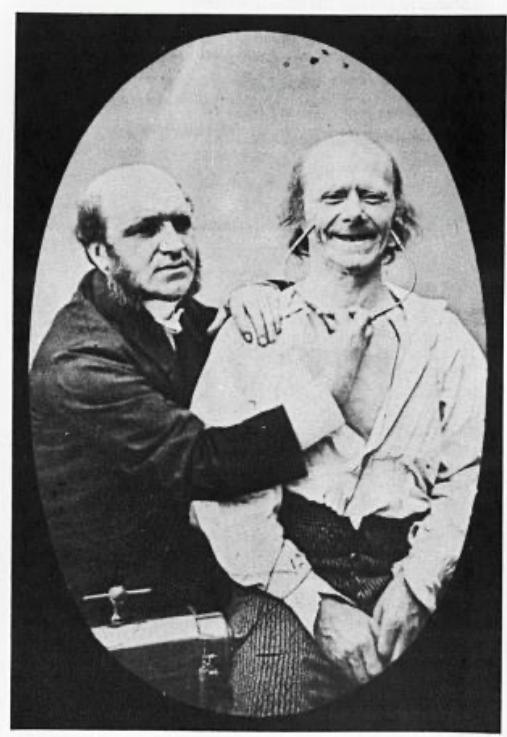




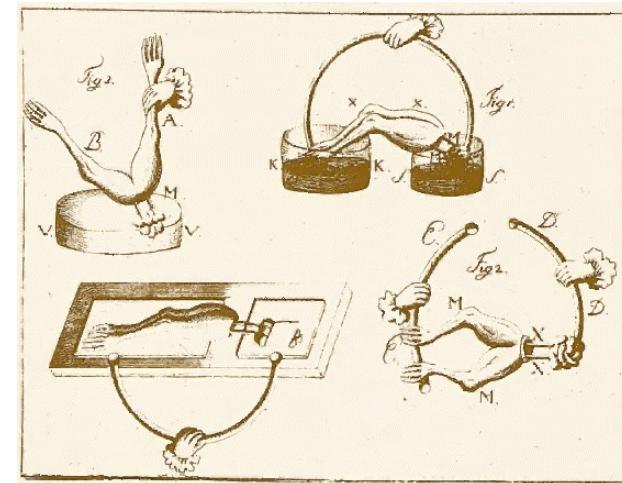
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Section 1- FUNDAMENTALS OF FUNCTIONAL
ELECTRICAL STIMULATION

Electrical Stimulation



- Use of torpedoes
- Galvani 1780
- Duchenne 1862
- Liberson 1961



Marcello Bracale: “Electrical and magnetic stimulation”
In: History of Bioengineering Treatment - E. Biondi and C. Cobelli
2001 - Patron Editore, Bologna, 299-324.

Functional electrical stimulation

“FES is the stimulation able to induce the contraction in a muscle without its neuronal control, in order to obtain a useful functional movement”

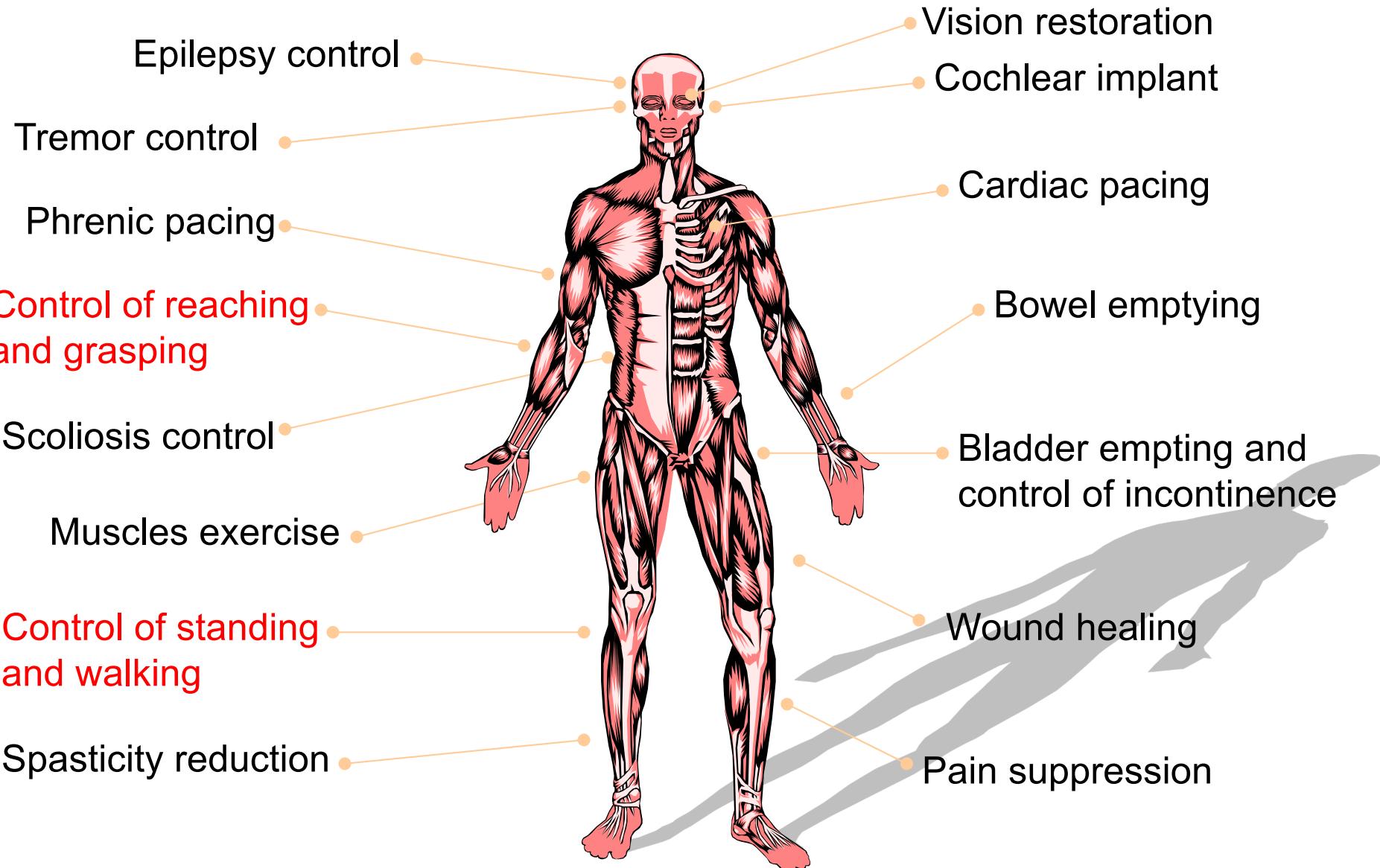
Vodovnik, L. 1971. Functional Electrical Stimulation of Extremities. In Advances in Electronics and Electron Physics, Academic Press.

“Functional electrical stimulation (FES) is the technique of applying safe levels of electric current to activate the damaged or disabled neuromuscular system in a coordinated manner in order to achieve the lost function. Neuro-prosthesis is a device that uses electrical stimulation to activate the nervous system. These initiate a physiological-like stimulation in the intact peripheral nerves, providing functional restoration of various body organs in the neurologically impaired individuals.”

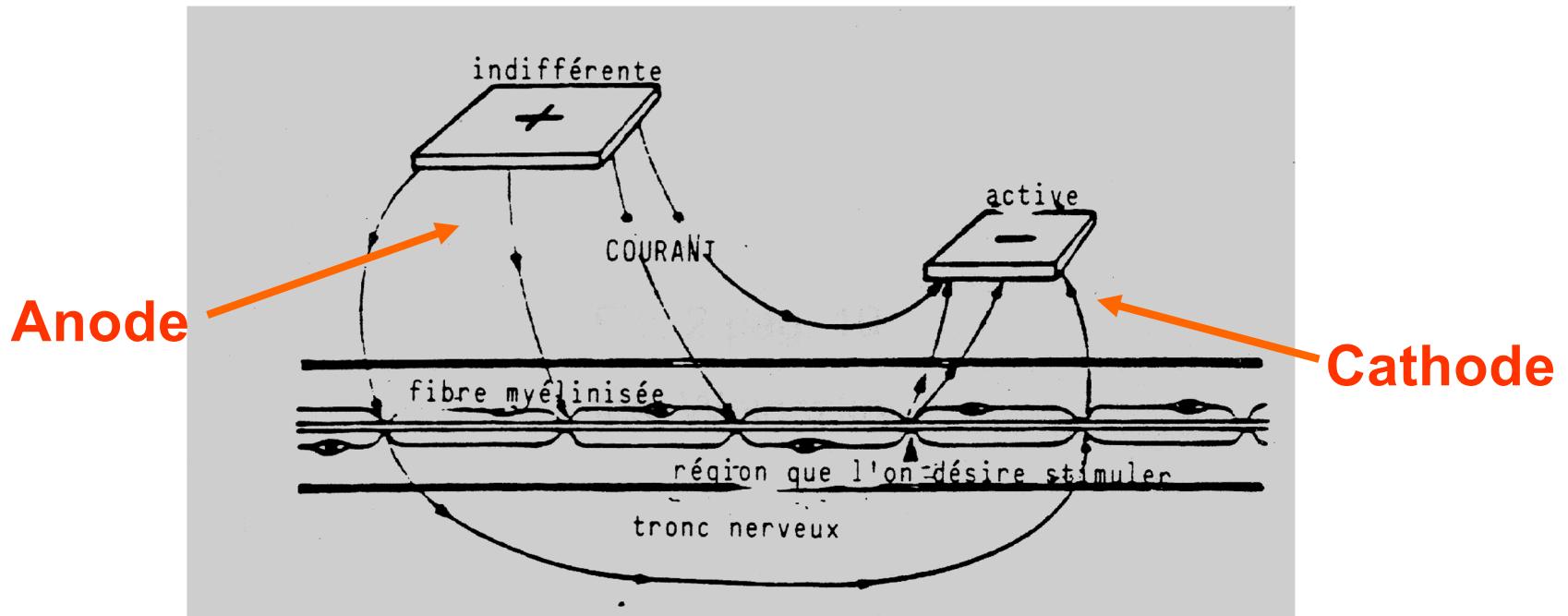
Hamid S, Hayek R. Role of electrical stimulation for rehabilitation and regeneration after spinal cord injury: an overview. *Eur Spine J.* 2008;17(9):1256–1269. doi:10.1007/s00586-008-0729-3

ES interventions and target disabilities

Applications of Electrical Stimulation



FES: Working Principle



Anode:

It sends a positive charge to the membrane which is HYPERPOLARIZED under the anode

Cathode:

The positive charge exits from the cathode; the membrane is DEPOLARIZED under the cathode

DEPOLARIZATION OVER THE THRESHOLD



Action Potential

Stimulation Parameters

- **Current Amplitude [A]**

(it excites the nerve; there is a current threshold)

- **Pulse width (PW, [μ s])**

(the alternative parameter able to adjust the charge)

- **Tension [V]**

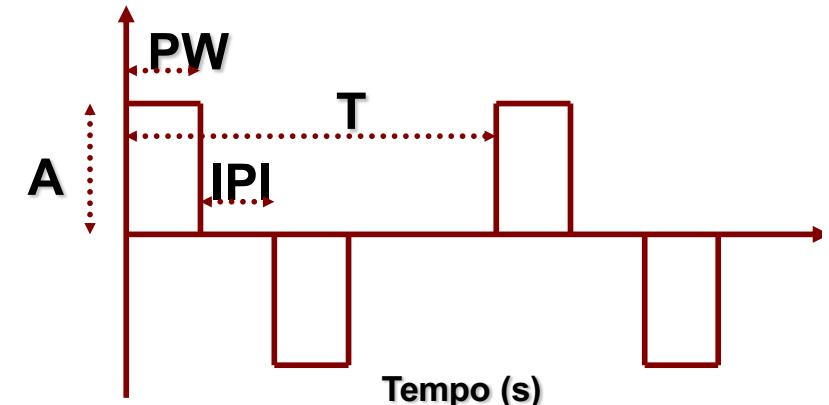
(it supports the current erogation)

- **Stimulus Frequency (1/T) [Hz]**

(it regulates the force of the mechanical action)

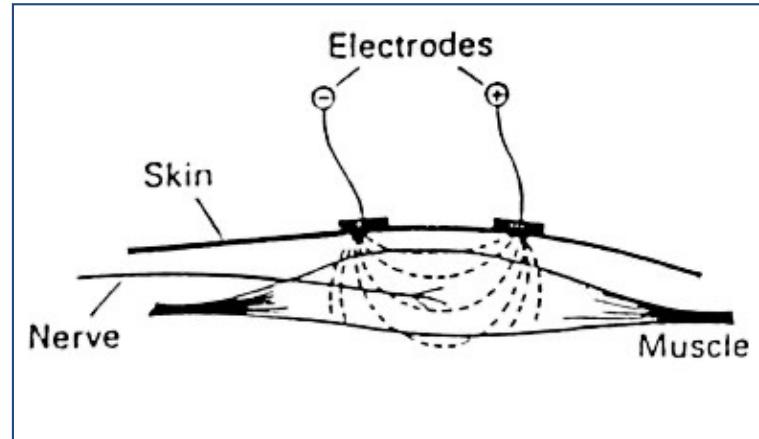
- **Stimuli shape**

(it limits possible tissue damage)



Technological Aspects: Electrodes

SURFACE



PERCUTANEUS

Monopolar Percutaneous Needle



Bipolar Percutaneous Hooks



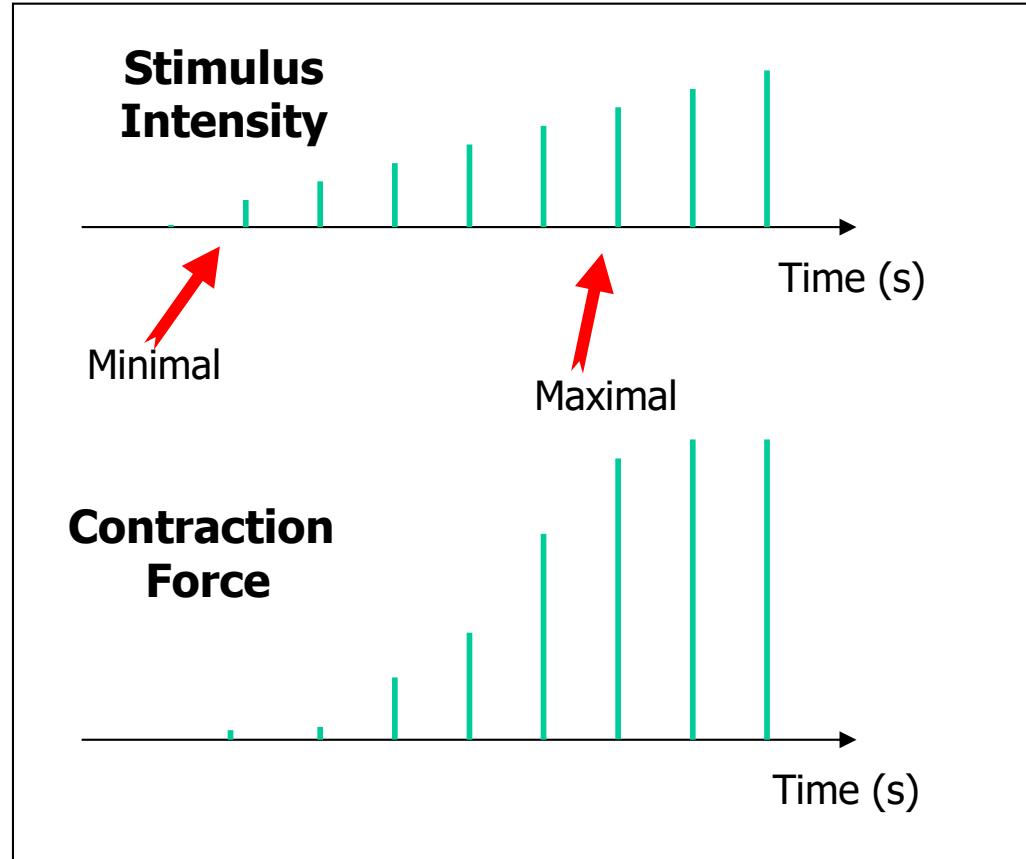
Natural Muscular Contraction

FORCE GENERATED
BY THE MUSCLE

$$F(t) = \sum_{i=1}^N F_i(t)$$

i: index of motor units

N = total number of motor units



Spatial summation

Natural Muscular contraction

- ASYNCHRONOUS ACTIVATION:

Force modulation

Turn over in the fiber activation

A continuous force is obtained with $f = 10 \text{ Hz}$

- PROGRESSIVE ACTIVATION



Type I Fibers

Type IIa Fibers

Type IIb Fibers

Type I fibers:

- Small diameter
- Deep
- Slow contraction
- Limited force ($0,6 \text{ kg/cm}^2$)
- Aerobic metabolism (oxidative)



SHORT RECOVERY PERIODS



RESISTANT TO FATIGUE

Type IIa fibers:

- Relatively big diameter
- Relatively fast contraction
- High Force (~~2,6-2,9 kg/cm²~~)
- Anaerobic and aerobic metabolism (glicolitic and oxidative)



MEDIUM RECOVERY PERIODS



MEDIUM RESISTANCE TO MUSCLE FATIGUE

Type IIb fibers:

- Big diameter
- Closer to Surface
- Fast contraction
- High force ($1,5-2 \text{ kg/cm}^2$)
- Anaerobic metabolism (glicolitic)



