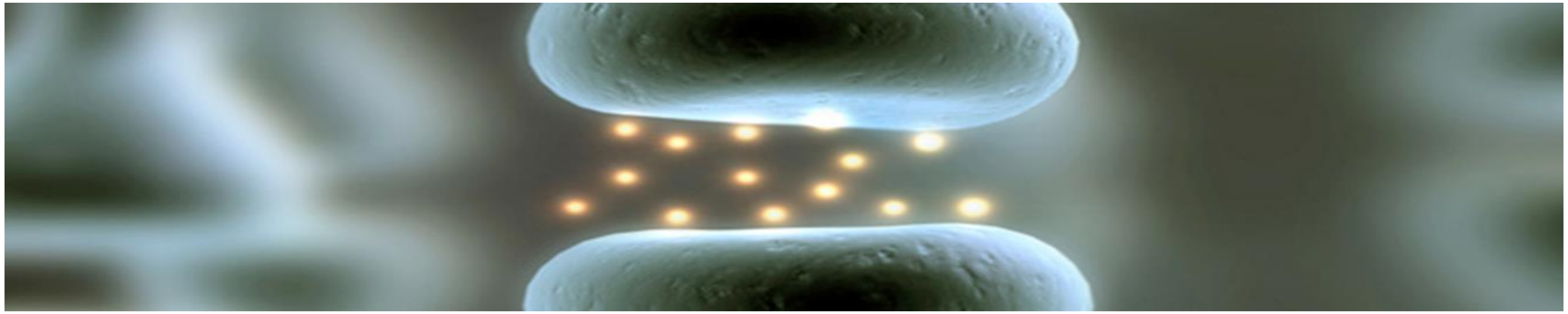
Implants designed to restore sensorimotor functions



Thomas Guiho – October 3rd 2023
M2 - Bionic
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 ?

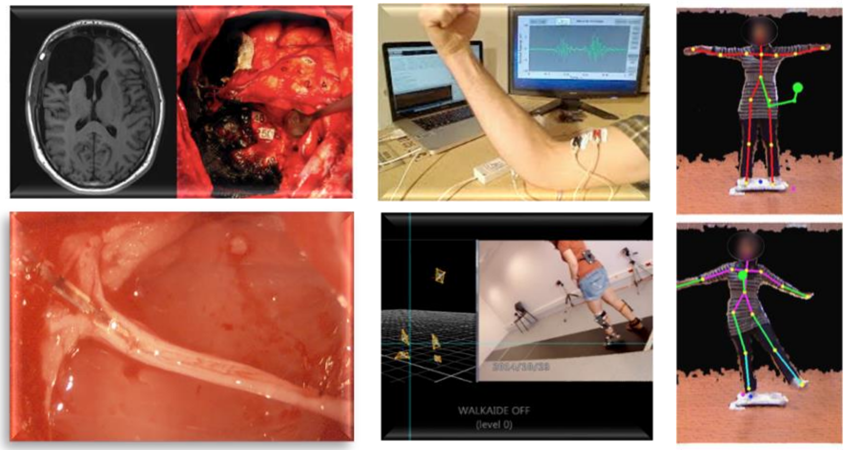
INRIA : National Institute for Research in Digital Science and Technlogy

Based in Montpellier and attached to the Sophia Antipolis center

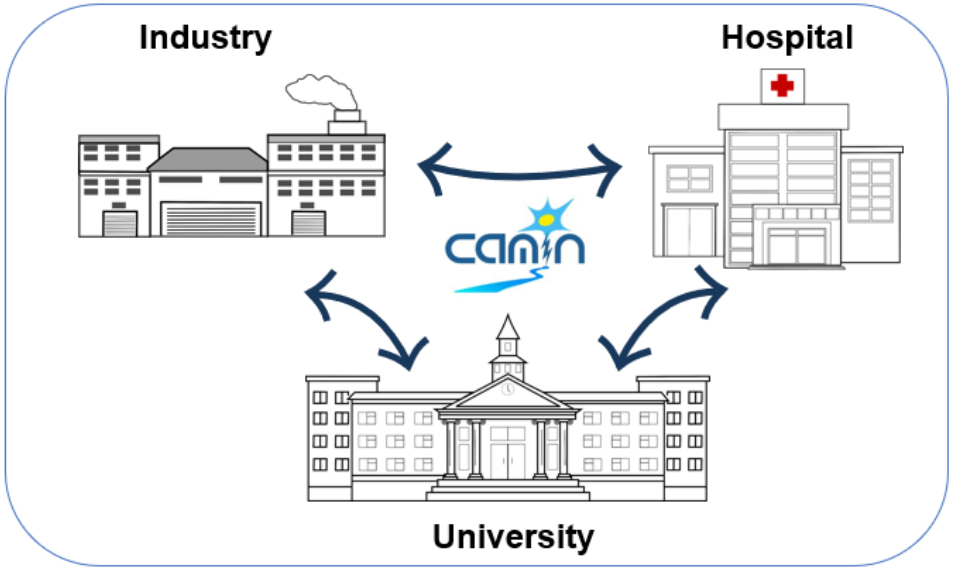
CAMIN : Dedicated to **Neuroprostheses**

Axes of research :

Exploration & analysis	**Assistance & restoration**
Electrophysiology Signal processing Sensors Technology Experimentation	Neuroprosthesis Automatic control Technology Experimentation




EXLORATION
ANALYSIS
movement
ASSISTANCE
RESTORATION


Industry
Hospital
camin
University


International collaborations
2 associated teams

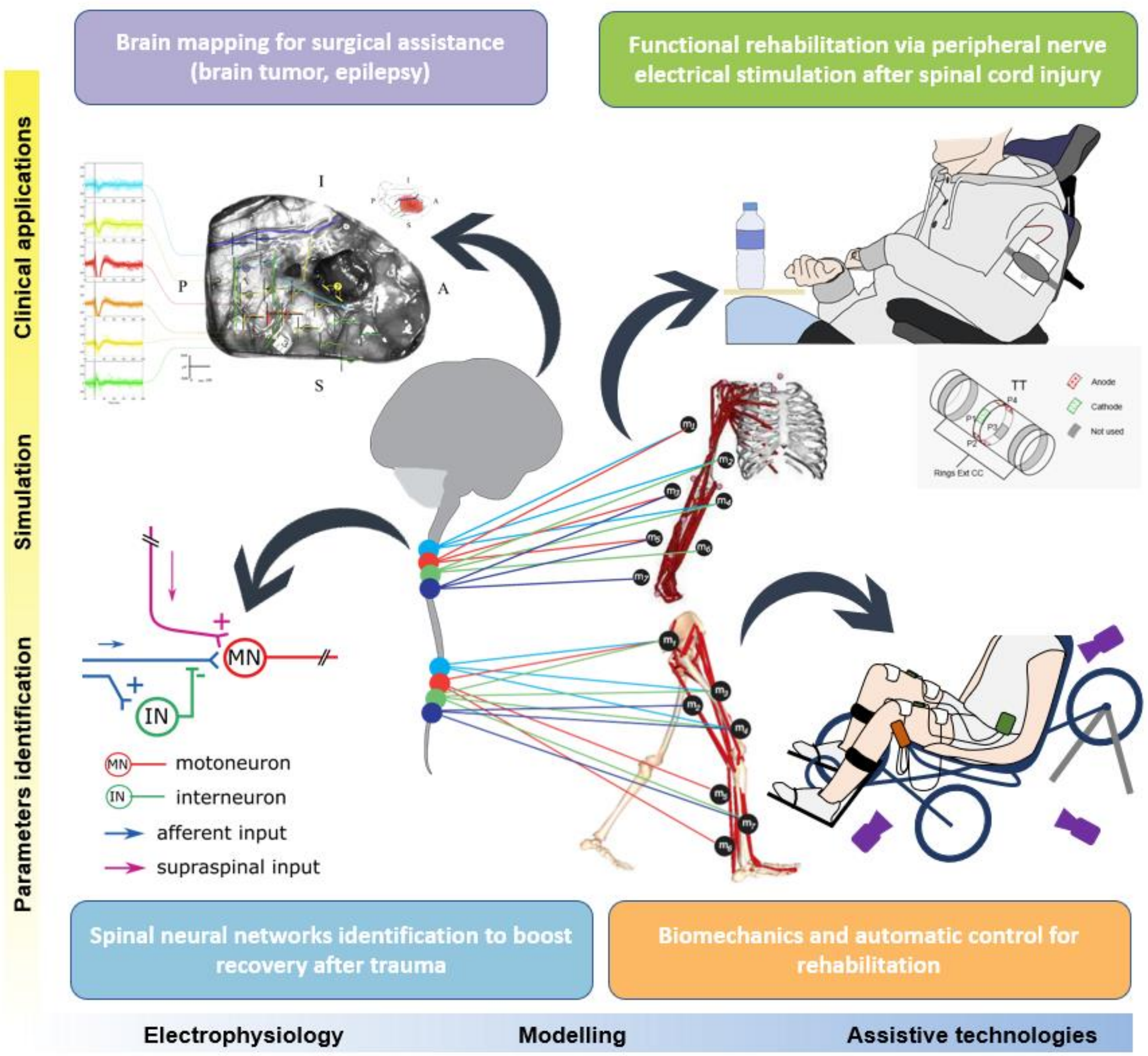
EXLORATION ANALYSIS
movement
ASSISTANCE RESTORATION

Keywords:

Sensorimotor disabilities

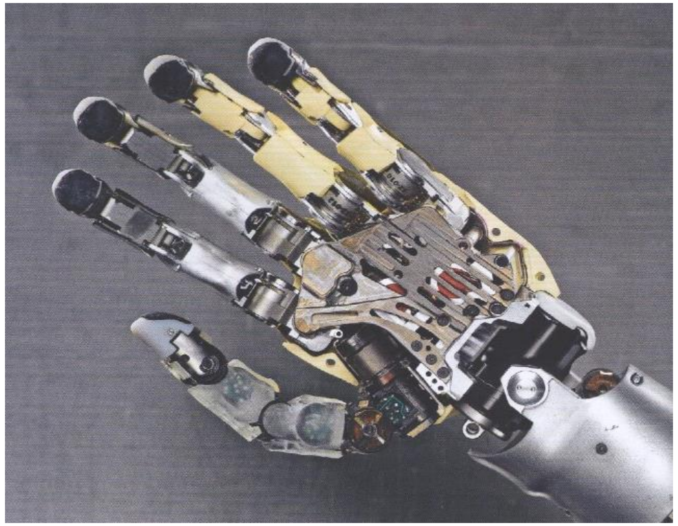
Nervous system
Biomechanics
Modeling
Simulation
Stimulation
Optimal control

Rehabilitation



B - Neuroprostheses ?

These devices, connected to the nervous system and responding to commands from the brain, are called neural or bionic prostheses.

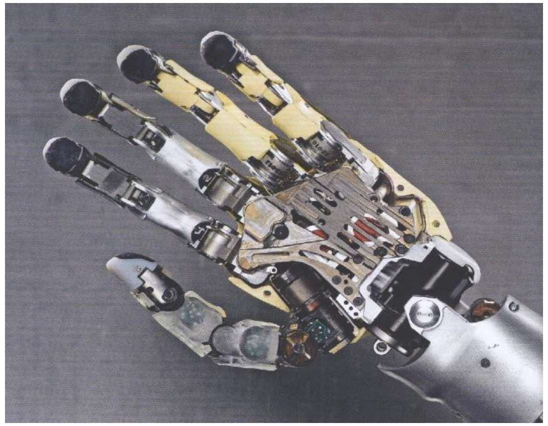


(National Geographic, February 2010)

B - Neuroprostheses ?

an .

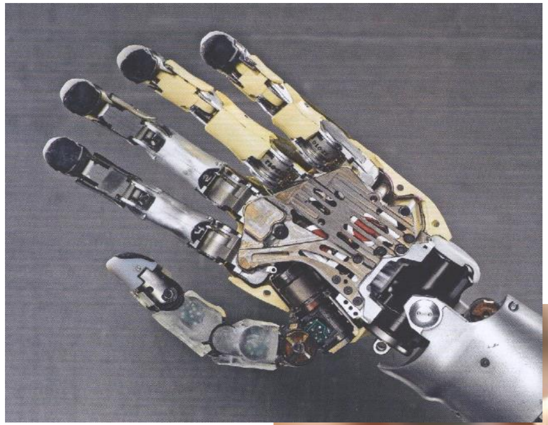
B - Neuroprostheses ?



Artificial **organ** that
replaces a living limb/organ

Artificial **device** that **acts**
on a living limb/organ
(mainly via the nervous system)

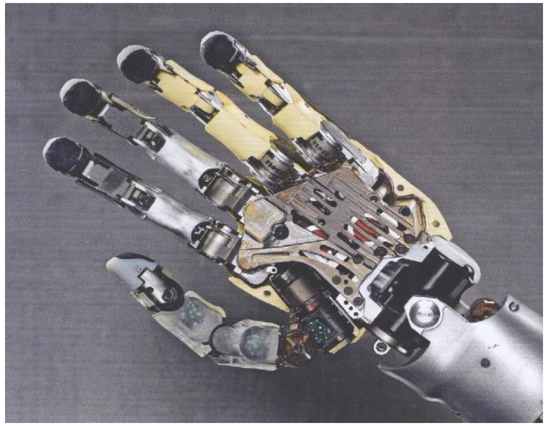
Neuroprostheses ≠ artificial organs… but confusion is easy !



Both neuroprostheses and artificial limb
Aimed at being controlled by the brain

Brain computer interface (**BCI**)

B - Neuroprostheses ?



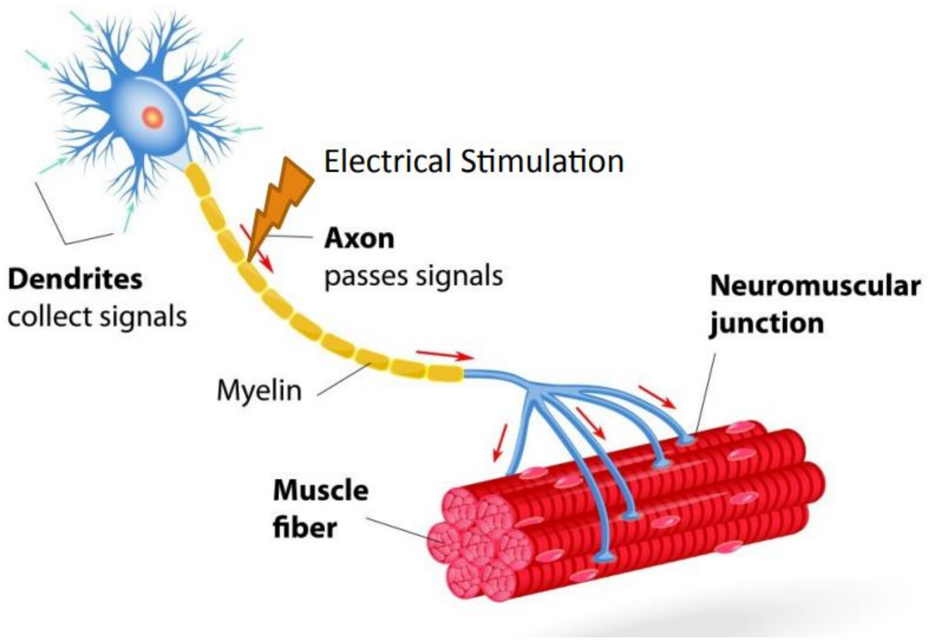
Artificial **organ** that **replaces** a living limb/organ

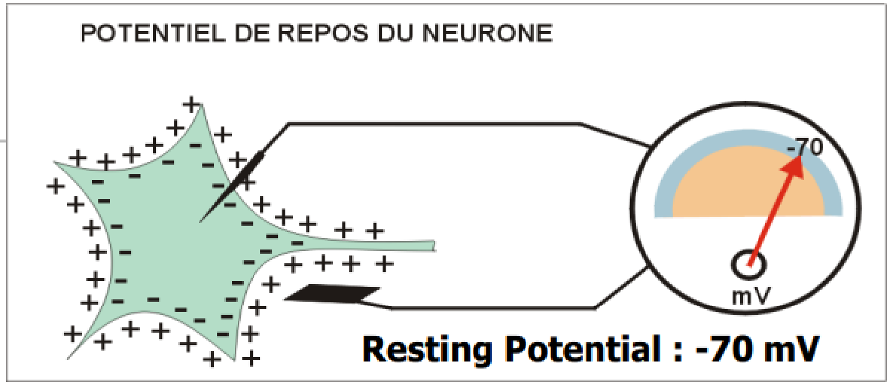
Artificial **device** that **acts** on a living limb/organ (via the nervous system)

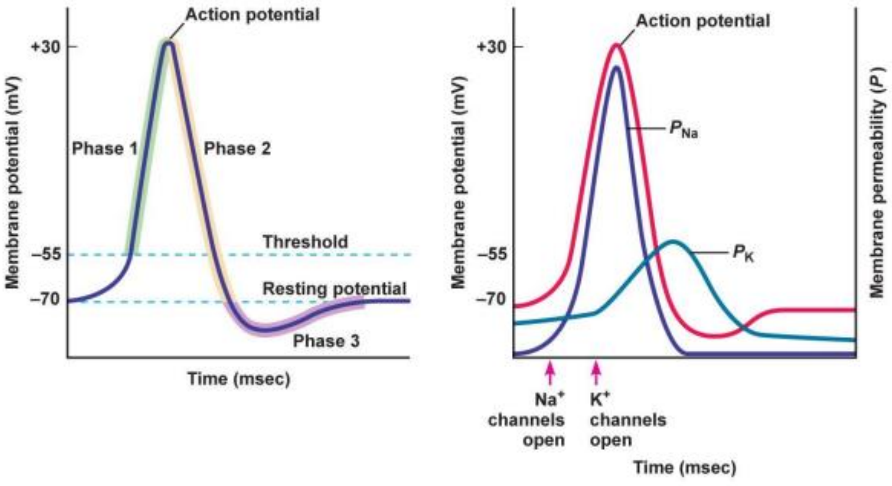
Albeit a lot in common:
Mechanics, electronics, microelectronics, computing, mathematics, etc.

