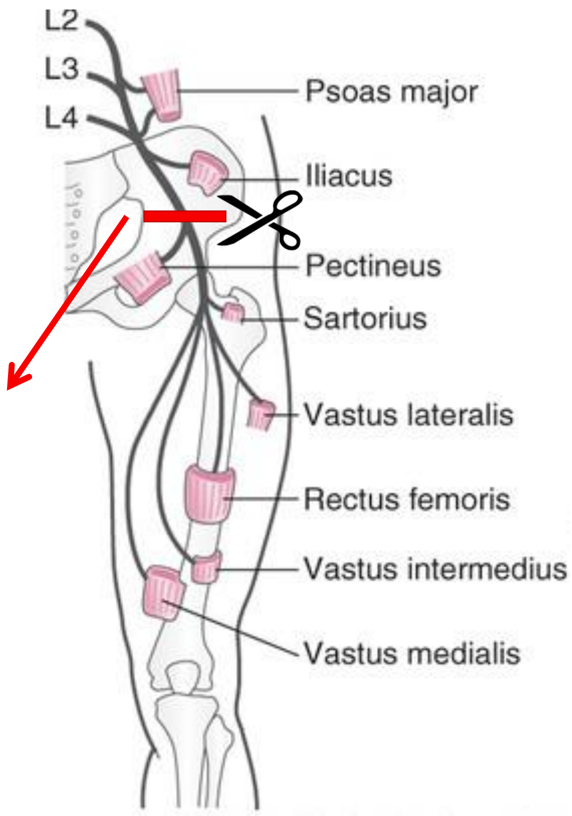
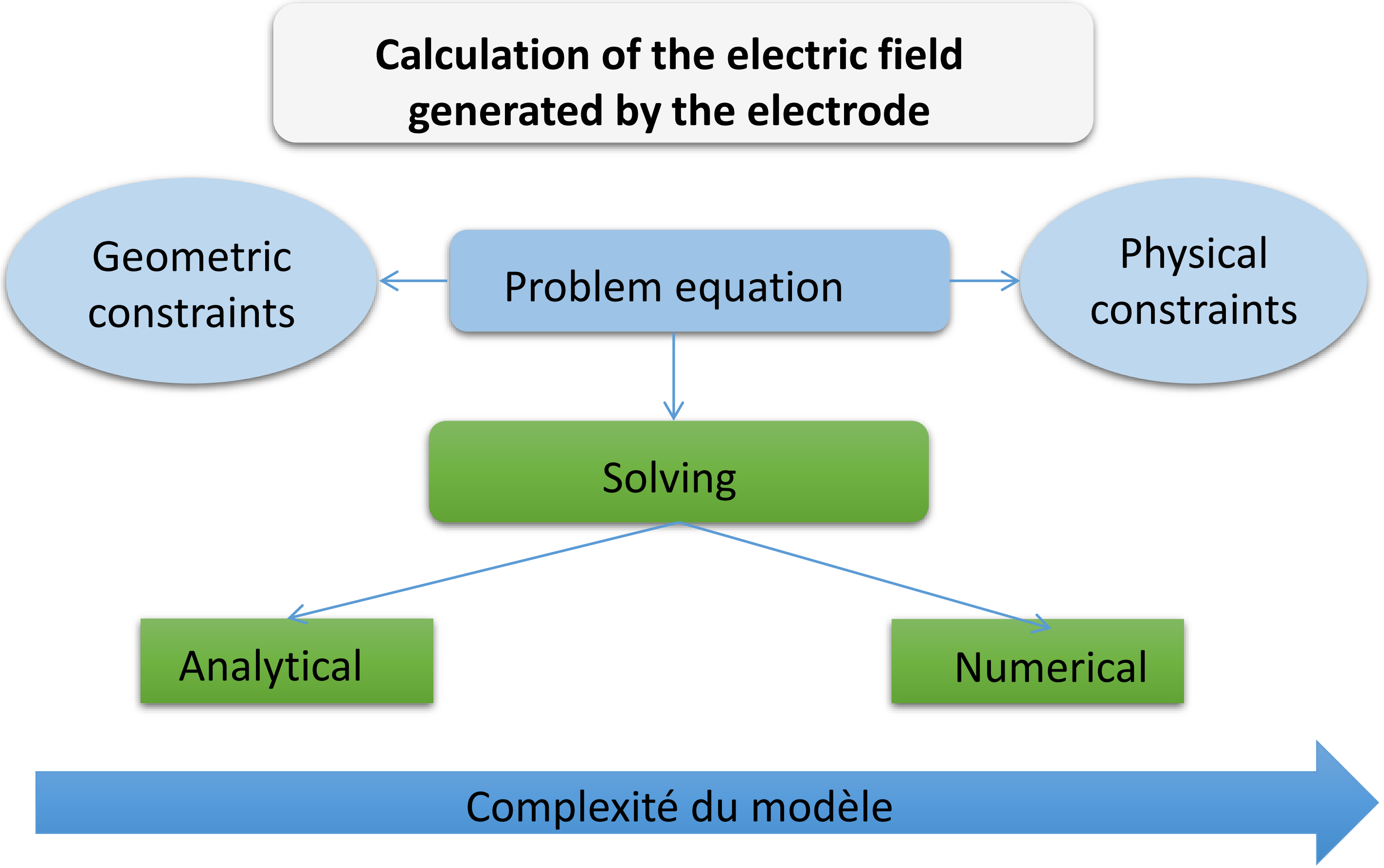



Muscular distribution of the femoral nerve
Moore& Roy, Rapid Review Gross and Developpement Anatomy © Elsevier

=> How can we improve the selectivity of Peripheral Nerve Stimulation

# Electrical Stimulation and SCI

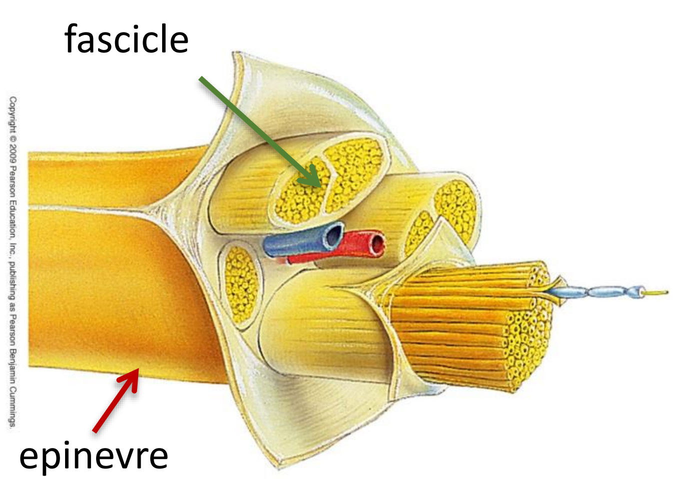
**Peripheral Nerve Stimulation and modelling**

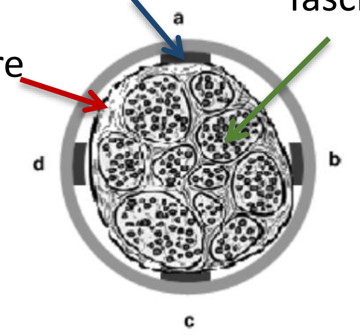


# Electrical Stimulation and SCI

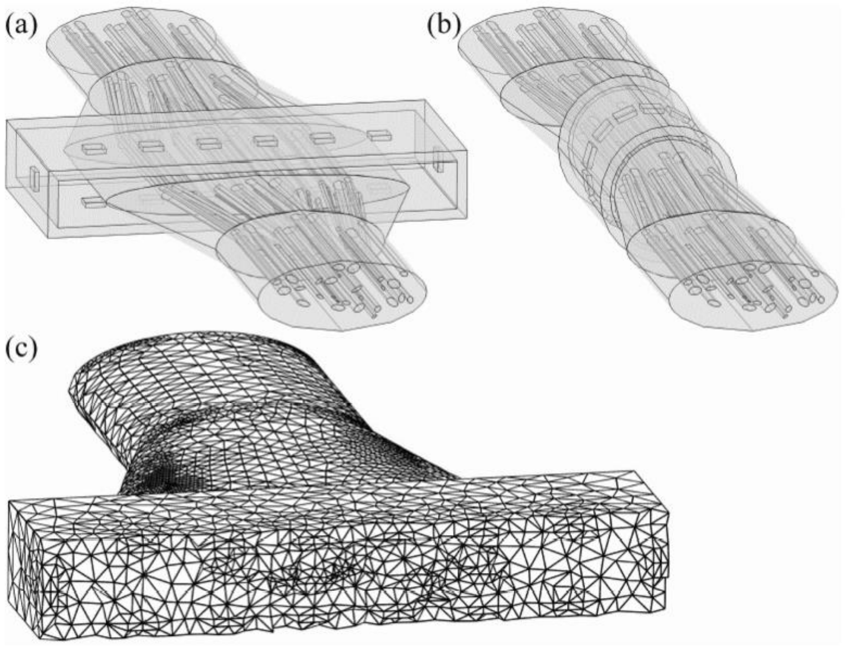
## Peripheral Nerve Stimulation and modelling

*Geometrical constraints*




*Nerve and electrode to be modelled*

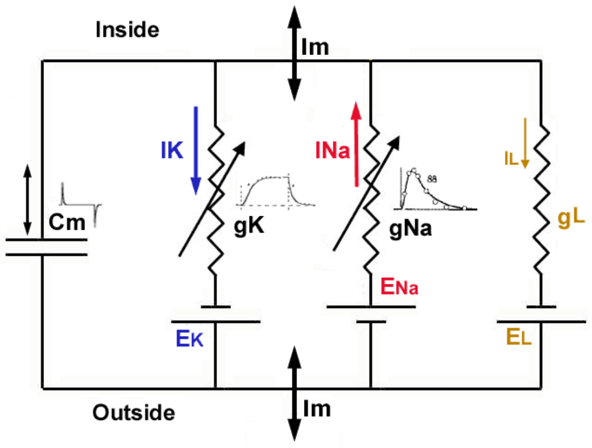



*Finite element model of the surrounding tissues*

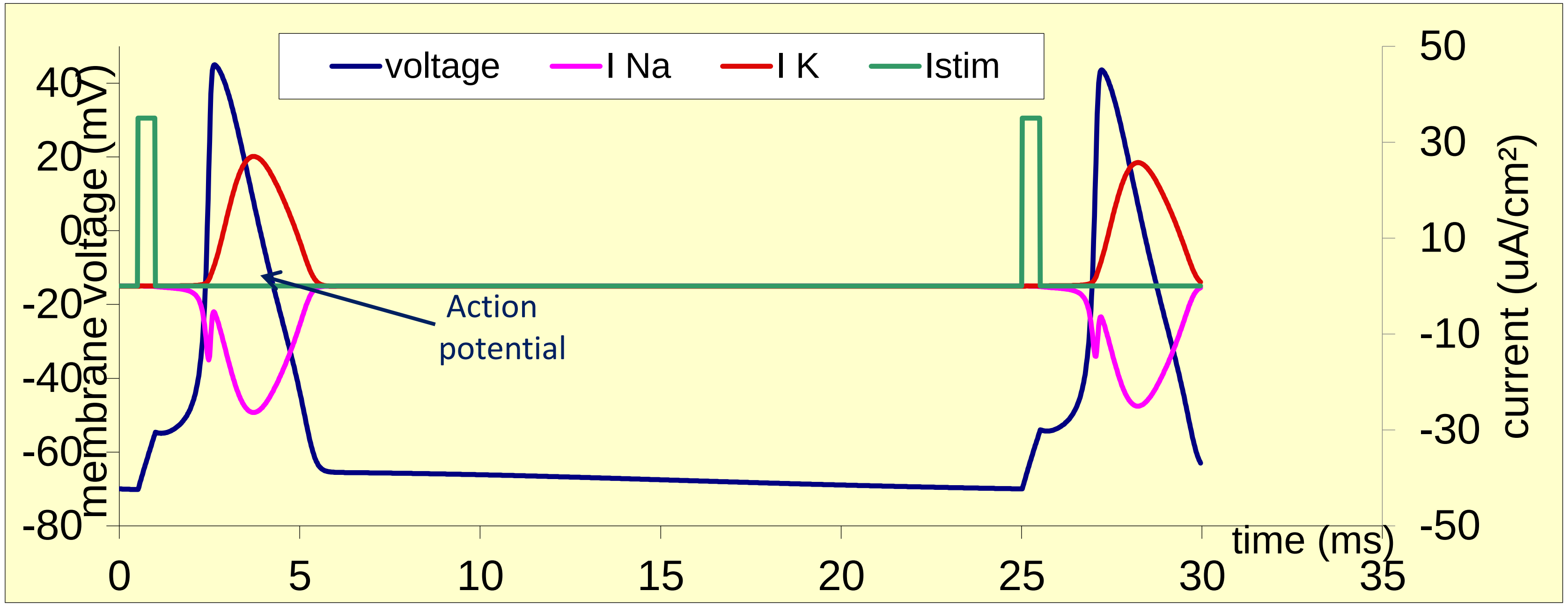
# Electrical Stimulation and SCI

**Peripheral Nerve Stimulation and modelling**

*Physical constraints – Example: Hodgkin Huxley*



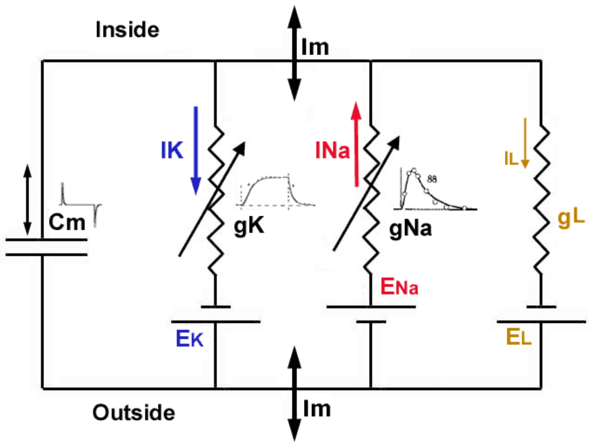

$$
\begin{aligned}
C\frac{dv}{dt} &= I - g_{Na}m^3h(V-V_{Na}) - g_K n^4(V-V_K) - g_L(V-V_L)\\
\frac{dm}{dt} &= a_m(V)(1-m) - b_m(V)m\\
\frac{dh}{dt} &= a_h(V)(1-h) - b_h(V)h\\
\frac{dn}{dt} &= a_n(V)(1-n) - b_n(V)n\\
a_m(V) &= .1(V+40)/(1-\exp(-(V+40)/10))\\
b_m(V) &= 4\exp(-(V+65)/18)\\
a_h(V) &= .07\exp(-(V+65)/20)\\
b_h(V) &= 1/(1+\exp(-(V+35)/10))\\
a_n(V) &= .01(V+55)/(1-\exp(-(V+55)/10))\\
b_n(V) &= .125\exp(-(V+65)/80)
\end{aligned}
$$