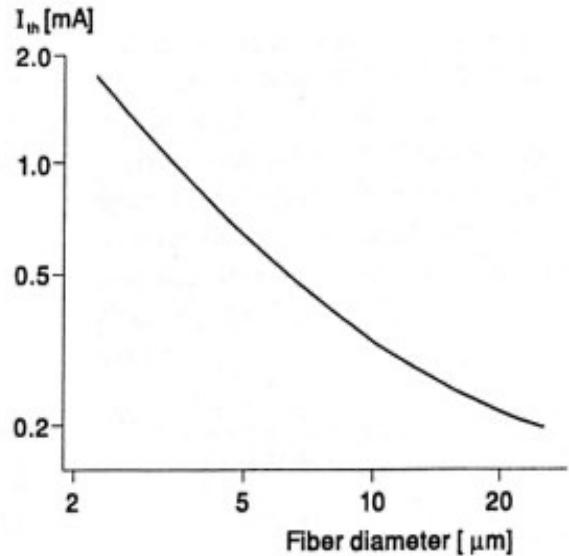
LONG RECOVERY PERIODS



FAST MUSCULAR FATIGUE

Artificial Muscular contraction

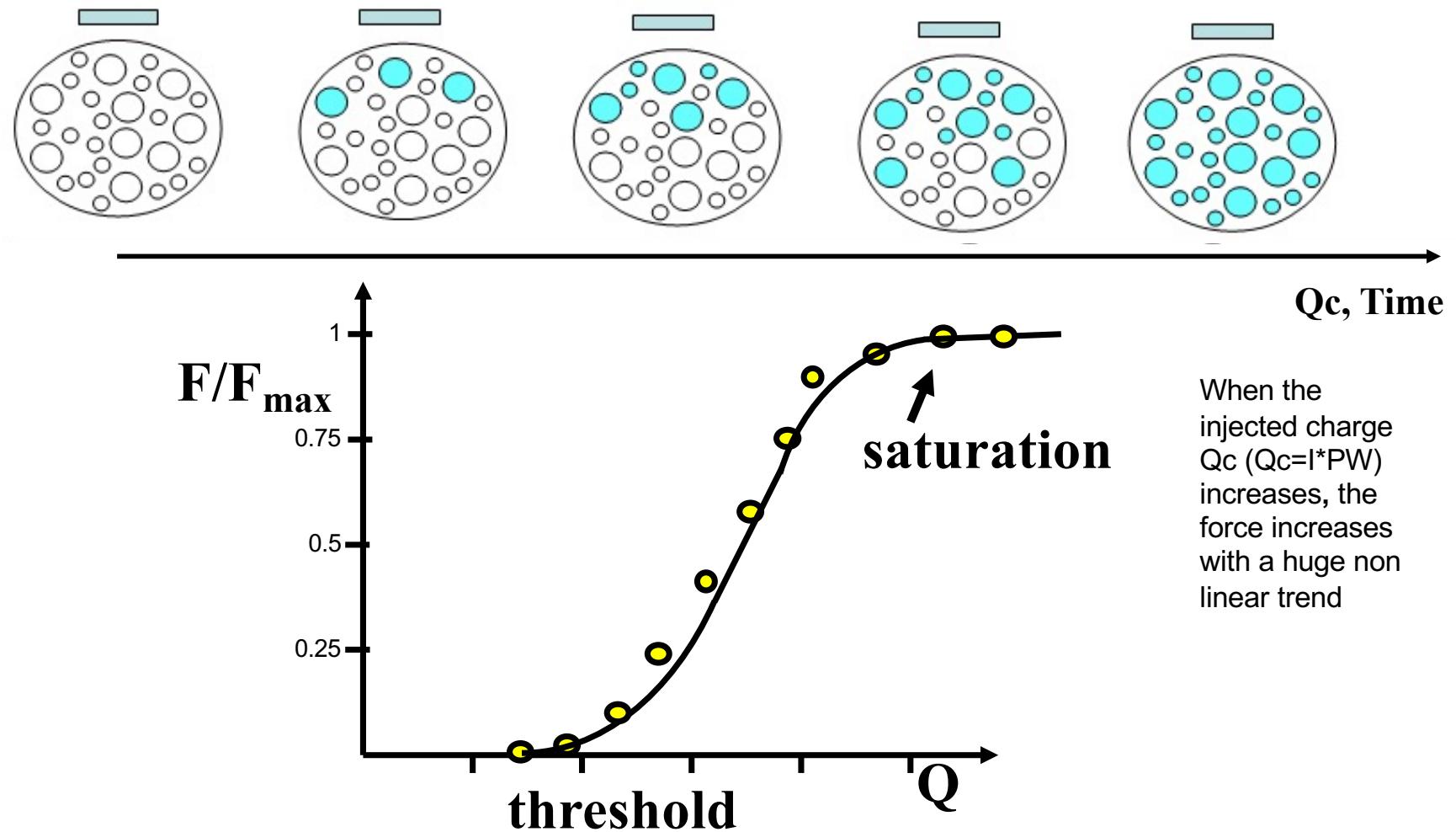
- Electrical stimulation activates the motor neuron (healthy!)
- Generation of an action potential that is not distinguishable from the physiological one



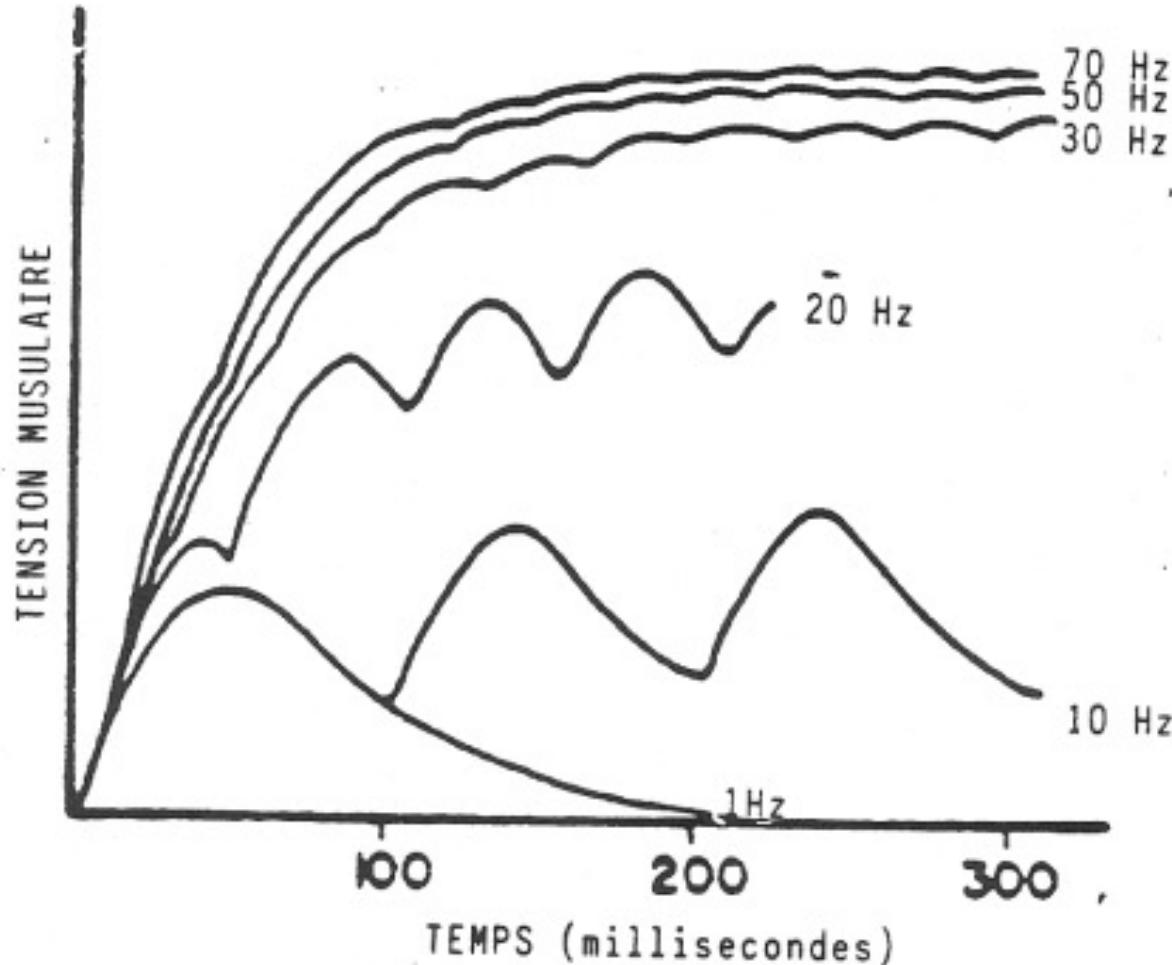
BUT

The artificial stimulation recruits fibers in a non-selective and spatially-fixed way and synchronously.

ARTIFICIAL FIBER RECRUITMENT



Force as a function of frequency



Temporal summation

NOTE: natural stable contraction is achieved by motor units recruitment at 10 Hz

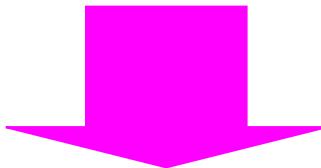
Comparison

ARTIFICIAL

- Synchronous fiber activation
- There is no “turn over” of motor units
- Recruitment order spatially fixed and (II - I)

PHYSIOLOGICAL

- Asynchronous fiber activation
- There is a “turn over” of the motor units
- Recruitment order (I-IIa-IIb)

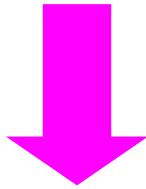


ARTIFICIAL ACTIVATION LIMITS

- Muscular fatigue
- It is difficult to modulate contractions

Changes for paretic muscles

- Reduction of the muscular fiber cross section (ATROPHY)
- Conversion of fibers: from type I (slow) to type II (fast)



NEED A MUSCULAR TRAINING PERIOD THROUGH
FES IN ORDER TO:

- Increase the muscular force and volume
- Increase the resistance to fatigue



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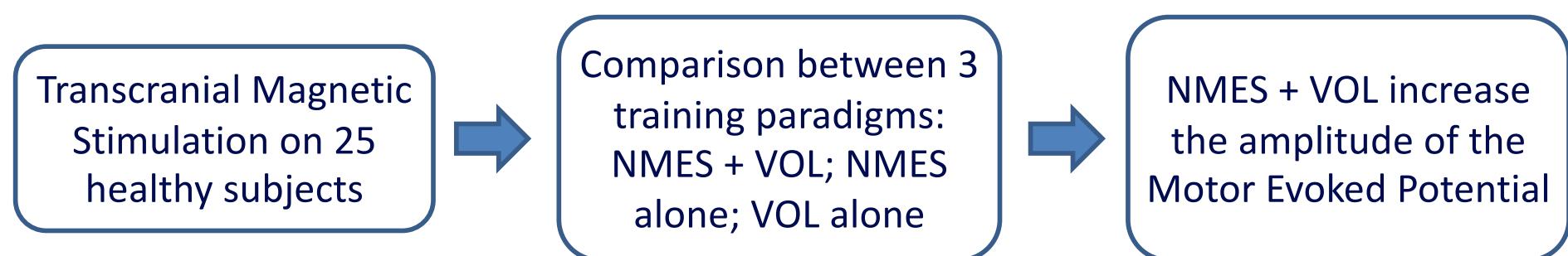
Section 2- THE NEURAL BASES OF FES FOR BRAIN PLASTICITY

FES EFFECTS FOR BRAIN PLASTICITY

NEUROPHYSIOLOGICAL HYPOTHESIS FOR IMPROVED MOTOR LEARNING

CORTICAL LEVEL

- 1) NMES-augmented voluntary activations increase cortical excitability with respect to voluntary activations alone or passive NMES [Barsi, 2008]



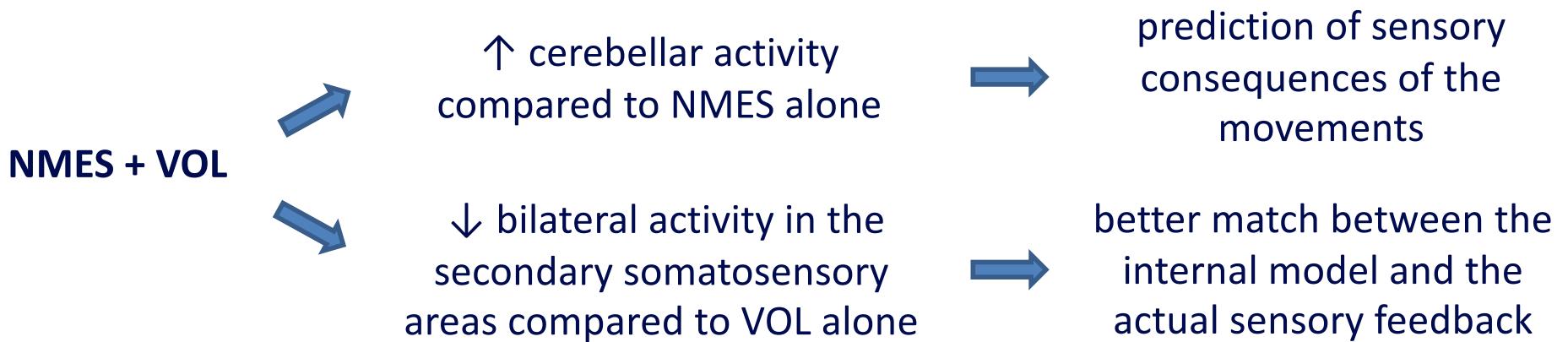
Cortical effects of FES and FES+VOL

NEUROPHYSIOLOGICAL HYPOTHESIS FOR IMPROVED MOTOR LEARNING

CORTICAL LEVEL

- 2) NMES combined with voluntary effort improves the prediction of sensory consequences of motor commands [Iftime-Nielsen, 2012]

fMRI study on 17 healthy subjects to compare cortical activity induced by NMES + VOL, NMES alone and VOL alone.

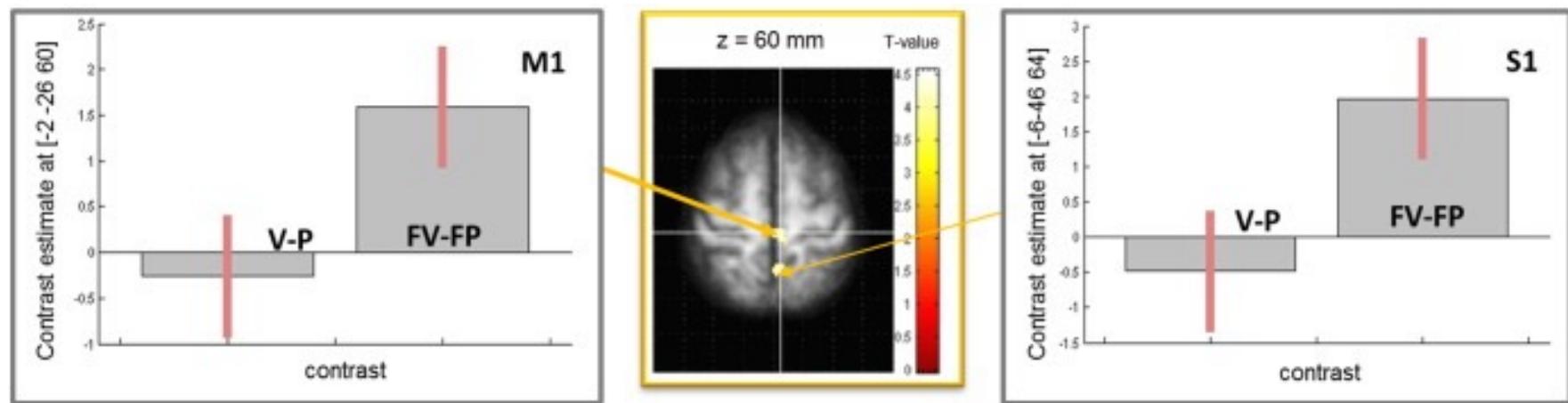


Neurophysiological hypothesis for improved motor learning

CORTICAL LEVEL

- 3) The NMES- augmented proprioception in the context of volitional intent produced a higher activation than NMES-augmented proprioception in the absence of volitional movement [Gandolla et al, 2014]

- ✓ fMRI study on 17 healthy subjects during ankle dorsi-flexion
- ✓ 2x2 factorial design, with volitional intention and NMES as factors:
 - V: only volitional; P: only passive; PV: passive + NMES; FV: volitional + NMES

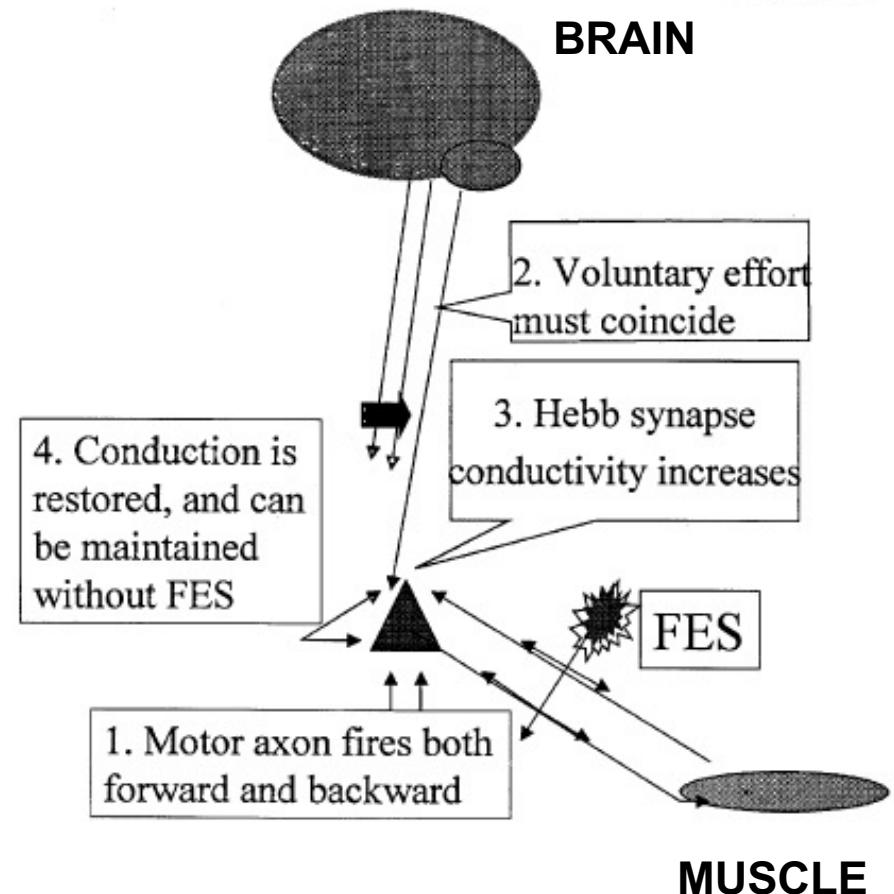


Neurophysiological hypothesis for improved motor learning

NMES antidromic impulses combined with coincident voluntary effort synchronize pre-synaptic and post-synaptic activity of the anterior horn cells



Restorative synaptic modifications at spinal level [Rushton, 2003]