C - Neuroprostheses -> Target excitable cells

Action Potentials





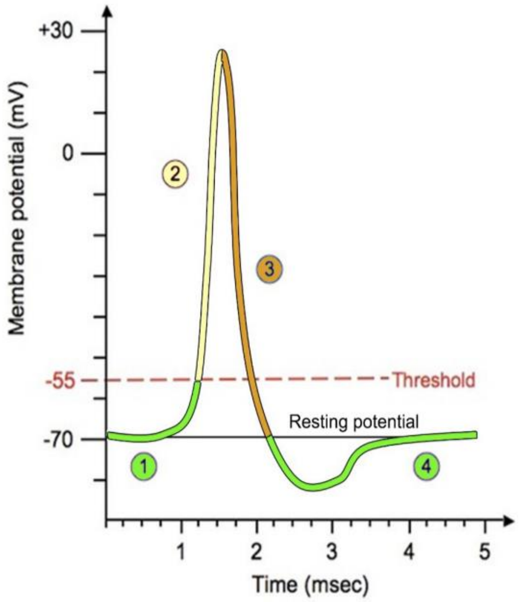


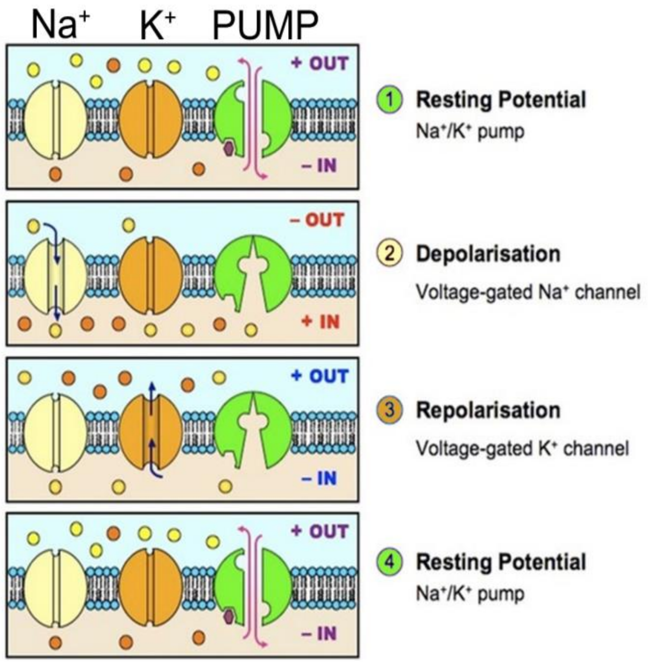
(a) Three phases of an action potential

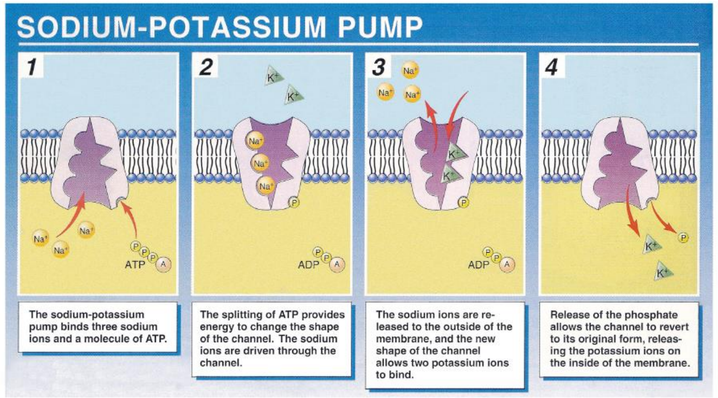
(b) Permeability changes for Na^+ and K^+ during an action potential

C - Neuroprostheses -> Target excitable cells

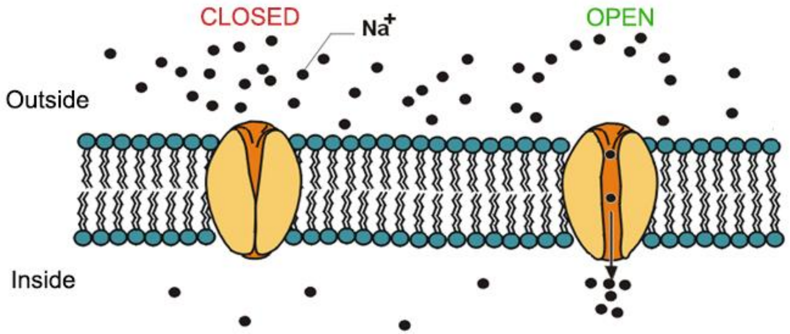
Action Potentials







sodium/potassium pump

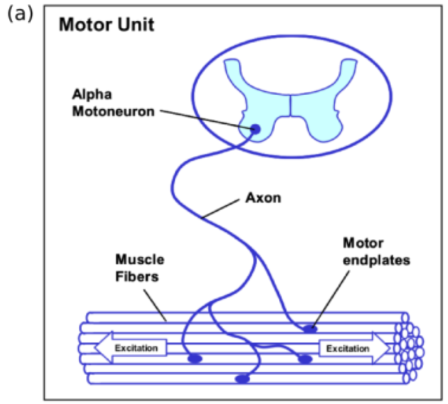


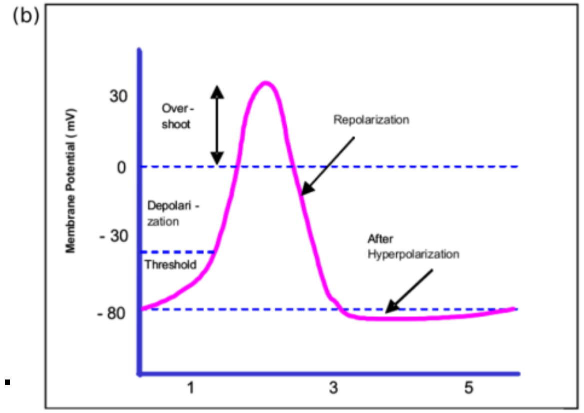
Voltage-gated Na+ channel

C - Neuroprostheses -> Target excitable cells

From motor neuron (MN) to muscle fibers (MF)

1. Activation of a MN with propagation of APs along the axon.
2. Release of transmitters at the motor plate.
3. Diffusion of ions (incoming Na+) at the semi-permeable membrane of the MFs (sarcolemma).
4. Formation of a motor plate potential in the MFs, followed by membrane depolarisation (AP).
5. Propagation of APs from the motor plate along the fibre, in both directions (1 to 5 m/s, 110mV).
6. Repolarisation, hyperpolarisation and return to resting potential of the MFs.

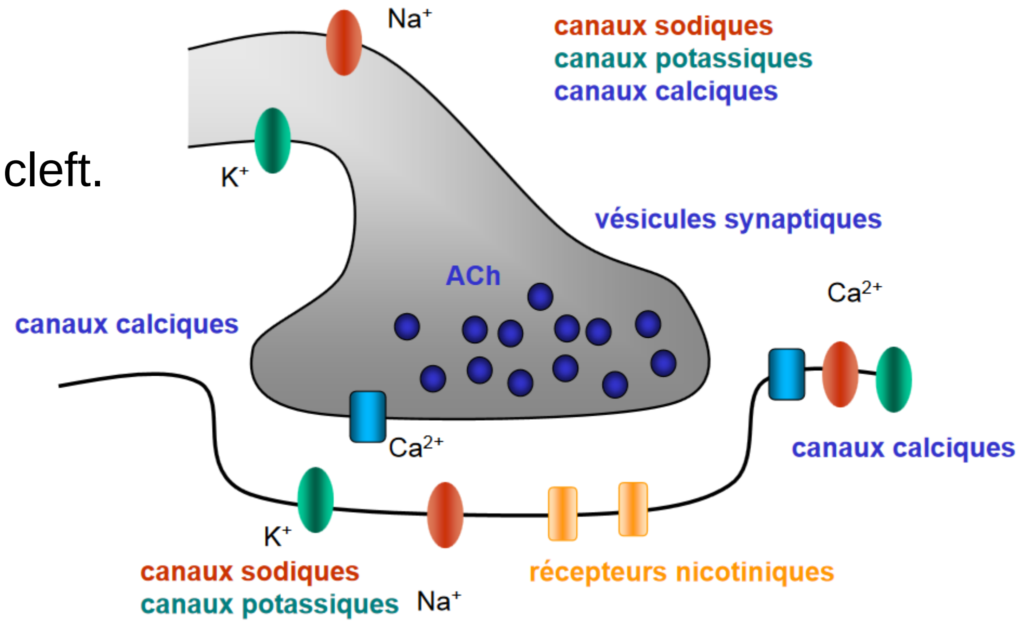




C - Neuroprostheses -> Target excitable cells

Biochemical cascade at the neuromuscular junction:

1. Arrival of PA at the axon terminal.
2. Ca^{2+} channels open
3. Massive influx of Ca^{2+} into the pre-synaptic element.
4. Displacement, fusion and release of ACh in the synaptic cleft.
5. Binding of ACh to nicotinic receptors.
6. Na+ channels open.
7. Na+ entry into the post-synaptic element.
8. Depolarisation of the post-synaptic membrane.
9. Degradation/recycling of Ach.

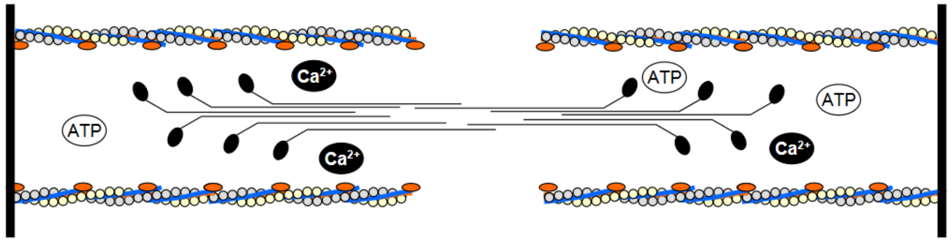


C - Neuroprostheses -> Target excitable cells

Ca2+ releases the sites :

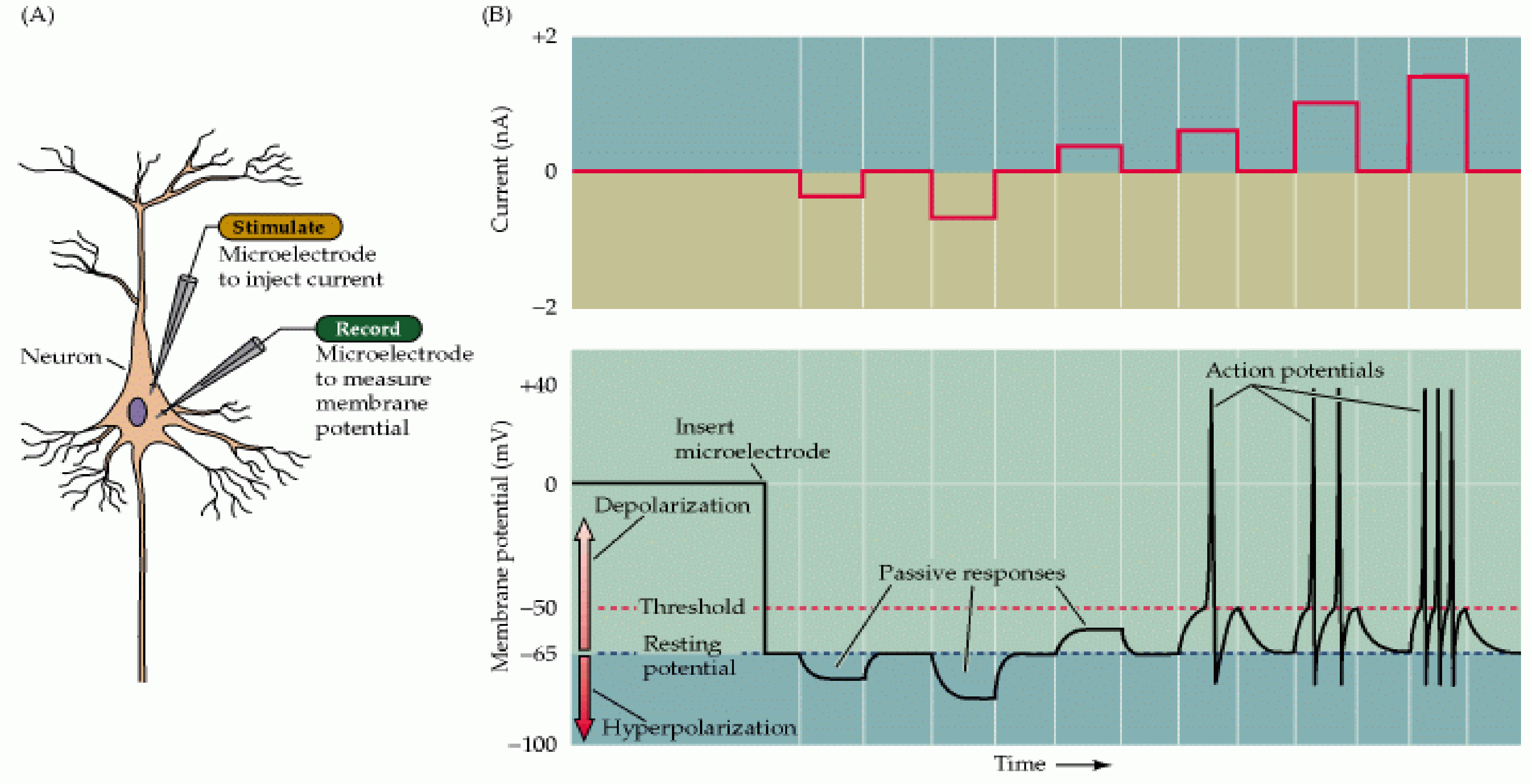
1. Myosin is attached to actin: acto-myosin complex.
2. ATP binds to the head of the thick myosin filament: actin unhooks.
3. The ATPase (enzyme in the myosin head) hydrolyses the ATP into ADP + Pi (inorganic phosphate). The myosin head can cling to the actin.
4. The ADP is detached from the myosin head.