# Electrical Stimulation and SCI

**Peripheral Nerve Stimulation and modelling**

*Physical constraints – Example: Hodgkin Huxley*

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\begin{aligned}
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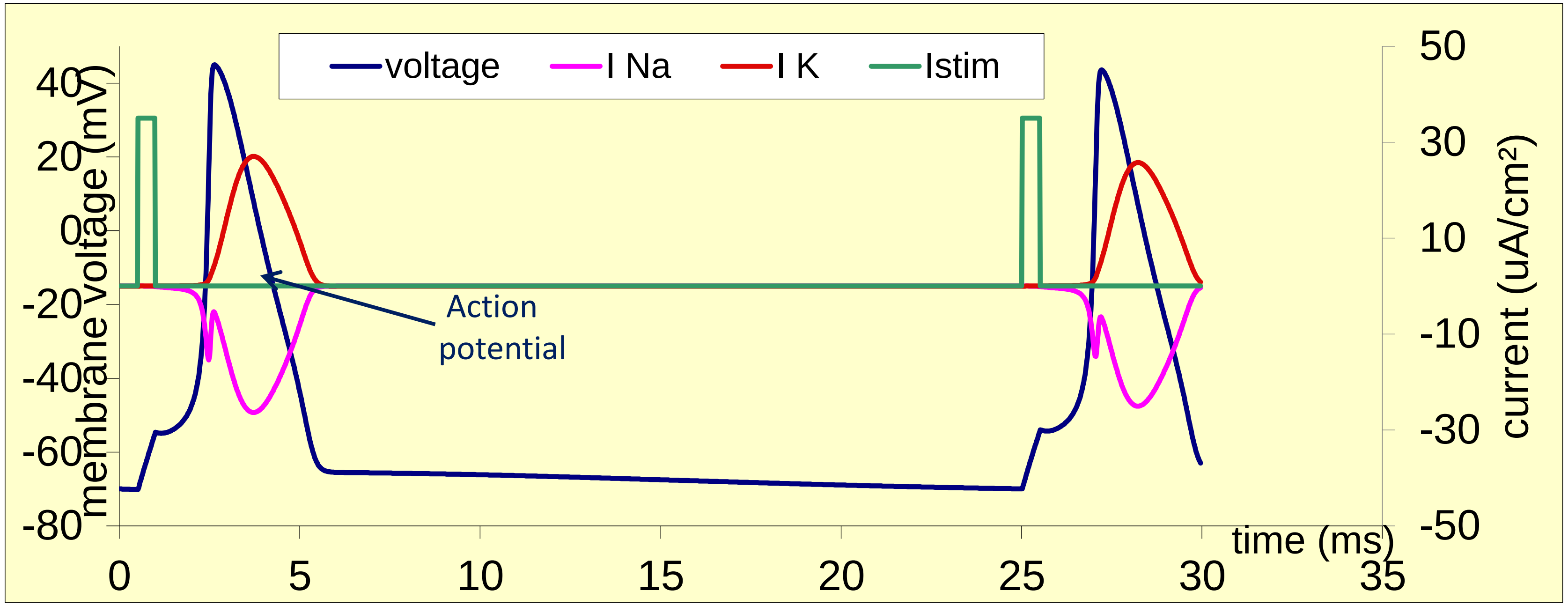
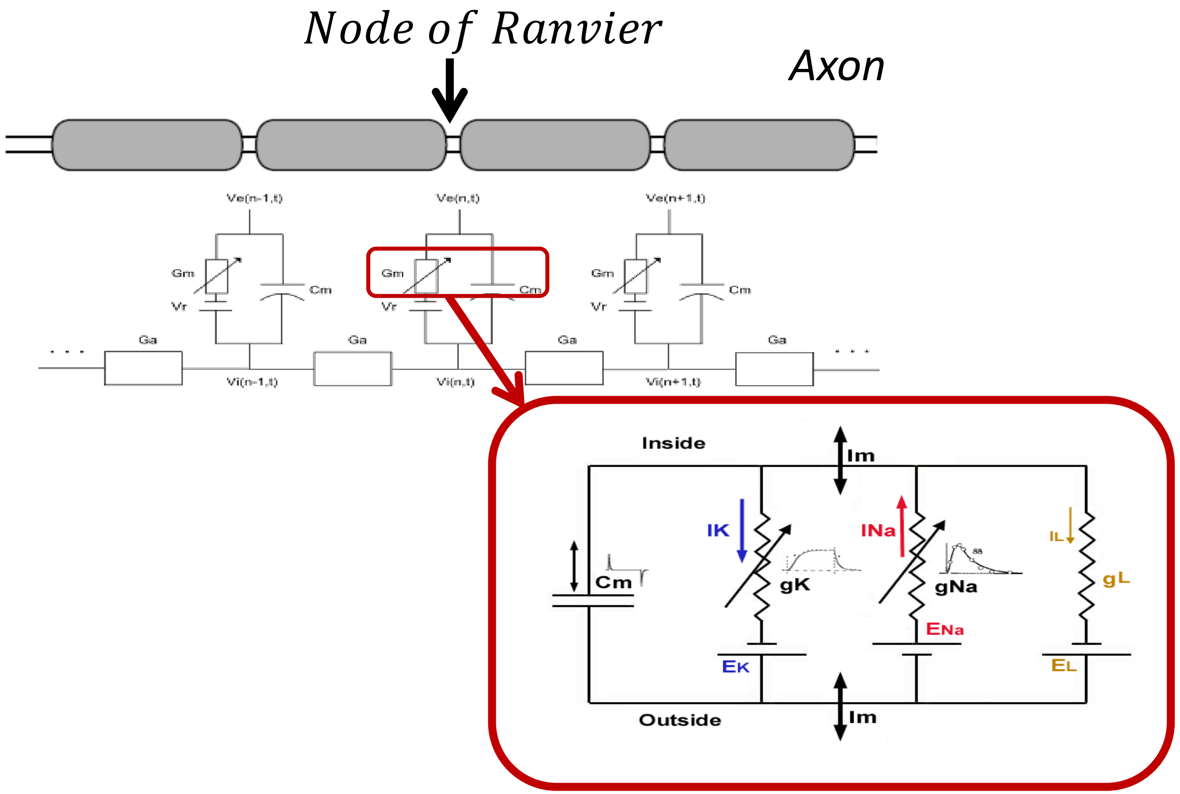
\frac{dh}{dt} &= a_h(V)(1-h) - b_h(V)h\\
\frac{dn}{dt} &= a_n(V)(1-n) - b_n(V)n\\
a_m(V) &= .1(V+40)/(1-\exp(-(V+40)/10))\\
b_m(V) &= 4\exp(-(V+65)/18)\\
a_h(V) &= .07\exp(-(V+65)/20)\\
b_h(V) &= 1/(1+\exp(-(V+35)/10))\\
a_n(V) &= .01(V+55)/(1-\exp(-(V+55)/10))\\
b_n(V) &= .125\exp(-(V+65)/80)
\end{aligned}
$$



# Electrical Stimulation and SCI

## Peripheral Nerve Stimulation and modelling

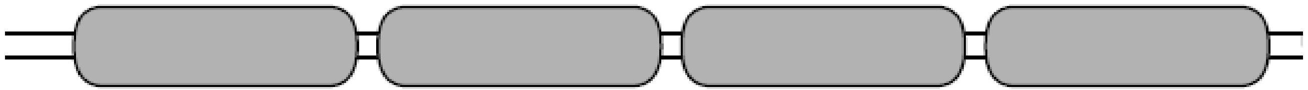
*Physical constraints – Example: Hodgkin Huxley*

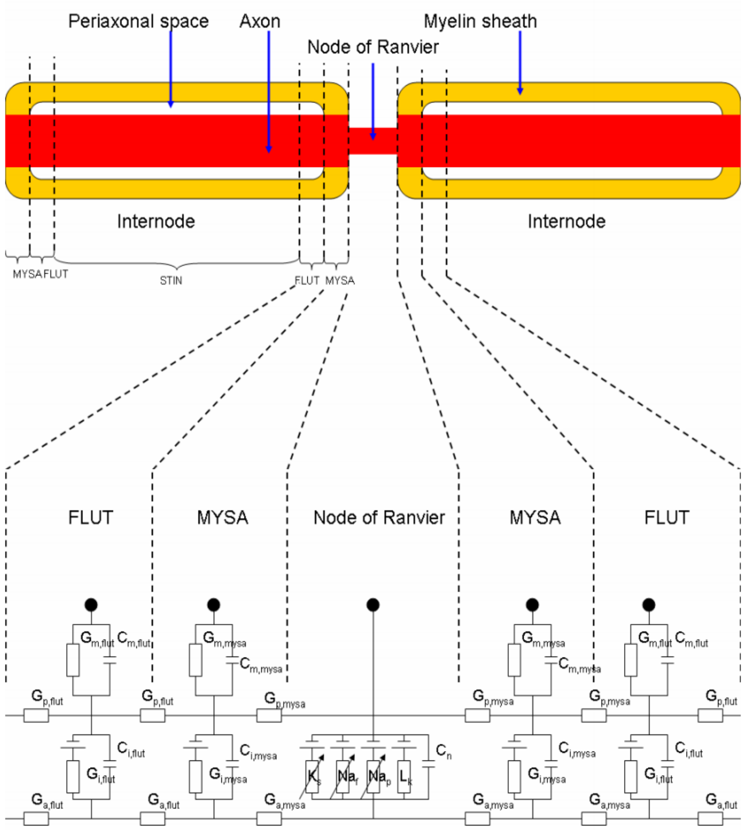


# Electrical Stimulation and SCI

## Peripheral Nerve Stimulation and modelling

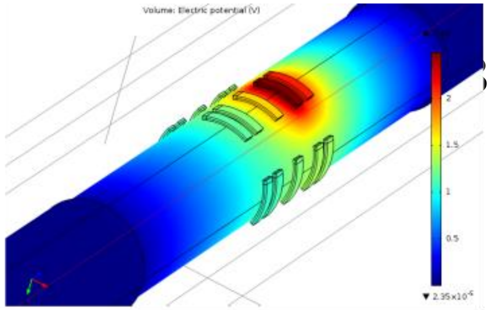
*Physical constraints – Example: MRG*



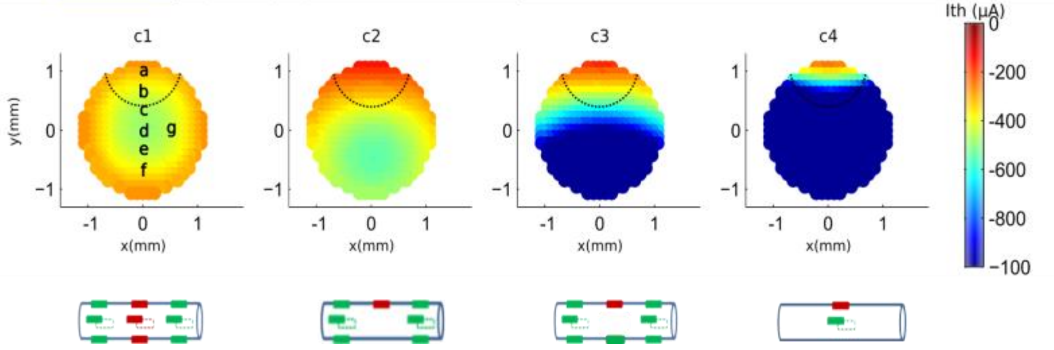


# Multi-contact cuff electrode

## –> A technological solution to the problems of selectivity and invasiveness




*Multicontact electrode adjustment by simulation*




- 3D spatial distribution of stimulation currents
- Model-based presets for clinical application

*Guiho et al, NER 2015*

**Toward complex multipolar selective neural stimulation***

Thomas Guiho[1], Olivier Rossel[1], Guillaume Souquet[2], Hernández Alfredo[3], Laure Laporte[4] Christine Azevedo - Coste[1] *IEEE, member*, David Andreu[1], David Guiraud[1] *IEEE, member, EMBS*

*Dali et al, JNE 2018*

J. Neural Eng. 15 (2018) 046018 (19pp) https://doi.org/10.1088/1741-2552/aabeb9

**Model based optimal multipolar stimulation without *a priori* knowledge of nerve structure: application to vagus nerve stimulation**

Mélissa Dali[1,7], Olivier Rossel[1,7], David Andreu[1], Laure Laporte[2], Alfredo Hernández[3], Jérémy Laforet[1,4], Eloi Marijon[5], Albert Hagège[5], Maureen Clerc[6], Christine Henry[2] and David Guiraud[1]

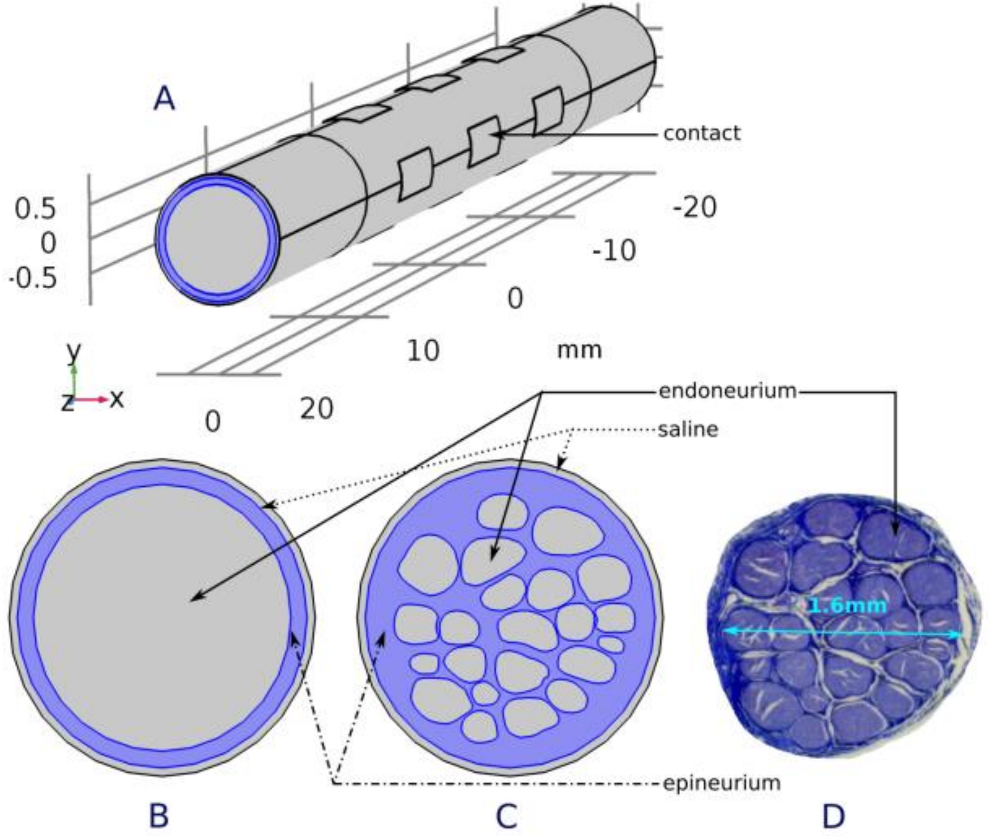
# Multi-contact cuff electrode

## –> A technological solution to the problems of selectivity and invasiveness

Parametric Identification and validation

Example:
Fascicles
– interindividual variability and No prior knowledge –

Impact of fasciculariaation - cross-section sudy (x and y)