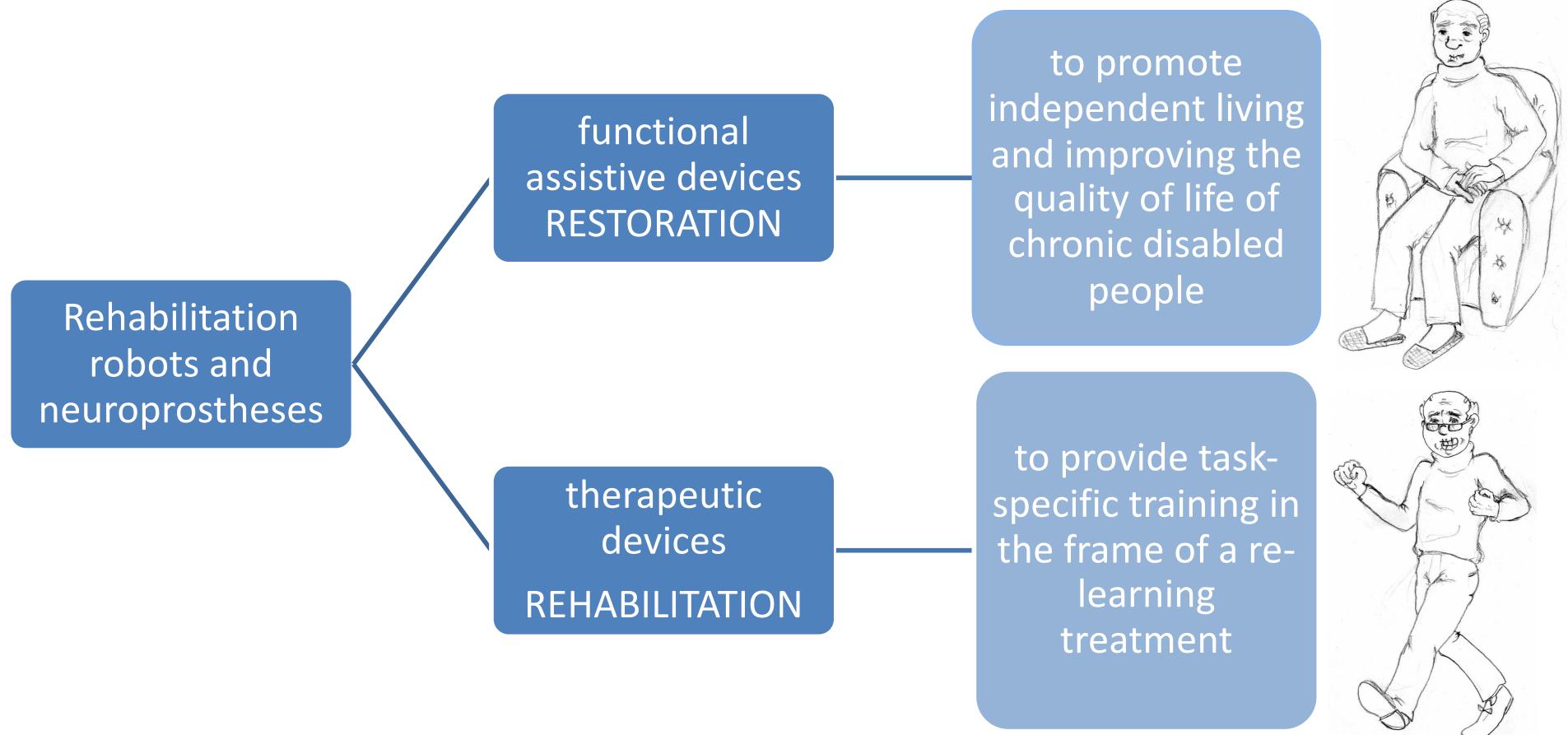




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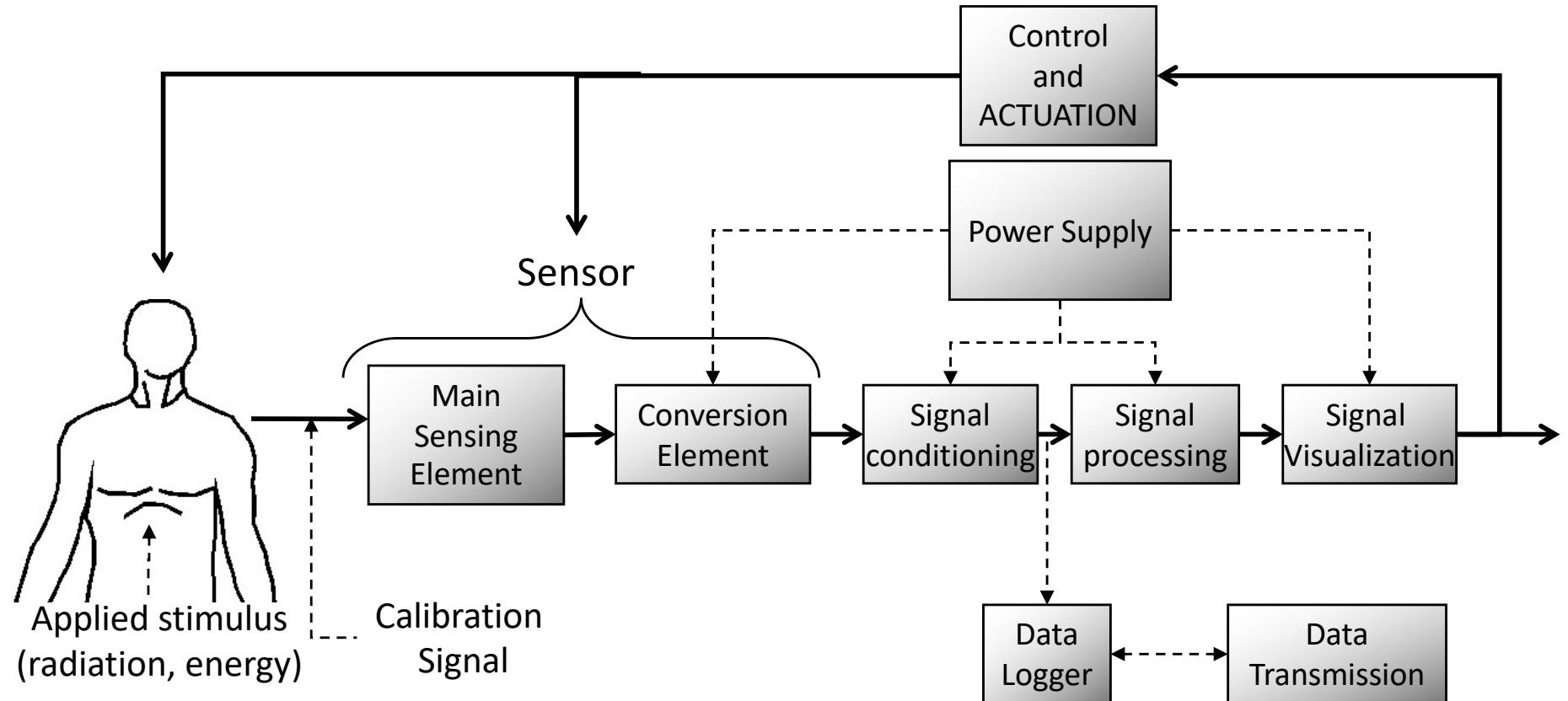
Section 3- HUMAN_MACHINE INTERACTION
INTERFACING NEUROPROSTHESES AND ROBOTS TO
SUBJECT INTENTION

Rehabilitation robotics: framework



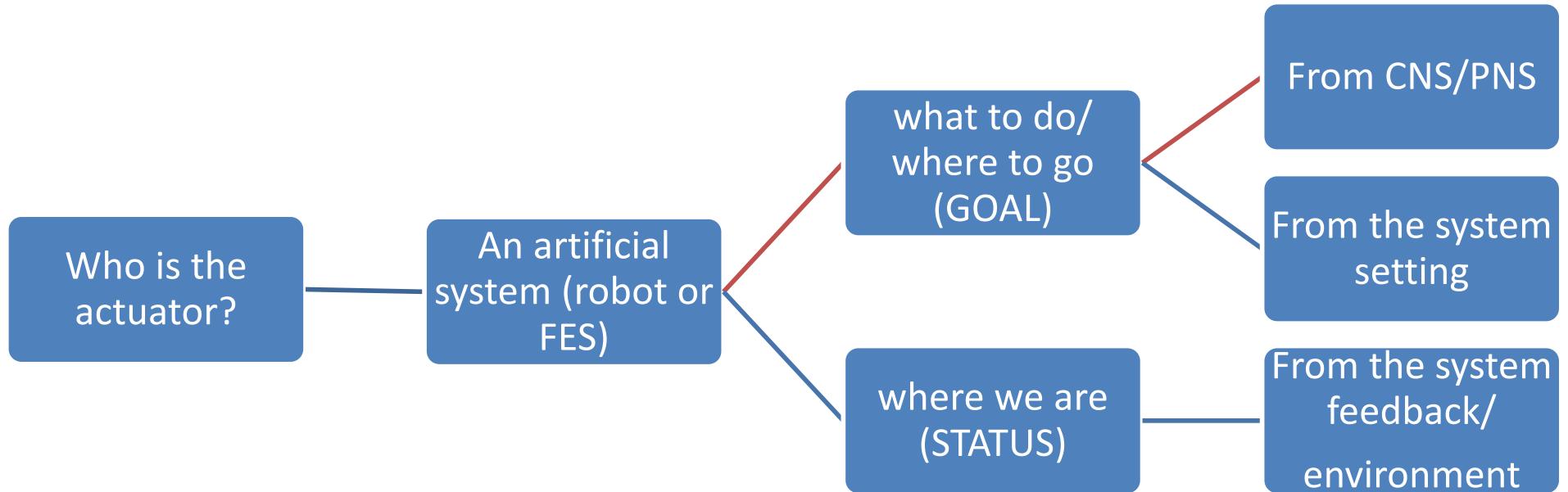
Interfacing devices (NP and ROBOTS) with subject: Sensors

Sensor: device able to convert a physical stimuli into a measureable and recordable signal



Adapted from Webster Medical Instrumentation

Neuroprostheses and robots



Goal of rehabilitation robotics and NP

Neuroplasticity: intrinsic capability of the nervous system to learn



goal of rehabilitation: effective use of neuroplasticity for functional recovery



Training aims people at

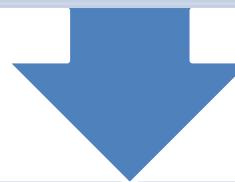
Practicing a task more intensively and safely

Progressing automatically in task difficulty

Achieving the desired movements

Motivating repetitive, intensive practice

reconnecting "intention" to "action"



ROBOTS + NEUROPROSTHESES

Goal of Assistive Neuroprostheses

Chronic damage inducing disability and preventing independent living

goal of restoration: provide the subject with a natural control of an efficient function

Assistive Neuroprostheses aim people at

Long-term regain of independent functions

reconnecting "intention" to "action"

Psychological benefits of natural control

ROBOTS+ NEUROPROSTHESES

Sensors to collect the motor command

Electroencephalogram
(EEG)

Field potential
recorded by scalp
electrodes
(BCI)

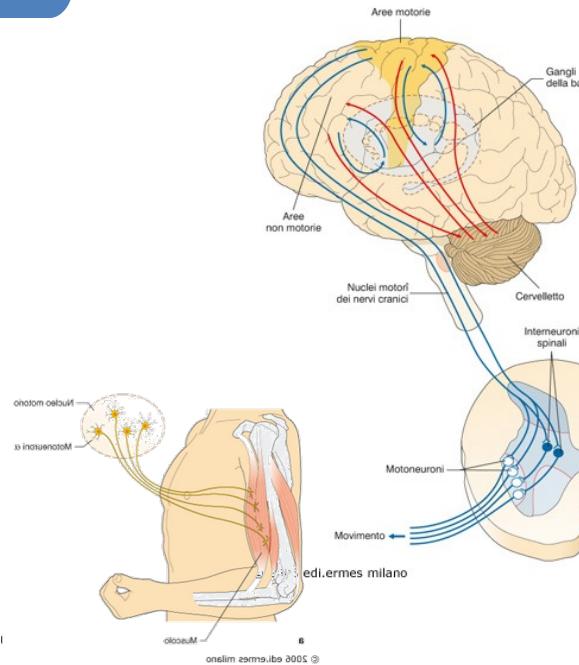
Electrocorticograms
(ECoG)

Field potentials
recorded by skull,
epidural or subdural
electrodes (Local FP)

Implantes Brain Arrays
(MEA)

Multiple single units
recordings or neural
population recording
(BMI)

Electromyogram
(EMG)



Electroneurogram
(ENG)

An overall picture

A Brain

Resolution:
Major benefit:
Clinical trials:

① EEG

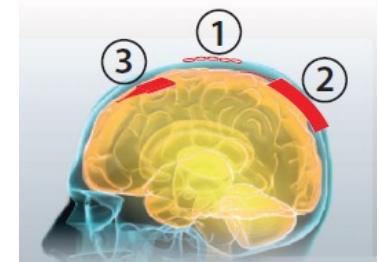
10 mm
No surgery
-236

② ECoG

2 mm
Clinical product
-5

③ Brain array

0.1 mm
Single neuron specificity
-6



B Peripheral nerves



Cuff electrode

Surface activation

LIFE electrode

Longitudinal activation

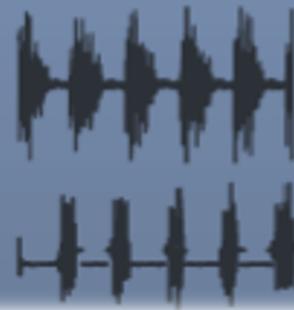
TIME electrode

Transverse activation

Selectivity →

C Muscles and kinematics

EMG sensors



Kinematic reconstruction



Implantable sensors



Adapted from Borton et al Sci Transl Med 5, 210 rv2, 2013

EEG-controlled Neuroprostheses (BCI)

Setting

Scalp electrodes
(wet or dry)

International electrodes
positioning 10-20

Signal pre-processing
(bandpass DC-100 Hz)

Data processing

Natural brain rhythms
modulation (motor
imagery) Event related
Synch/desync ERD/ERS

Movement related
potentials (MRP)

Visual Event
potential(SSVEP)

Event- related Potential
(P300)

Problems/Challenges

Time for setting up

Each session calibration
(about 30 minutes)

Required training of the
subject

BCI illiteracy

Multi Electrodes Arrays controlled robots (BMI)

Setting

Cortical arrays of electrodes
(4x4mm)

One single implantation in M1 (hand area, Hochberg; two for Collinger)

Signal pre-processing (spike detection, spike sorting , spike classification)

Data processing

Spike decoding
observation-based seven dimensional neural decoder of firing rate

model that linearly related neural firing rate to movement velocity

orthoimpedance attenuated the brain-command component perpendicular to the ideal seven-dimensional trajectory

Problems/challenges

Surgery

Each session calibration
(about 15 minutes)

Required training of the subject (three times per week for 13 weeks; each session was about 4 h, Collinger et al)

Illiteracy? few tested people so far

Is the simplest, cheapest and most usable solution?

BMI Some examples



Collinger et al Lancet 2013; 381: 557–64



Hochberg LR et al Nature 2012; 485: 372–75

ENG-controlled robots

Setting

Peripheral nerves activity

Cuff electrodes /transversal
Electrodes

Data processing

Triggering of Drop foot
stimulations

Control of hand
neuroprostheses (Tombini
et al): efferent fibers
MOTOR NP

Problems/Challenges

Surgery

Required training of the
subject

Illiteracy? few tested people
so far

EMG-controlled robots

Setting

Signal generated by muscular contraction

(Mostly) Surface electrodes

Band 10-500Hz

Data processing

Triggering of Impedance control robots

Triggering of FES by other muscles

Triggering of FES by the same target muscle
(Blanking circuit)

Myocontrolled NP
(Blanking circuit + extraction of volitional control)

Problems

Electrodes positioning, electrode-skin contact instability and calibration at each session (about 15 min)

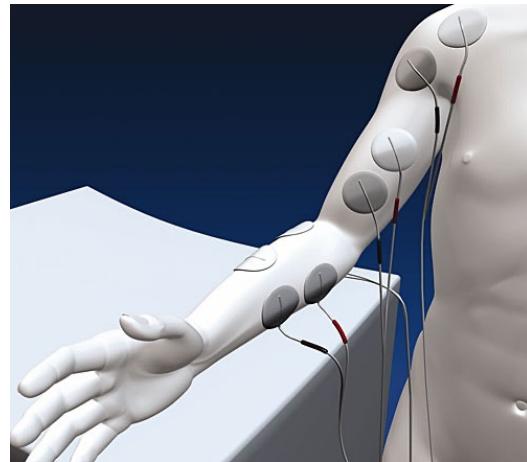
Crosstalk from adjacent muscles

Same muscle control only if a weak but functional activation is still present

In the case of other muscles control the resulting task is rather unnatural

EMG triggered FES

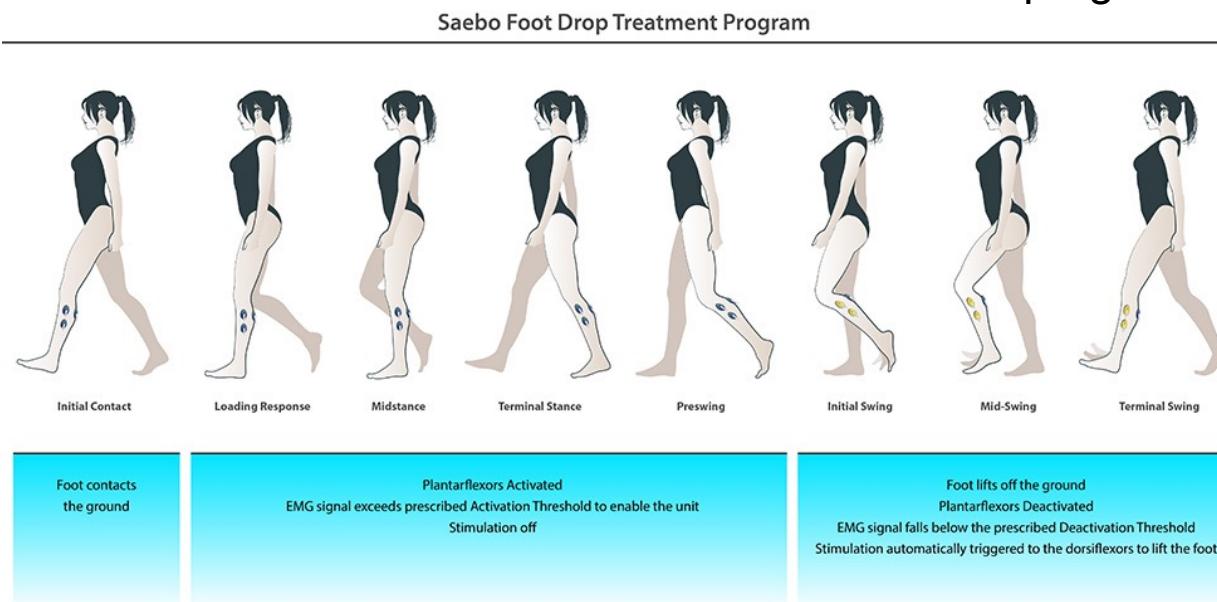
STIWELLmed4
EMG trigger of 4
channel
stimulation



Biomove



Saebo Myotrac Infinity
EMG trigger +
Reciprocal EMG Triggered Stimulation
program.



Technical challenges to make myocontrolled NP

TWO DIFFERENT SOLUTIONS OF MYOCONTROLLED NEUROPROSTHESES

1) *EMG-TRIGGERED NMES*

Residual volitional EMG is used to **trigger** the onset of a **predetermined simulation sequence** applied in an **open-loop modality** to the same muscle used for control.