organisation des myofilaments dans le sarcomère



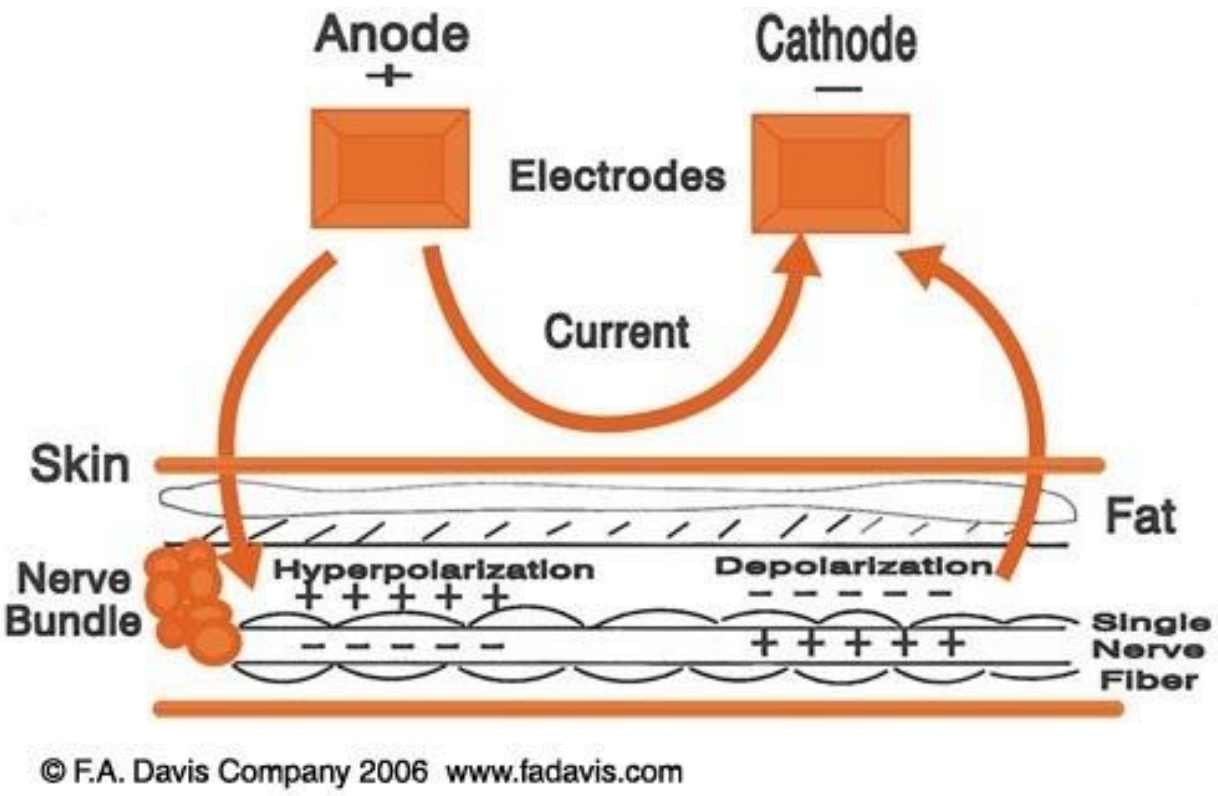
chaînes légères : responsables de l'activité ATPasique.
De cette activité ATPasique dépend la vitesse du cycle de contraction ainsi que la consommation d'ATP.

D - Principle of Electrical Stimulation



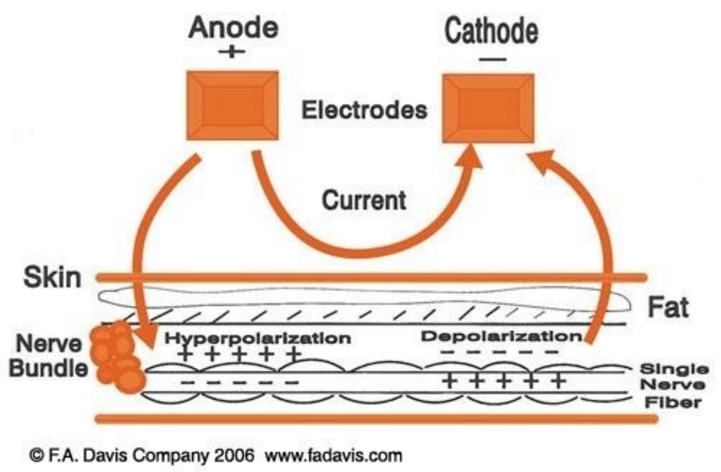
Induice an Action Potential (AP) in both directions

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

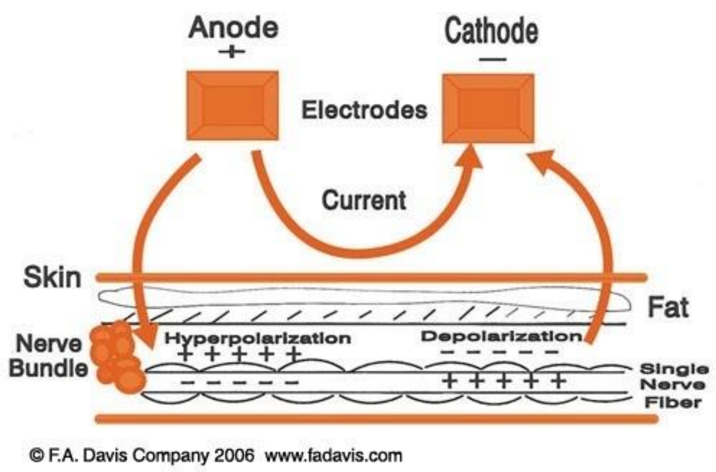
D - Principle of Electrical Stimulation

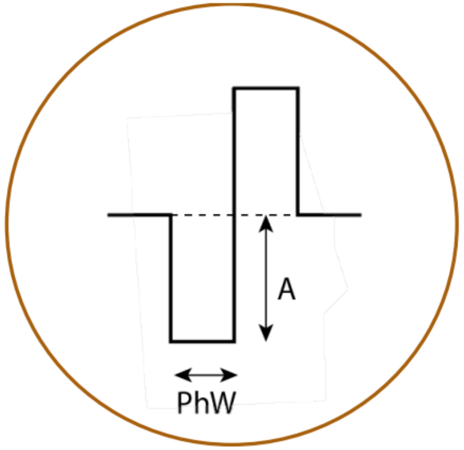
Alternating Current (AC) – Biphasic

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



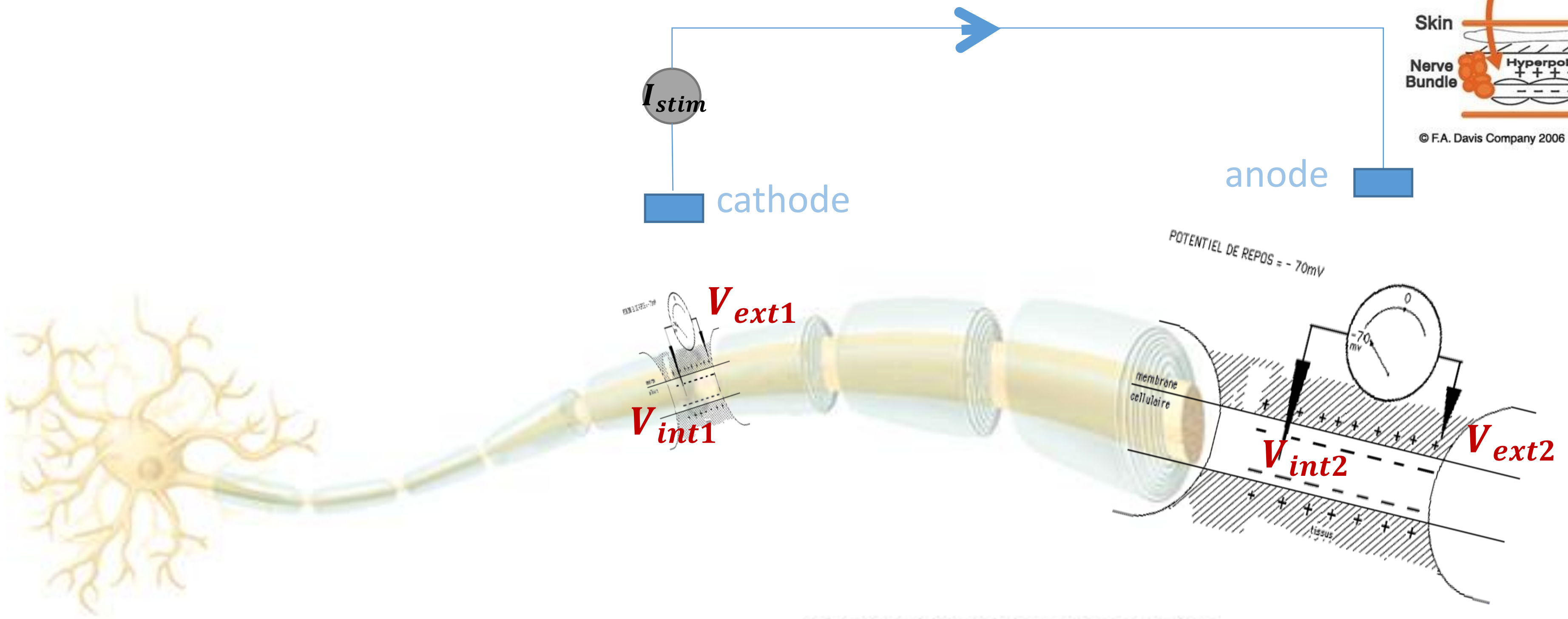


Most modern stimulators use
- Current controlled stimulation
- Biphasic charge balanced pulses

A	Current amplitude
PhW	Phasewidth
F	Frequency

D - Principle of Electrical Stimulation

Alternating Current (AC) – Biphasic



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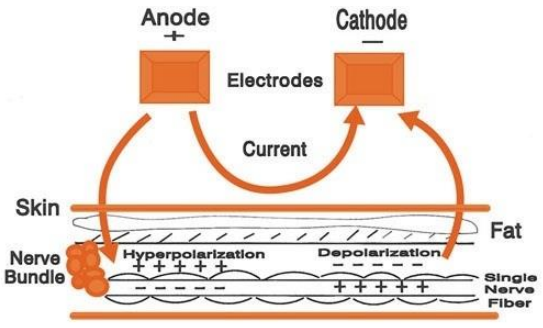

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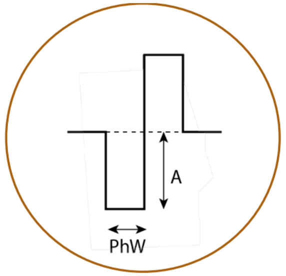


Most modern stimulators use

- Current controlled stimulation
- Biphasic charge balanced pulses

A	Current amplitude
PhW	Phasewidth
F	Frequency

D - Principle of Electrical Stimulation

Direct Current (DC) VS Alternating Current (AC)

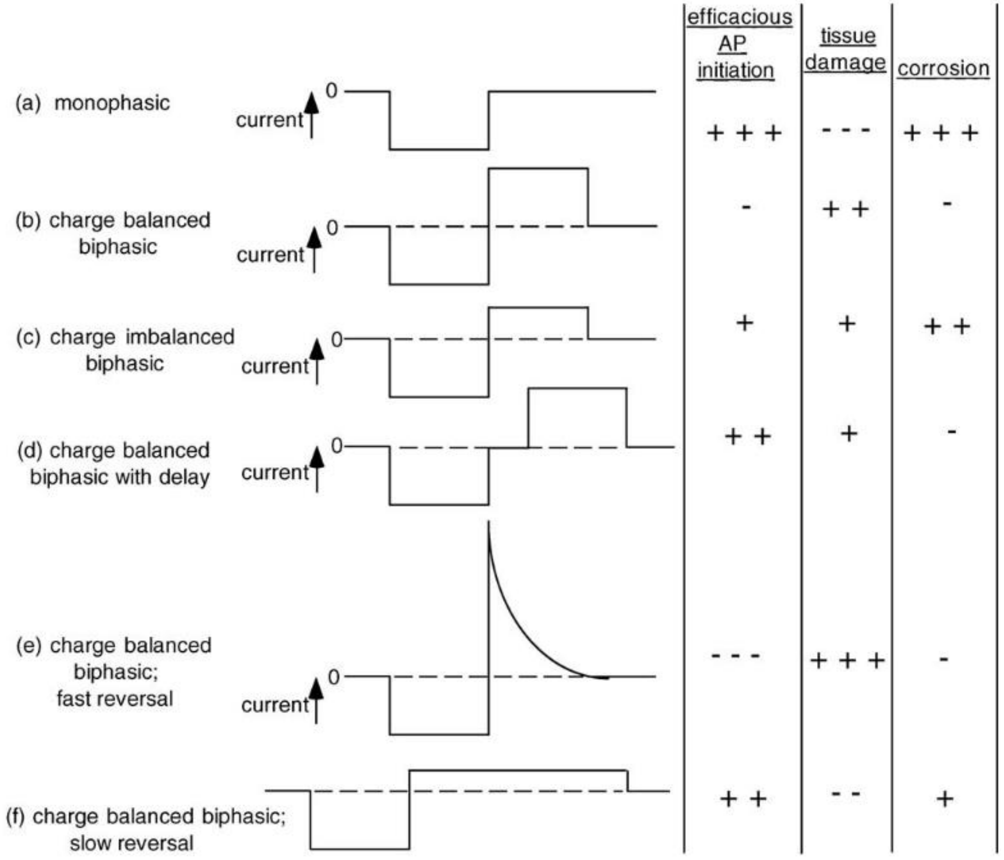
Efficiency

VS

Tissue damage

VS

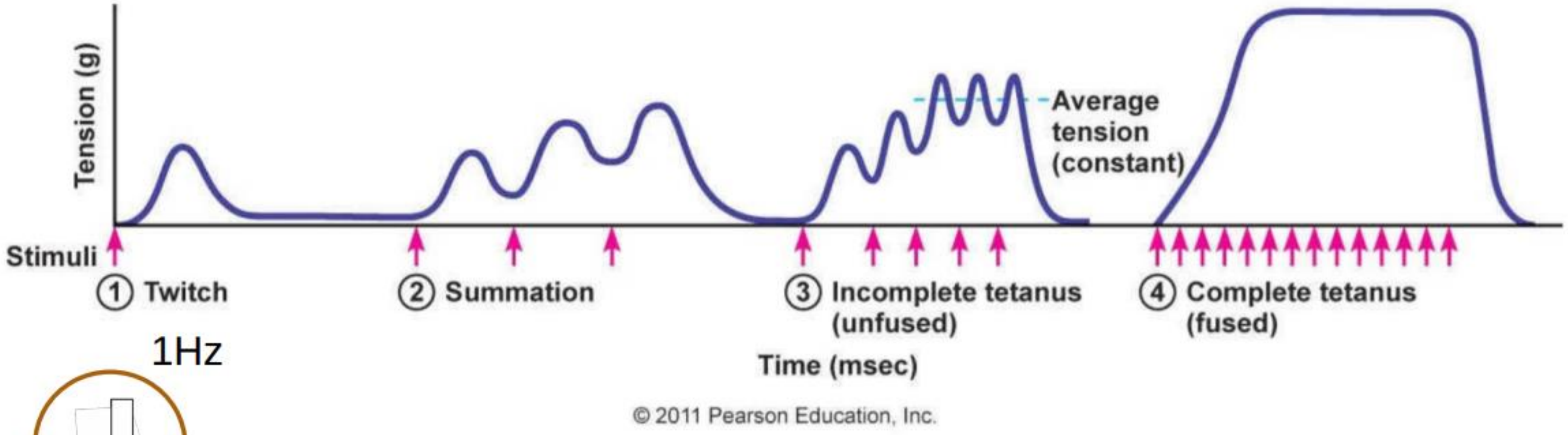
Corrosion



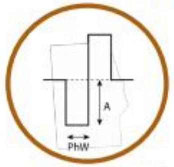
From Merrill et al., Journal of Neuroscience Methods. 2004.

D - Principle of Electrical Stimulation

Impact of stimulation frequency



1Hz



Single twitch : ~1Hz

Unfused tetanus : ~10Hz

Fused contraction : ~40Hz

Implants designed to restore sensorimotor functions

Introduction – Neuroprotheses?