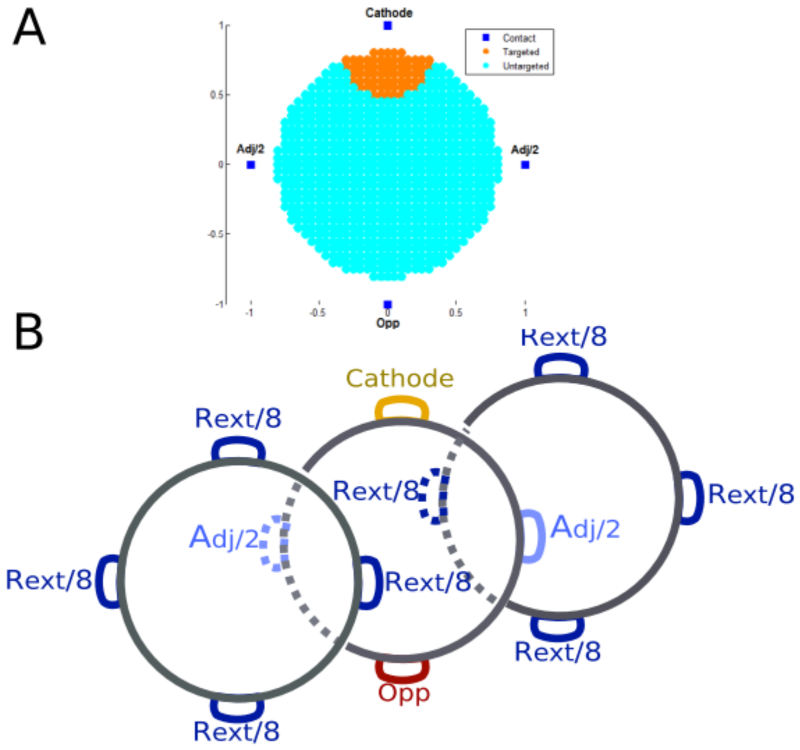
# Multi-contact cuff electrode

## –> A technological solution to the problems of selectivity and invasiveness

<u>Parametric Identification and validation</u>

*Example:*

Electrode design
distribution of contacts along the x, y and z axes

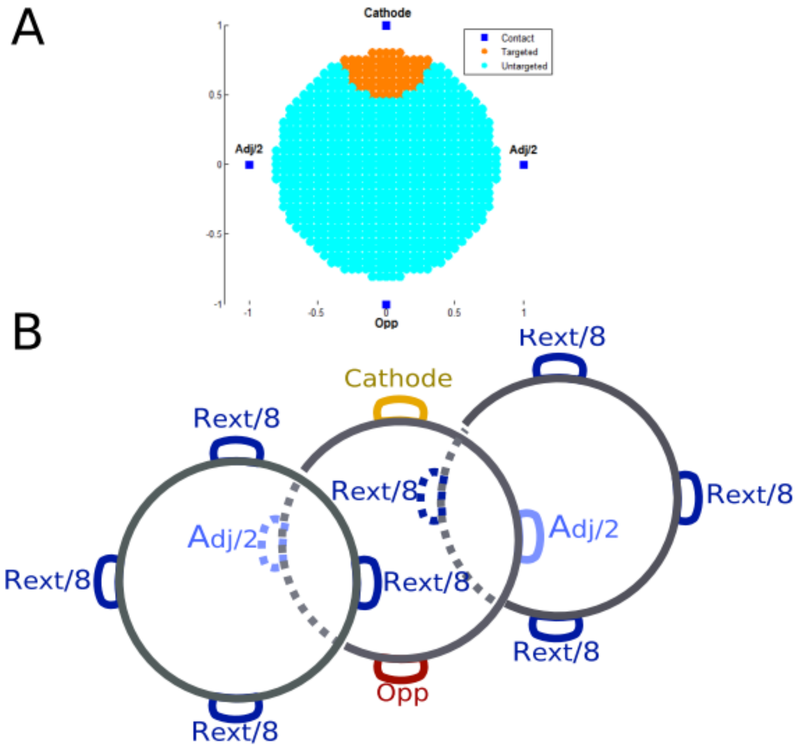


# Multi-contact cuff electrode

## –> A technological solution to the problems of selectivity and invasiveness

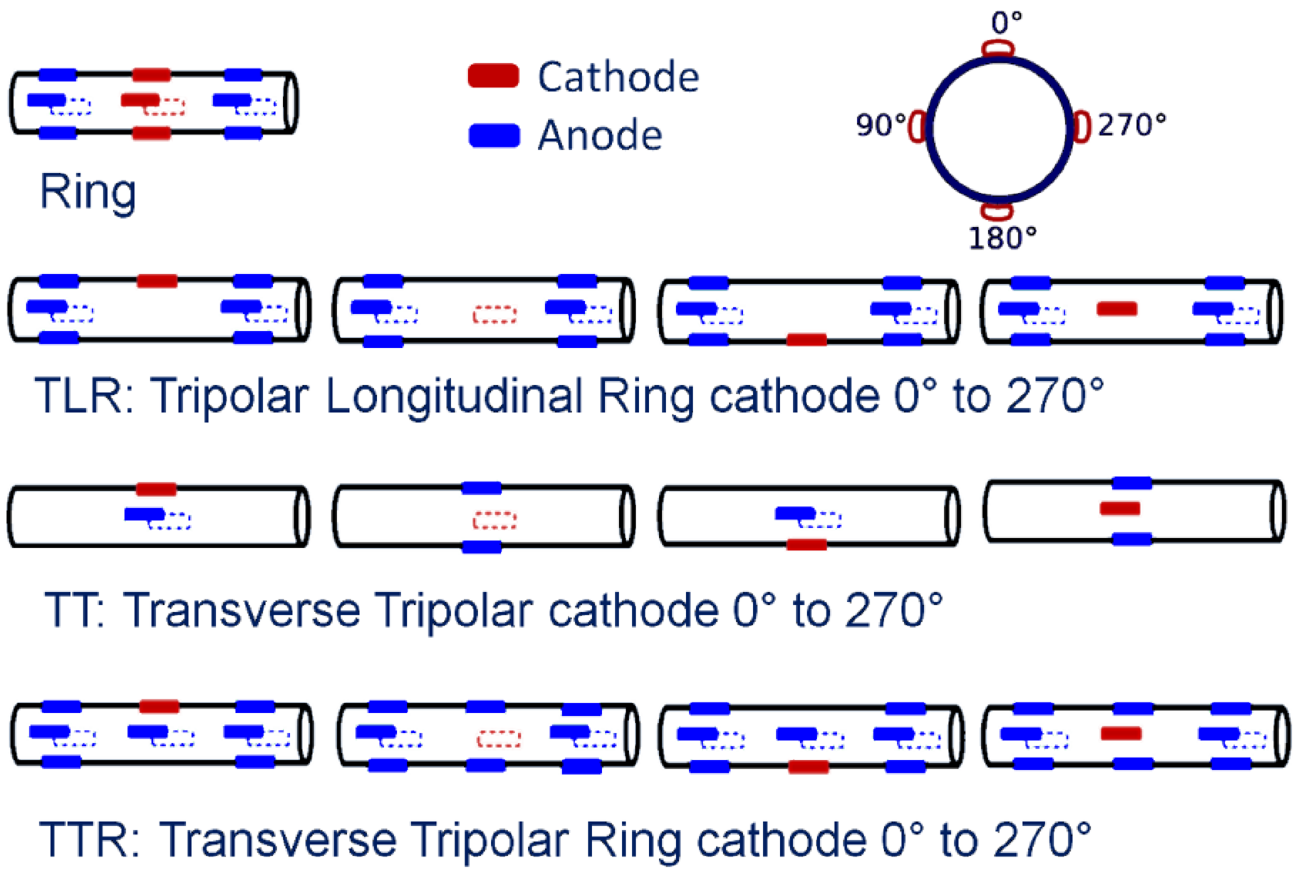
<u>Interest of the Model:</u>

-> Testing a large number of configurations in silico
-> Reduce the field of possiblities
-> Compliance with the 3R for the use of animals in research



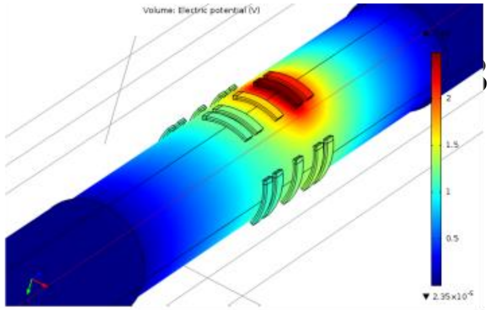
# Multi-contact cuff electrode

–> A technological solution to the problems of selectivity and invasiveness



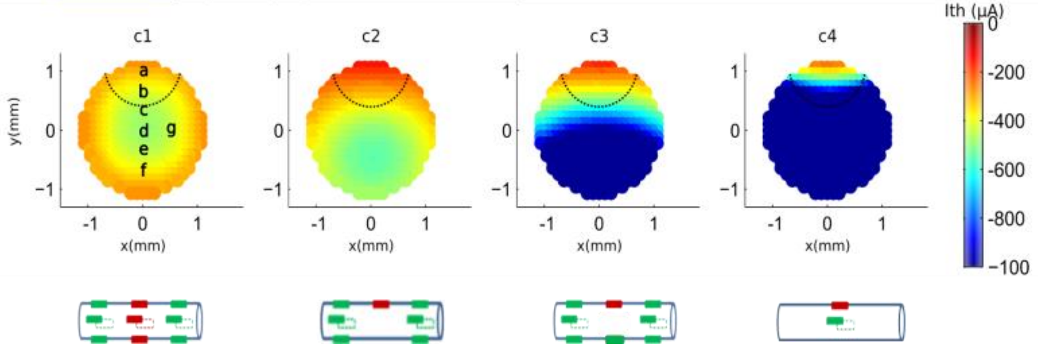
# Multi-contact cuff electrode

## –> A technological solution to the problems of selectivity and invasiveness



*Multicontact electrode adjustment by simulation*

- 3D spatial distribution of stimulation currents
- Model-based presets for clinical application




*Guiho et al, NER 2015*

**Toward complex multipolar selective neural stimulation***

Thomas Guiho[1], Olivier Rossel[1], Guillaume Souquet[2], Hernández Alfredo[3], Laure Laporte[4]
Christine Azevedo - Coste[1] *IEEE, member*, David Andreu[1], David Guiraud[1] *IEEE, member, EMBS*

*Dali et al, JNE 2018*

J. Neural Eng. 15 (2018) 046018 (19pp) https://doi.org/10.1088/1741-2552/aabeb9

**Model based optimal multipolar stimulation without *a priori* knowledge of nerve structure: application to vagus nerve stimulation**

Mélissa Dali[1,7], Olivier Rossel[1,7], David Andreu[1], Laure Laporte[2], Alfredo Hernández[3], Jérémy Laforet[1,4], Eloi Marijon[5], Albert Hagège[5], Maureen Clerc[6], Christine Henry[2] and David Guiraud[1]

# Assessment of the approach

## -> Selective configuration -> Animal experiments

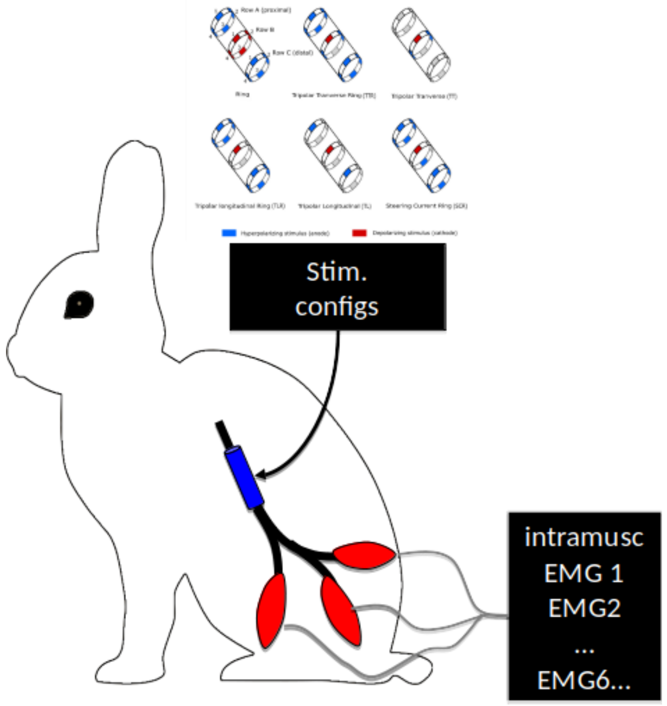
*Dali et al, PlosOne* 2019

PLOS | ONE    PUBLISH    ABOUT

**Relevance of selective neural stimulation with a multicontact cuff electrode using multicriteria analysis**

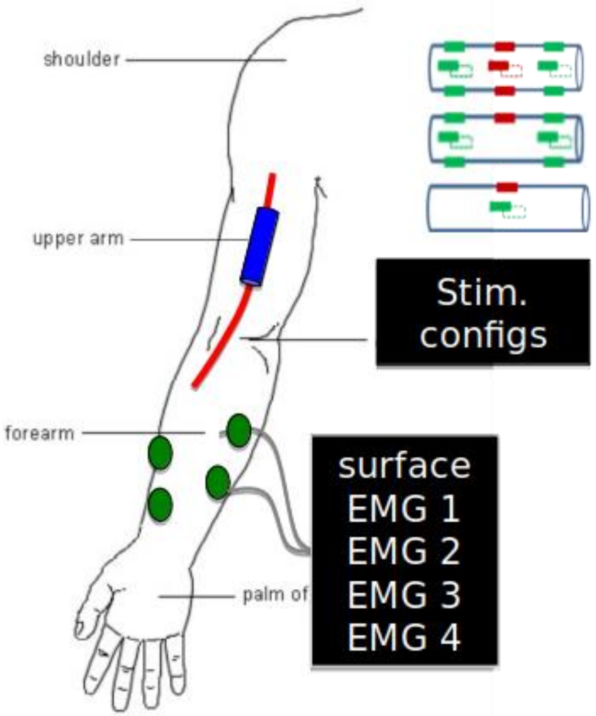
Mélissa Dali, Lucie William, Wafa Tigra, Hubert Taillades, Olivier Rossel, Christine Azevedo, David Guiraud

Published: July 2, 2019 • https://doi.org/10.1371/journal.pone.0219079



# Assessment of the approach

## -> Selective configuration -> Animal experiments




*Tigra et al, JNER 2020*

*ClinicalTrials NCT03721861*


BMC Part of Springer Nature

Journal of NeuroEngineering and Rehabilitation

Research | Open Access | Published: 19 May 2020

**Selective neural electrical stimulation restores hand and forearm movements in individuals with complete tetraplegia**

Wafa Tigra, Mélissa Dali, Lucie William, Charles Fattal, Anthony Gélis, Jean-Louis Divoux, Bertrand Coulet, Jacques Teissier, David Guiraud & Christine Azevedo Coste

*Journal of NeuroEngineering and Rehabilitation* 17, Article number: 66 (2020) | Cite this article

# Agilis project: Offering an implanted solution for upper limb restoration using electrical stimulation

**Constraints** :

- As less invasive as possible (surgical procedure)
- As efficient as possible (precision of gestures)
- Lessons from FreeHand

# Context:

**Tétraplegia**: Complete lesion of the spinal cord at cervical level, resulting in paralysis of all four limbs.

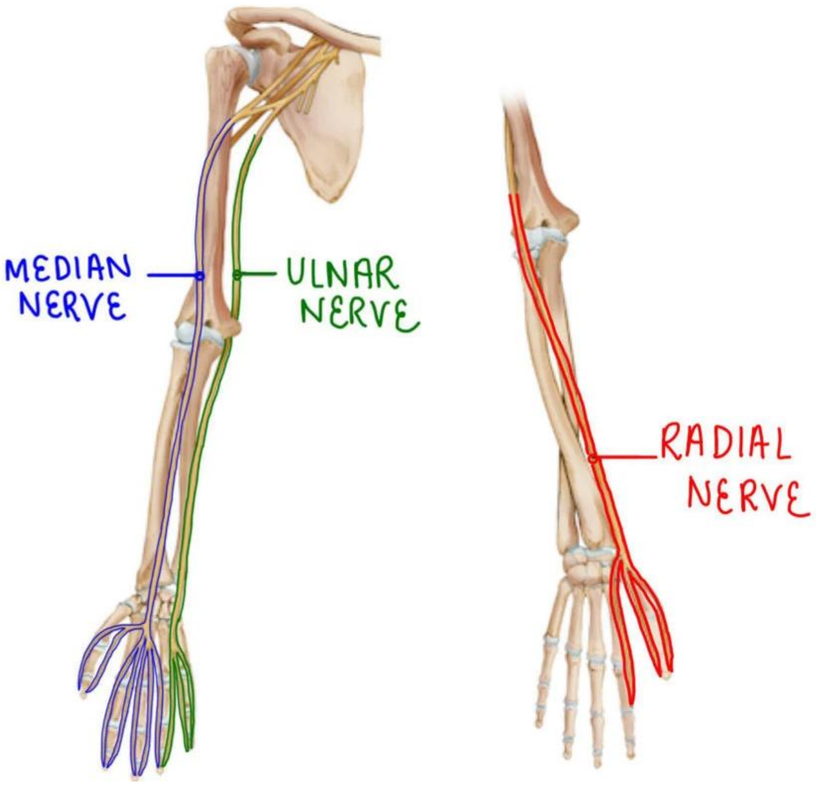
**Aim: Restore wrist and finger movement**

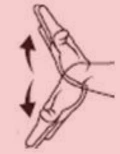
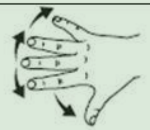
- Grip objects independently
- Improved quality of life

**Collaboration with start-up Neurinnov**
-> Development and marketing of an active implantable medical device: Neuroprosthesis

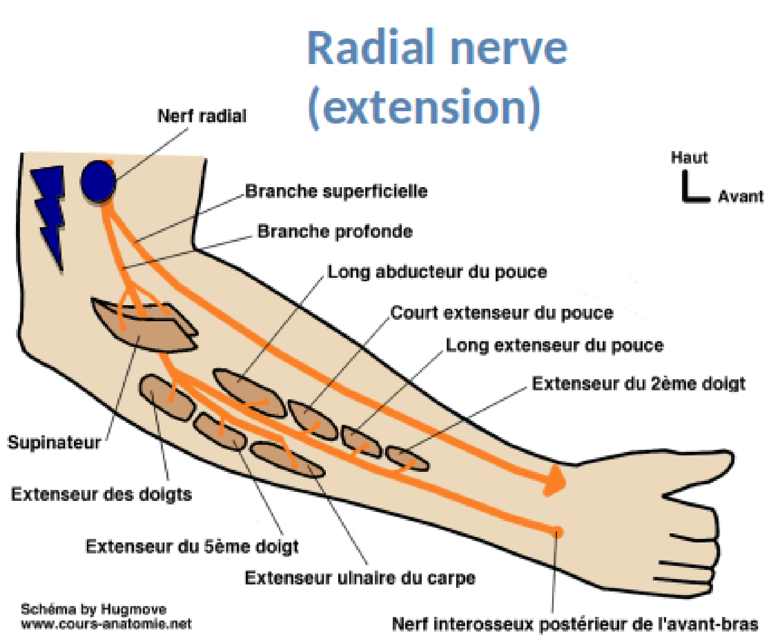
*C4 AIS A spinal-cord injured patient*

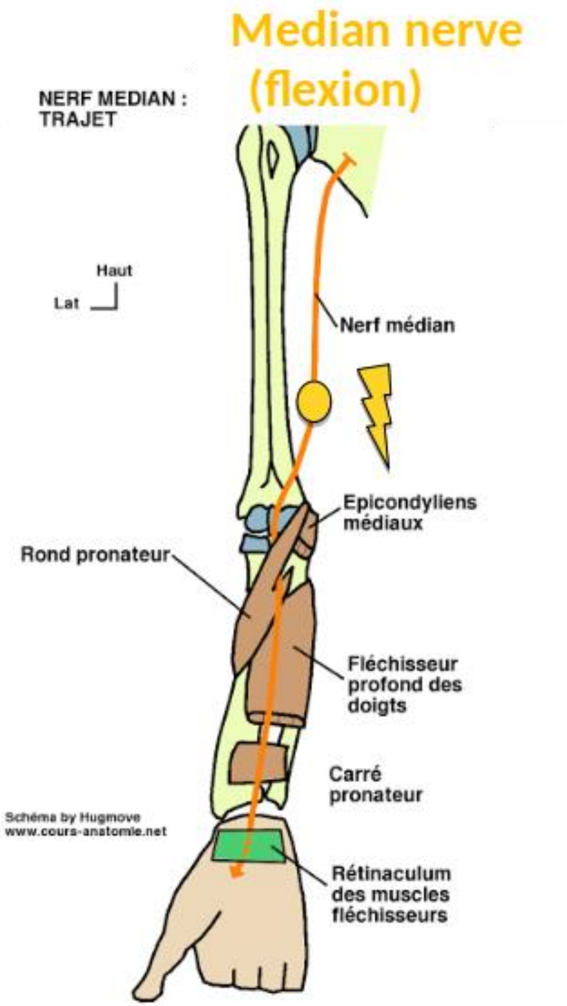
# Neurophysiology of the upper limb - In (very) brief