2) *EMG-CONTROLLED NMES*

Residual volitional EMG is used to **modulate the stimulation intensity** in a **closed-loop modality** to the same muscle used for control.

Myocontrolled NP

TWO DIFFERENT SOLUTIONS OF MYOCONTROLLED NEUROPROSTHESIS

	EMG-TRIGGERED NMES	EMG-CONTROLLED NMES
PROS	Simple to implement → EMG signal is measured only before NMES starts	Assure the synchronization between NMES and voluntary effort
CONS	No guarantees about the synchronization between NMES and voluntary effort	More complex technological solutions are needed for the design

EMG signal during hybrid muscle contractions

Hybrid muscle activations: muscle contractions both volitional and electrically induced [Langzam, 2006]

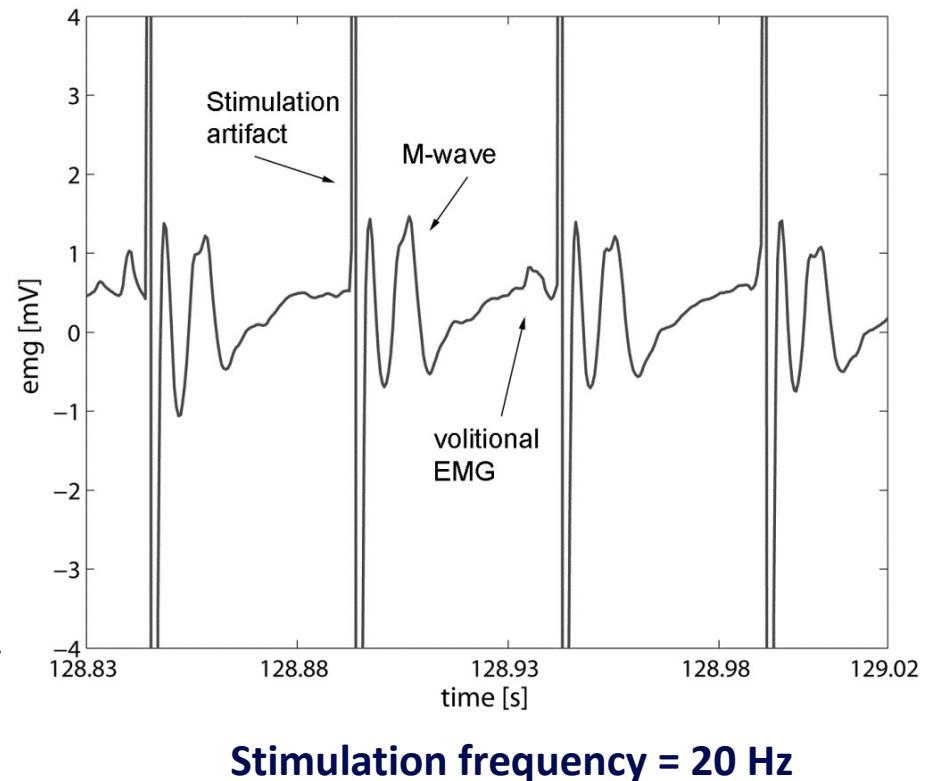
Stimulation artifact: spike lasting few ms due to the electric field generated by the stimulation current

M-wave: compound action potential due to the synchronous firing of the electrically elicited muscle fibers (some mV)

H-reflex: second waveform determined by the orthodromic sensory volley

F-wave: small second compound action potential due to the antidromic efferent stimuli

Volitional EMG: stochastic signal with an amplitude of at least one magnitude less than the M-wave



Devices for EMG recording during FES

Standard amplification unit for EMG recordings can not be used in the presence of NMES



The **stimulation artifact** is the result of a potential difference produced by the stimulation current between the EMG electrodes → it **can not be rejected by the differential amplifier**

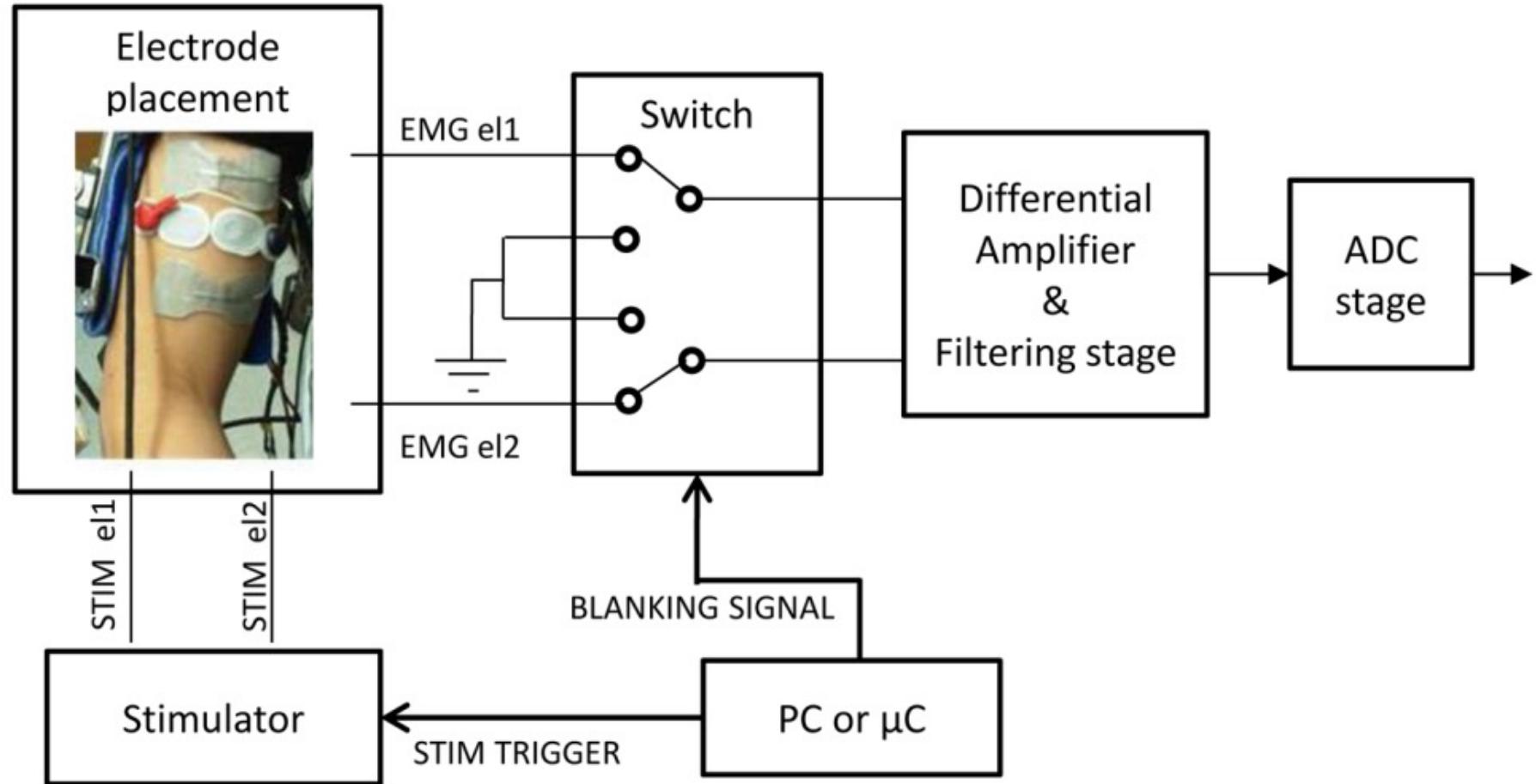


Since its amplitude is one to three orders greater than the M-wave, it can **saturate or even damage the amplifier of a standard EMG circuit**

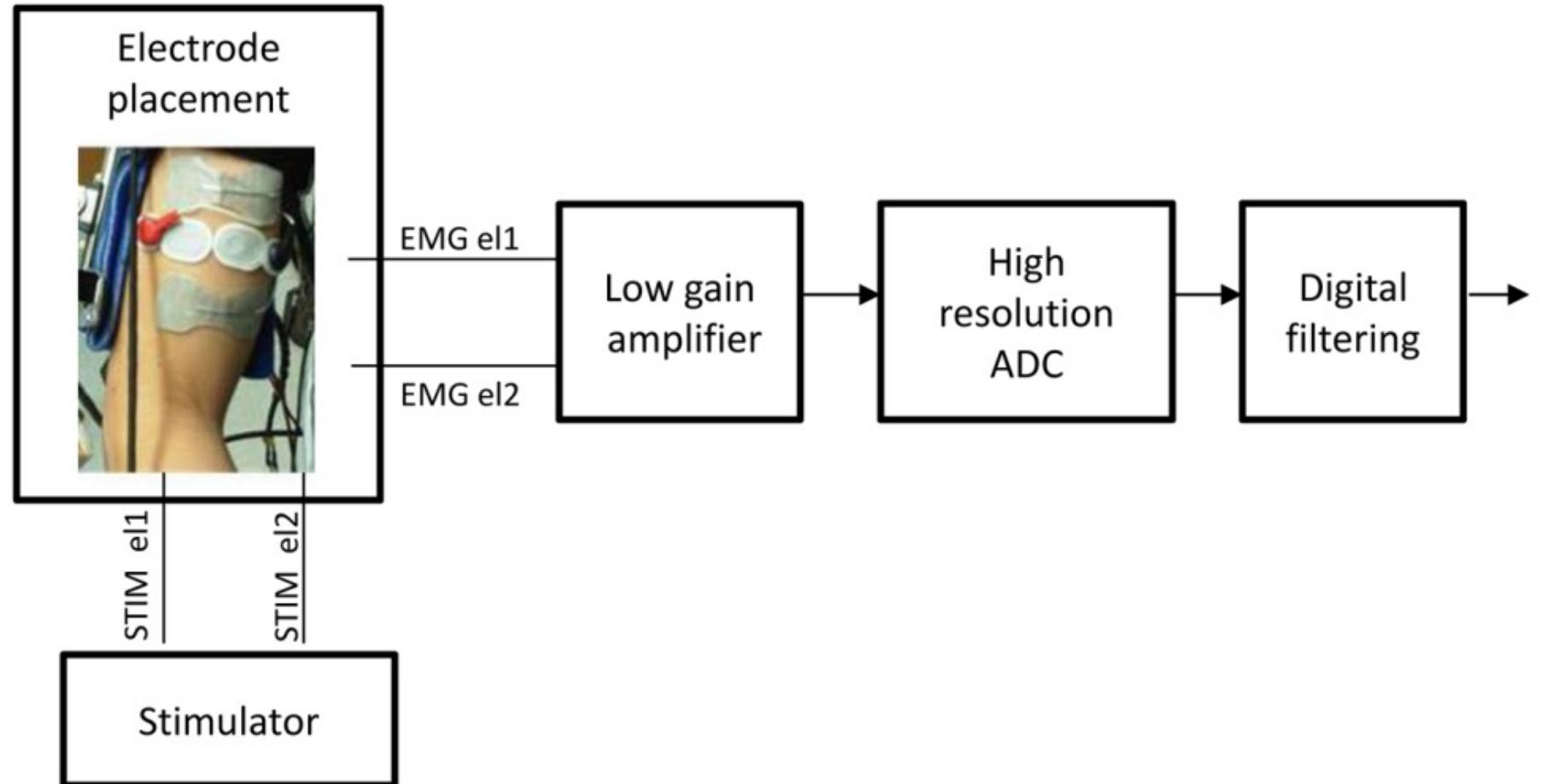


Different solutions have been proposed to face the problem of the **suppression of the stimulation artifact**.

Devices for EMG recording during FES - Blanking



Devices for EMG recording during FES – low gain amplifier



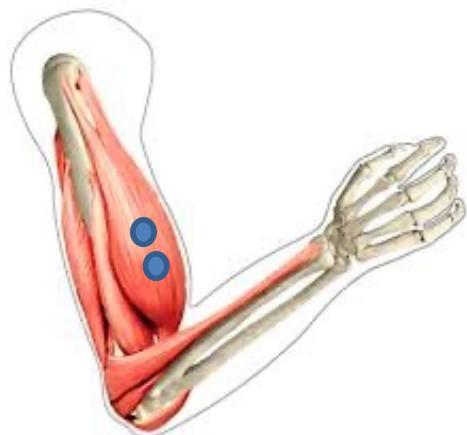
Devices for EMG recording during FES

RECORDING AND STIMULATION ELECTRODE

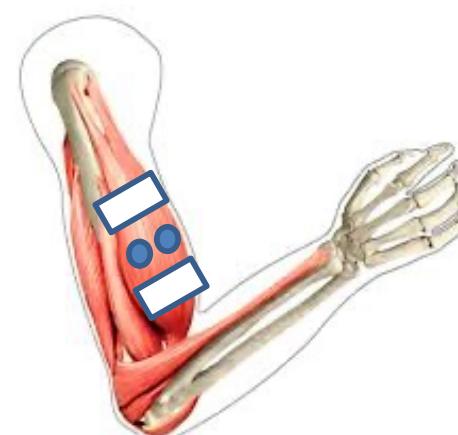
Standard solution: separate recording and stimulation electrodes

The relative placement of the electrodes affect the capability of the system to suppress the stimulation artifact

Regular placement for
EMG recordings
(SENIAM guidelines)



This placement is
preferred in the presence
of NMES [Frigo, 2000]



Higher common mode
component of the
stimulation artifact

- Stimulation electrode
- Recording electrode

Extract volitional EMG from hybrid contraction recording

Blocking window [Langzam, 2006]

The signal is zeroed for the first 20 or 25 ms of each inter-pulse period.

The volitional EMG is estimated from the remaining part of the inter-pulse period.

→ The M-wave is not completely removed

High-Pass filter [Muraoka, 2002; Schauer, 2004]

Assumption: 20-30 ms after the stimulation pulse, only low-frequency electrically-induced components superpose the volitional EMG

Blocking window + high-pass filter with a cut-off frequency between 200 and 330 Hz

Extract volitional EMG from hybrid contraction recording

Linear Prediction Adaptive filter [Sennels, 1997]

Assumption: the volitional EMG is a band-limited Gaussian signal and the M-wave is time-variant

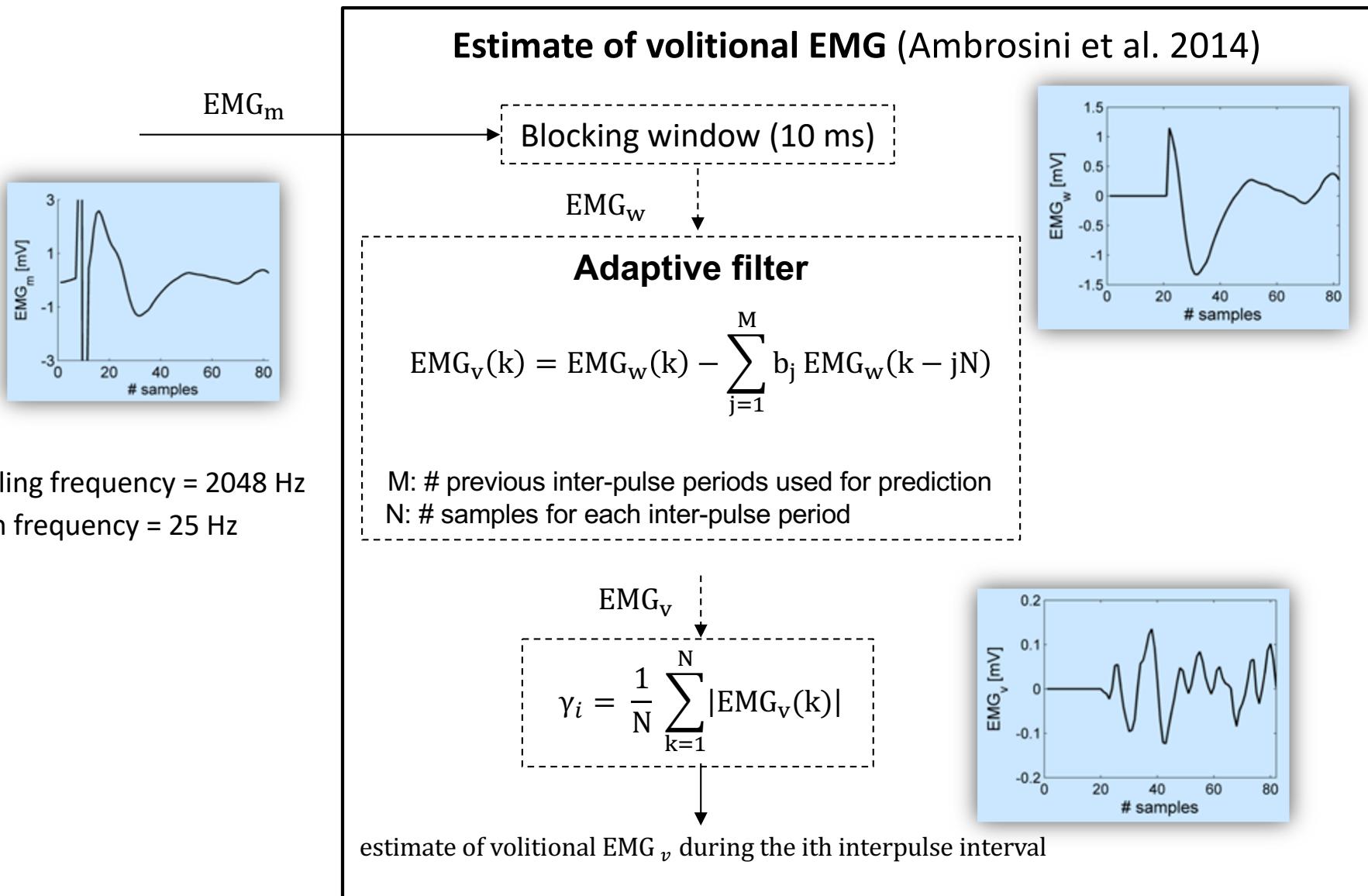
$$EMG_v(n) = EMG_r(n) - \sum_{j=1}^M b_j EMG_r(n - jN)$$

M number of previous inter-pulse periods used for prediction (6)

b_j filter coefficients computed by solving a least square algorithm that minimizes the output energy of the current inter-pulse period