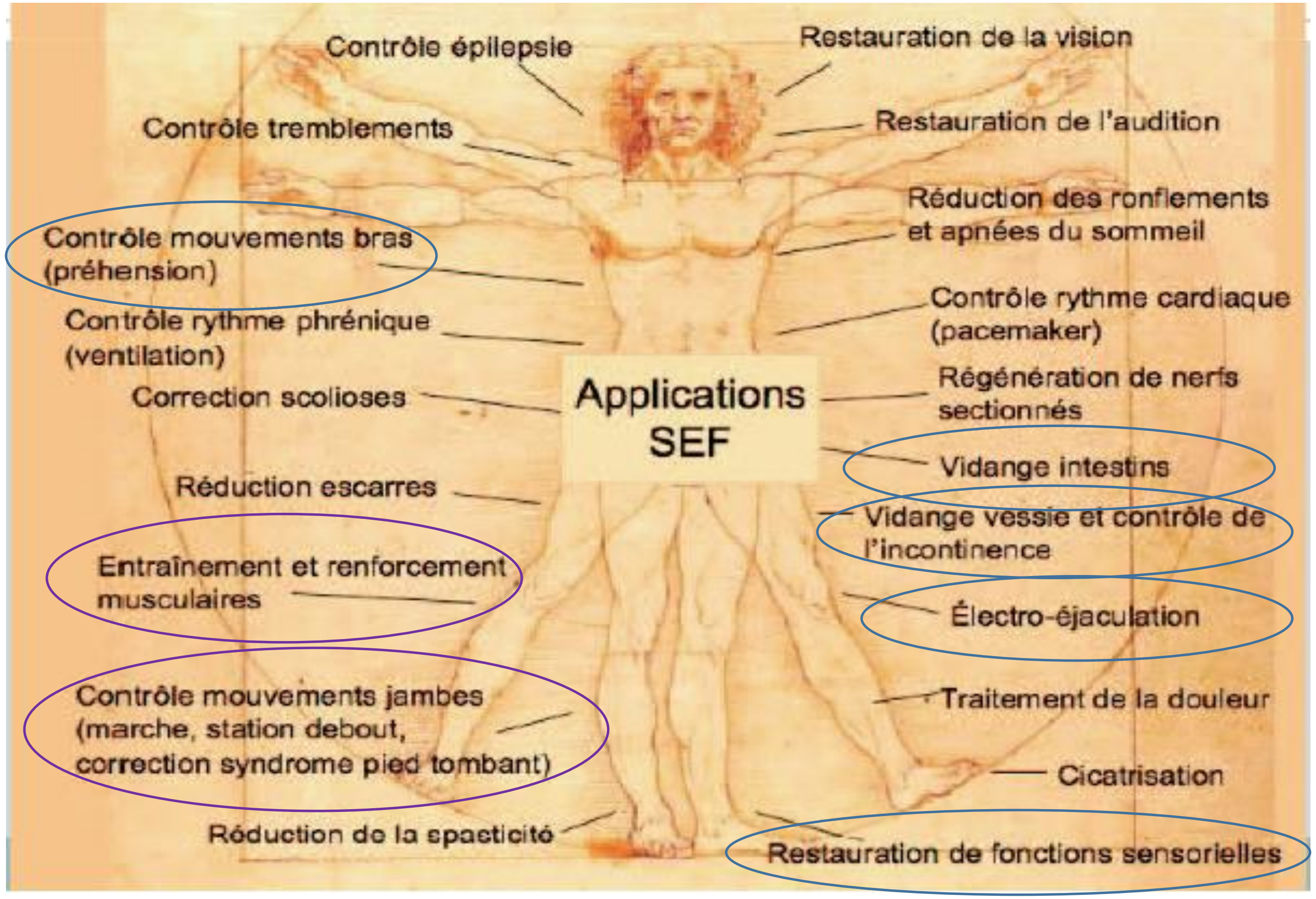
Application domains

Marketed technologies

Research perspectives

Beyond stimulation…

Areas of application



Areas of application

Categories

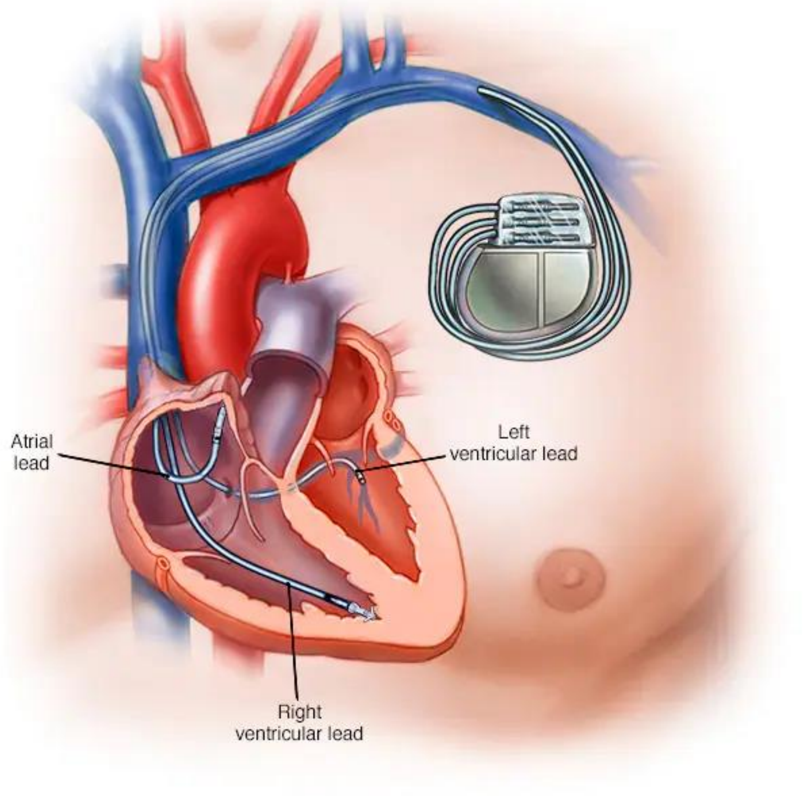
- Assistive
- Replacing
- Rehabilitation
- Recreational

• Pacemaker	(Bradyarrhythmias) & ICD
• Cochlear implants	(Deafness & Hearing loss)
• Diaphragm pacing	(Central Hypoventilation Syndrome) (The failure of automatic control of breathing)
• Drop-foot stimulator	(Post Stroke Hemiplegia)
• Bladder control	(e.g. Paraplegia)
• Hand grasping control	(e.g. Tetraplegia or Post Stroke Hemiplegia)
• Rowing & Cycling	(Paraplegia or Tetraplegia)

Areas of application

A - Pacemaker

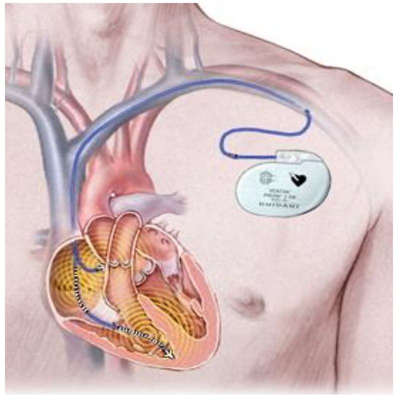
- Dilatation of the right or left heart
- Hypertrophy of the heart muscle
- Heart rhythm abnormalities: extrasystoles, tachycardias, bradycardias, etc.
- Abnormalities of the intracardiac conduction pathways.
- The ECG can also be altered by numerous medication or metabolic conditions...



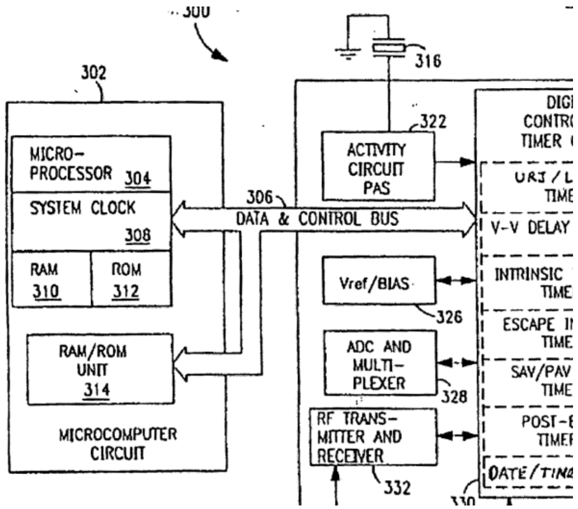
Areas of application

A - Pacemaker -> Taking pathology into account:

- Development of a 3 (or 5) letter code such as: XXX or XXXXX
  - The first letter = chamber driven by stimulation
    - A (Atrium) / V (Ventricle) / D (Double) / O (None)
  - The second letter = chamber listened to
    - A (Atrium) / V (Ventricle) / D (Double) / O (None)
  - Third letter = response to detected activity
    - I (Inhibition) / T (Training) / D (Double Response) / O (None)
- Bonus: The 4th and 5th letters found on some pacemakers:
  - The fourth letter = frequency modulation
    - R (Frequency modulation) / O (None)
  - The fifth letter = multisite training for arrhythmia control
    - P (training if bradycardia) / S (shock if tachyarrhythmia) / D (dual function) / O (none)



http://www.questmachine.org/

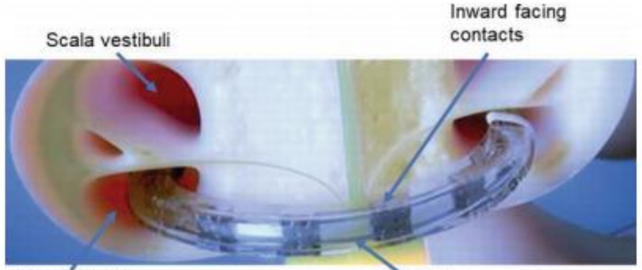


https://wiki.engr.illinois.edu/

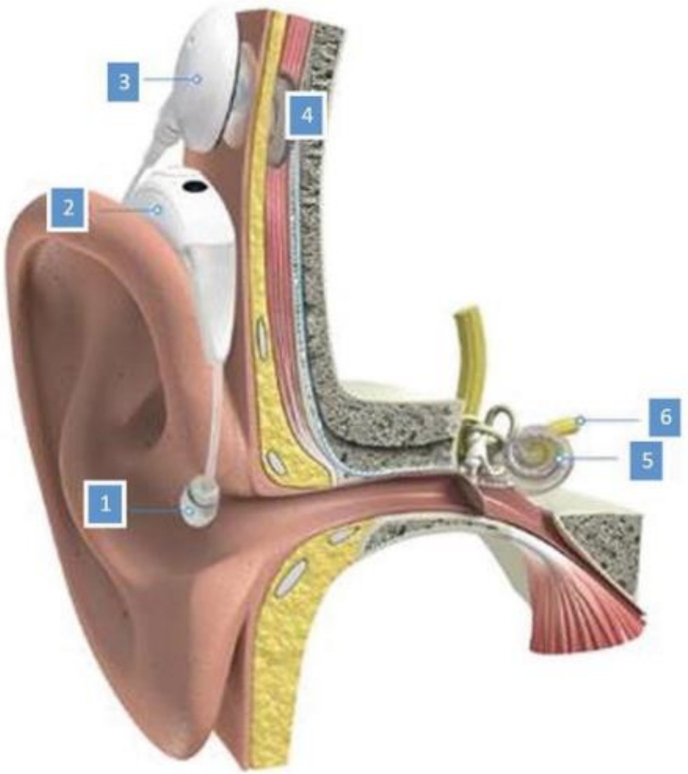
Areas of application

B - Cochlear implant

-> Cochlear implants (Deafness & Hearing loss)
~600 000 implants in 2016
Used for more than 40 years



View of how an electrode array is positioned within the scala tympani of the cochlea, here with the electrode contacts facing towards the modiolar wall behind which the spiral ganglion cell bodies are located



The components of a behind the ear (BTE) model of cochlear implant showing (1) the T-mic placed in the external ear canal, (2) BTE sound processor, (3) radio frequency transmitting headpiece, (4) the implant body, (5) intra-cochlear electrode array and (6) the auditory nerve.

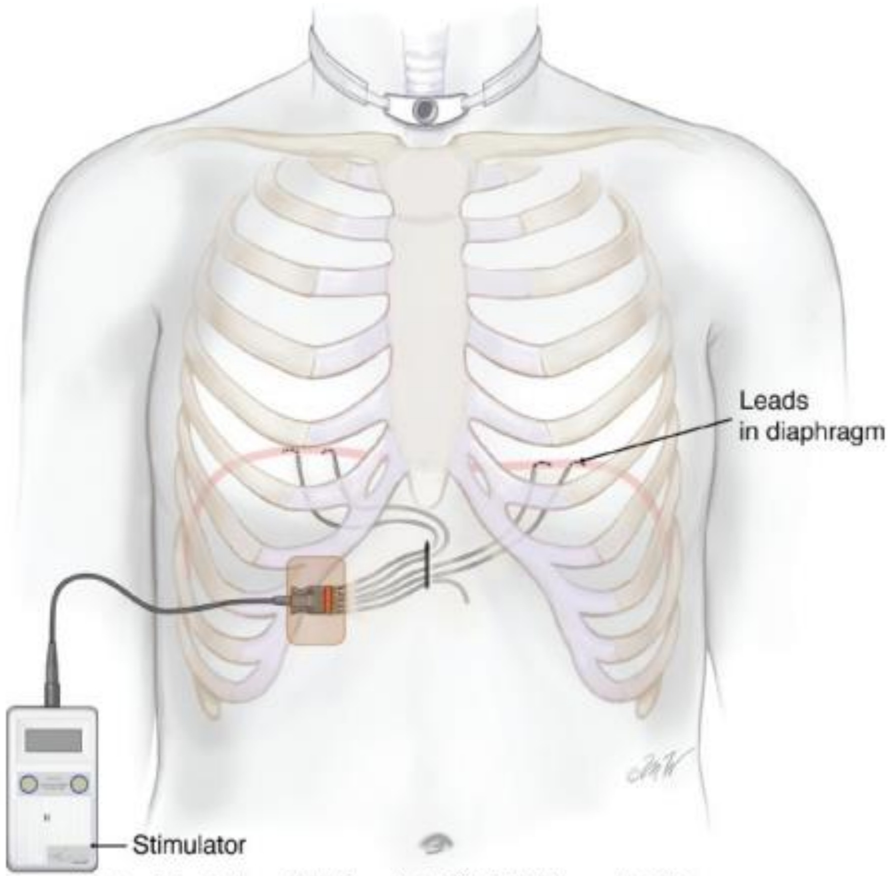
https://www.intechopen.com/books/the-human-auditory-system-basic-features-and-updates-on-audiological-diagnosis-and-therapy/electrical-stimulation-of-the-auditory-system

Areas of application

C - Diaphragm Pacemaker

-> Diaphragm pacing (Central Hypoventilation Syndrome)
Acquired & Congenital
Aka : Ondyne syndrome

Failure of the automatic control of breathing.