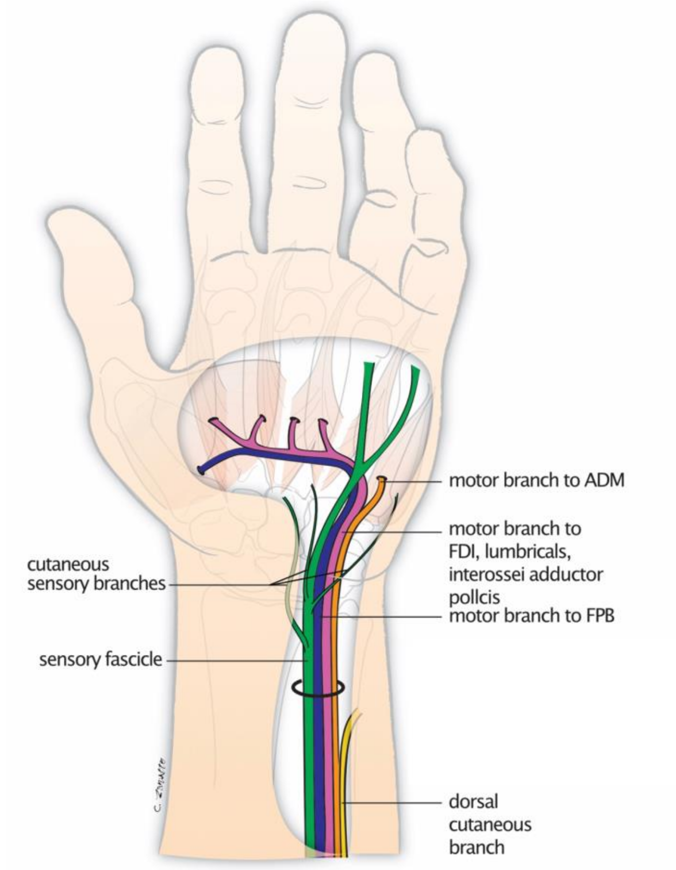

| Sensation | | Motor Function | |
|---|---|---|---|
| **Radial Nerve**<br>Palpate webbing space between thumb and index finger, including dorsal surface of hand |  | **Radial Nerve**<br>The ability to extend wrist and fingers at the knuckle joint<br>If cast is over hand only assess extension of fingers |  |
| **Median Nerve**<br>Palpate webbing space between thumb and index finger, including palmer surface of hand |  | **Median Nerve**<br>The ability to bring thumb and little finger together so they are touching |  |
| **Ulna Nerve**<br>Palpate between little finger and distal ring finger on palmar and dorsal surface of hand |  | **Ulna Nerve**<br>The ability to abduct all fingers |  |

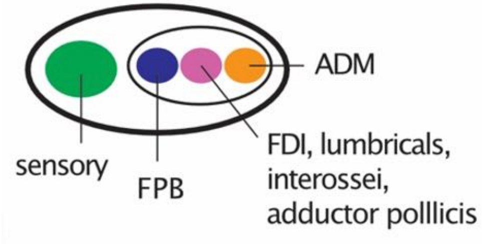
# Neurophysiology of the upper limb - In (very) brief



# Neurophysiology of the upper limb - In (very) brief



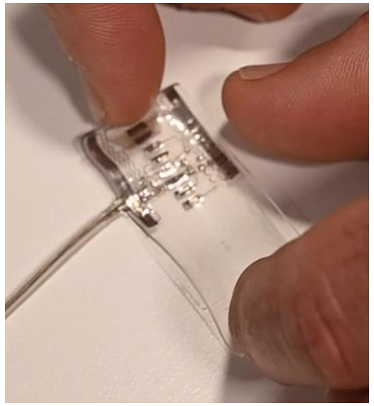



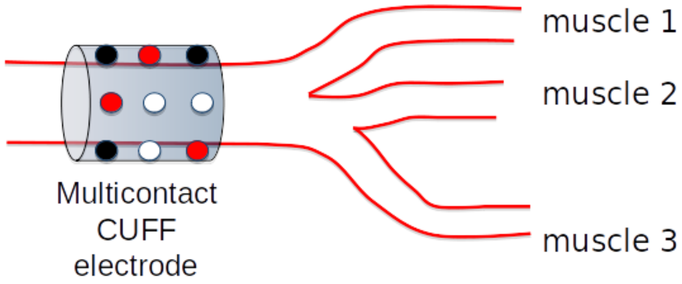

**Caracteristic**:
- Topological and functional organisation of nerve fibres

**Consequence**:
- Possibility of reducing the number of electrodes…
- While retaining motor selectivity

# Multicontact cuff electrode

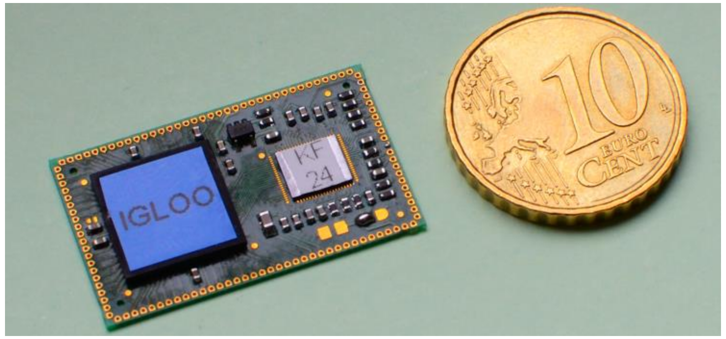
–> A technological solution to the problems of selectivity and invasiveness

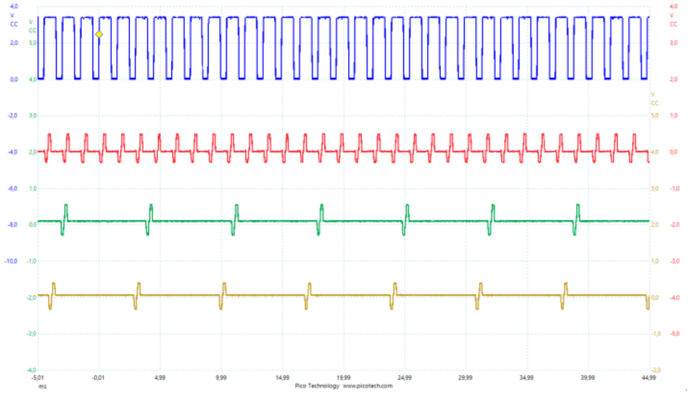


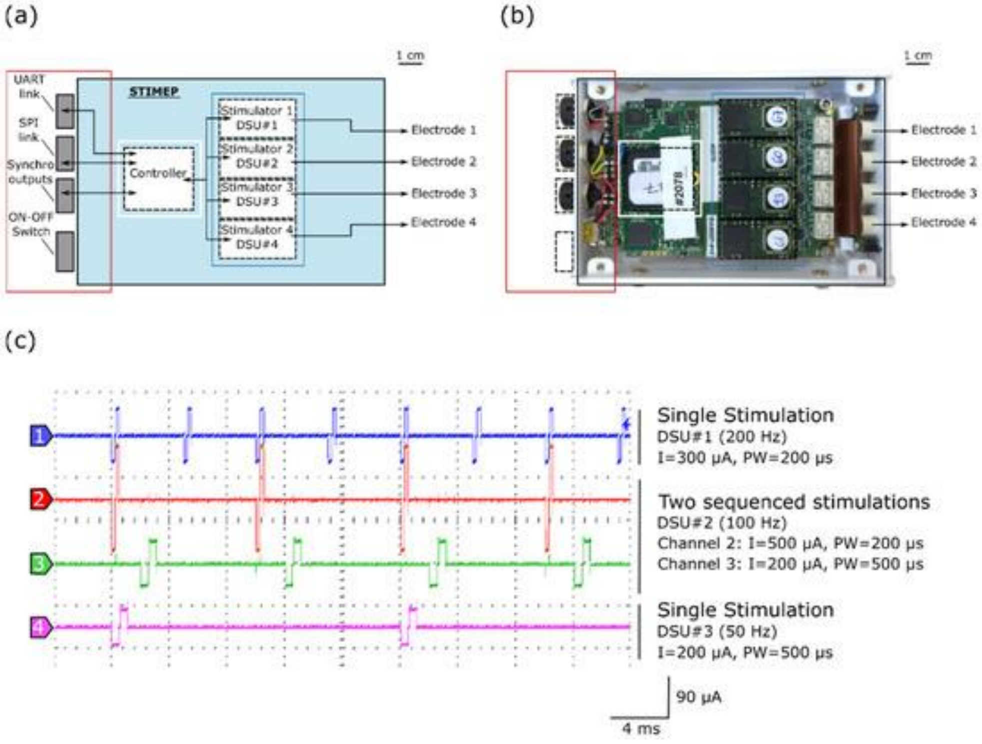

# Selective stimulation approach

## –> Multicontact cuff electrode and stimulation device

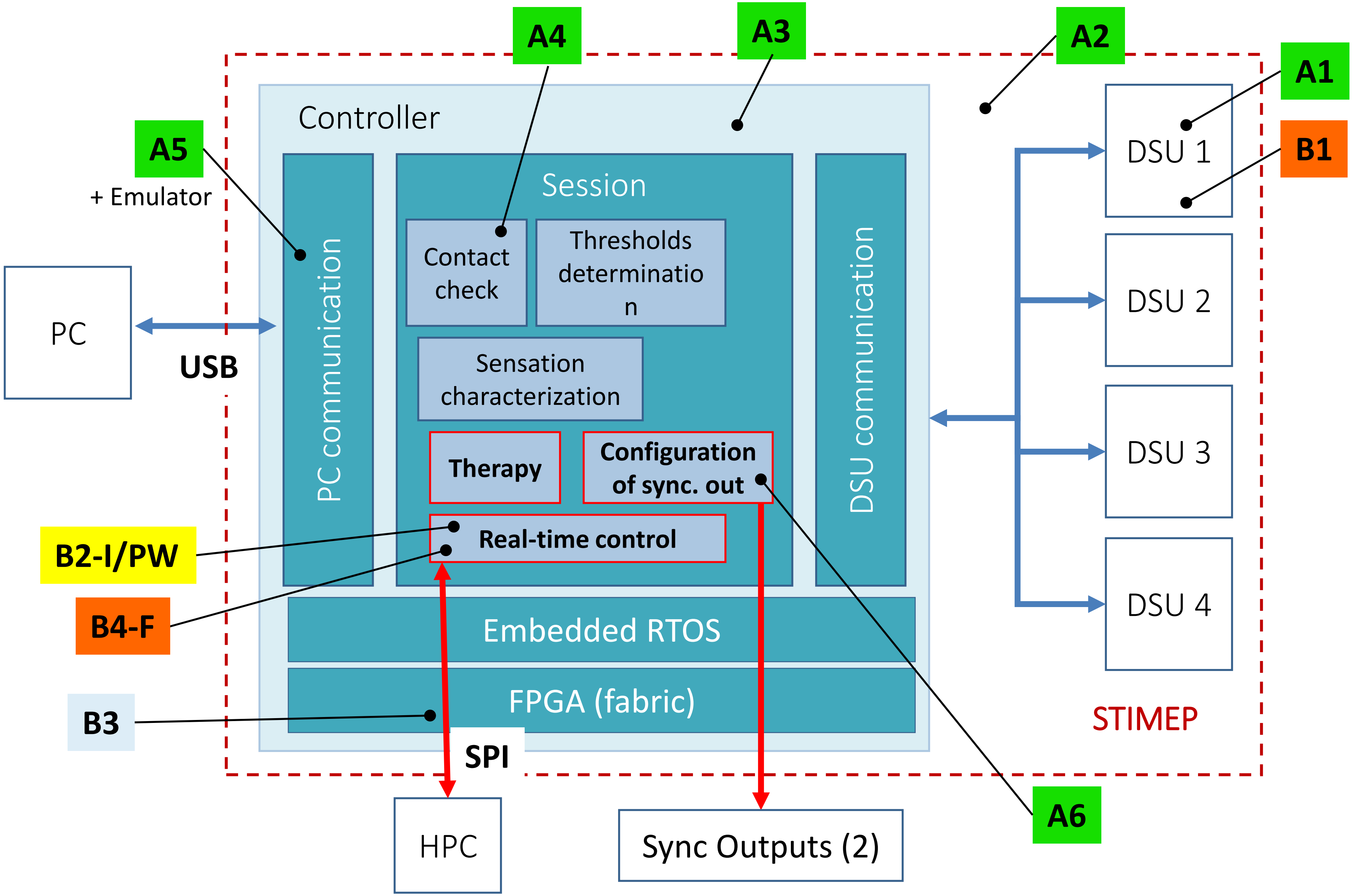



*Based on Andreu, Guiraud and Souquet, JNE* 2009

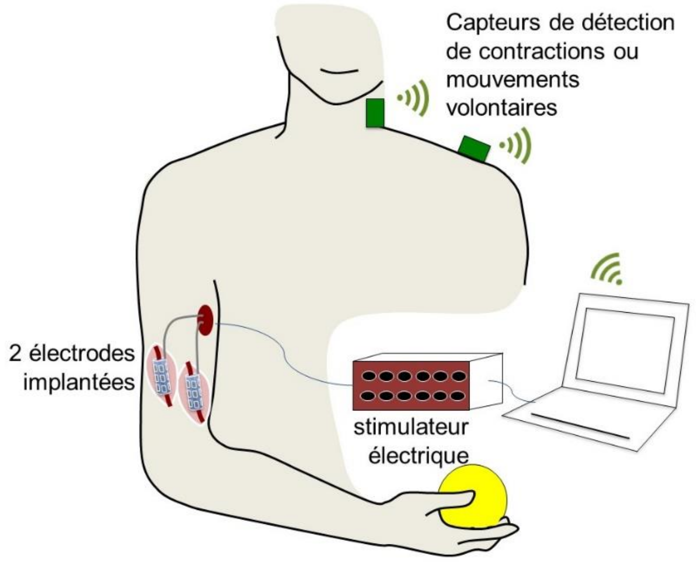


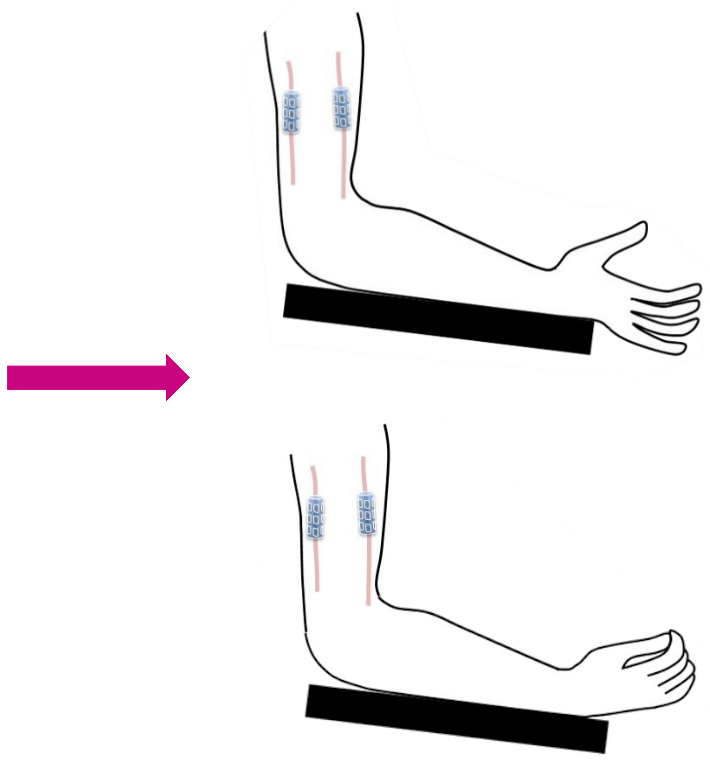
# STIMEP software – Architecture & Activities



# Agilis project (Phase 1 &2)

## Schematic operation of the system

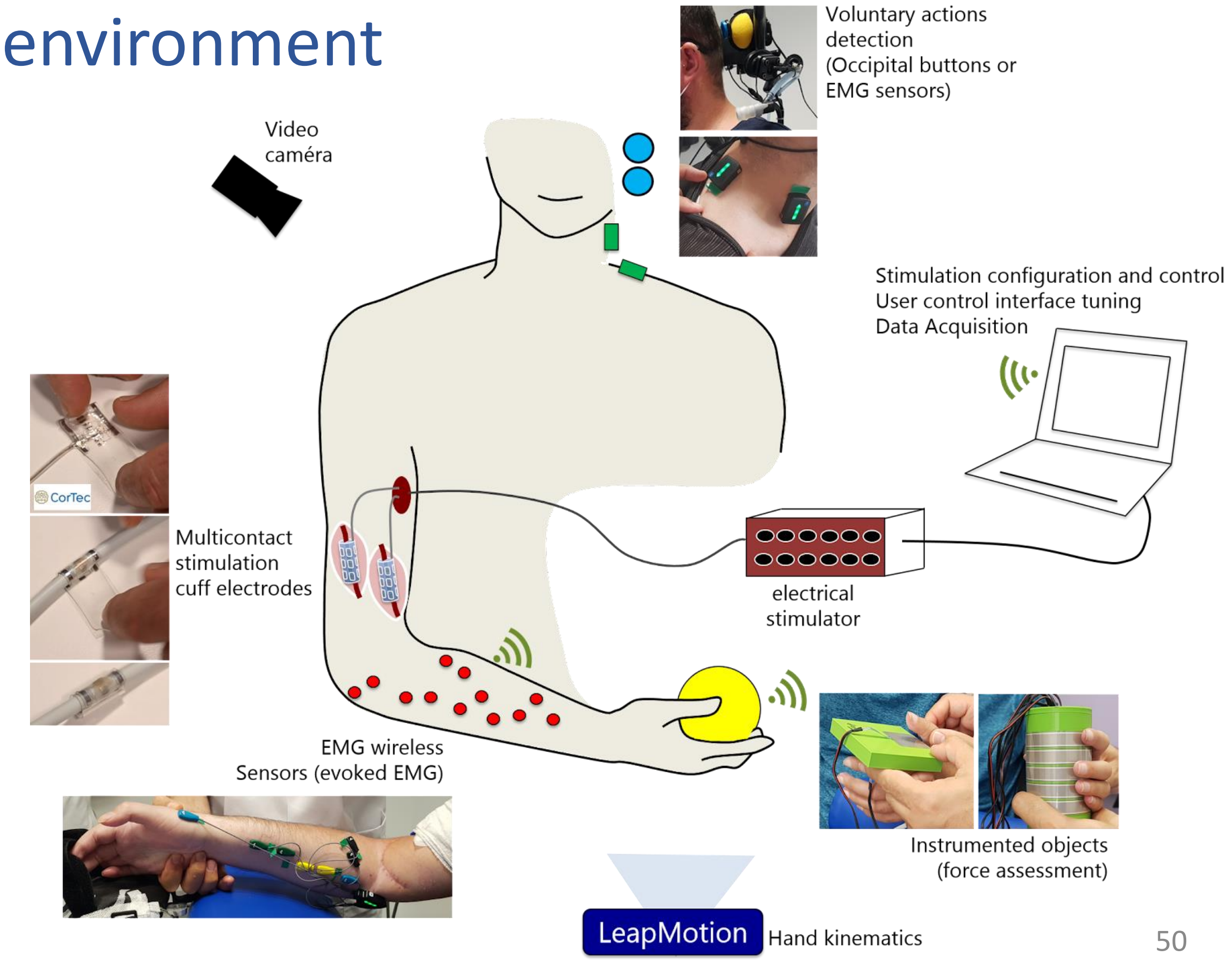


- The patient controls the stimulator using residual movements
- Restoration of hand opening and grasping of objects
- 4 Patients