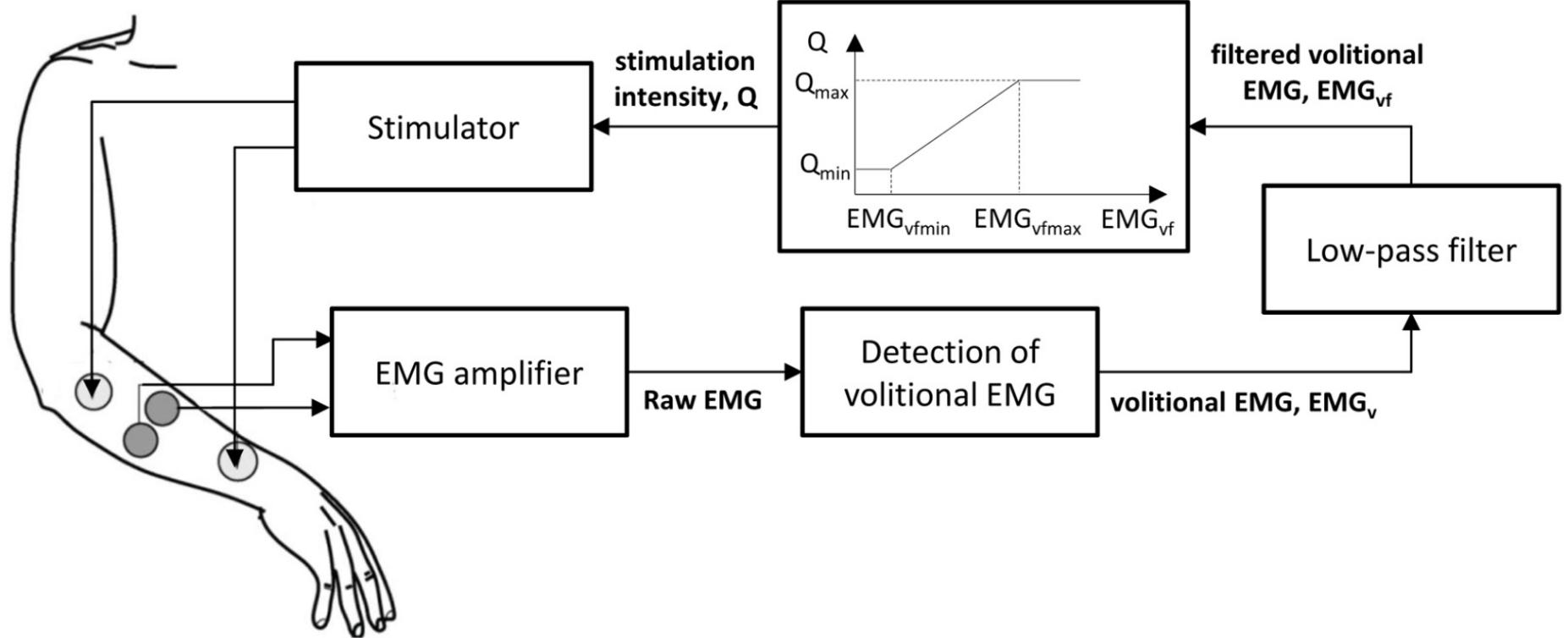
b_j are updated at a rate equal to the stimulation frequency

Linear prediction adaptive filter



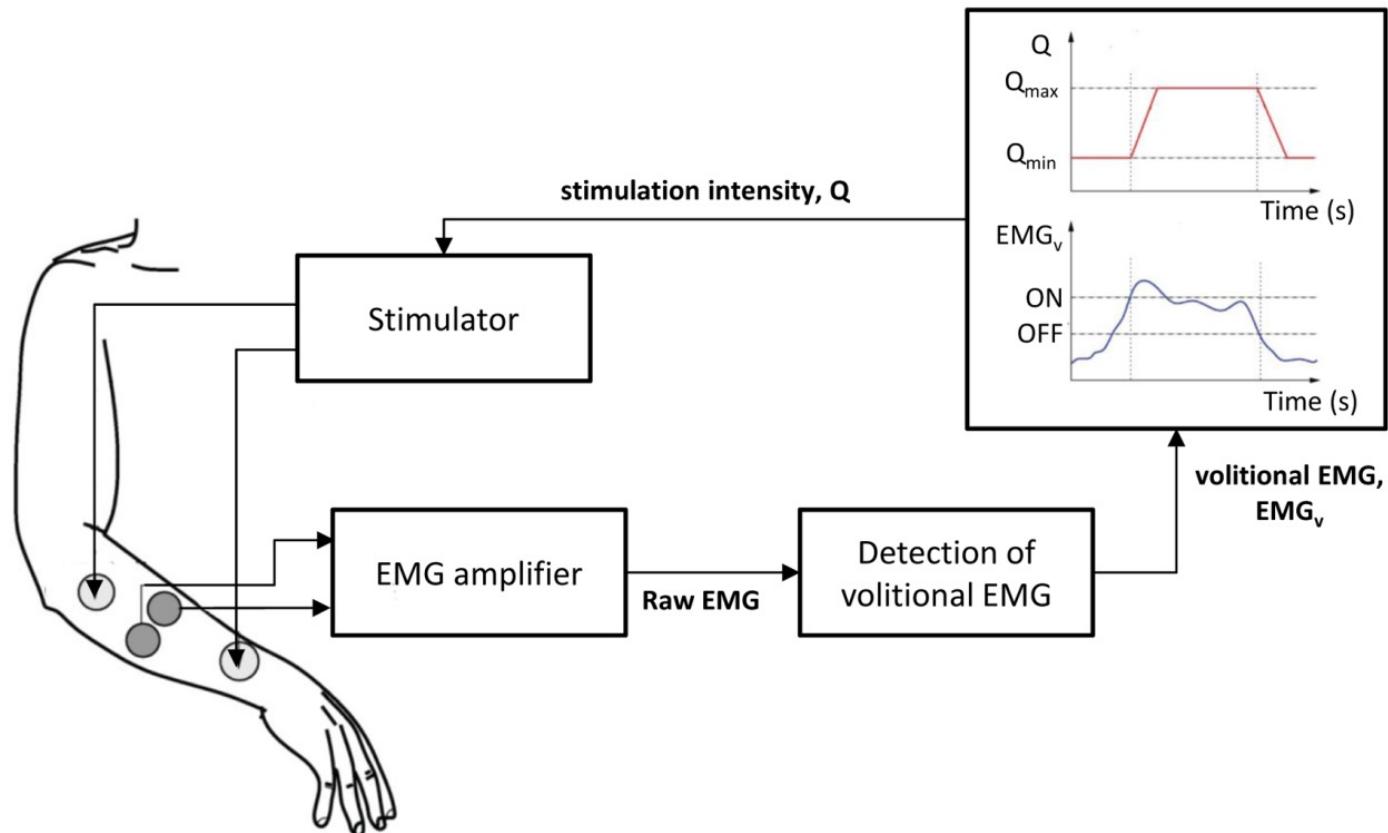
Design myocontrolled NP: control strategies

PROPORTIONAL CONTROLLER



Design myocontrolled NP: control strategies

ON/OFF CONTROLLER



Design myocontrolled NP: control strategies

Only few clinical applications of EMG-controlled neuroprostheses exist.

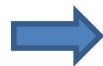
- 1) EMG-proportional controller supports hand functions during daily life activities in people with Spinal Cord Injury [Thorsen 1999, 2001, 2006]



assistive system

stimulation of a muscle closed to the one used for control

- 2) EMG-proportional controller improves hand functions in post-stroke patients [Fujiwara 2009; Shindo 2011]



rehabilitative purposes

same electrodes for stimulation and recordings

stimulation of the same muscle used for control

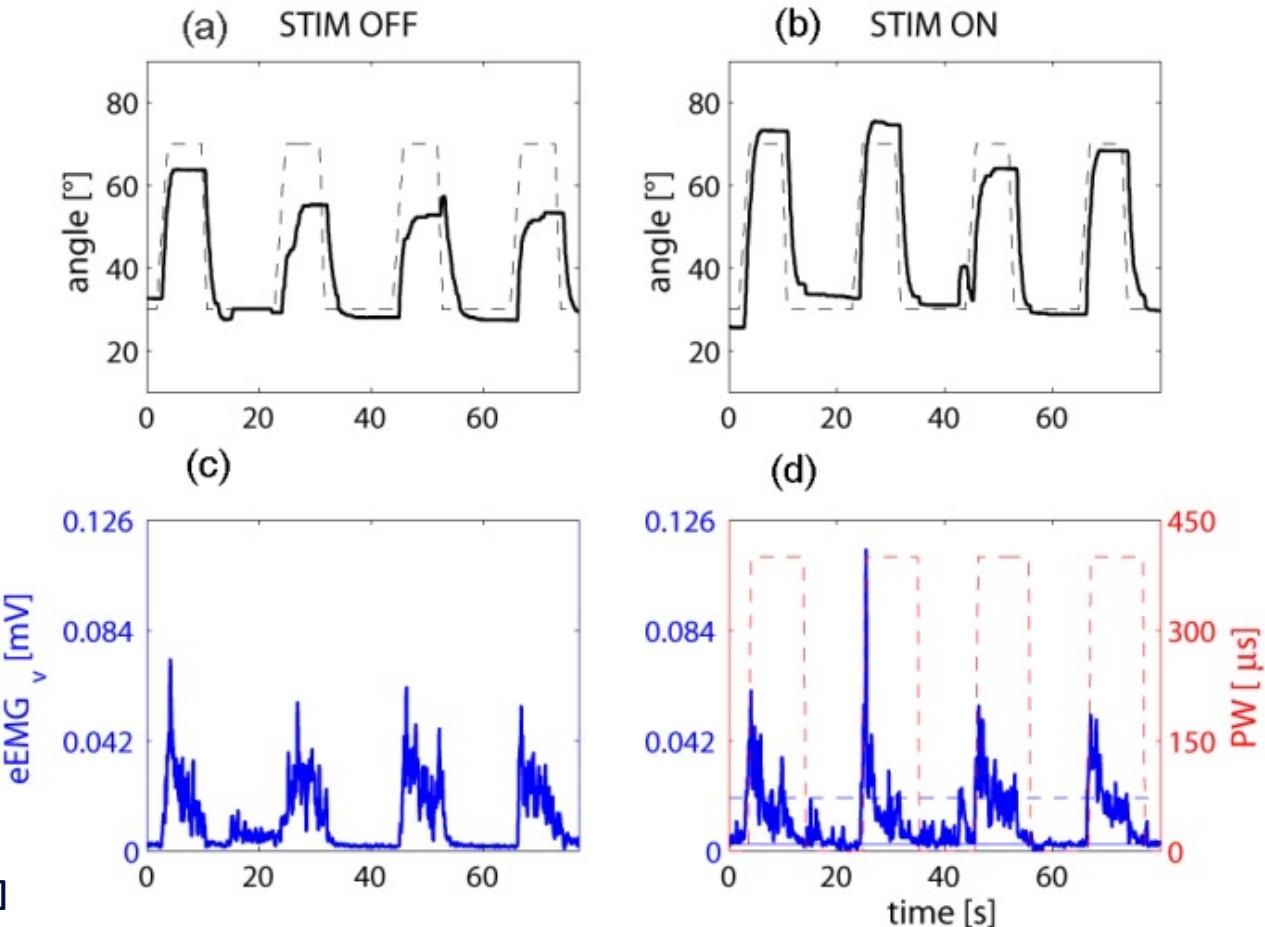
Example of applications

Test of the ON/OFF controller

Task: elbow flexion-extension with and without myocontrolled-NMES support

Participants: 2 healthy subjects and 3 people with Spinal Cord Injury

The neuroprosthesis was integrated with a passive exoskeleton for weight relief to further support the patients.



[Ambrosini et al, JEK, 2014]

Conclusions

Restoration /rehabilitation

Sensors to connect intention to action: neuroprostheses

- Motor NP/Robots
 - EEG controlled NP
 - MEA controlled NP
 - ENG controlled NP
 - EMG controlled NP

TAKE HOME MESSAGES

The main resource is always brain neuroplasticity

The optimal sensor and NP solution depends on the target of the application and the disability

BCI neuroprostheses and Artificial Intelligence (Sept 2018)

Brain–computer interface (BCI) neurotechnology has the potential to reduce disability associated with paralysis by translating neural activity into control of assistive devices. Surveys of potential end-users have identified key BCI system features, including high accuracy, minimal daily setup, rapid response times, and multifunctionality. These performance characteristics are primarily influenced by the BCI’s neural decoding algorithm, which is trained to associate neural activation patterns with intended user actions. Here, we introduce a new deep neural network decoding framework for BCI systems enabling discrete movements that addresses these four key performance characteristics. Using intracortical data from a participant with tetraplegia, we provide offline results demonstrating that our decoder is highly accurate, sustains this performance beyond a year without explicit daily retraining by combining it with an unsupervised updating procedure, responds faster than competing methods, and can increase functionality with minimal retraining by using a technique known as transfer learning. We then show that our participant can use the decoder in real-time to reanimate his paralyzed forearm with functional electrical stimulation (FES), enabling accurate manipulation of three objects from the grasp and release test (GRT). These results demonstrate that deep neural network decoders can advance the clinical translation of BCI technology.



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Section 4- CONTROLLERS FOR NEUROPROSTHESES,
MANAGING FATIGUE USING ANN CONTROLLERS

AIM

To modulate the current stimulus during the movement according to the characteristics of the biological systems to control (non linearity and time variability) so to achieve an accurate, smooth and robust task completion

EXISTING CONTROL STRATEGIES :

- FEEDFORWARD
- FEEDBACK
- MODEL BASED
- ADAPTIVE CONTROLLERS
- CONTROLLERS BASED ON ARTIFICIAL NEURAL NETWORKS

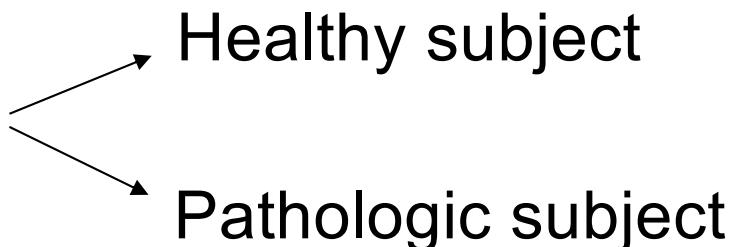
Choose a simple movement

Develop a novel control system

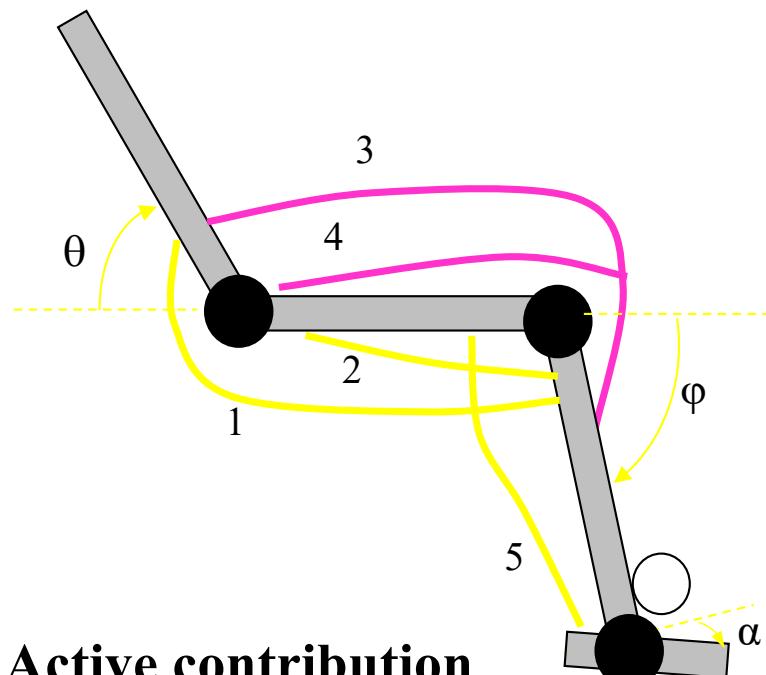
TWO STEPS:

1) Simulation trials

2) Experimental trials



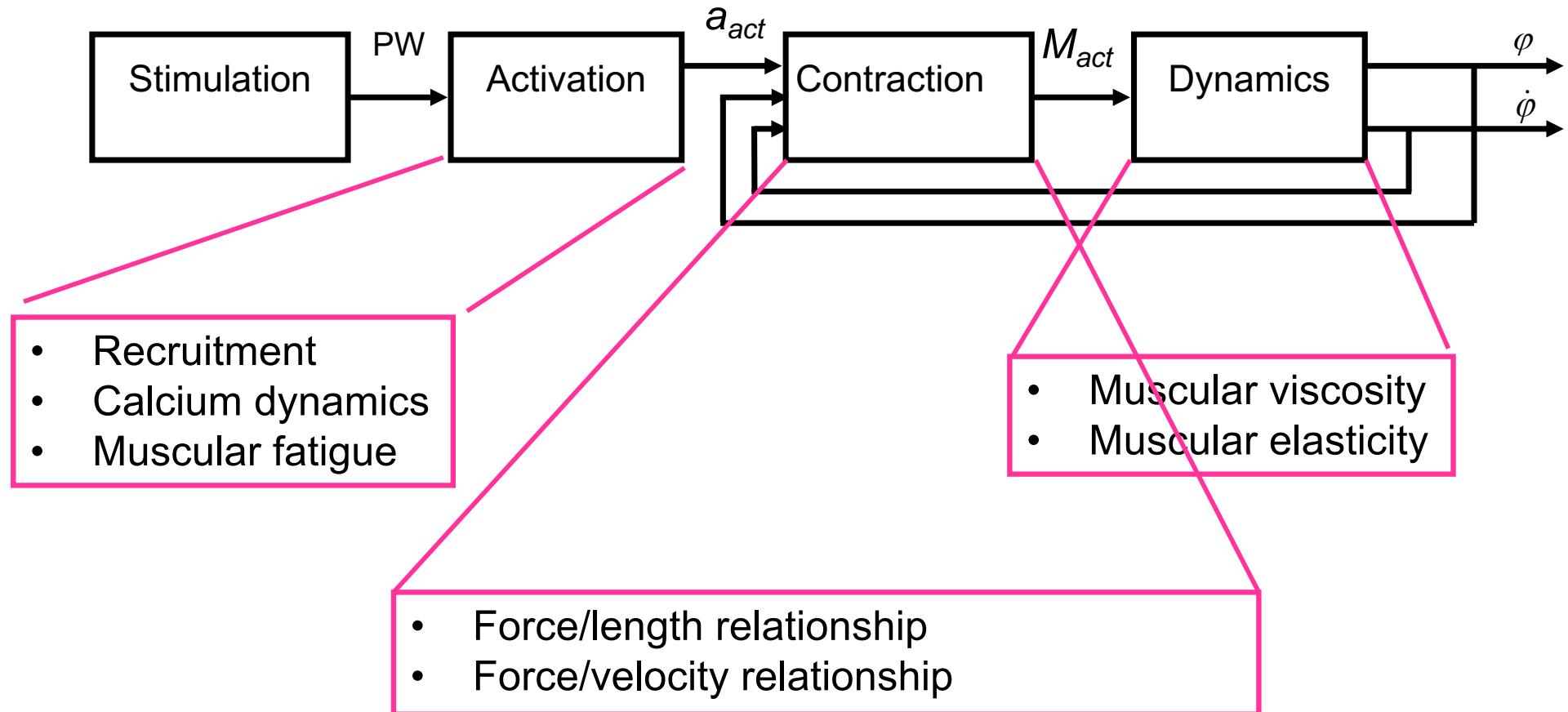
PLANT



Active contribution
Passive contribution

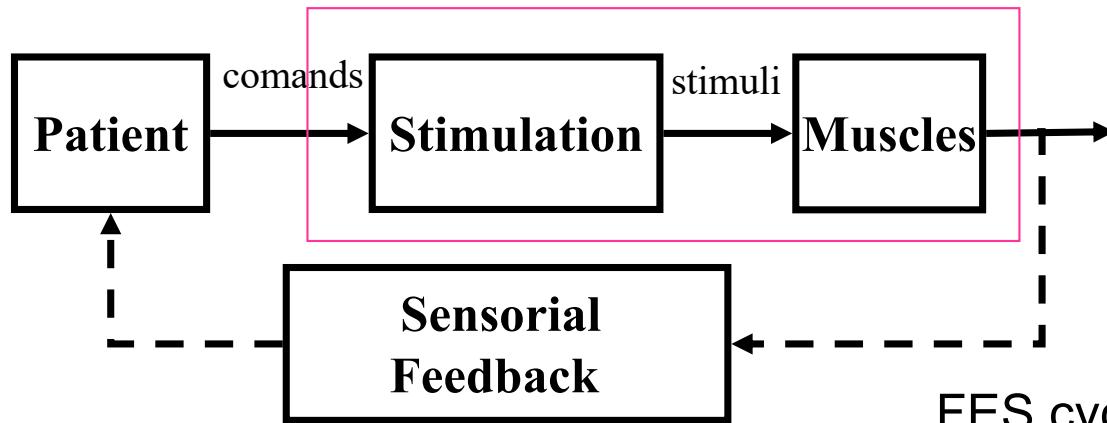
1. Biceps femoris caput lungum,
semitendinosus, semimembranosus
2. Biceps femoris caput brevis
3. Rectus femoris
4. Vasti
5. Lateral and medialis gastrocnemius