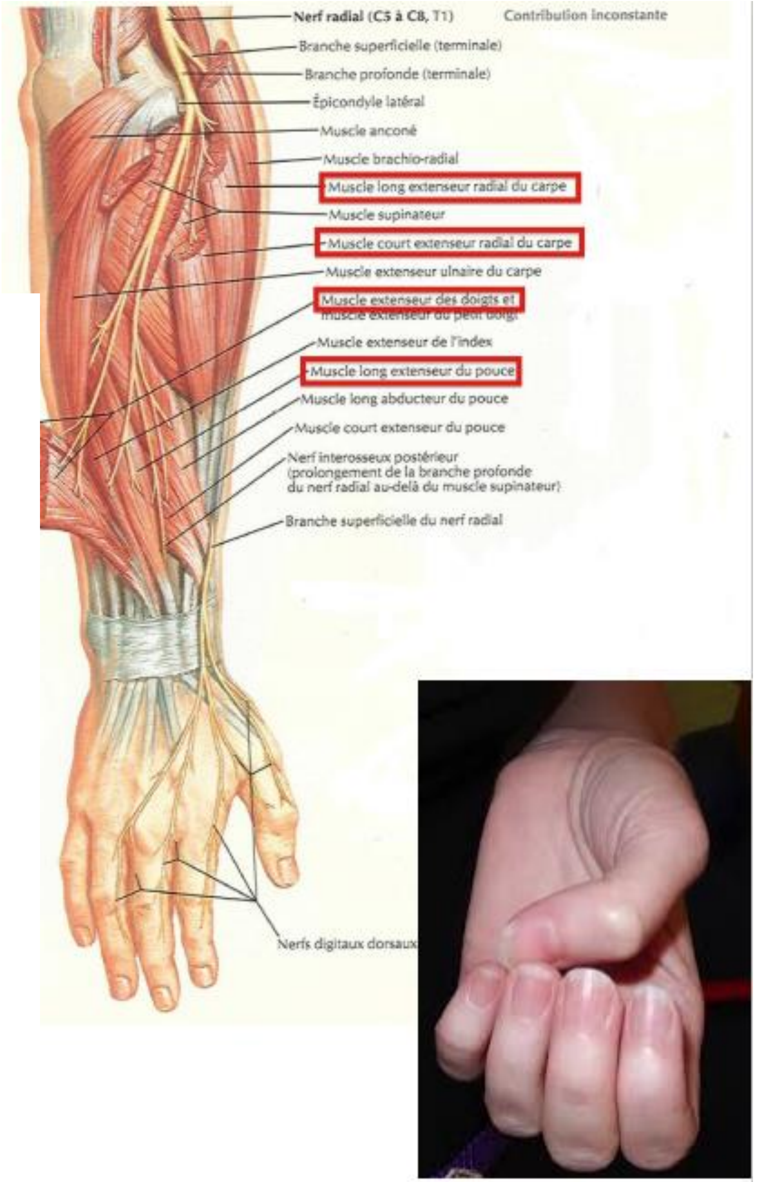


Source: D. J. Sugarbaker, R. Bueno, Y. L. Colson, M. T. Jaklitsch, M. J. Krasna, S. J. Mentzer, M. Williams, A. Adams: *Adult Chest Surgery*, 2nd Edition: www.accesssurgery.com

Areas of application

D - Stroke -> Hand Grasping Stimulator

- Partial loss of voluntary control in muscles of the paretic limbs
- Apparition of <u>Hypertonia*</u> in some muscles.
  Treatment by regular stretching and Botulinum toxin injection
  (Often the superficial flexors of the fingers and the thumb, locking the hand in a closed position)
- A hand which is not functional any more because of the inability to open and achieve prehension.
- Complex neurological context
  (Brain-damaged patients, cognitive abilities sometimes diminished, Aphasia, <u>agonistic/antagonistic contractions</u>)

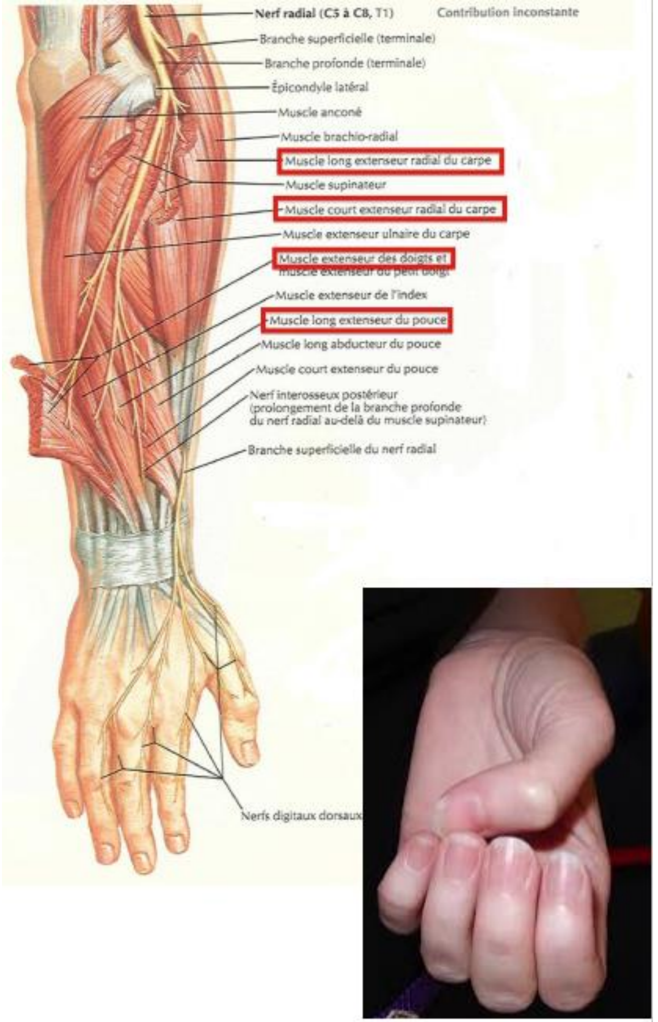


<u>*Hypertonia</u> = Permanent increase of muscle tone in a resting muscle.

Areas of application

D - Stroke -> Hand Grasping Stimulator

- Strokes are the N°1 cause of acquired handicap in adults.
- 134 000 hospitalisations for first-case strokes in France in 2012, and increasing due to the ageing population.
- ~50% of patients retain severe deficiencies due to the stroke.
- ~80% of these patients retain a prehension deficit following the stroke.
- No therapeutic alternative currently allows significant improvements in the prehension abilities of these patients.



https://www.inserm.fr/information-en-sante/dossiers-information/accident-vasculaire-cerebral-avc
https://www.irdes.fr/recherche/questions-d-economie-de-la-sante/234-parcours-de-soins-des-personnes-hospitalisees-pour-un-accident-vasculaire-cerebral.pdf

Areas of application

D - Stroke -> Drop Foot Stimulator

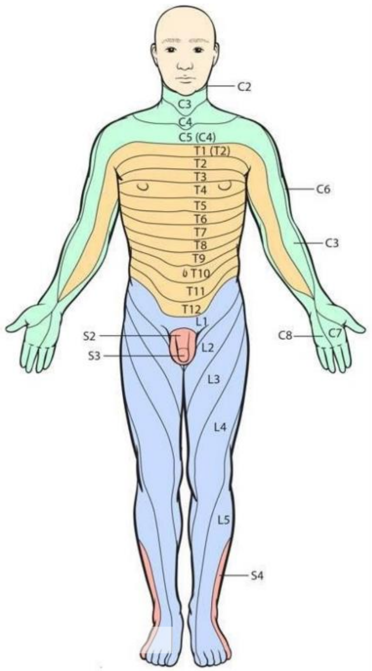
-> Drop foot syndrome (Post Stroke Hemiplegia)

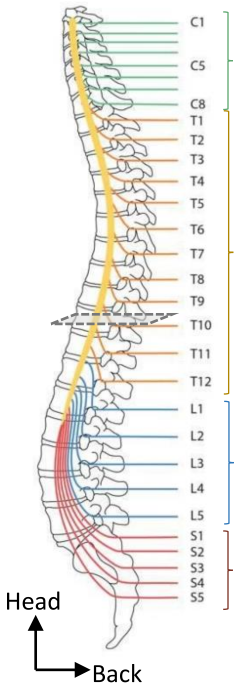
Inhibited foot dorsiflexion resulting in lack of propulsion and raising of the foot supposed to help when clearing the ground to go to the swing phase.

Creating abnormality in the gait cycle and resulting in compensative walking patterns inducing body asymetry.

Implants designed to restore sensorimotor functions

In a context of spinal cord injuries (SCI)





<u>Niveau</u> :

Cervical

Thoracic

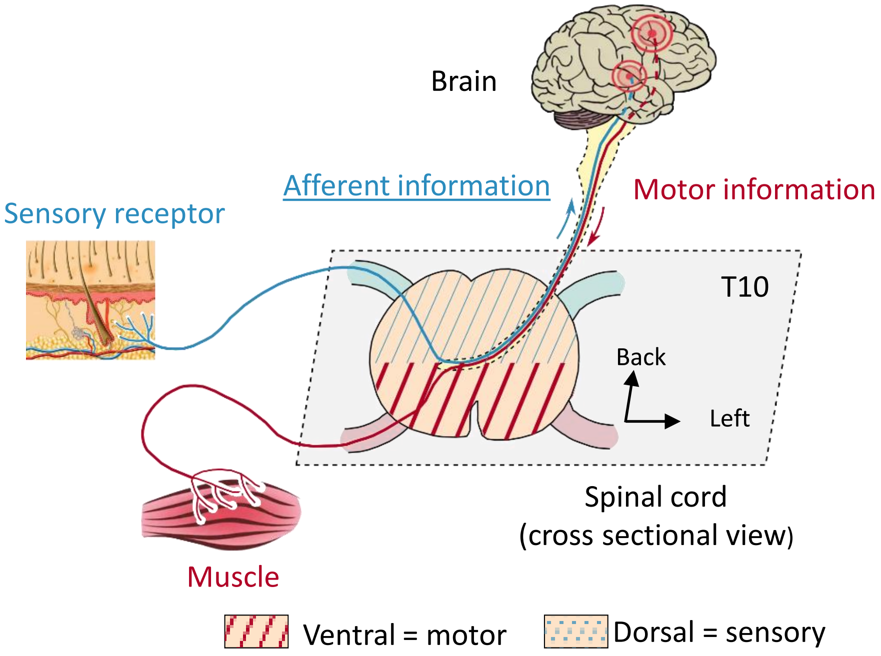
Lumbar

Sacral

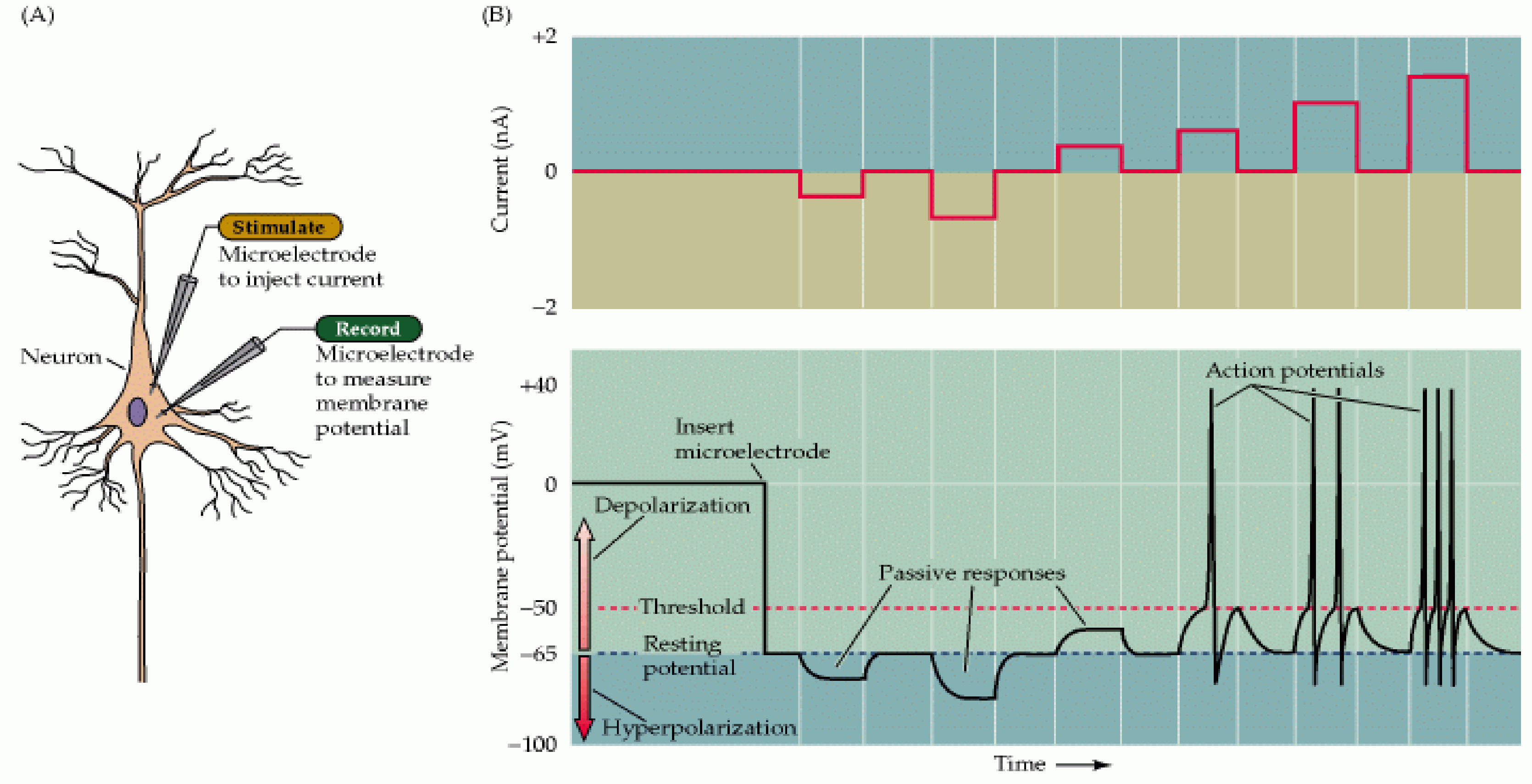
<u>In case of lesion</u> :

Level C6
(Tétraplegia)

Level T6
(Paraplegia)

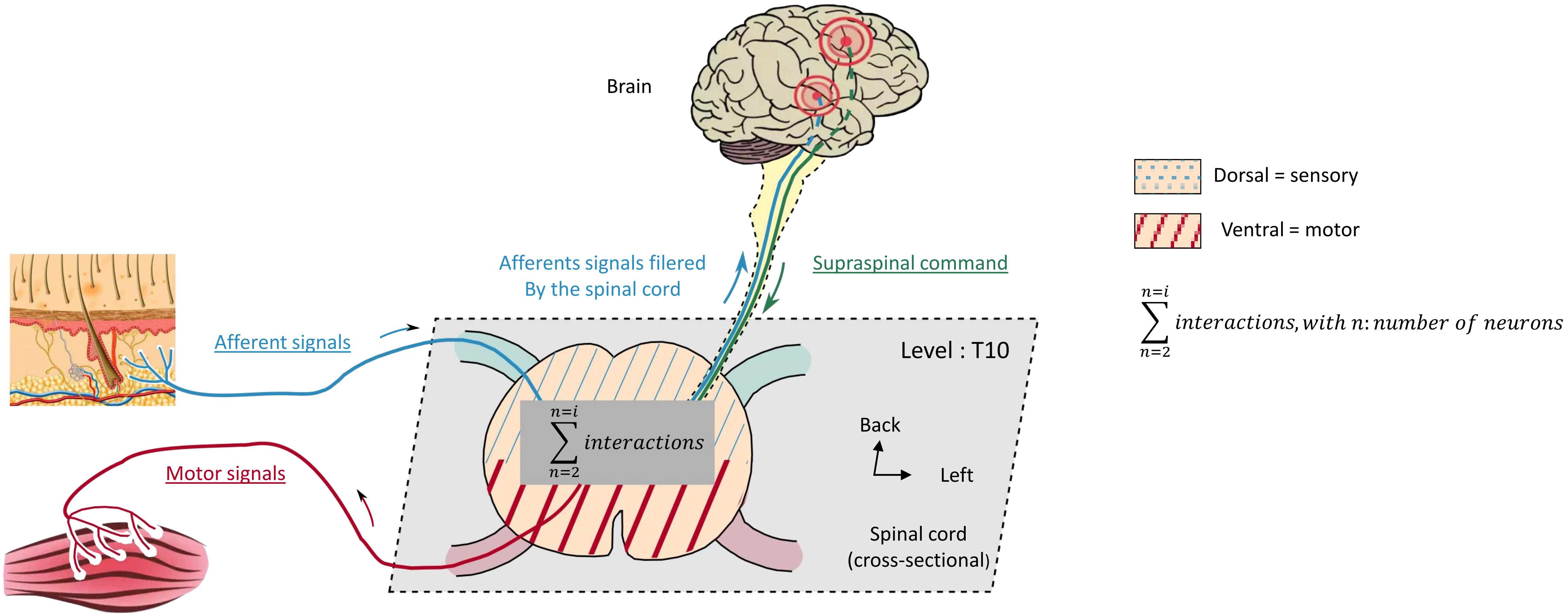


A - Electrical Stimulation and SCI



Induice an Action Potential (AP) in both directions

A - Electrical Stimulation and SCI



A - Electrical Stimulation and SCI

Target <-> Strategies

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

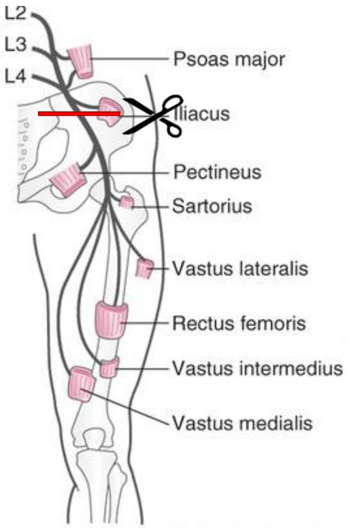
-> Muscle stimulation

-> Peripheral nerve stimulation

-> Spinal cord stimulation

Expertise of CAMIN team

New axis of research



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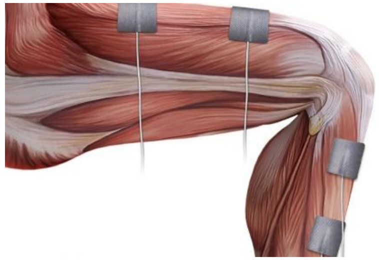
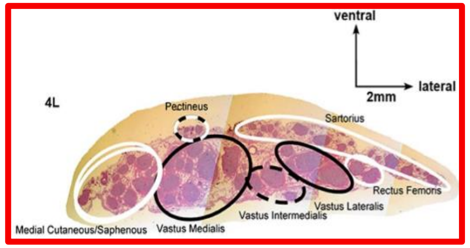
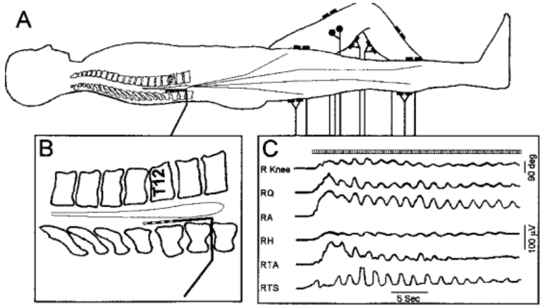