# Agilis project (Phase 1 &2)

## A complex sensor and software environment



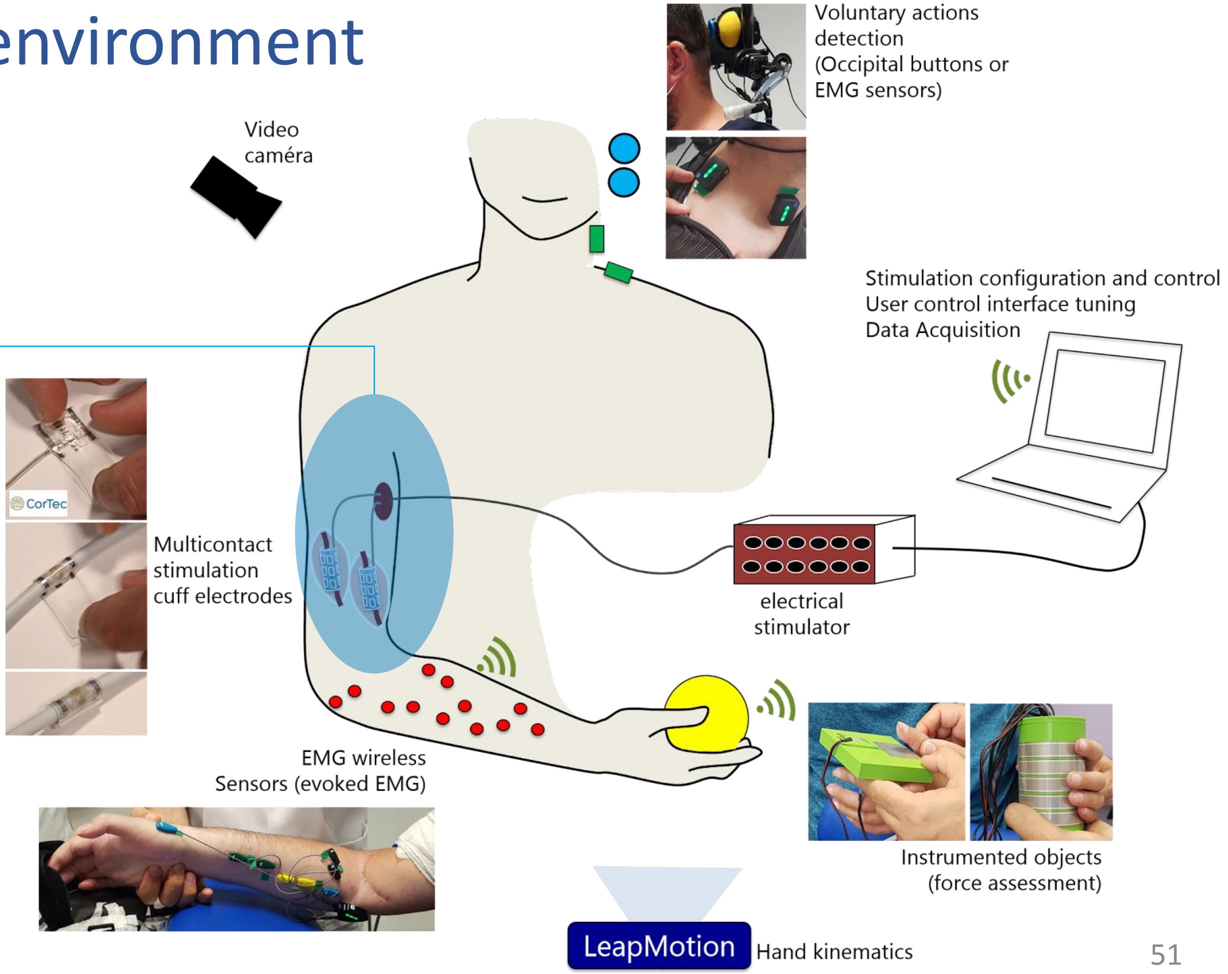
# Agilis project (Phase 1 &2)

## A complex sensor and software environment

*The investigated solution:*

Implanted multi-contact electrodes
(30 days)

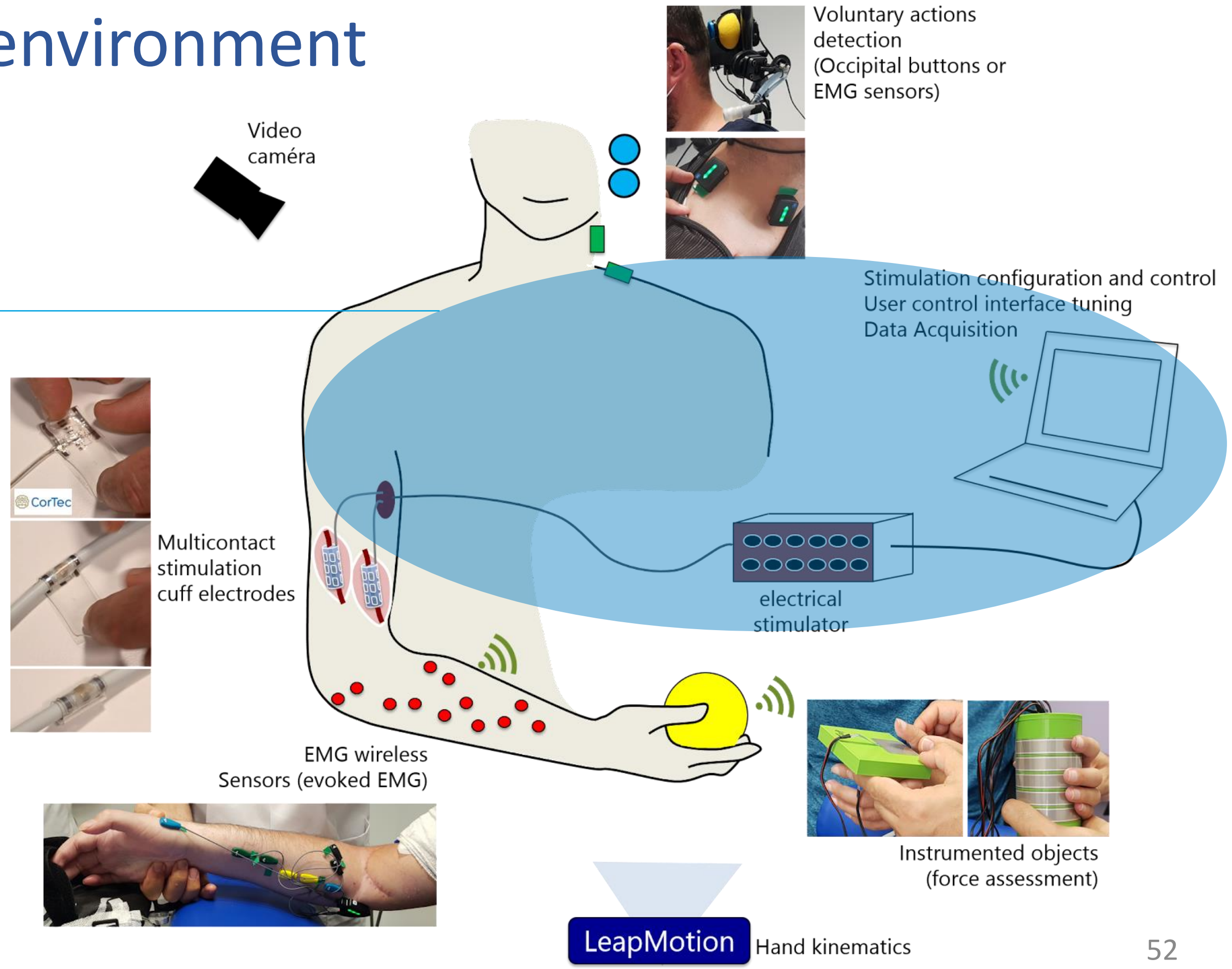
*Agilis 2020 (2 nerves)*



# Agilis project (Phase 1 &2)

## A complex sensor and software environment

Stimulator connected to electrodes and control devices



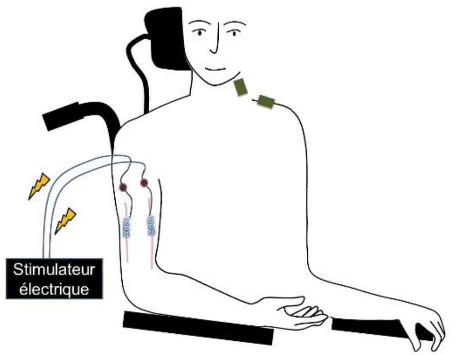

*Stimulation device (Neurinnov)*

# Agilis project (Phase 1 &2)

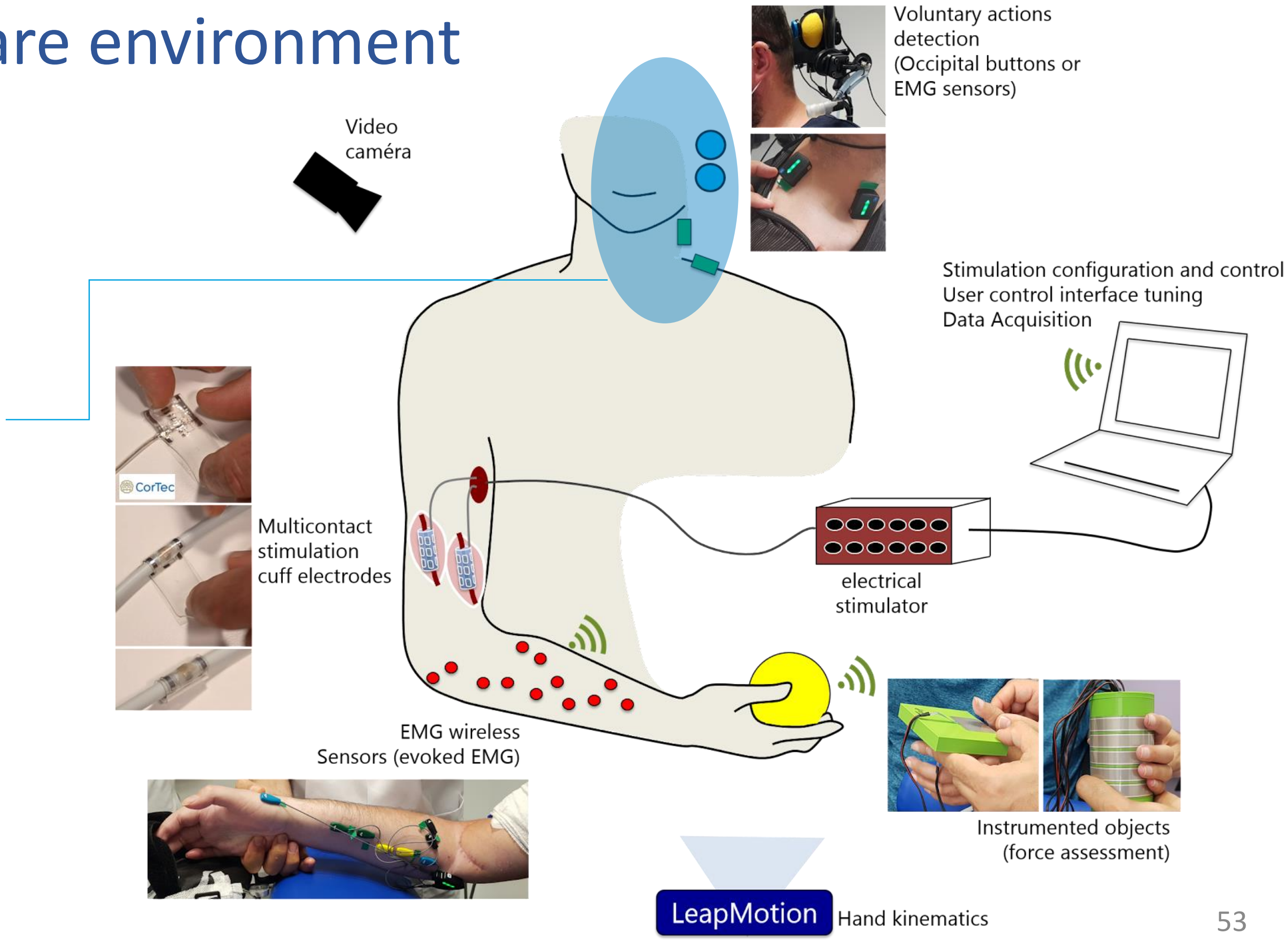
## A complex sensor and software environment

Controlled by the patient :

- Detection of voluntary contractions using EMGs
- Voice command



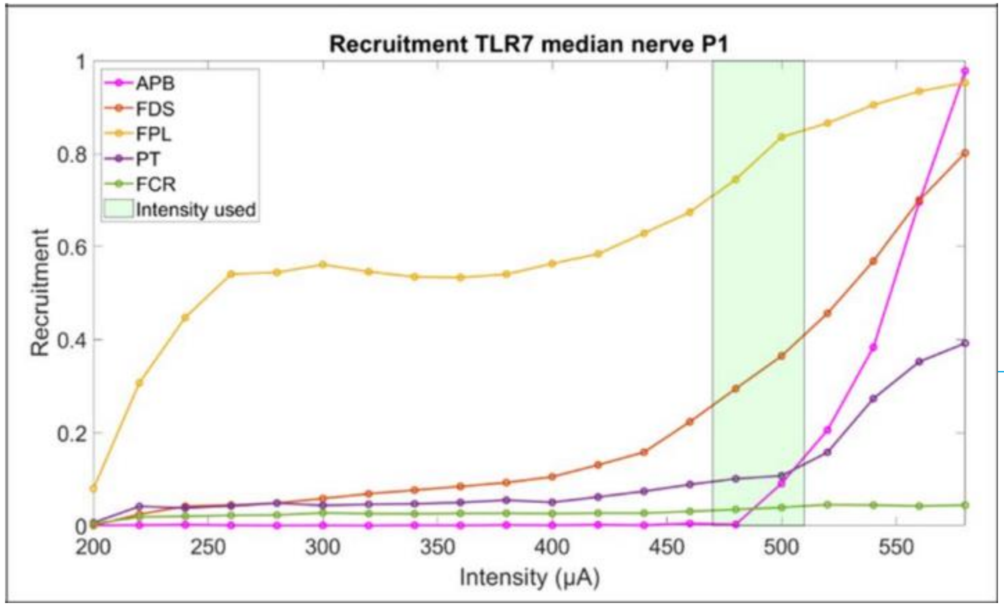

*Agilis 2020 (2 nerves)*

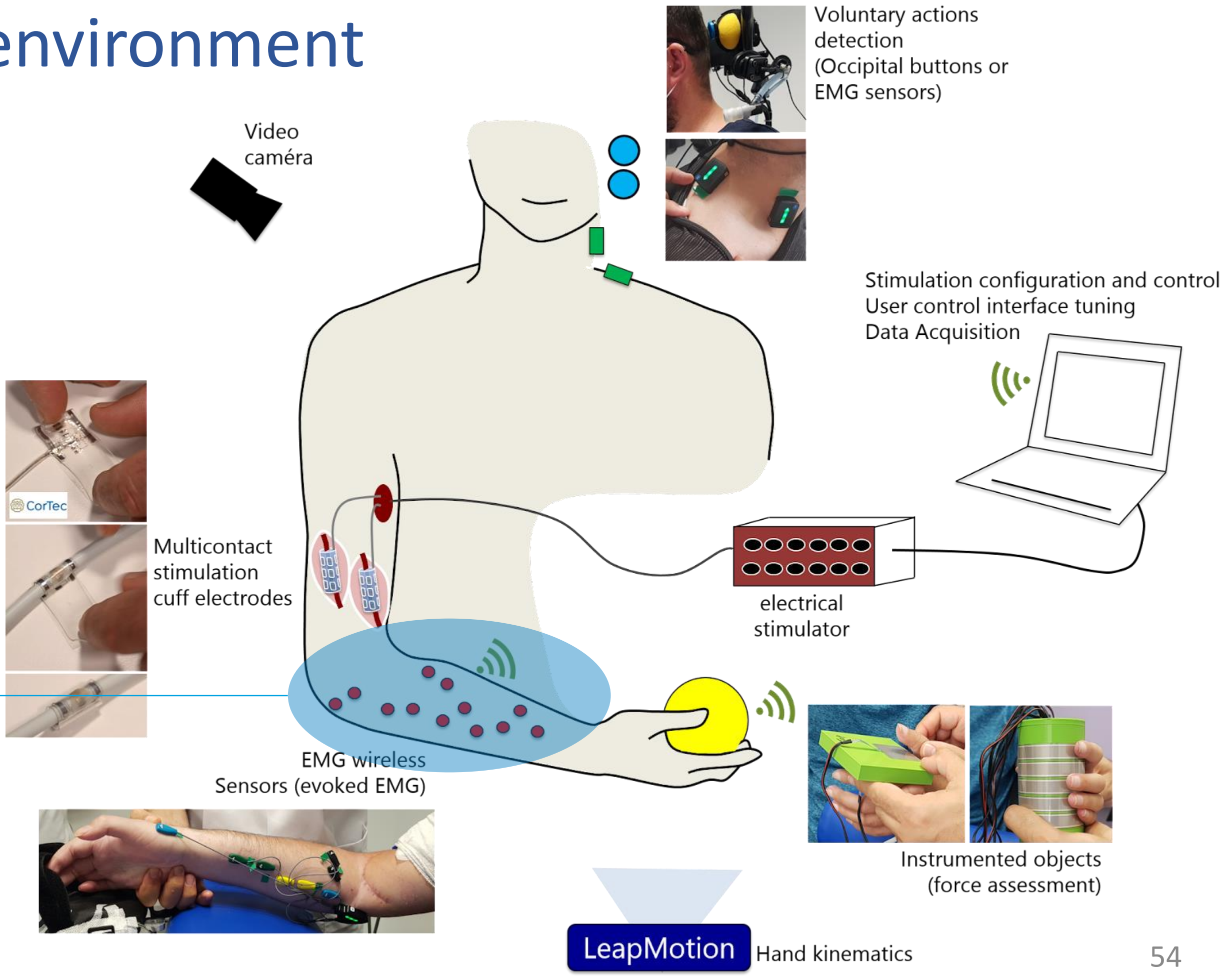


# Agilis project (Phase 1 &2)

## A complex sensor and software environment

EMGs to analyse muscle responses :