Simulation: biomechanical neuro-muscular model



Riener et al., 1997

Feed-forward Control (OPEN LOOP)



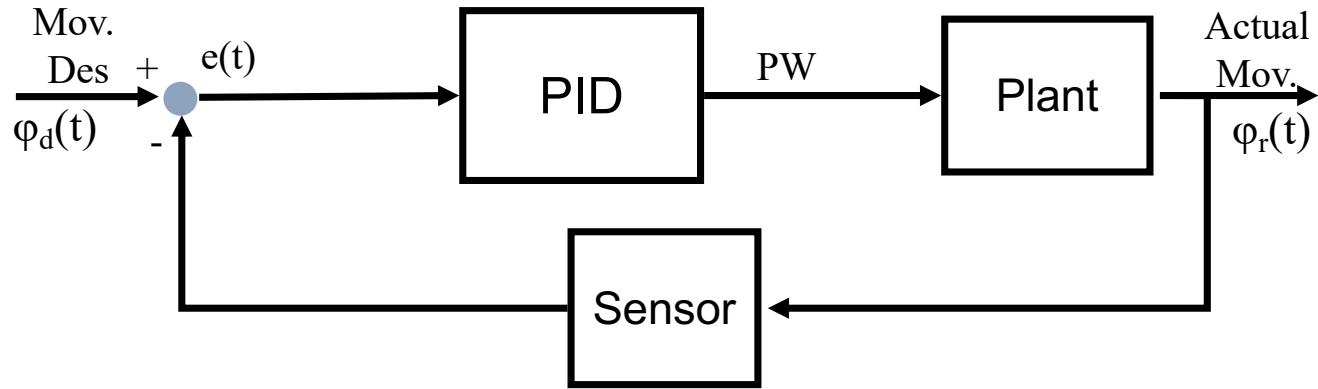
FES cycling controlled on crank angle is a feedforward automatic controller....

Fixed Stimulation trains

Stimulation triggered by manual or heel switches or measures of the task

- No disturbances' compensation
- Necessity of direct control by the patient
- Produces fixed and jerky movements
- Not adaptable to fatiguing muscles

PID controller

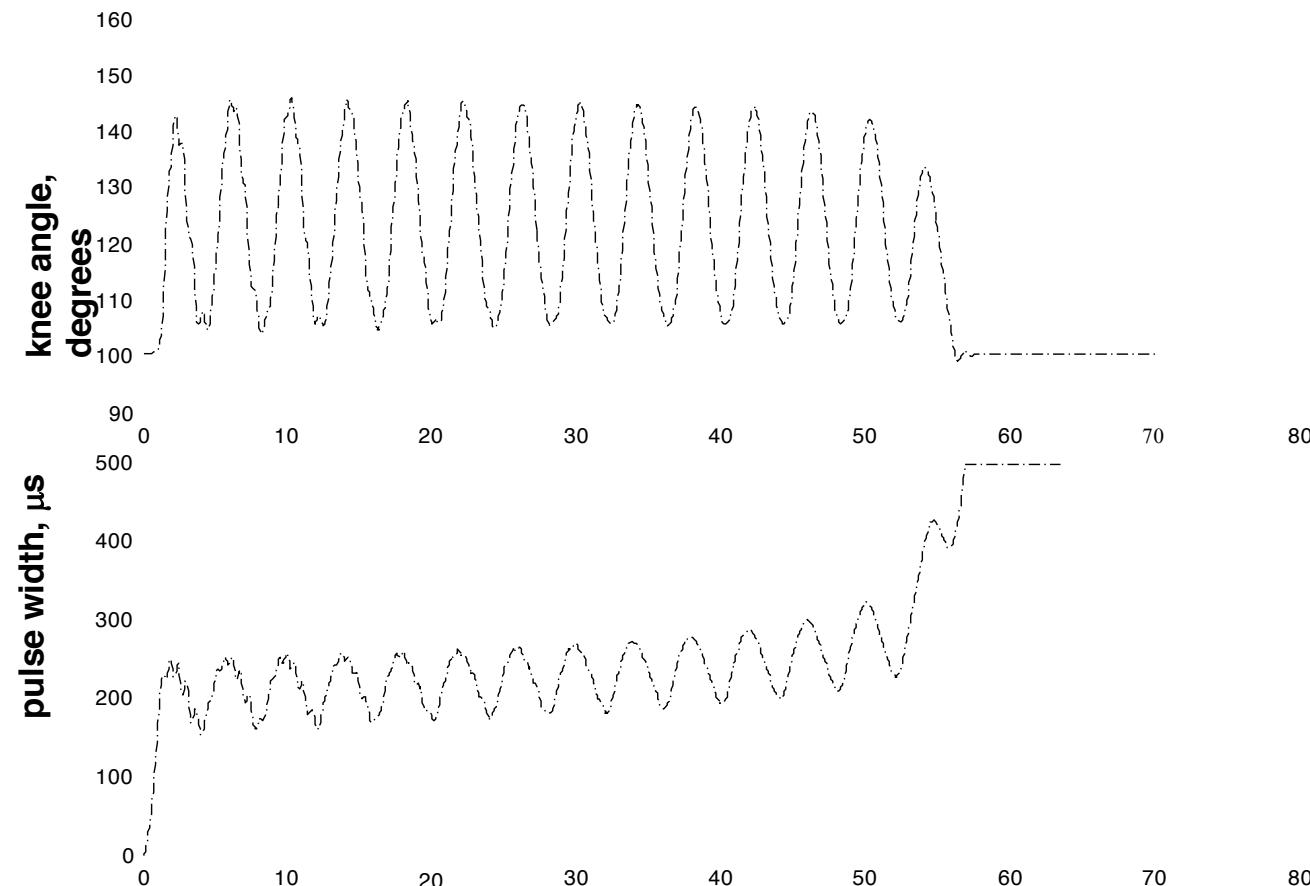


Stimulation changes according to the error between the desired and obtained signal

Compensation of unforeseen events

$$pw(t) = K_p \cdot e(t) + K_d \frac{de(t)}{dt} + K_i \cdot \int_0^t e(t) dt$$

Feedback controller

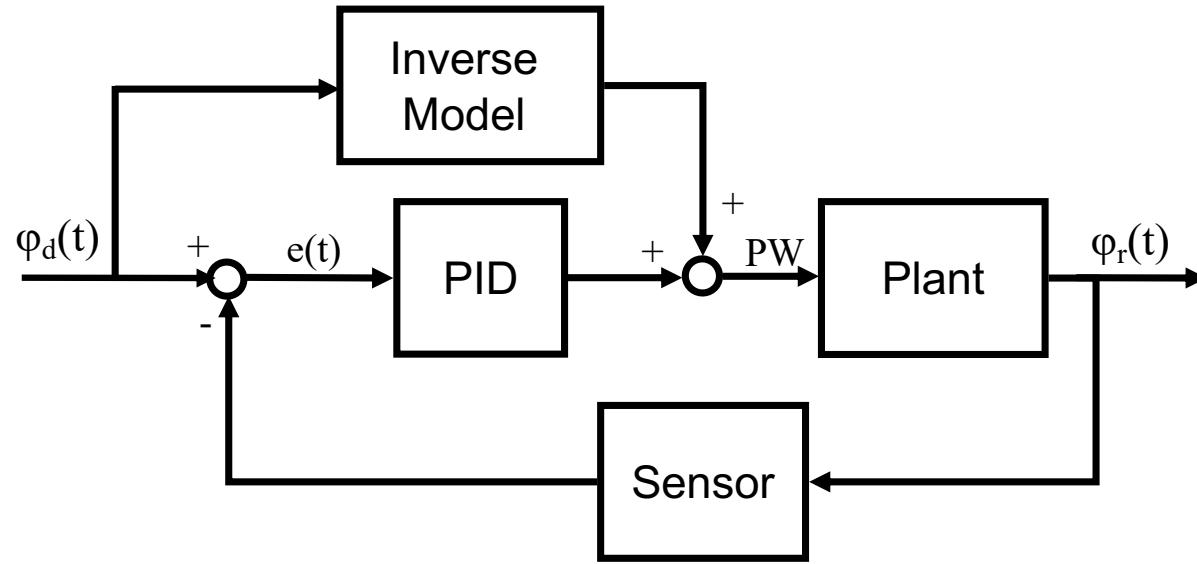


LIMITS

- Linear controller to pilot a non linear and time variant system
- Difficult identification of the controller coefficients
- Delay in the control due to the dominant pole to stabilize the feedback

Impossible to compensate fast disturbances

Model-based control

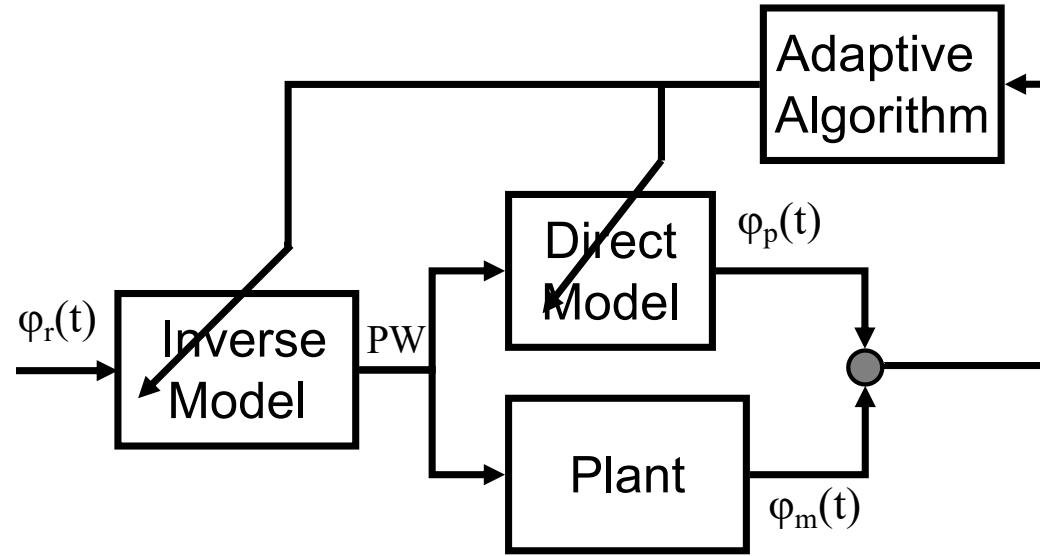


Reduction of the controller delay thanks to the introduction of the feedforward inverse model

LIMITS

- Inversion of the neuro-musculo-skeletal system
- Modellization with fixed parameters of a time variant system
- Difficultly to customize on a single subject

Adaptive controllers



Adaptive systems can follow angular trajectories when they are affected by muscular fatigue or external disturbances

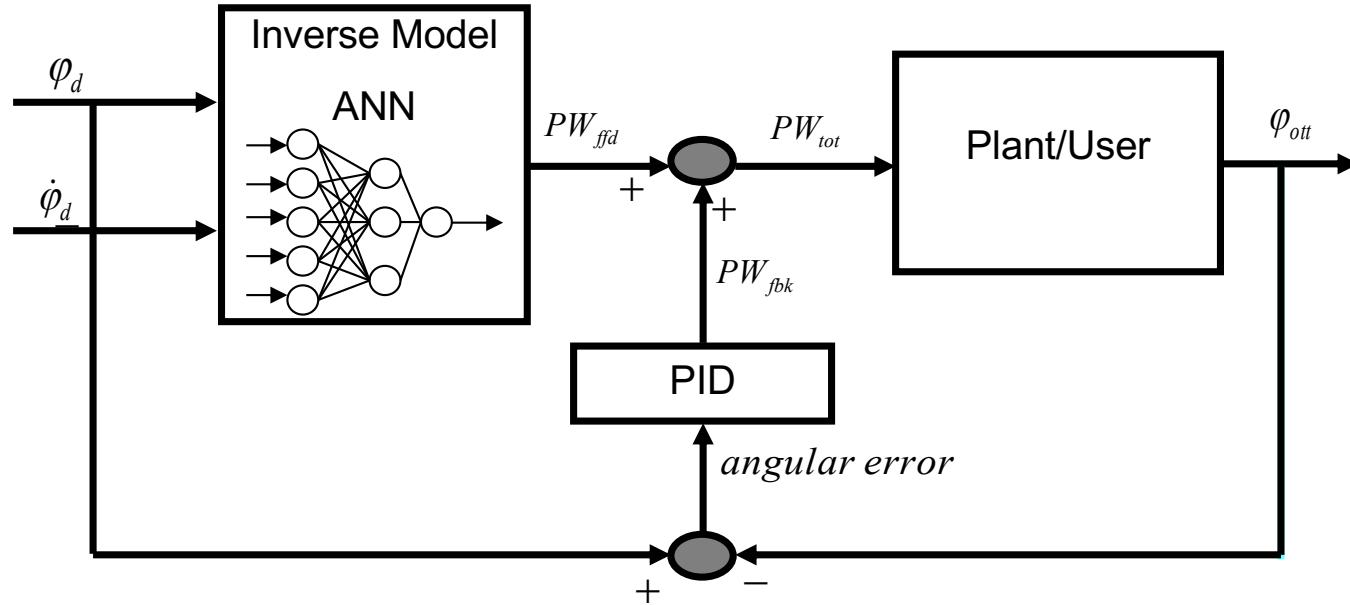
LIMITS

- Inversion of the neuro-musculo-skeletal system
- Convergence problems of the algorithm used to estimate the parameters

WHY?

- ✓ Black Box approach
- ✓ Generalization
- ✓ Adaptability
- ✓ Identification and control of non linear and time variant systems
- ✓ Availability of training set data?

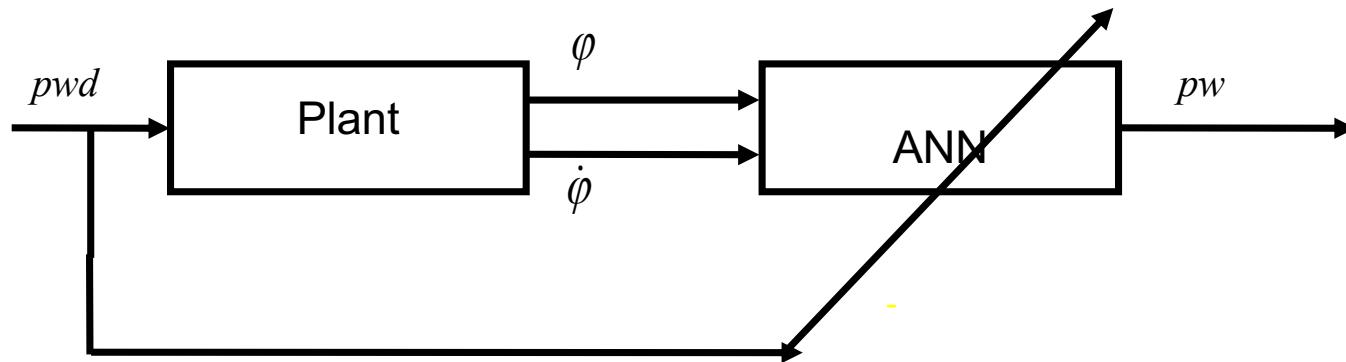
Neural Inverse Model



- ✓ Quadriceps Stimulation for knee flexion/extension
- ✓ GOAL: assure repetitions of knee flex/ext for muscular conditioning
 - ✓ Problem of fatigue controls more than trajectory tracking!
- ✓ Can we collect a training set ?