Central Nervous System:

[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

A - Electrical Stimulation and SCI

Compensating for motor impairment: existing solutions

Assistive robotics

Auxiliary nurses

Assistance dogs

Limitations :

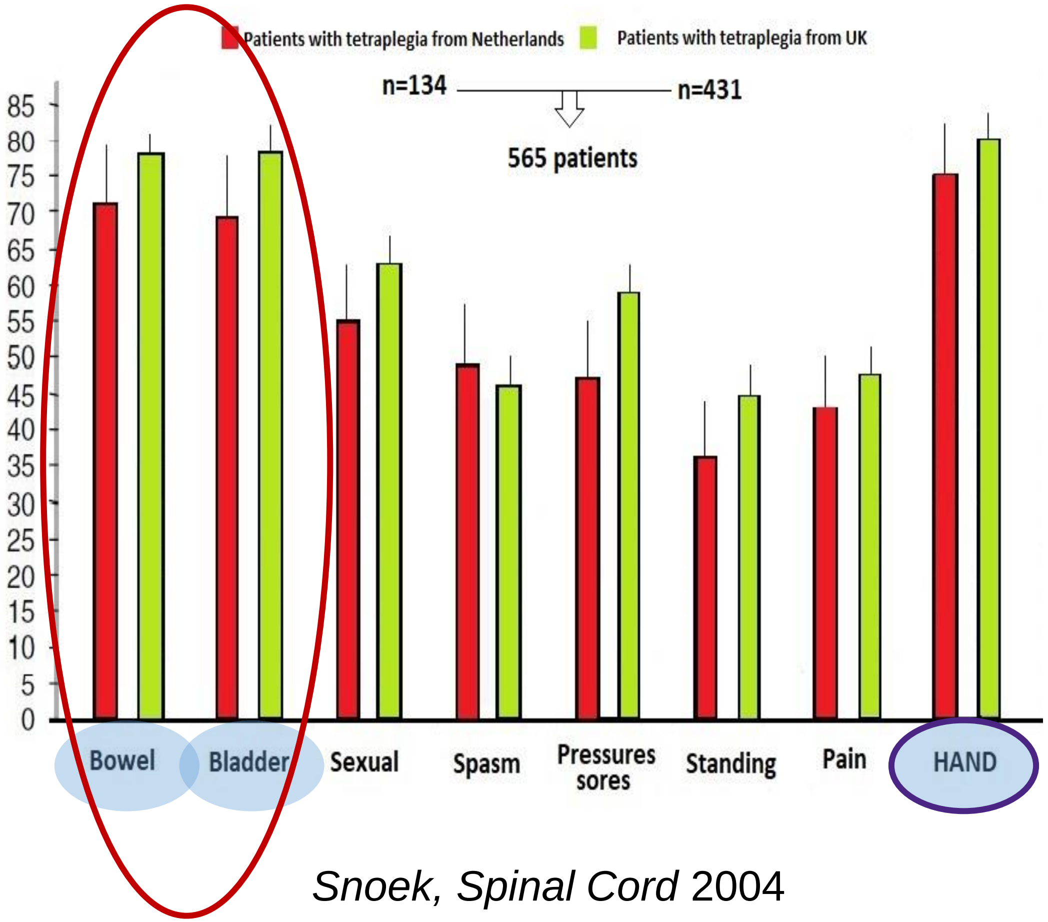
- Lack of independence in everyday life
- Bulky
- Lack of privacy
- Action is “delegated”
- Stigmatising effect

A - Electrical Stimulation and SCI

Context

Perceived impact of restoration of various functions on quality of life in a panel of tetraplegic patients.

- **Level of independance**
- **Quality of life**



Snoek, Spinal Cord 2004

A - Electrical Stimulation and SCI

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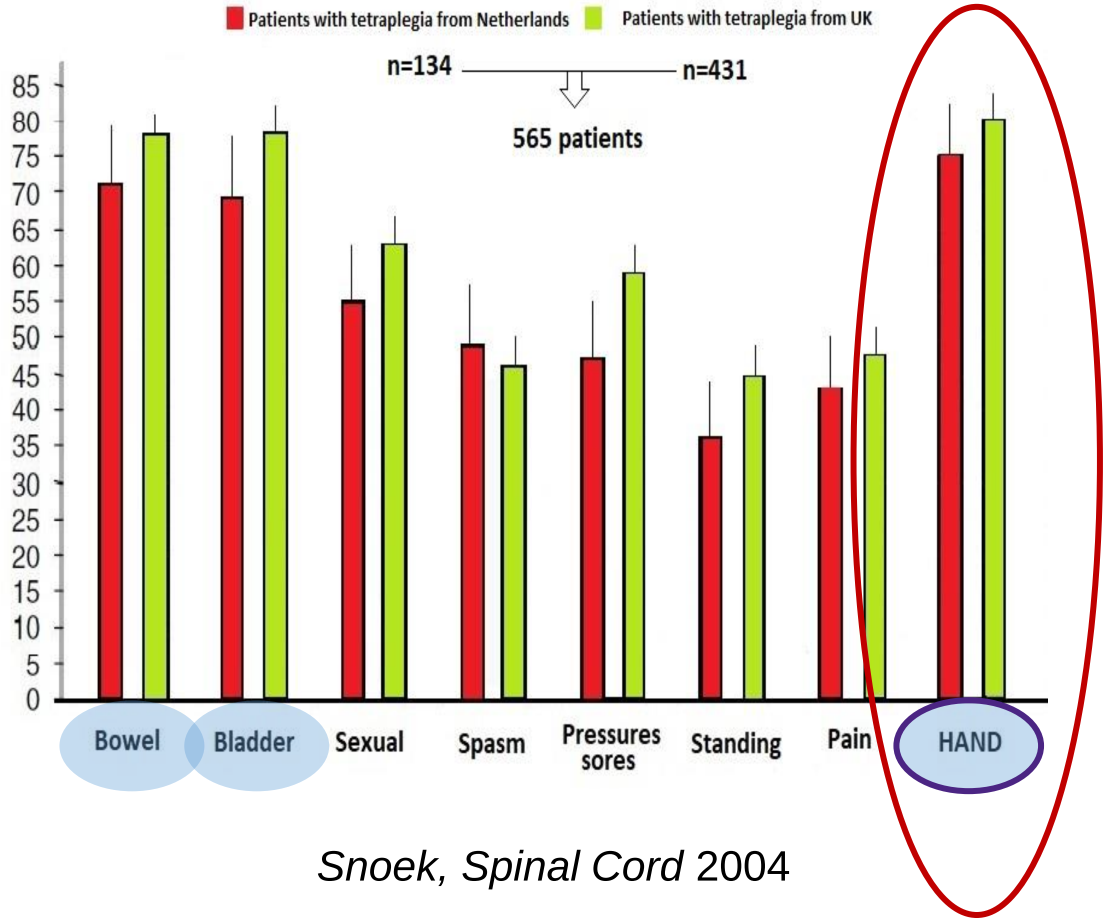


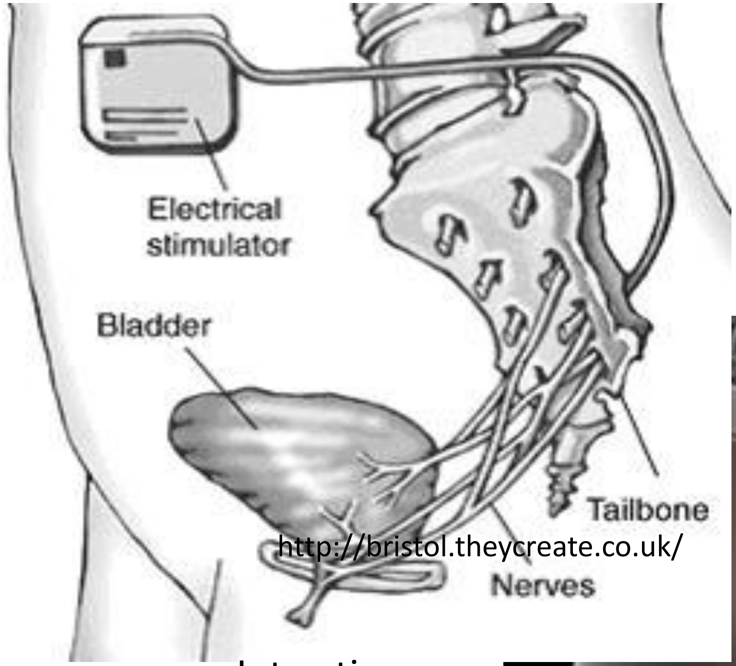
Snoek, Spinal Cord 2004

Functional Electrical Stimulation and SCI

A - SCI -> Visceral functions

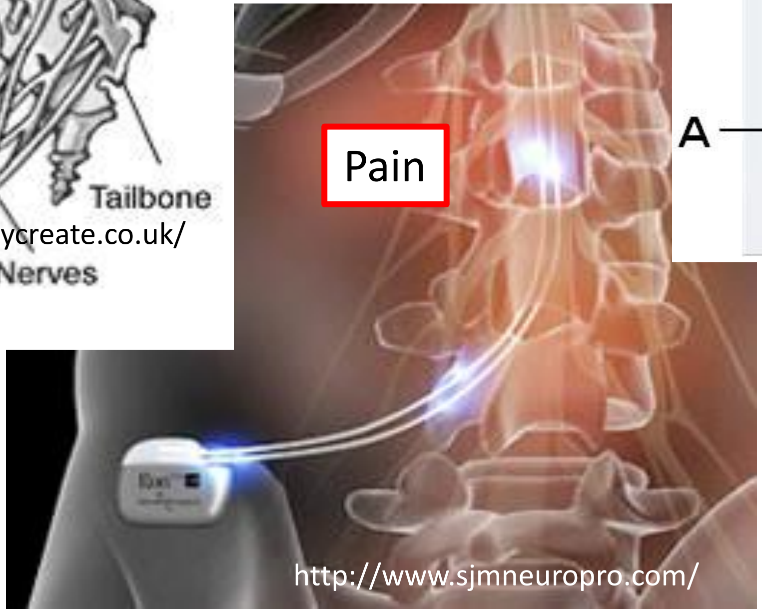
Incontinence

Micturition

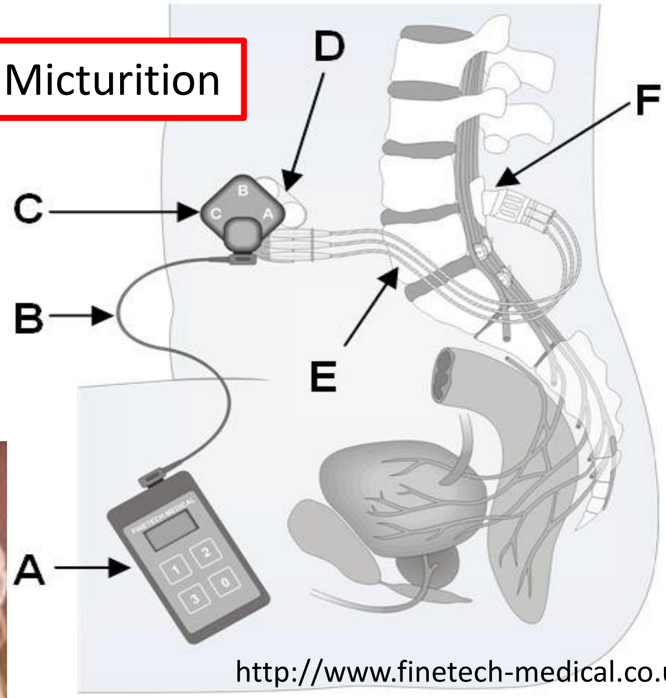


Interstim
(Medtronic, USA)

Pain



Eon
(ANS, St Jude, USA)

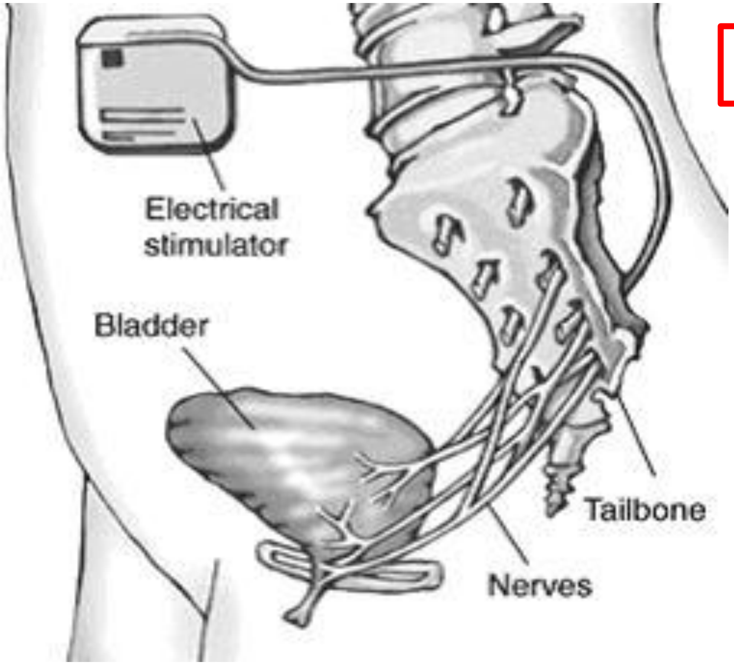


Brindley
(Finetech, UK)

Stimulation on the same sites …
COHABITATION ?