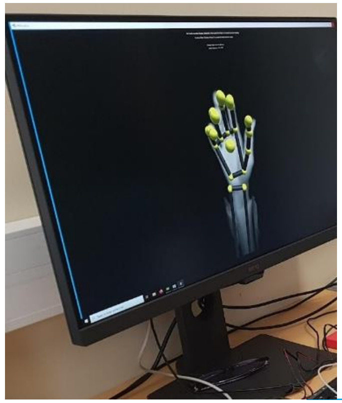


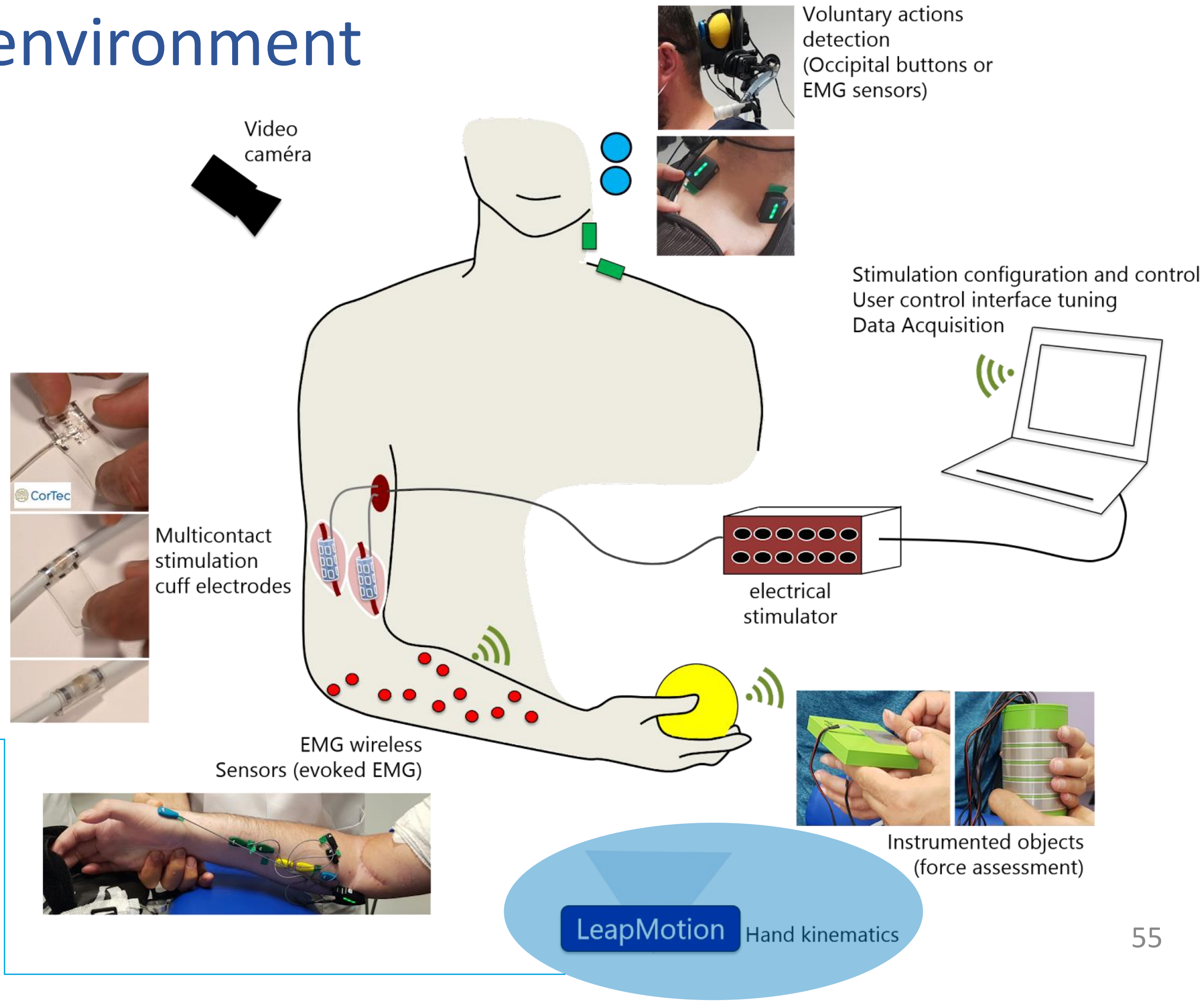
# Agilis project (Phase 1 &2)

## A complex sensor and software environment

Motion capture :
Kinematics and dynamics



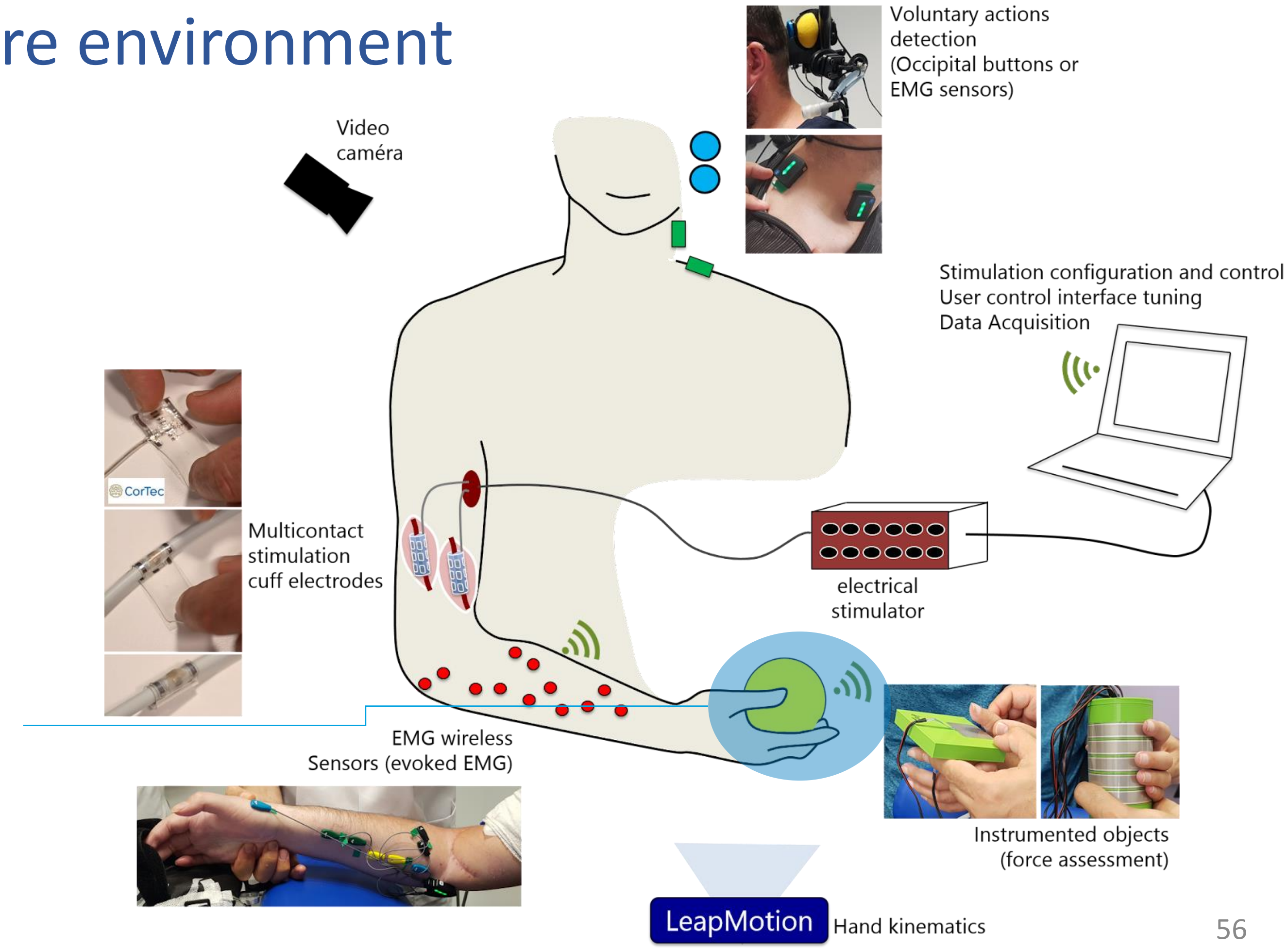
*Agilis 2022 (3 nerves)*



# Agilis project (Phase 1 &2)

## A complex sensor and software environment

Motion capture :
Gripping force




*Agilis 2020 (2 nerves)*

# Agilis project – Phase 2

## *Results (2020)*

# Agilis project – Phase 2

## *Results (2023)*

# Agilis project – Phase 2

## *Results (2023)*

# Agilis project -> Future work

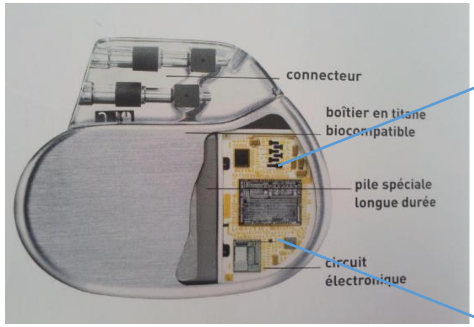
## *Research perspectives*

- Looking for even greater selectivity (3rd nerve, advanced stimulation strategies)
- Automate stimulation according to the objects approached by the patient's hand (camera in hand)
- Automatic selection of stimulating configurations thanks to on-line biomechanical analysis of movements
- Optimum on-line control, computer vision, etc.