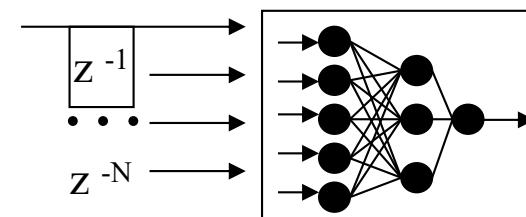
Inverse model identification: NN training set collection

TRAINING

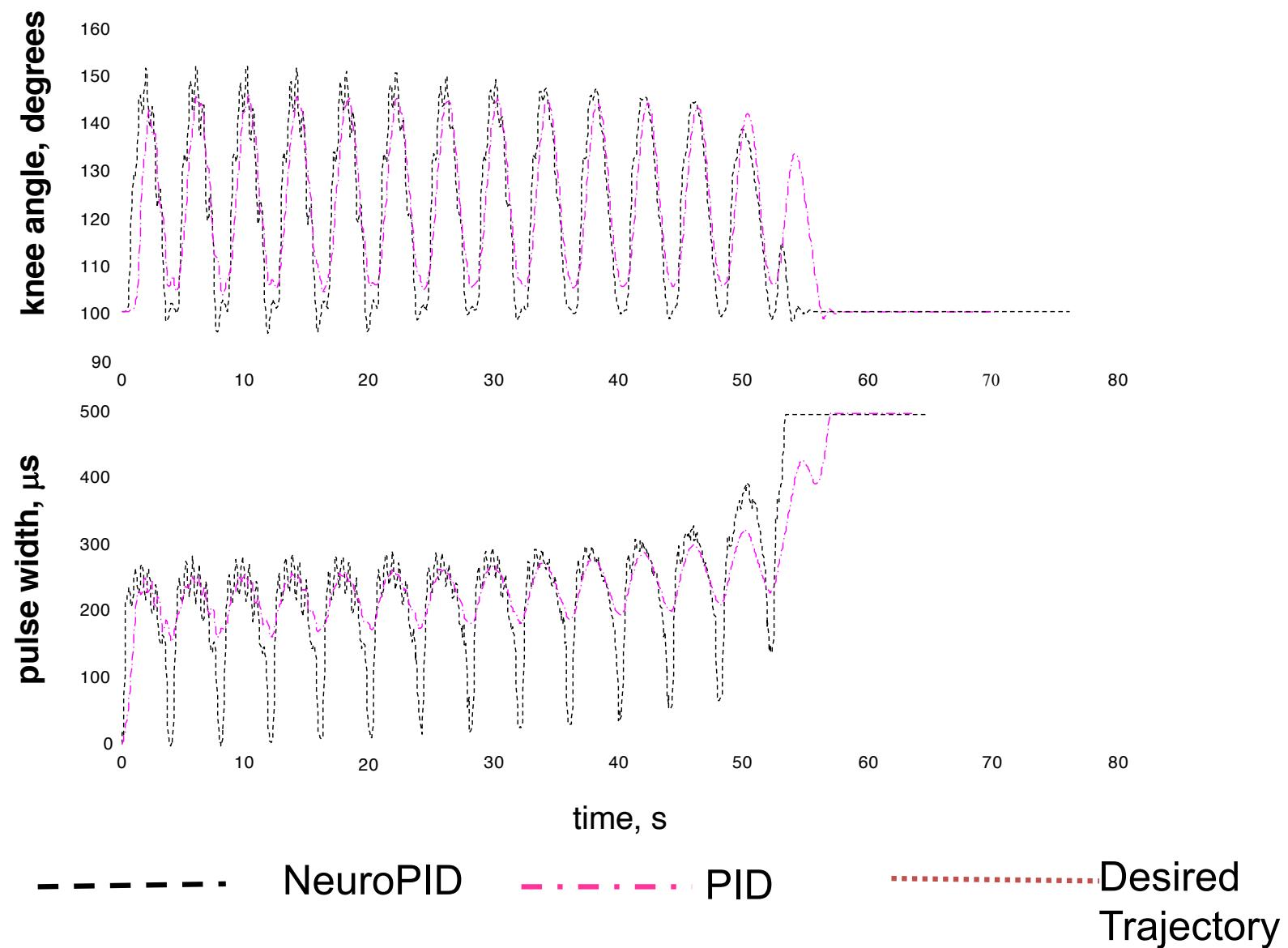


NETWORK CHOICE

- ✓ Multi layer perceptron with time delay in the inputs in order to identify the system time variability

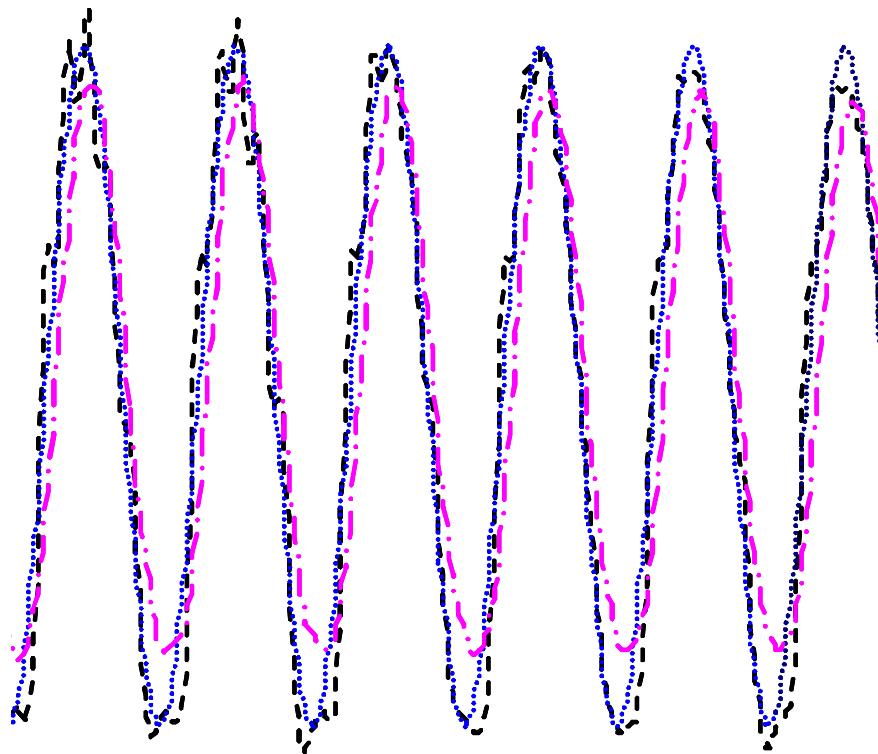


PID vs NeuroPID

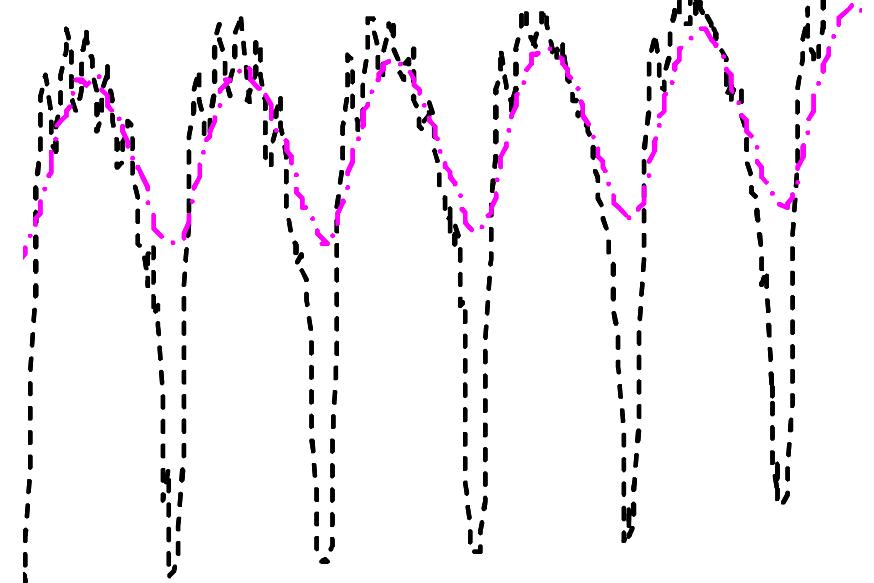


PID vs Neuro PID

Angle



Pulsewidth



----- NeuroPID

- - - - - PID

Desired
trajectory

It comprises a neural inverse model and a PID as a feedback controller

- Reduces the delay effect of the PID controller
- Overstresses the system in order to follow the desired trajectory
- Overcomes the problem of intermediate solicitations

However....

- A huge improvement with respect to the PID alone is not obtained and instead the training of the ANN inverse model is required

ERROR MAPPING CONTROLLER

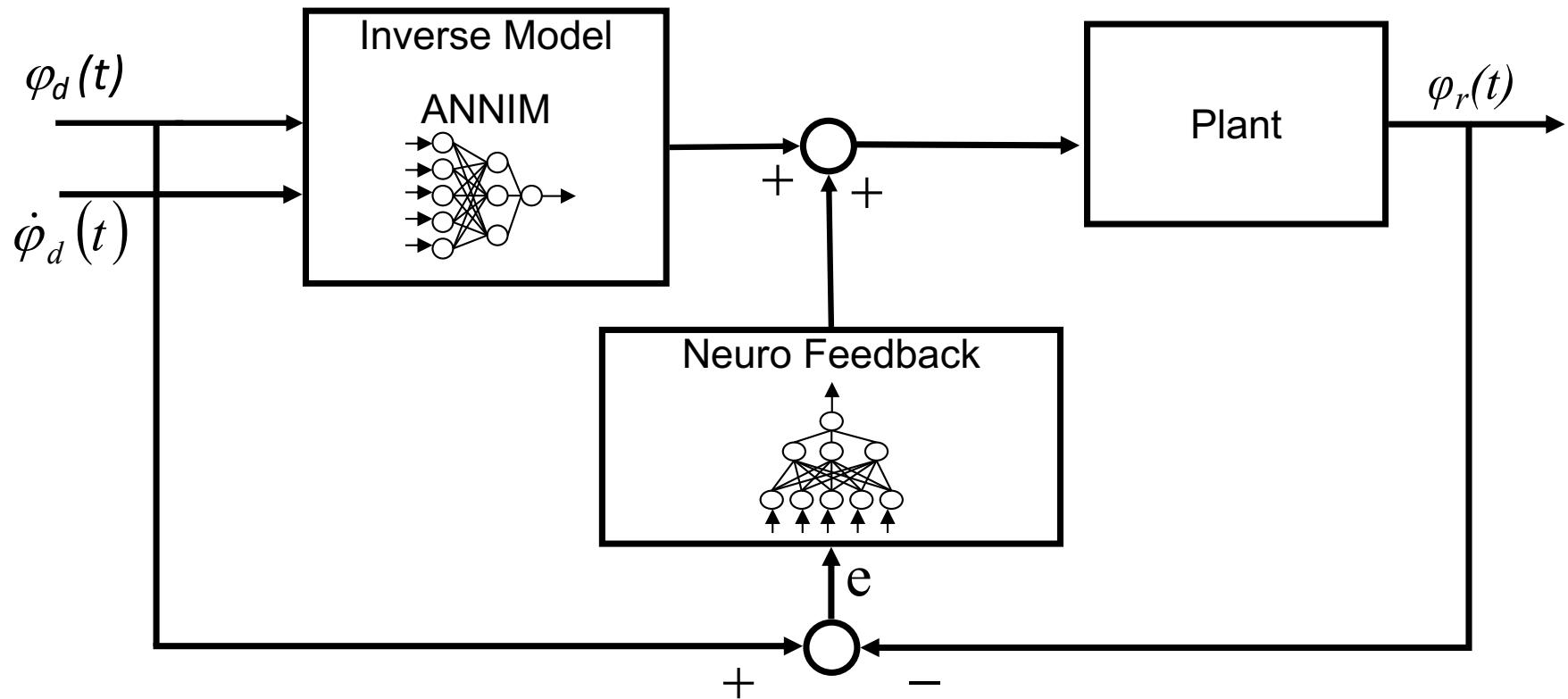
OBJECTIVE:

To make the control system able to map the muscular fatigue of the subject and not only the trajectory tracking problem

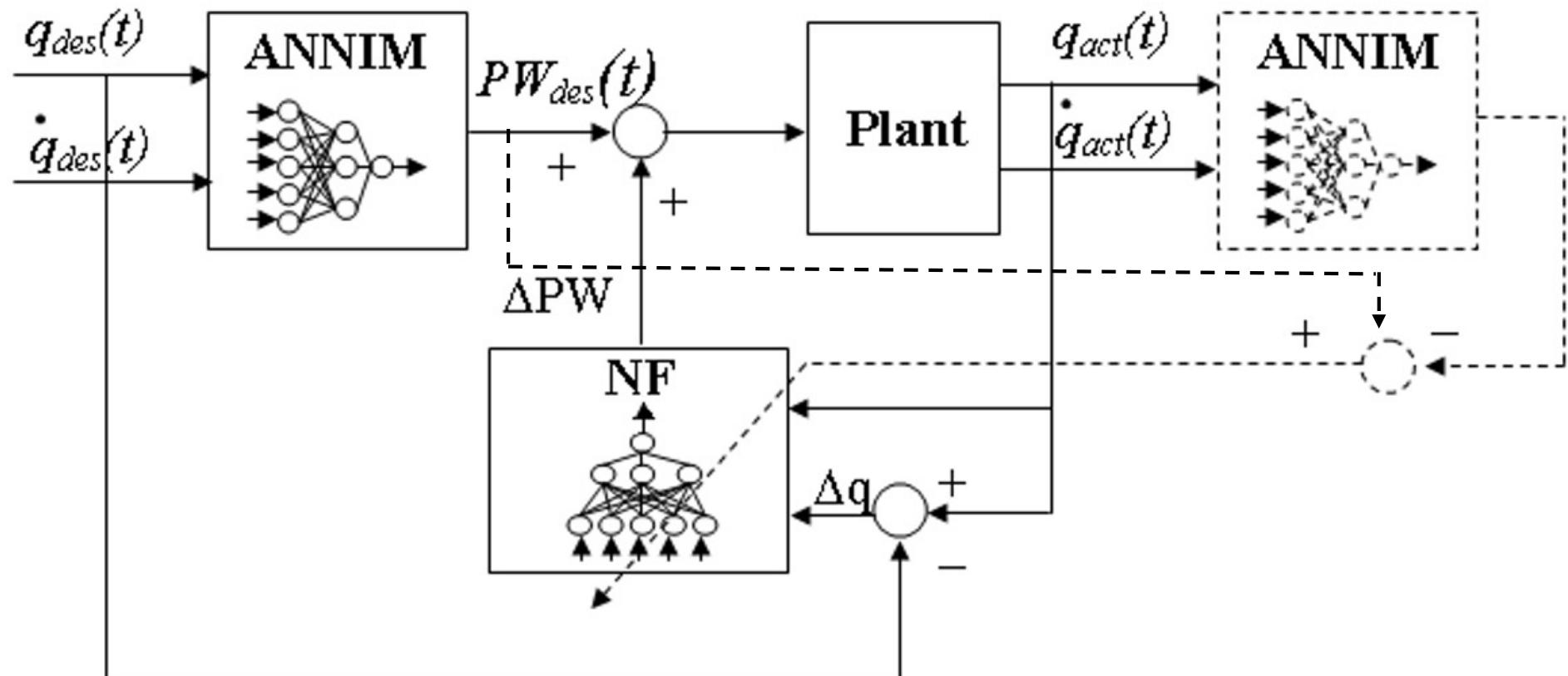
<http://www.jneuroengrehab.com/content/3/1/25>

Neurofeedback

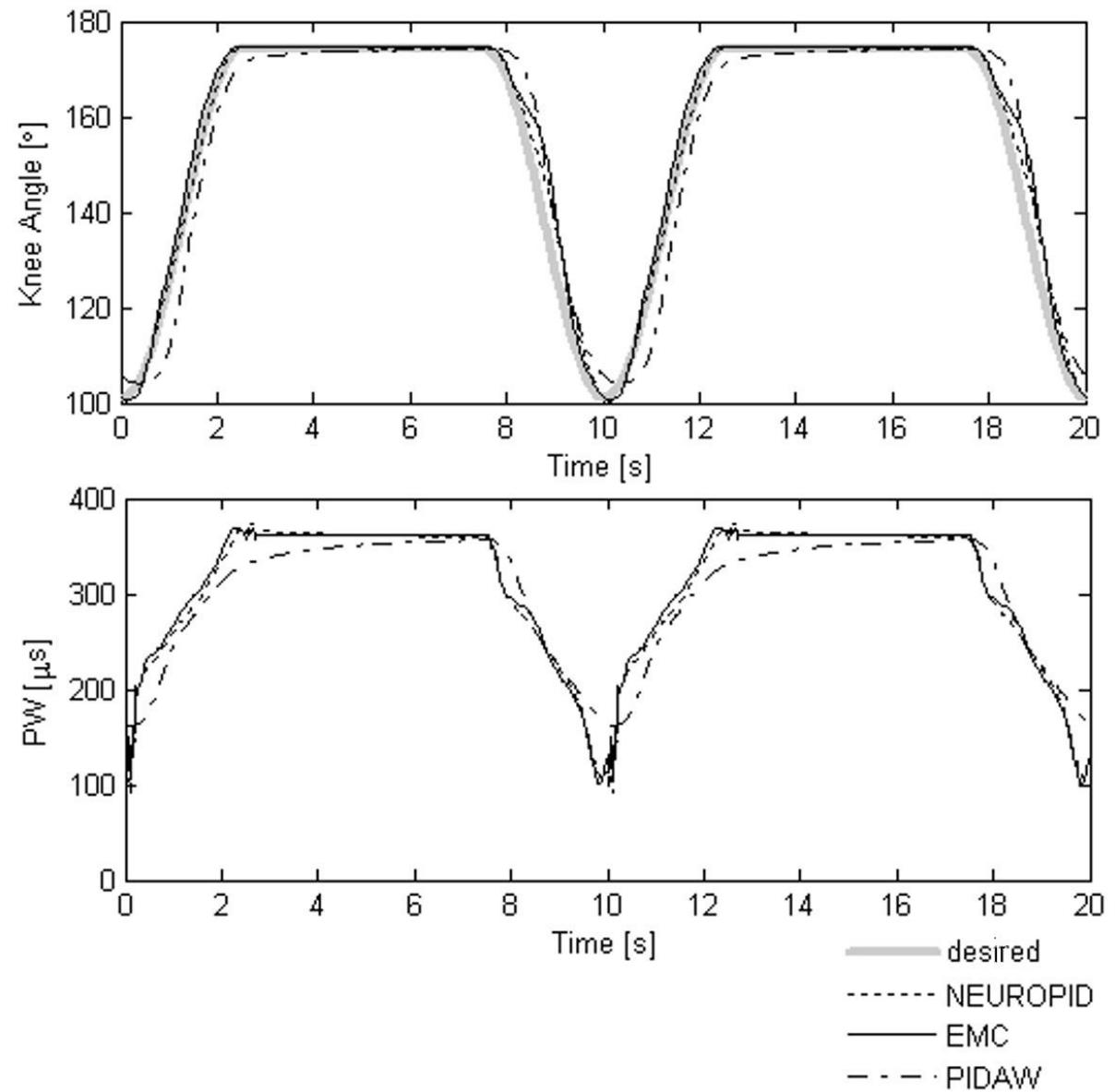
Control the stimulation patterns adapting the **time variability** to the muscular properties of a **single subject**