Functional Electrical Stimulation and SCI

A - SCI -> Visceral functions (Interstim implant, Medtronic USA)



http://bristol.theycreate.co.uk/

Incontinence

Interstim
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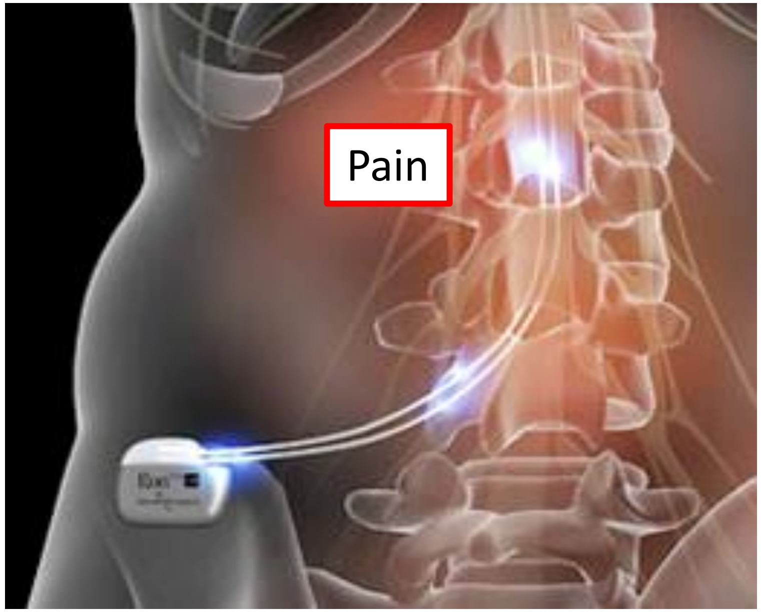


Functional Electrical Stimulation and SCI

A - SCI -> Visceral functions (Finetech Brindley Bladder Control System)

- External control : Only {electrode + antenna + generator} are implanted

Finetech Brindley Bladder Control System

(VOCARE, NeuroControl in USA)

Controller

Functional Electrical Stimulation and SCI

A - SCI -> Visceral functions (Finetech Brindley Bladder Control System)

A - Electrical Stimulation and SCI

Target <-> Strategies

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

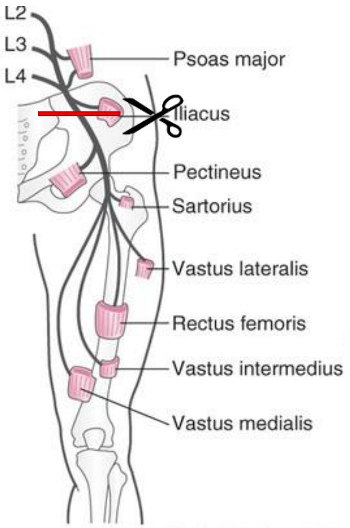
-> Muscle stimulation

-> Peripheral nerve stimulation

-> Spinal cord stimulation

Expertise of CAMIN team

New axis of research



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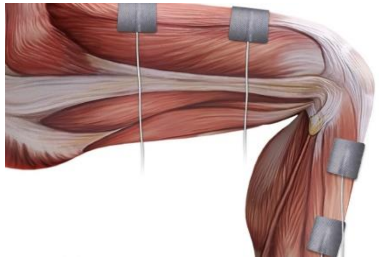

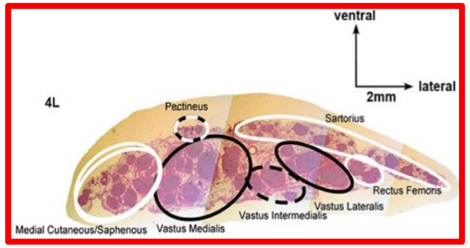

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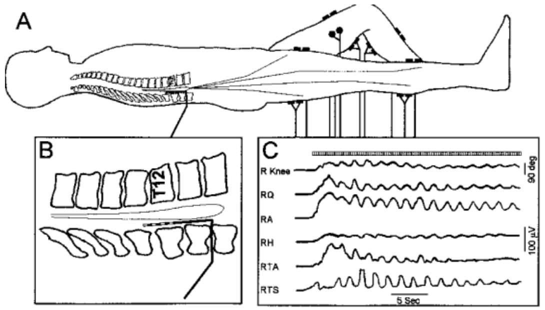

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Fuctional Electrical Stimulation and SCI

B – Upper limb function: surgery: Tendon transfer

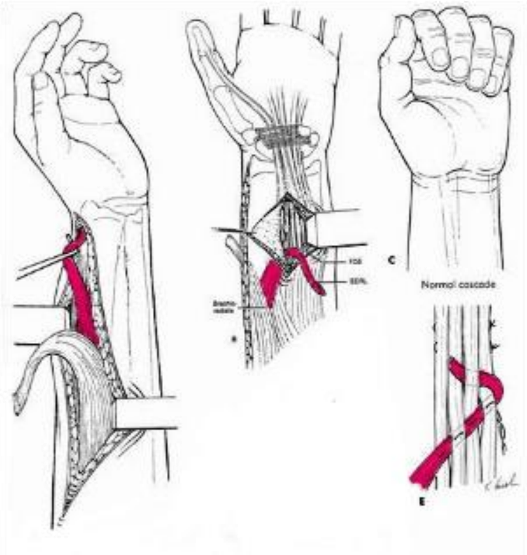
Approaches :

- 2 muscles with preserved synergistic action
- Repositioning of the tendon of one of the two muscles on a new insertion site

New muscle action

Tenodesis Effect

Tendon transfer surgery

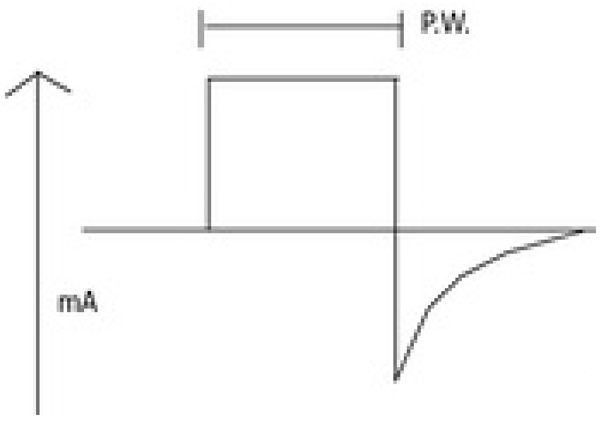


Limitations :

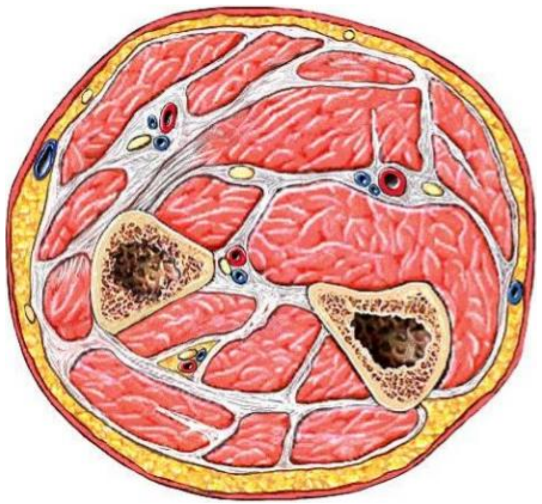
- The clamping force is moderate
- Initial synergic movement is impacted
- Not possible for all patients (synergy)

Functional Electrical Stimulation and SCI

B – Upper limb function: SCI -> Hand Grasping



Simple stimulation pattern

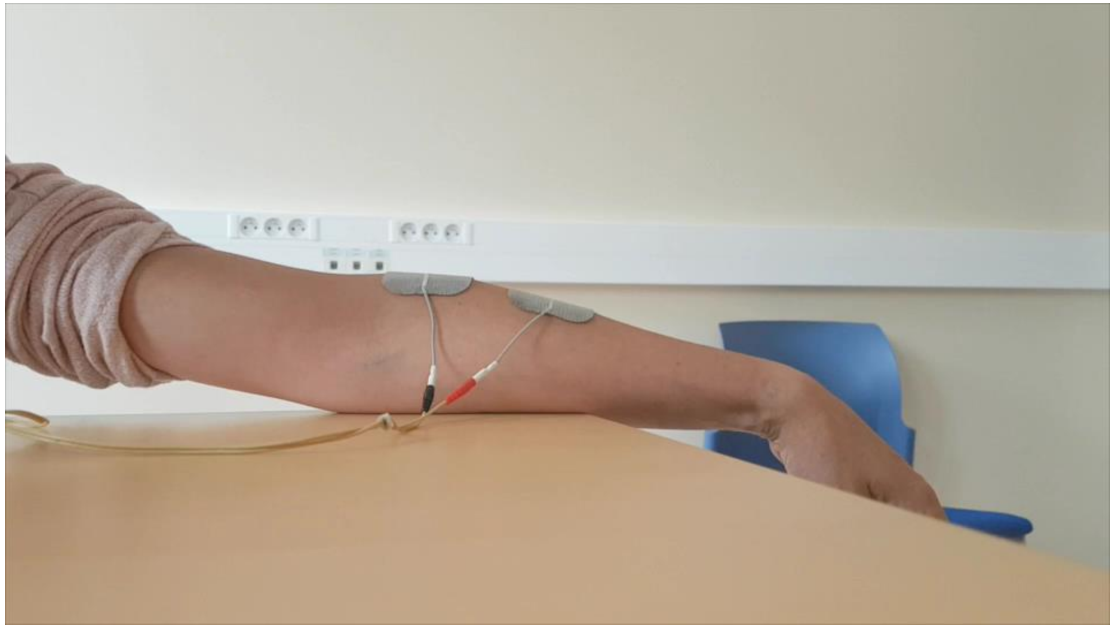


Arm muscles:
Small / In depth

External / implanted
stimulation

Functional Electrical Stimulation and SCI

B – Upper limb function: SCI -> Hand Grasping

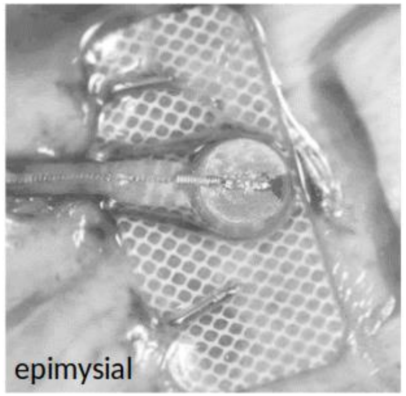


Surface electrodes -> Electrode matrix

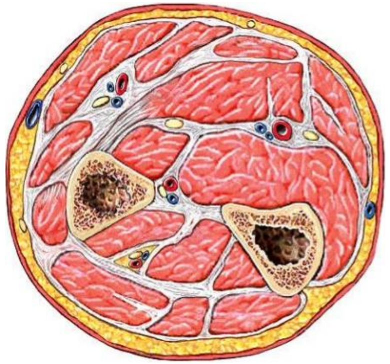
PopovićManeski et al, 2013

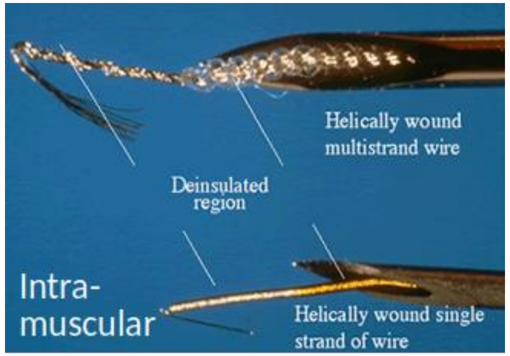
Functional Electrical Stimulation and SCI

B – Upper limb function: SCI -> Hand Grasping



Electrodes de surface -> Electrodes implantés





Functional Electrical Stimulation and SCI

B – Upper limb function -> Hand Grasping -> FreeHand System (Neurocontrol, USA, out of market)

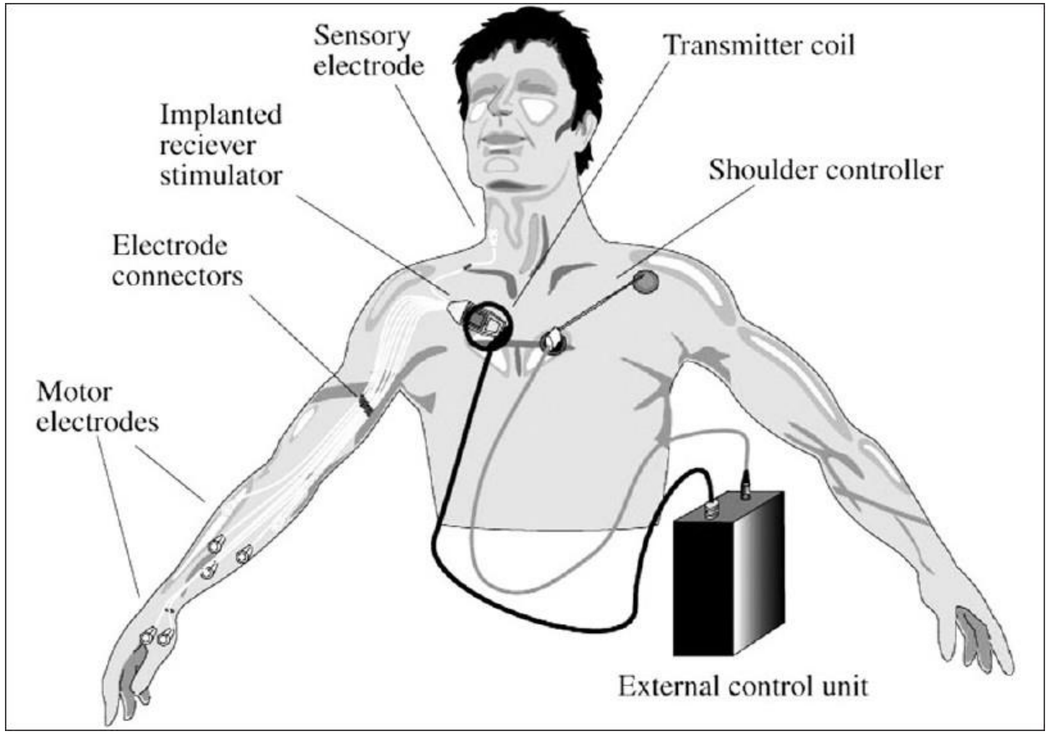
Specifications :

- Up to 12 epimysial and intramuscular electrodes
- Human Machine interface: Opposite shoulder movements
- Around 300 patients implanted worldwide

Intervention :

- Surgery: 6 Hours (general anaesthetic)
- Immobilisation for 3 weeks post-surgery

Kilgore et al. J. Bone Jt. Surg. (1997).