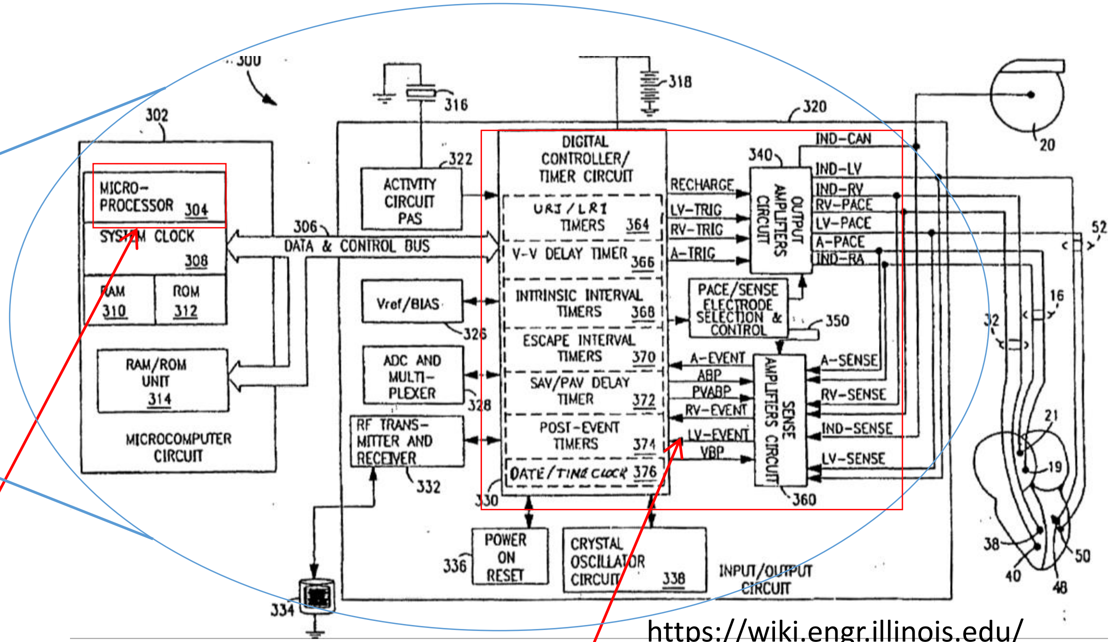
# Agilis project -> Future work

## *Research perspectives*

- Develop the implant

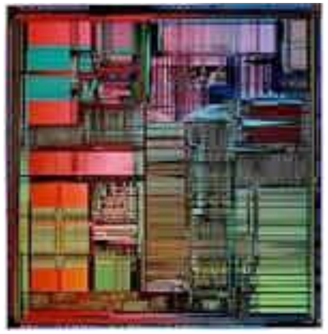



http://pacemaker-tpe.e-monsite.com/



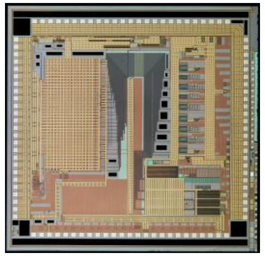

https://wiki.engr.illinois.edu/

Micro-processor



Stimulation parameters

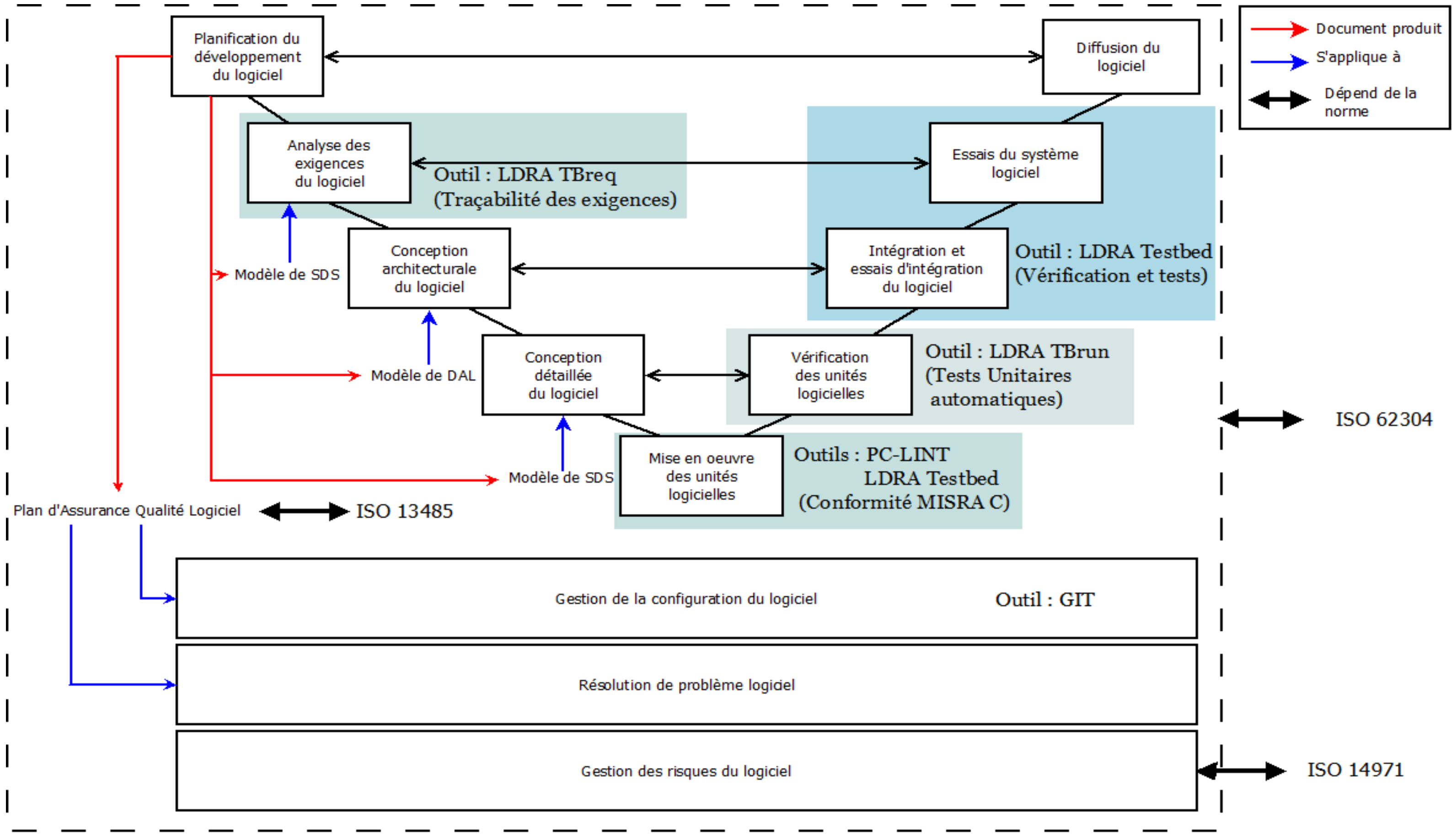
ASIC



Stim & mesure

# Agilis project -> Future work

## *Research perspectives*

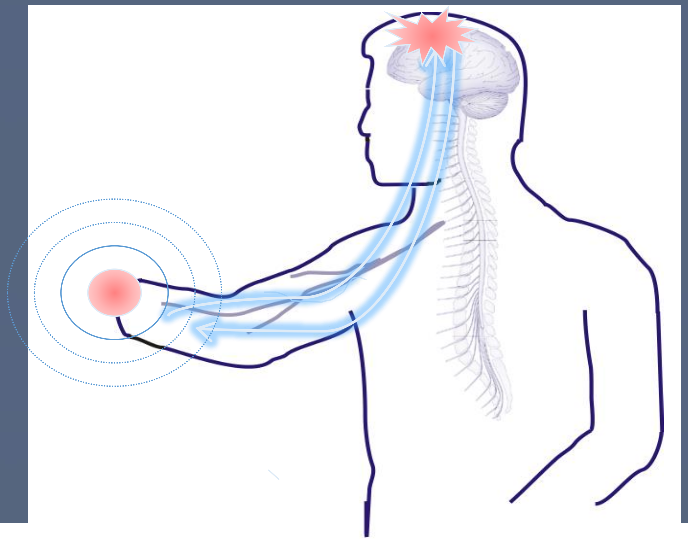


# Peripheral Nerve Stimulation

Intrafascicular electrodes

# *Intrafascicular Electrodes - Phantom limb pain management*

Natural sensory feedback for phantom limb modulation and therapy

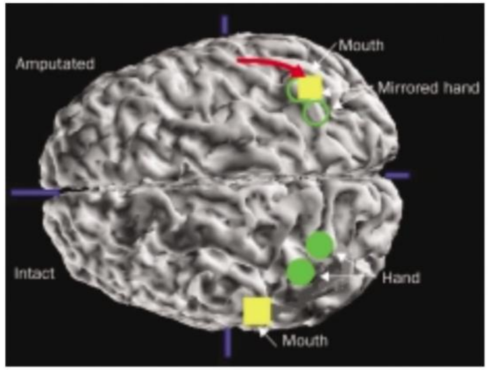


# *Intrafascicular Electrodes - Phantom limb pain management*

## EPIONE: Sensory feedback for phantom limb modulation and therapy

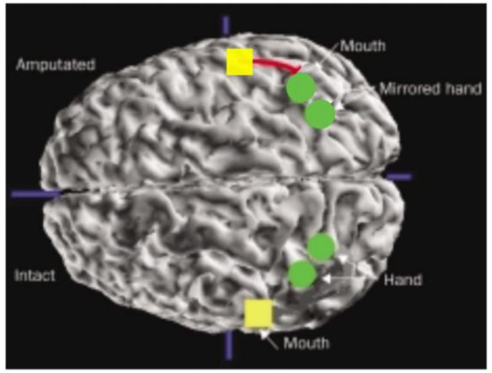
### Observation:

- Amputation → Reduction or loss of sensory feedback
  → Changes in cortical representation
  → Development of neuropathic pain



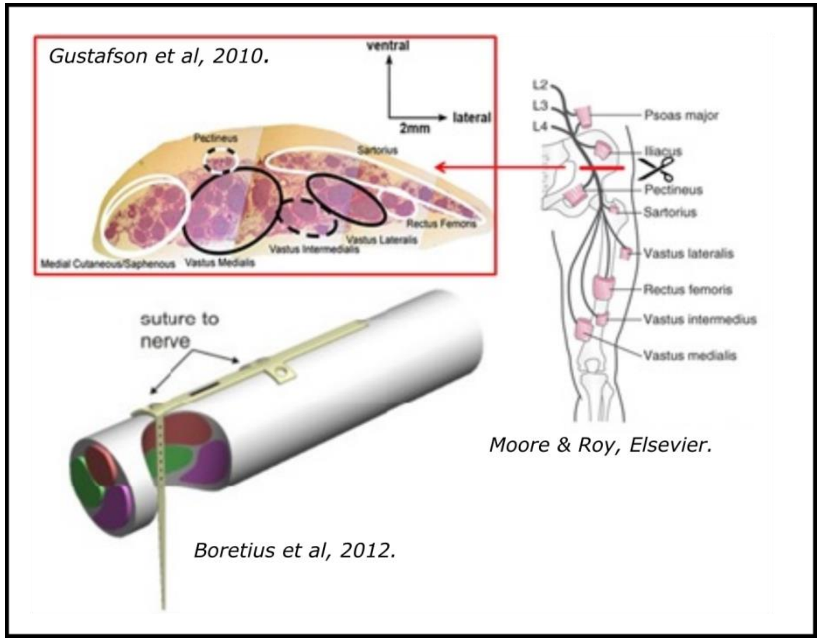

### Hypothesis:

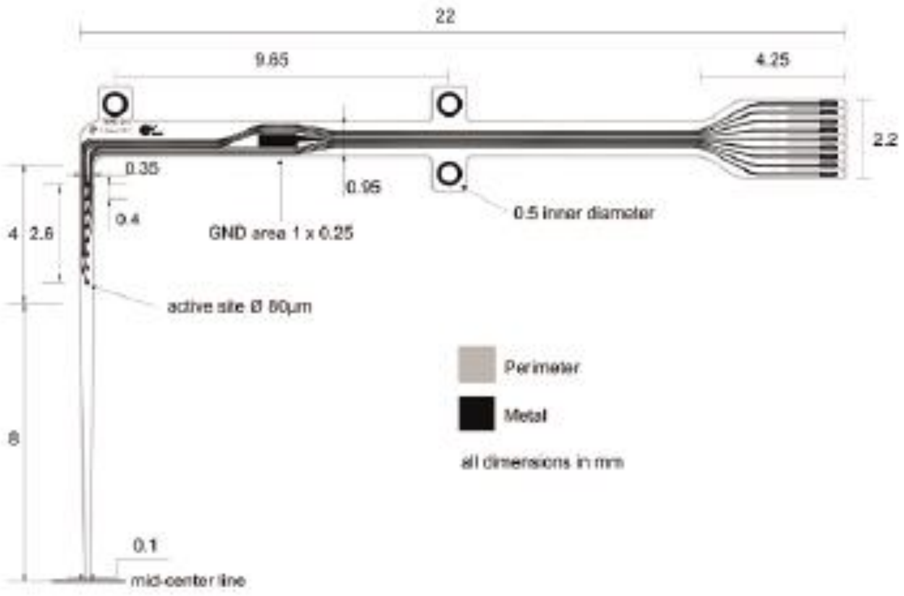
- Research project → Stimulation to replace the sensory feedback
  → Revert the cortical representation
  → Back to a normal representation
  → Phantom limb pain reduction



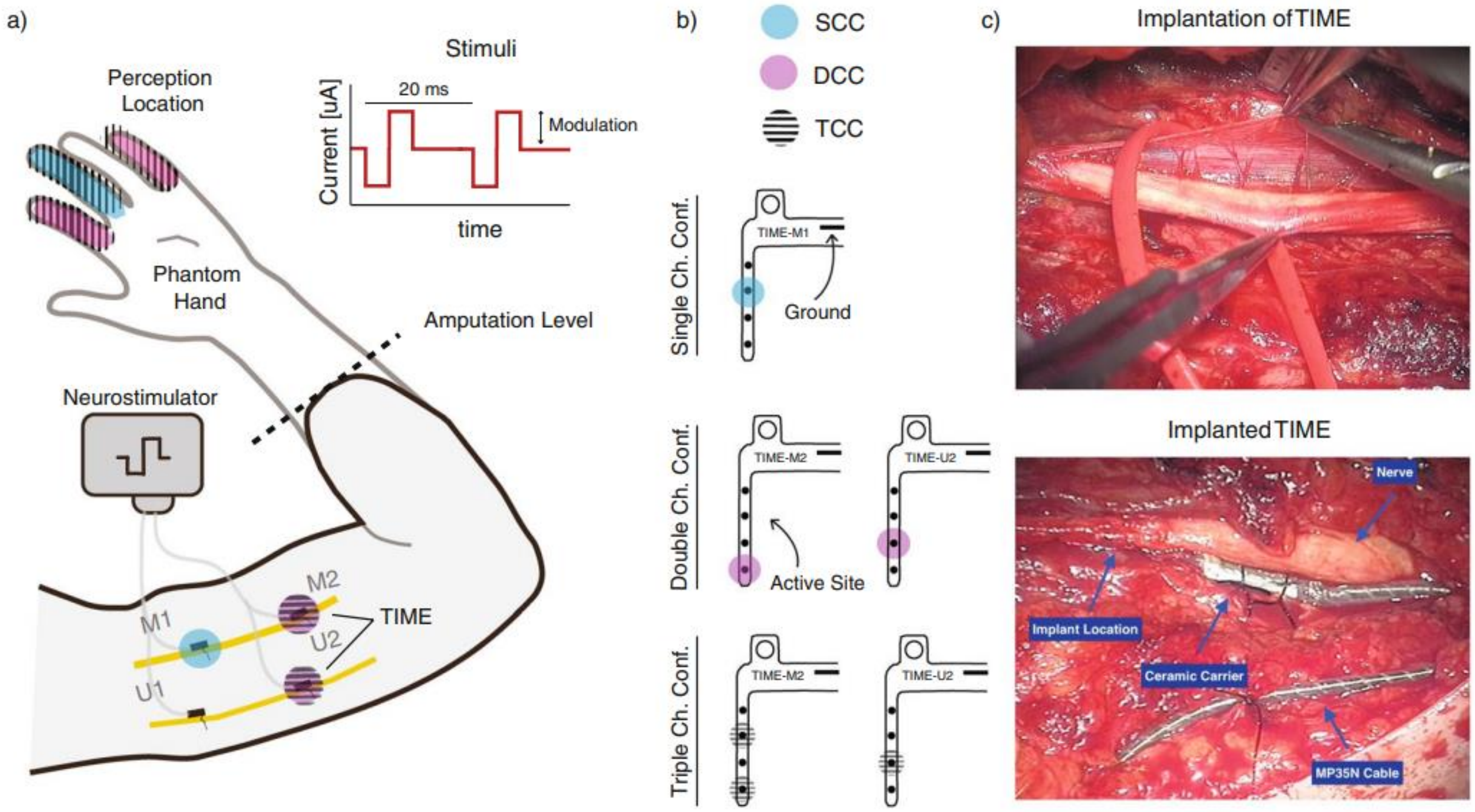
# TIME electrode

–> An other technological solution to the problems of selectivity and invasiveness

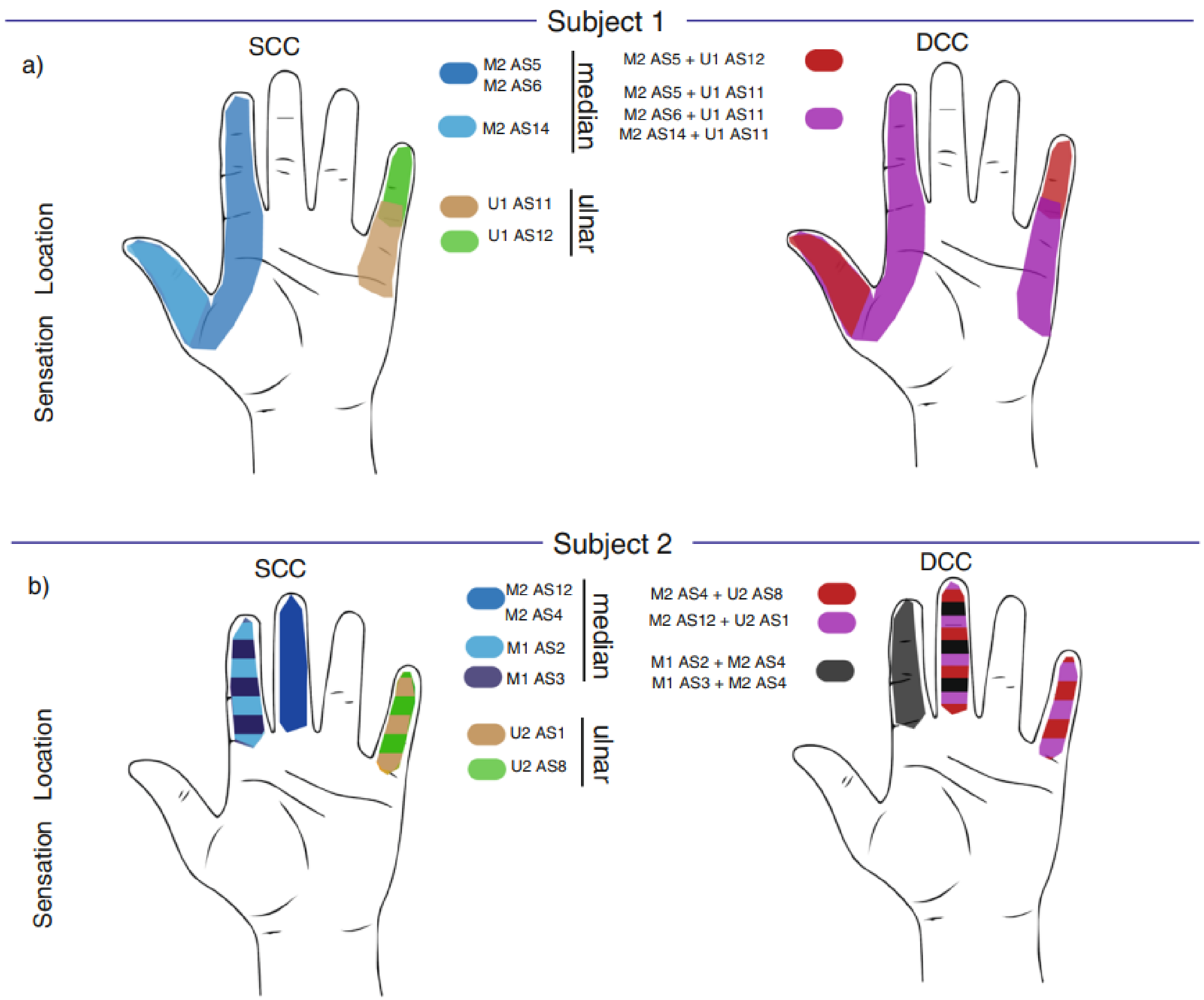


# *Phantom limb pain management*



# *Phantom limb pain management*



# Spinal cord Stimulation

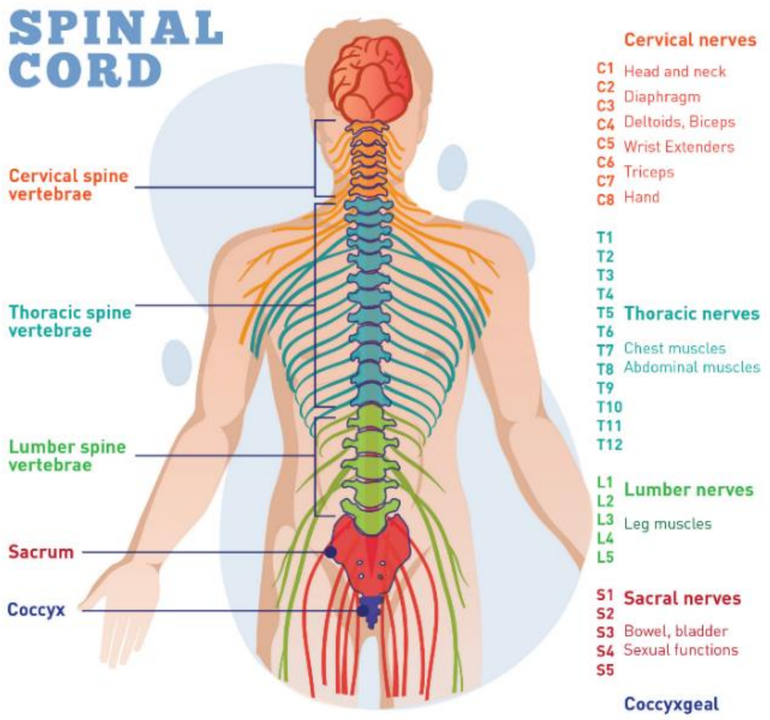
In a context of SCI

# *Spinal cord*

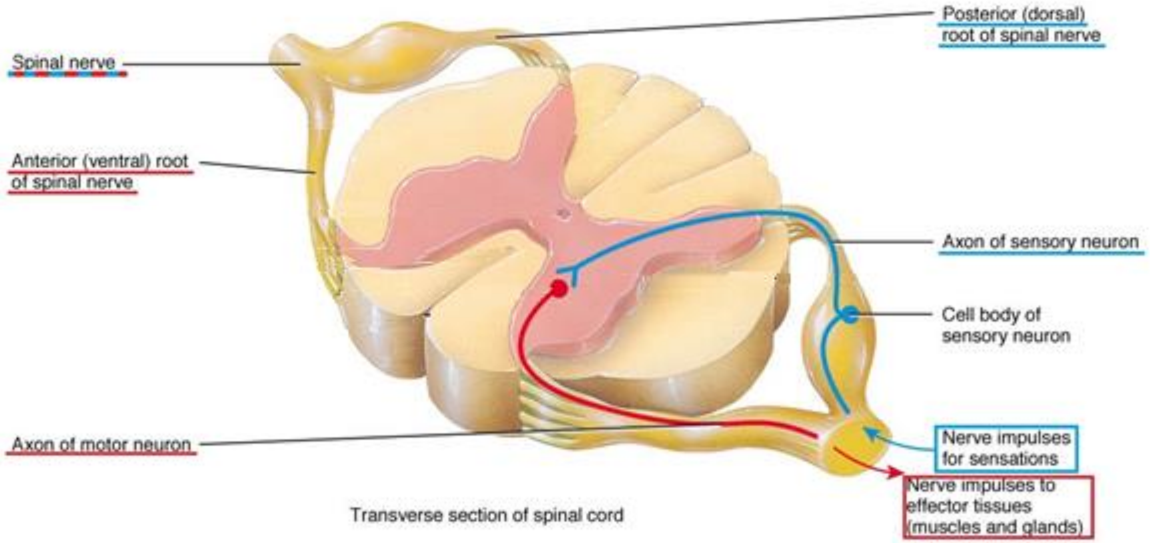
Protected by the spine (*vf – la colonne vertebrale*)
- Pre-existing neural networks
- First level of signal processing (reflexes etc.)