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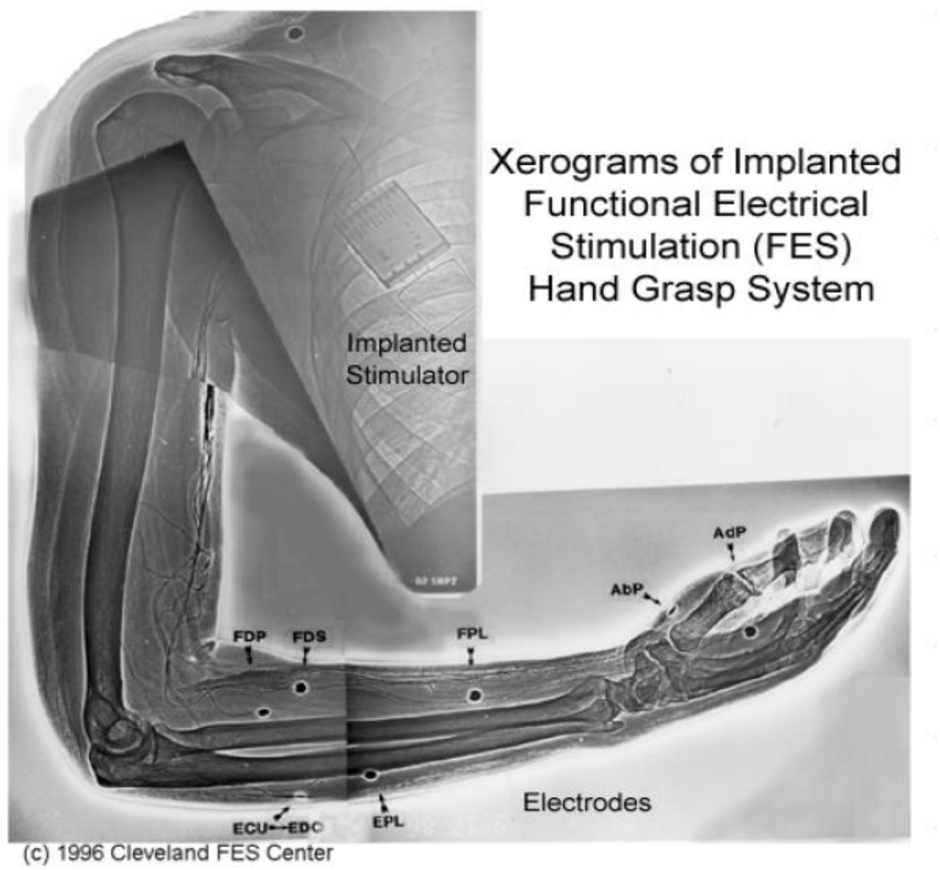
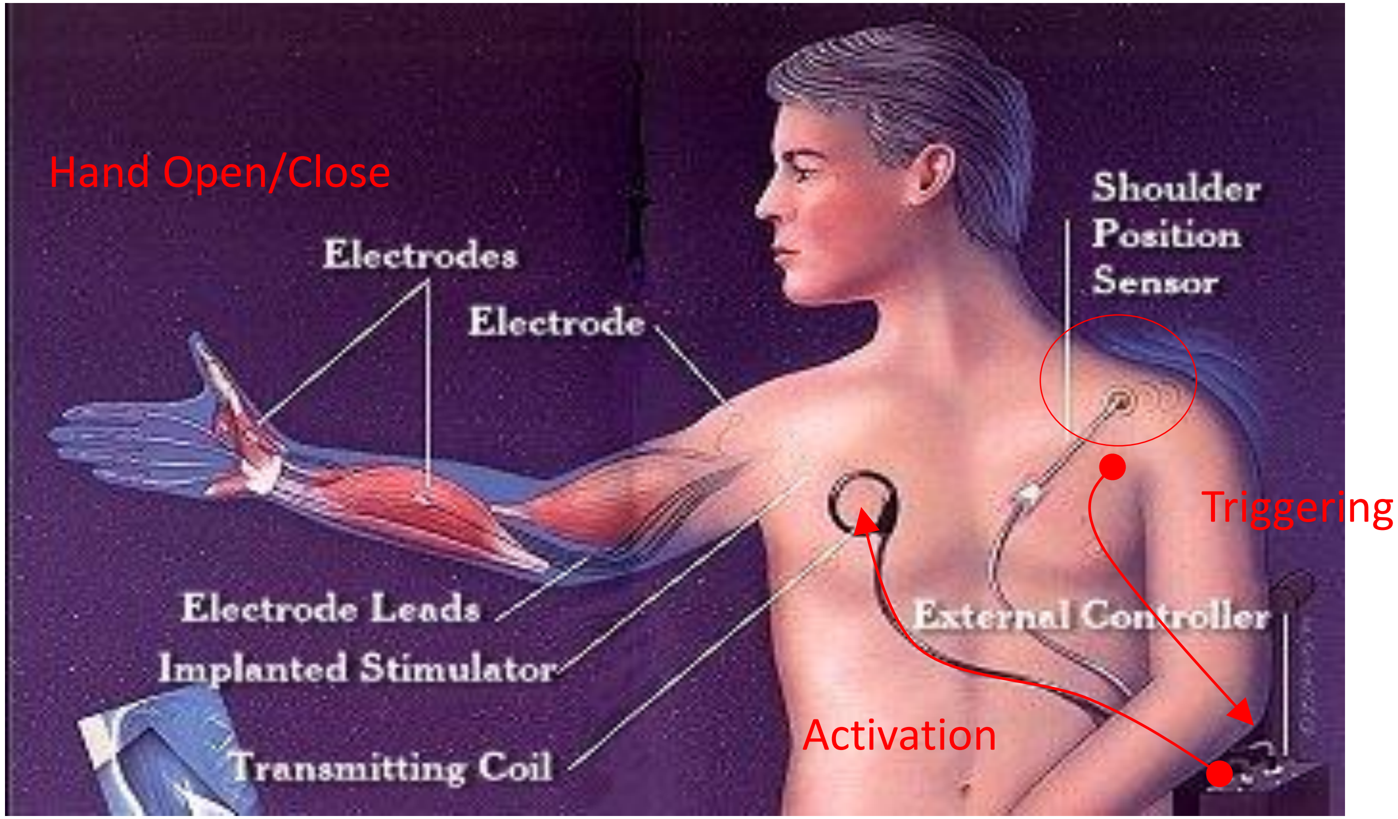




Free Hand System (NeuroControl)

Functional Electrical Stimulation and SCI

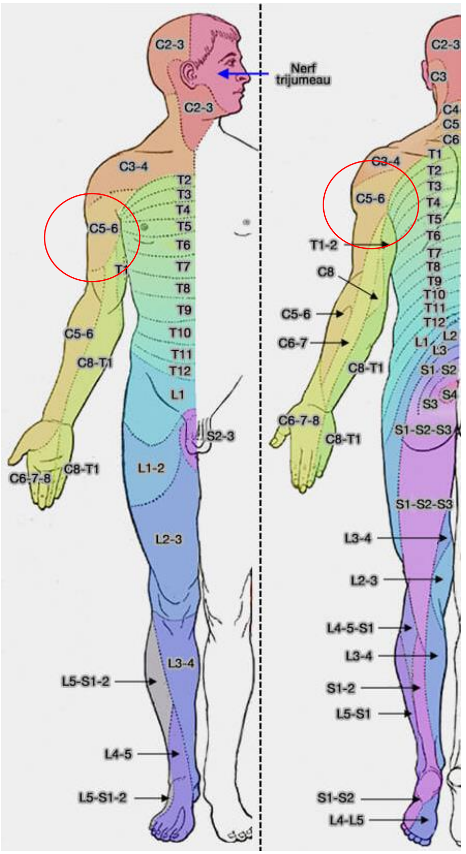
B – Upper limb function -> Hand Grasping -> FreeHand System (Neurocontrol, USA, out of market)

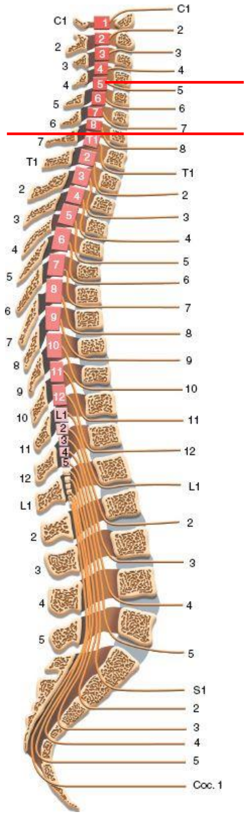
Case study :

- Woman
- Traumatic tetraplegia
- Lesional profile: C5 incomplete and C7 complete
- Right Handed

Functional goals (n=4) :

- Writing
- Facial care and make-up
- Eating and drinking
- Self catheterization





Functional Electrical Stimulation and SCI

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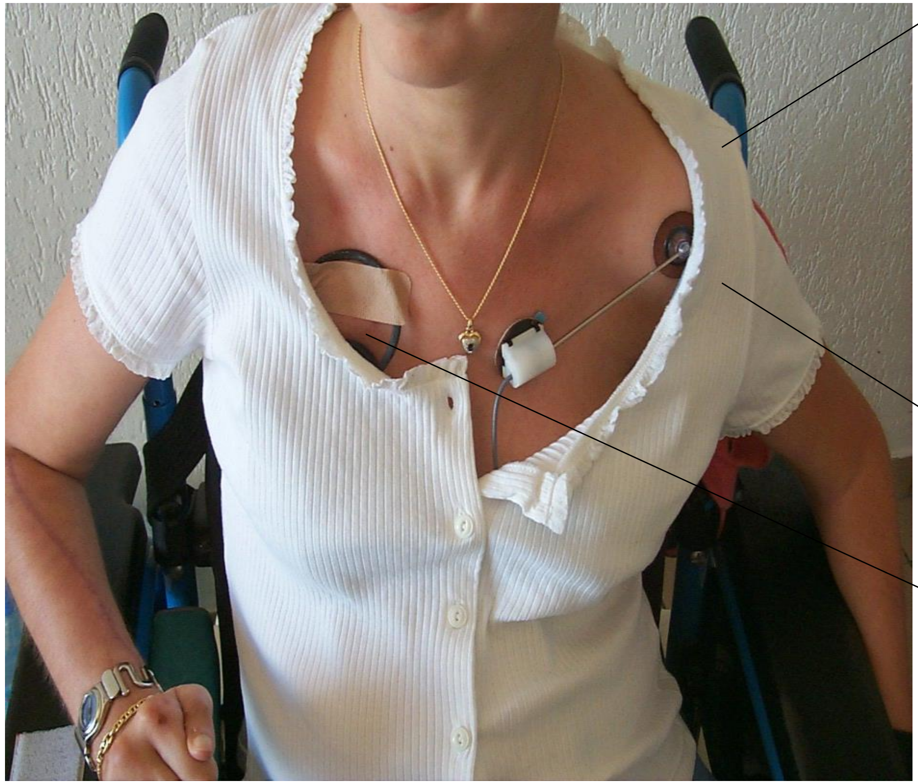
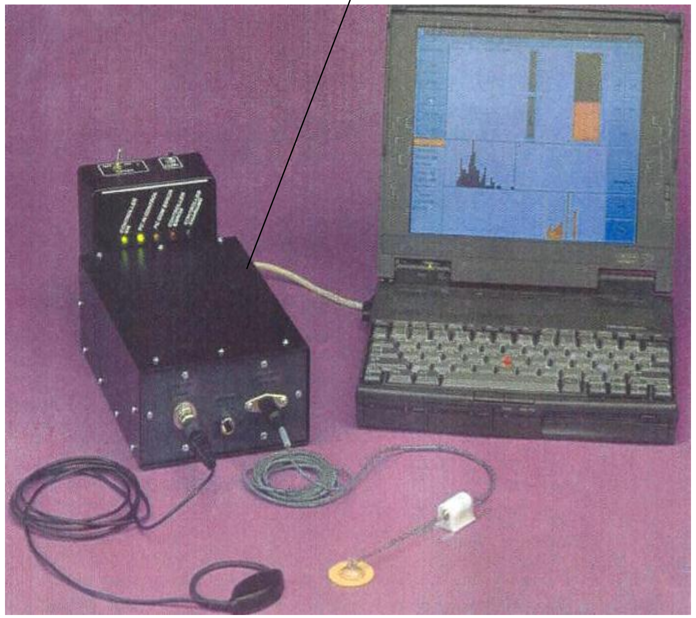


Opposite shoulder movement:
Top / Front / Back / Bottom

Sensor position

Inductive link

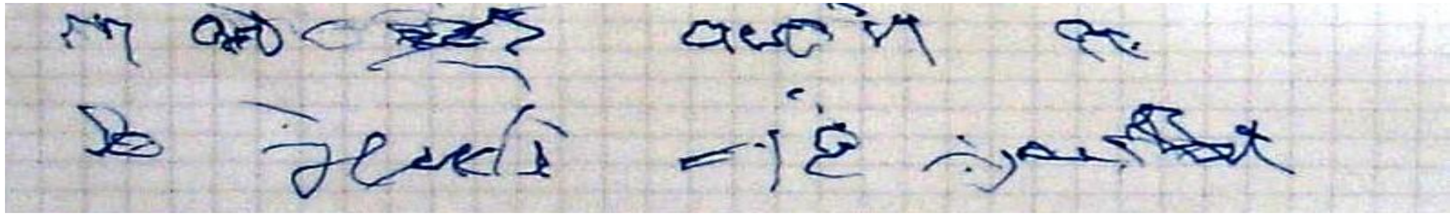
External control unit



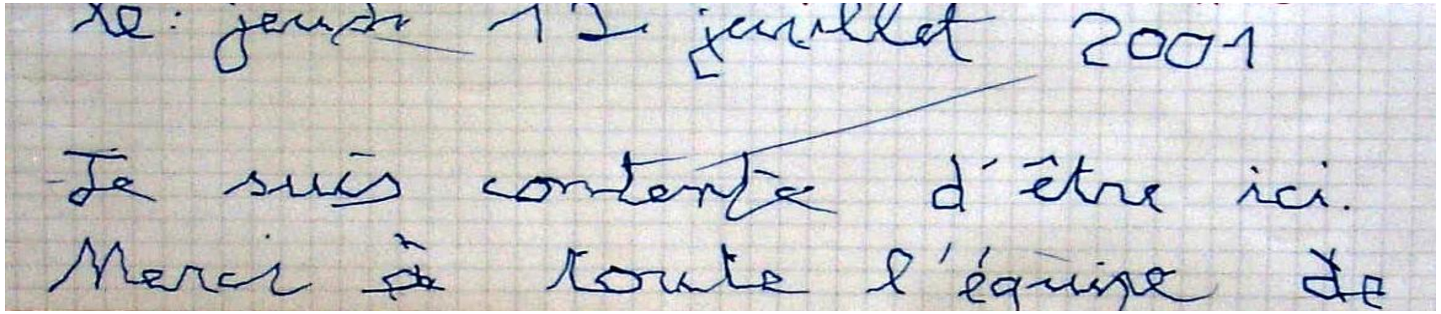
Functional Electrical Stimulation and SCI

B – Upper limb function -> Hand Grasping -> FreeHand System (Neurocontrol, USA, out of market)

Without stimulation



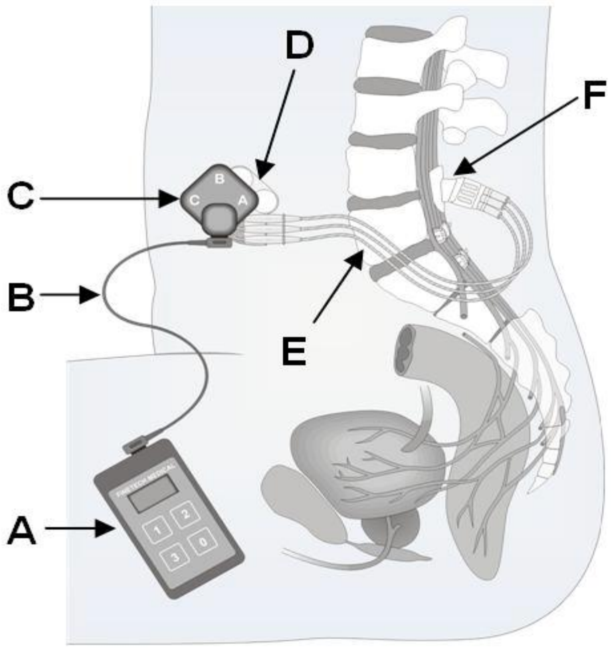
With stimulation (4 month post-surgery)



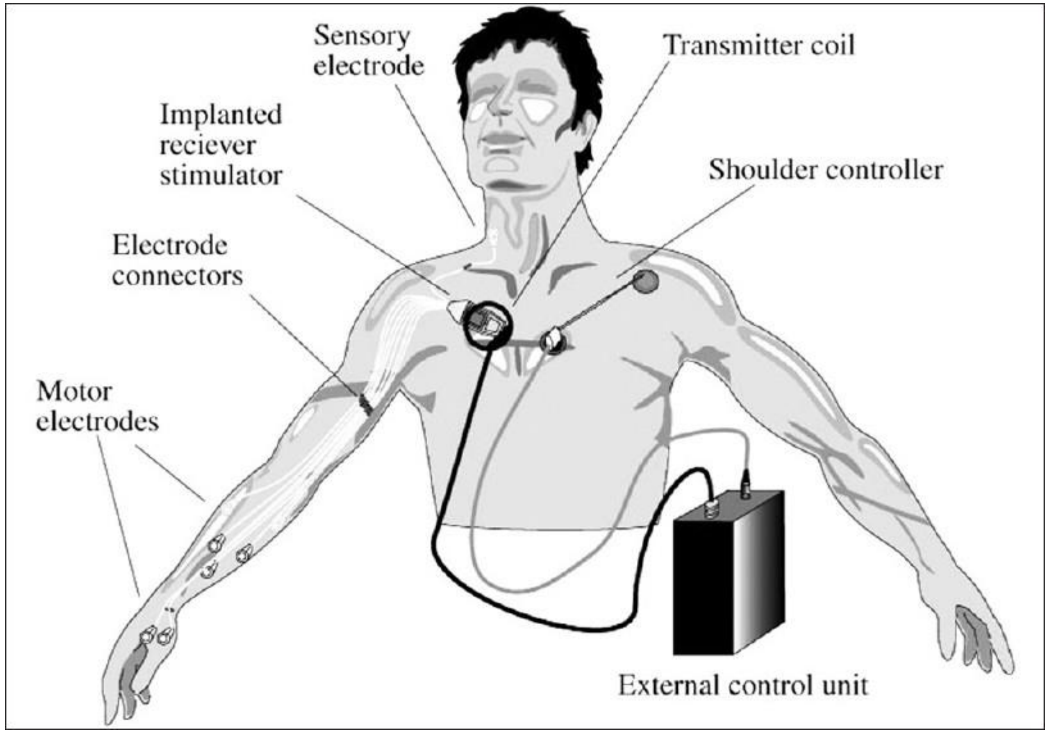
Courtesy of Dr Charles Fattal (Perpignan, France)

Functional Electrical Stimulation and SCI

Marketed implant to rehabilitate functions after SCI



Brindley implant: Around 2500 patients…
But decline of implantation



FreeHand System: 300 patients worldwide…
But out of market

Implants designed to restore sensorimotor functions

Thank you for your attention