Its functional unit
- The spinal level (*vf – le niveau medullaire*)
  - -> Dedicated to a specific territory (C4 level for example)
  - -> Spreads the motor command
  - -> Gathers sensitive information from the periphery

In case of spinal cord injury
- Communication breakdown between the brain and the periphery
- Motor and sensitive impairments below the lesion
- Sublesional spinal networks: Intact but loss of supraspinal driving command
  - -> Spinal cord stimulation for reactivation?



# *Spinal cord – The spinal level*

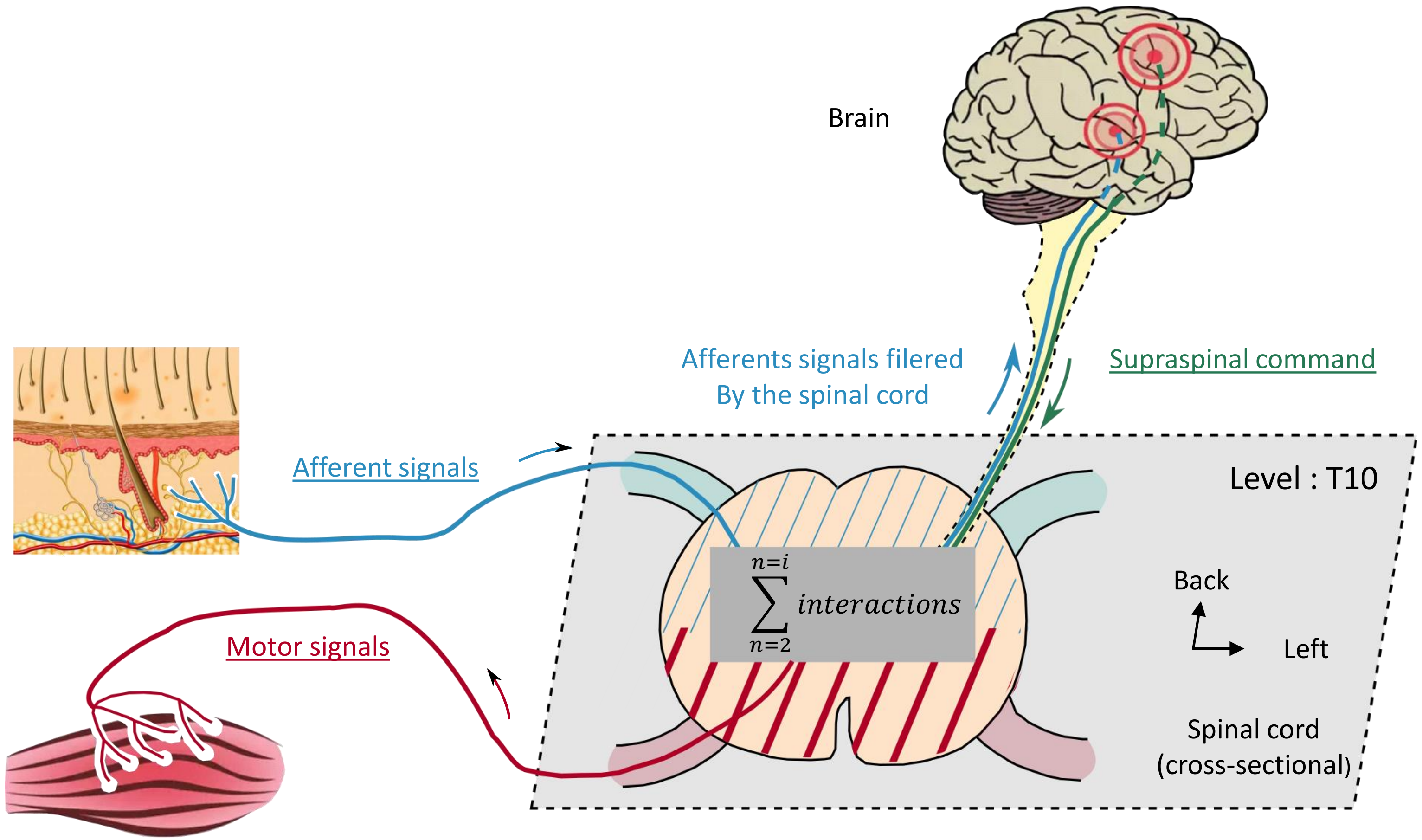



Anatomically
- Grey matter
  -> Cell body packed within the cord in a butterfly shape
- White matter
  -> Nervous fibres at the periphery gathered in tracts

Functionally
- Dorsal spinal cord and dorsal root -> exclusively sensitive
- Ventral spinal cord and ventral root -> exclusively motor
- Left side -> left part of the body / Right side -> right part

Spinal cord stimulation
- Promote spinal cord excitability by dorsal stimulation
  -> Spectacular results in the past few years in person with SCI
  -> Partial functional and volitional recovery

# *Spinal cord – Multiple interactions*



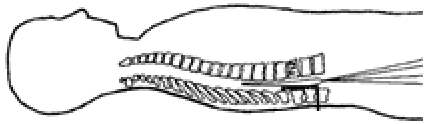

Dorsal = sensory

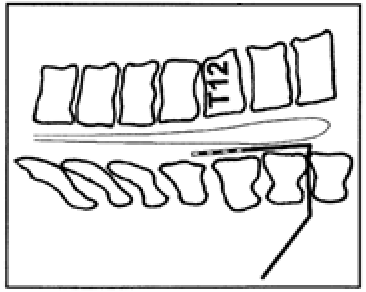
Ventral = motor

$$\sum_{n=2}^{n=i} interactions, with\ n: number\ of\ neurons$$

# *Improvements of motor tasks after spinal cord injuries: SCS + Training*

–> Epidural stimulation + Intense locomotor treadmill training







Recovery of Over-Ground Walking after Chronic Motor Complete Spinal Cord Injury

Claudia A. Angeli, Ph.D., Maxwell Boakye, M.D., Rebekah A. Morton, B.S., Justin Vogt, B.S., Kristin Benton, B.S., Yangshen Chen, Ph.D., Christie K. Ferreira, B.S., and Susan J. Harkema, Ph.D.

N Engl J Med 2018; 379:1244-1250 September 27, 2018

–> Transcutaneous stimulation + Training for grip strength

Gad P, Lee S, Terrafranca N, Zhong H, Turner A, Gerasimenko Y and Edgerton V R 2018 Non-invasive activation of cervical spinal networks after severe paralysis *J. Neurotrauma* 35 2145–58

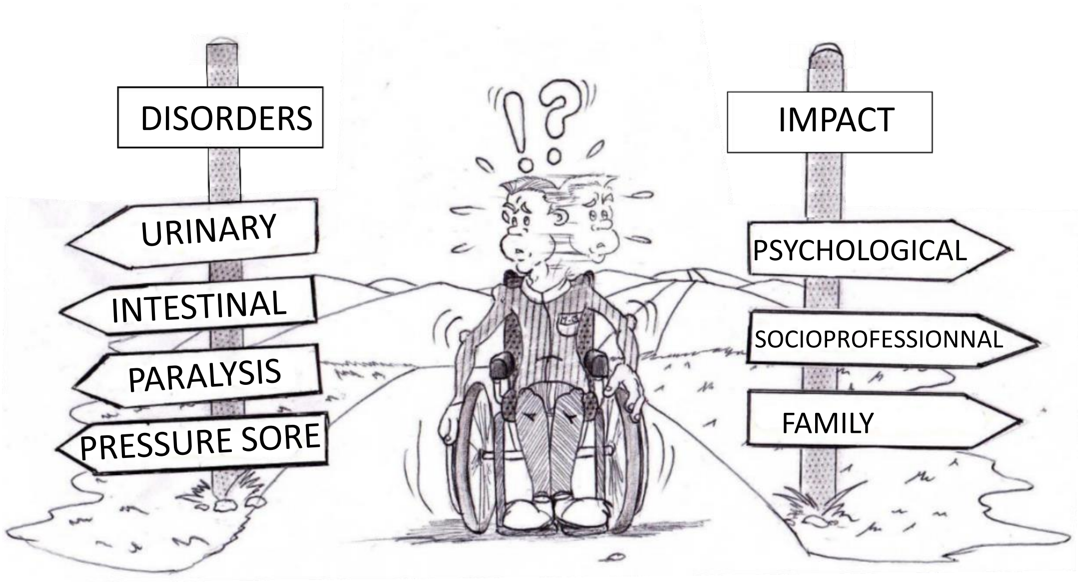
Training:
--> Provide task-specific afferent feedback

Stimulation:
--> Potentiate spinal cord excitability

- Mechanism of action of SCS -> potentiate afferences
- Interaction SCS <-> supraspinal input -> Boost plasticity

# *Spinal cord stimulation*

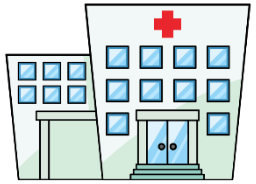
*Spinal Cord Injury*

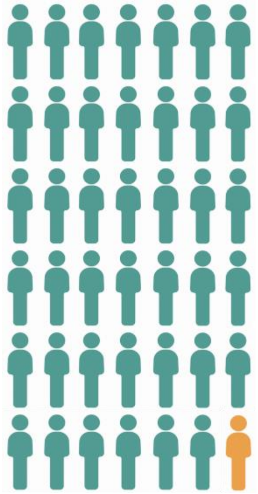



*In clinic : Spinal cord stimulation*


*Generally beneficial*
*but…*

*Limited Approach…*



*Limited… in its current form because empirical…*

# Spinal cord stimulation - illustration of the approach

Article

## The neurons that restore walking after paralysis

### 1) The journal

nature

**Aims & Scope**

*Nature* is a weekly international journal publishing the finest peer-reviewed research in all fields of science and technology on the basis of its originality, importance, interdisciplinary interest, timeliness, accessibility, elegance and surprising conclusions. Nature also provides rapid, authoritative, insightful and arresting news and interpretation of topical and coming trends affecting science, scientists and the wider public.

**2021 Journal Metrics**

2 year Impact Factor (2021) - 69.504

5- year Impact Factor (2021) - 63.580

Immediacy index - 17.085

Eigenfactor® score - 1.11428

Article Influence Score - 25.568

2-year Median - 31

### 2) The authors

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Neurotechnologies and Neur…

| | Toutes | Depuis 2018 |
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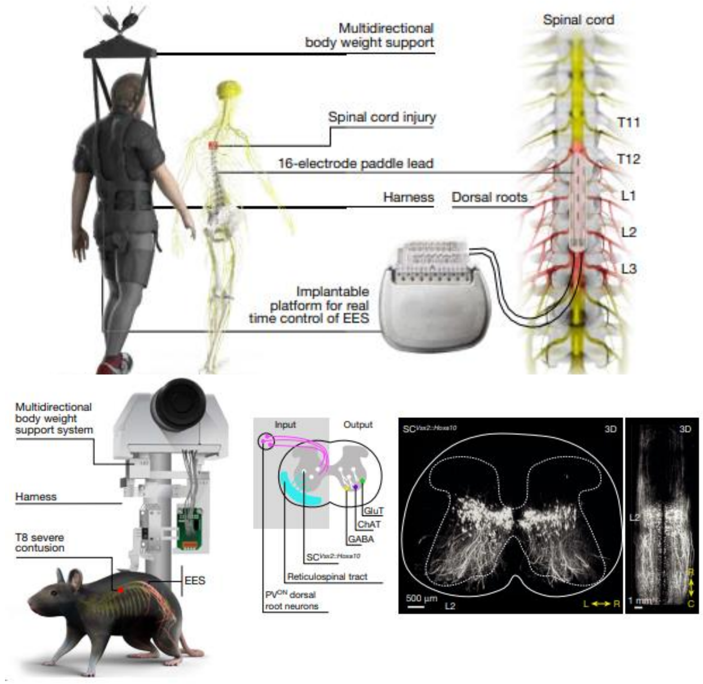
| Citations | 15450 | 9540 |
| indice h | 62 | 49 |
| indice i10 | 110 | 106 |

| TITRE | CITÉE PAR | ANNÉE |
|---|---|---|
| Electronic dura mater for long-term multimodal neural interfaces<br>IR Minev, P Musienko, A Hirsch, Q Barraud, N Wenger, EM Moraud, …<br>Science 347 (6218), 159-163 | 856 | 2015 |
| Restoring voluntary control of locomotion after paralyzing spinal cord injury<br>R Van den Brand, J Heutschi, Q Barraud, J DiGiovanna, K Bartholdi, …<br>science 336 (6085), 1182-1185 | 821 | 2012 |
| Transformation of nonfunctional spinal circuits into functional states after the loss of brain input<br>G Courtine, Y Gerasimenko, R Van Den Brand, A Yew, P Musienko, …<br>Nature neuroscience 12 (10), 1333-1342 | 754 | 2009 |

### 3) The paper

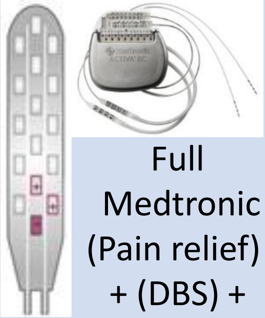
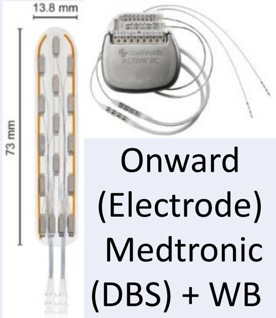
Nature | Vol 611 | 17 November 2022

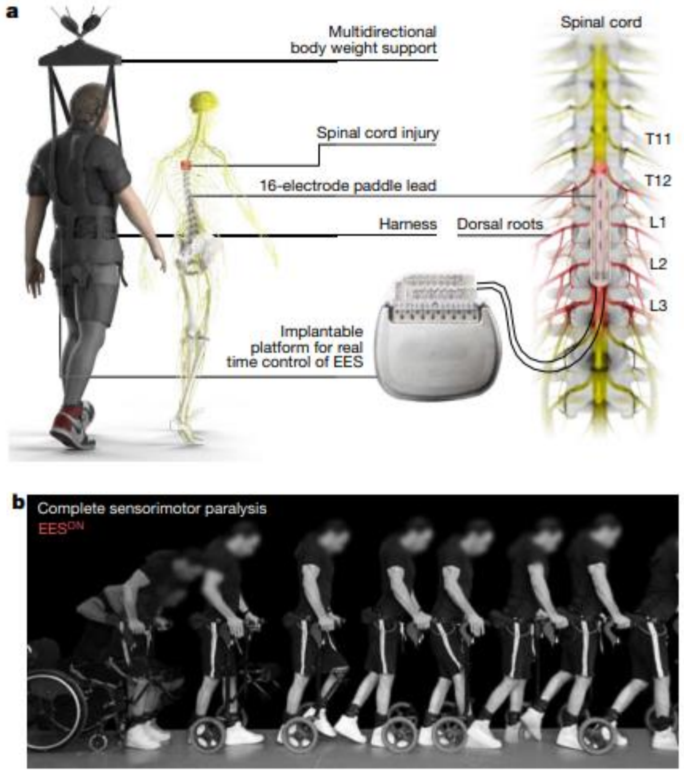
*No keyword section*



# *Spinal cord stimulation - illustration of the approach*

9 Participants: 2 Groups *Clinical study (STIMO): EES Rehab protocol = Closed-loop EES + neurorehab w/ support (4 or 5/week)*

| Participants | Implant | Acute phase | After 5 months of EES Rehab |
|---|---|---|---|
| Group A:<br>N=6;<br>Severe or complete motor paralysis but some degree of sensation in the legs | <br>Full Medtronic (Pain relief) + (DBS) + WB (Custom Wireless Bridge) | 1) « EES immediatly enabled to improve or regain ability to walk while supported in the robotic interface »<br>2) « Volitional control over the amplitude of their steps w/ EES » (except 1 from Group B) | 1) « Weight-bearing capacities improved considerably over time, which enabled the participants to walk outdoors with $EES^{ON}$ and an assistive device for stability »<br>2) « Participants who exhibited residual functions before EES displayed an increase in motor scores » + « walking in absence of EES in 4 participants» |
| Group B:<br>N=3;<br>Complete sensorimotor paralysis | <br><br>Onward (Electrode) Medtronic (DBS) + WB | | |



# *Spinal cord stimulation - illustration of the approach*

9 Participants: 2 Groups *Clinical study (STIMO): EES Rehab protocol = Closed-loop EES + neurorehab w/ support (4 or 5/week)*

Immediate effect – Acute phase

Biomimetic EES protocols immediately enabled all nine participants to improve or regain the ability to walk while supported in the robotic interface (Extended Data Fig. 1a). Moreover, the participants, including two with complete sensorimotor paralysis, could exert volitional control over the amplitude of their steps when EES was turned on (Extended Data Fig. 1b).

# Thank you for your attention