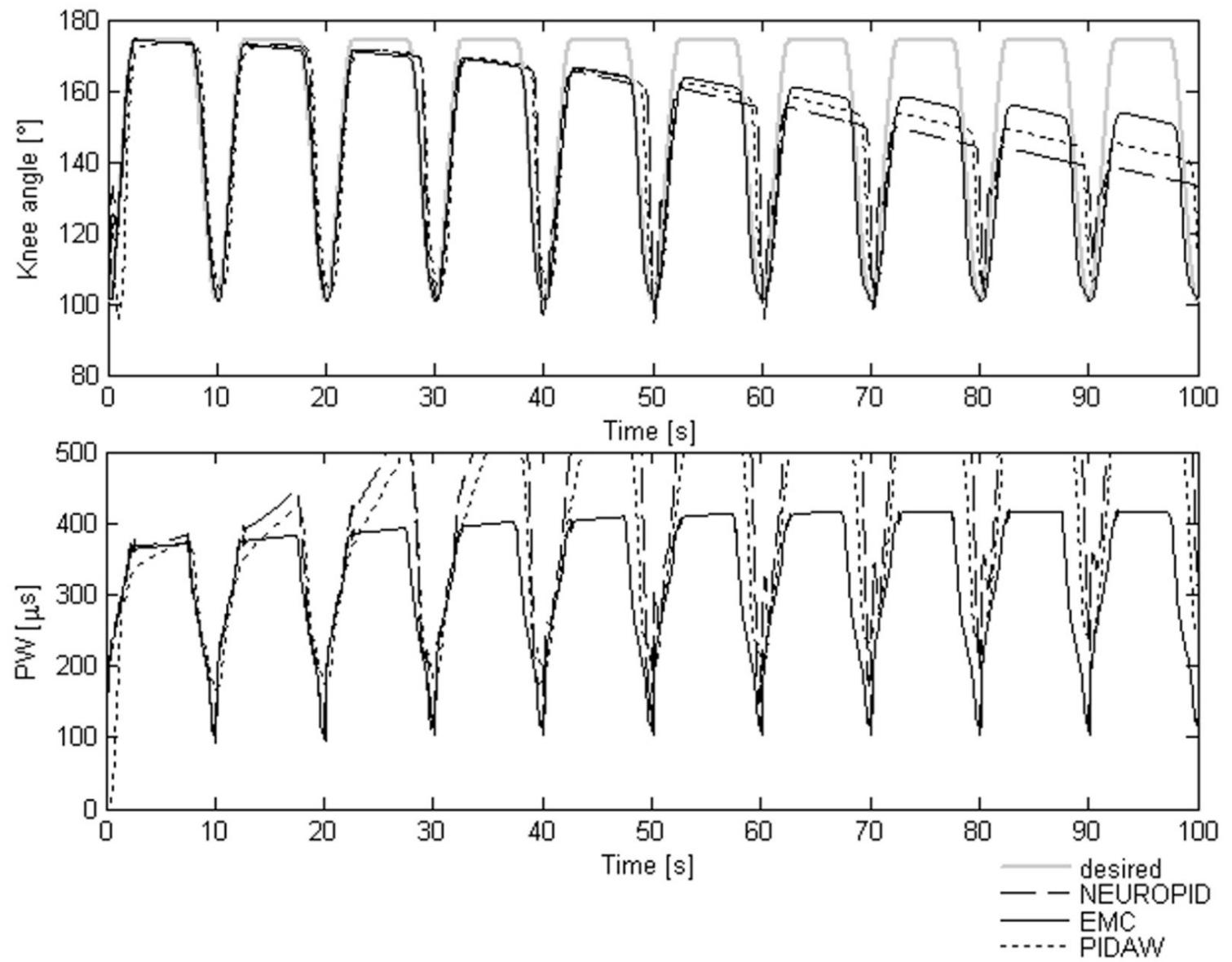
Training Problem



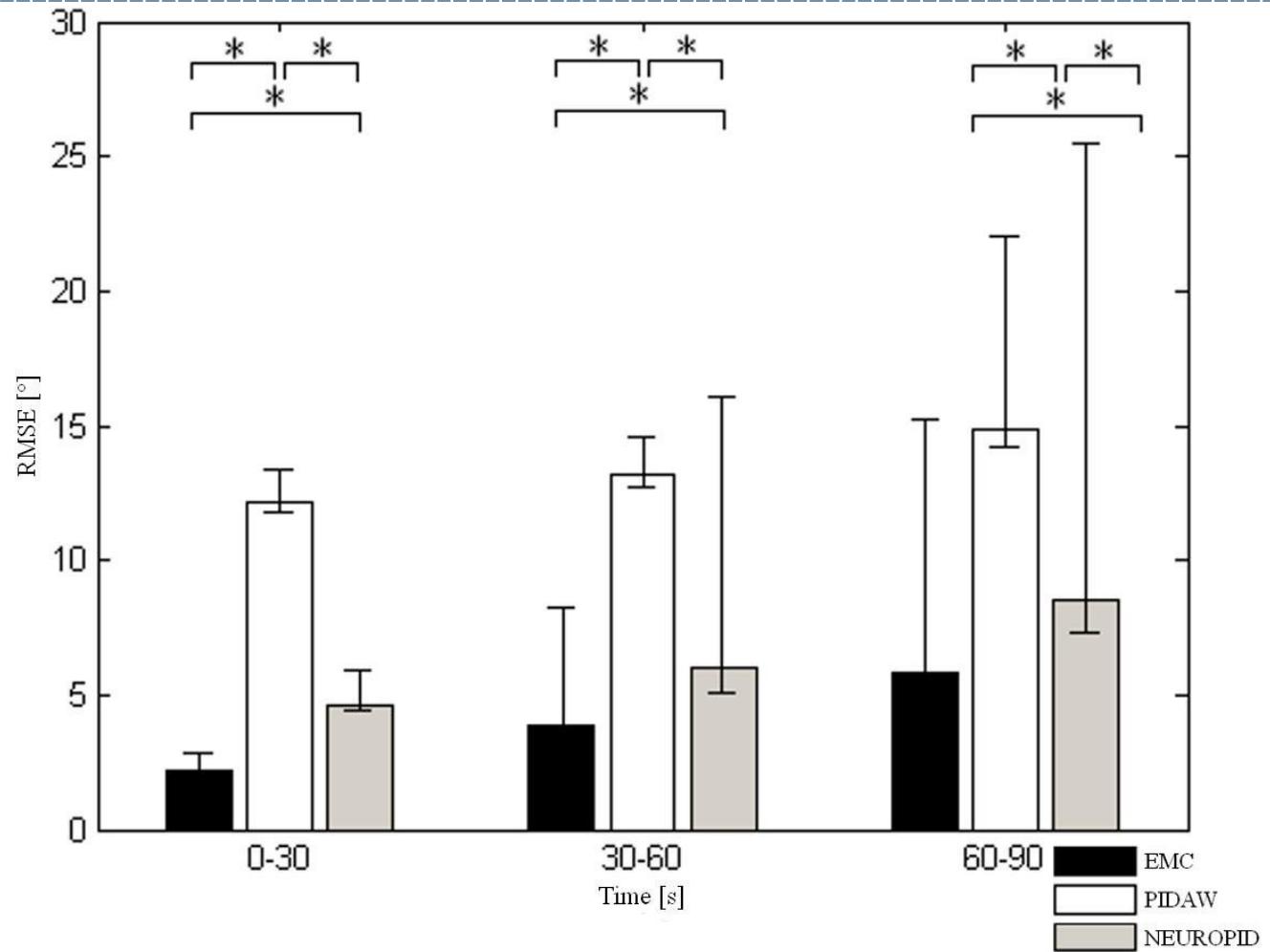
Tracking ability



How to manage muscular fatigue



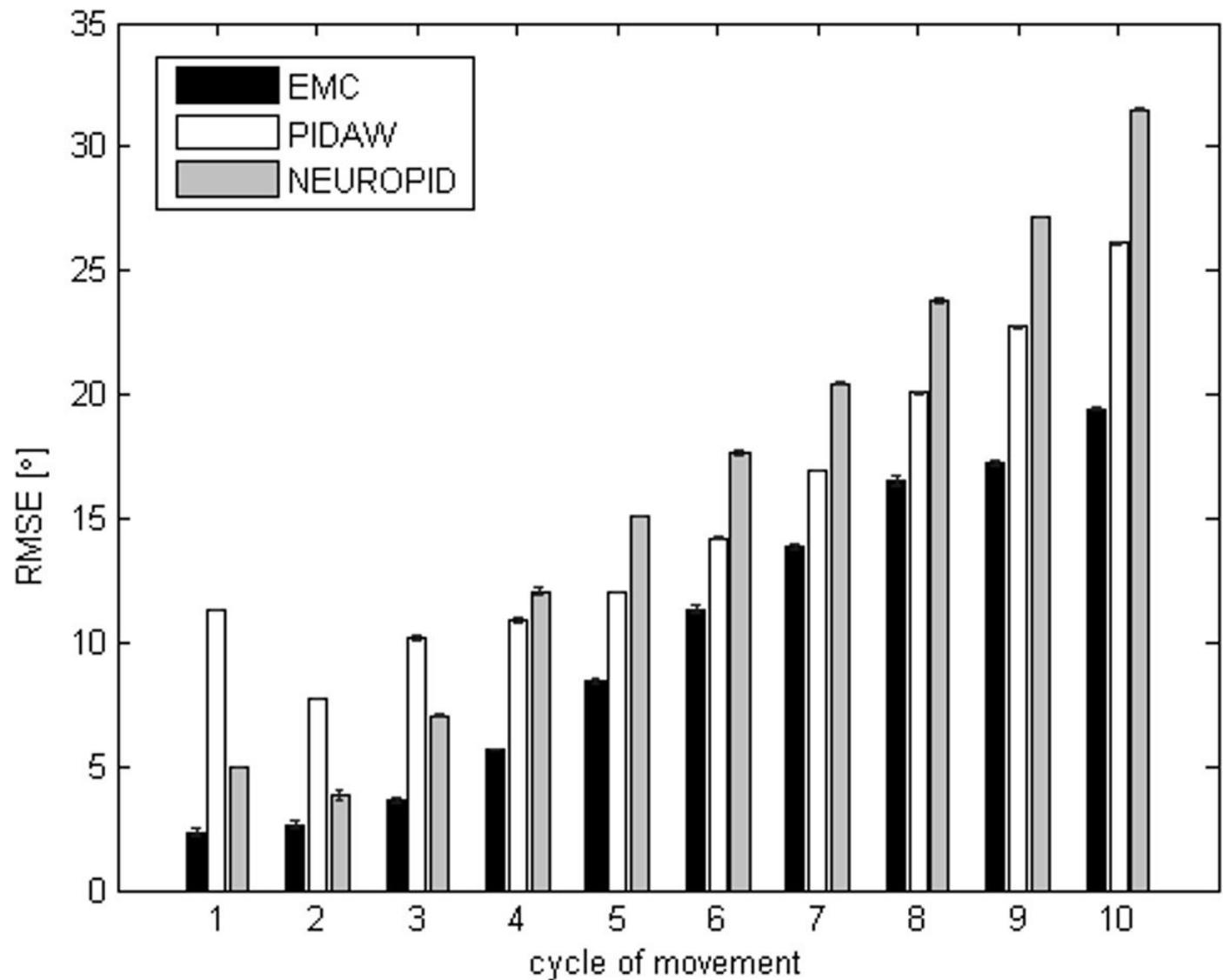
How to manage muscular fatigue



Evaluation of untrained disturbances

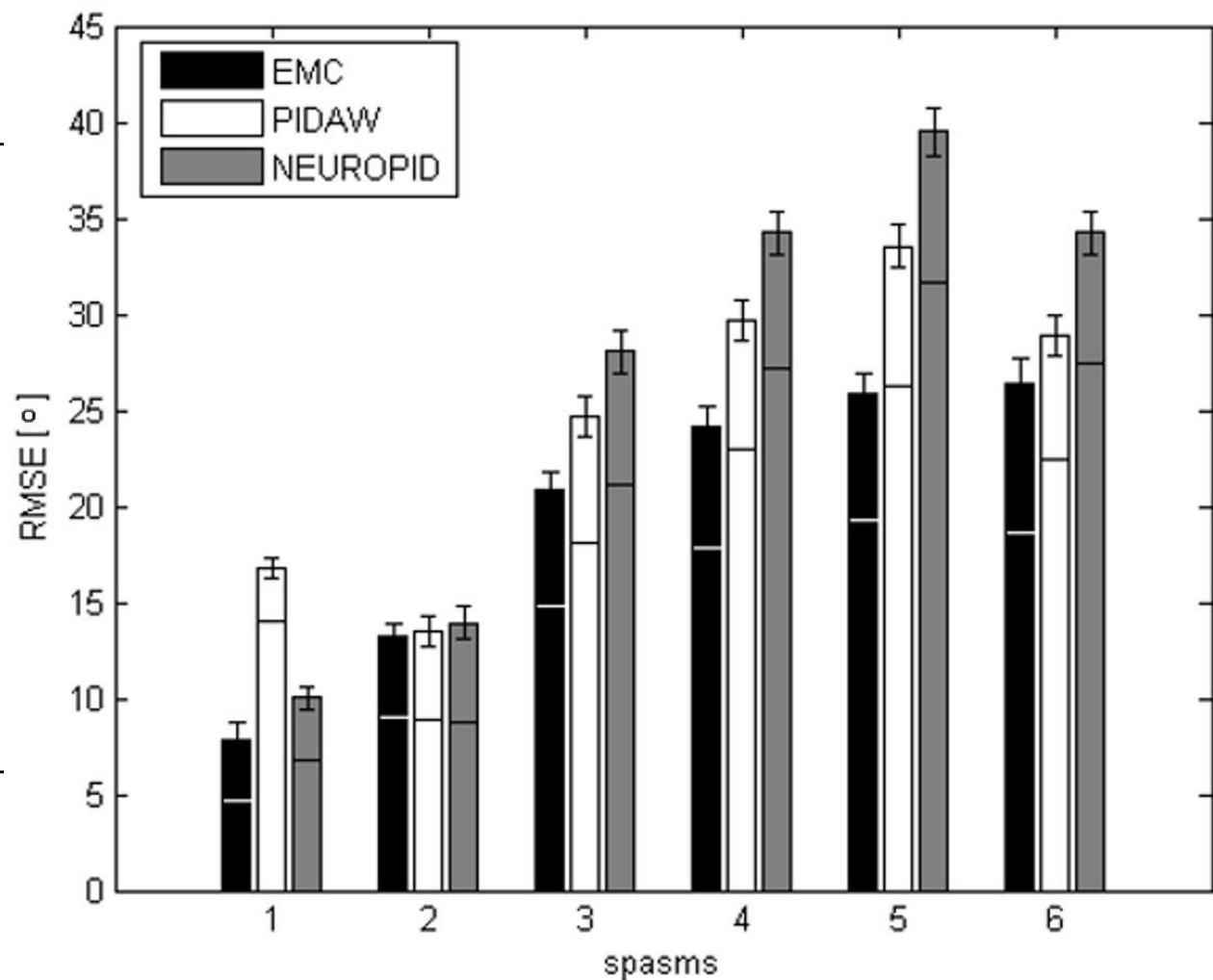
1)Distributed noise

Erroneous placement of electrodes, not well stucked electrodes, changes in the muscular condition, erroneous placement of the electro-goniometer



2) Spasms

SPASM	start (s)	Phase of movement
1	1.5	Raising/ext
2	20	Raising
3	38	Return
4	52	Extension
5	64	Extension
6	75	Extension



The angular error increase is due to the spasm (second part of each bar) and it is the same for all the controllers independently on the instant in which the spasm is simulated during the movement; also the ANN , even if the spasms where not presented in the TS, showed good generalization ability on spasms

Inter and intra- subject variability

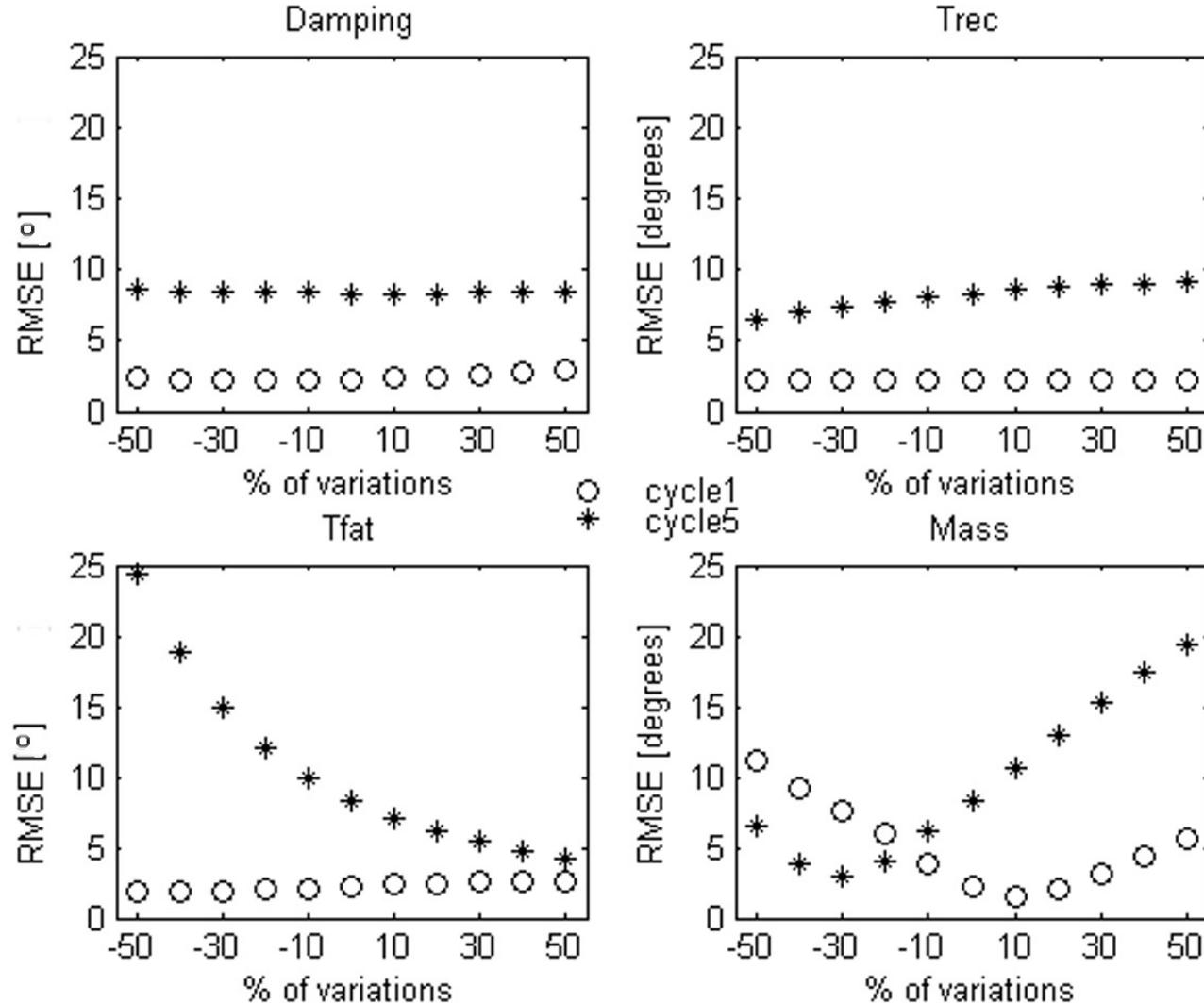
Objective:

When the subject changes and when the session day changes, the features of the system to be controlled also change...

RE-CALIBRATION TIME and/or GENERALIZATION CAPACITY

1) ROBUSTNESS

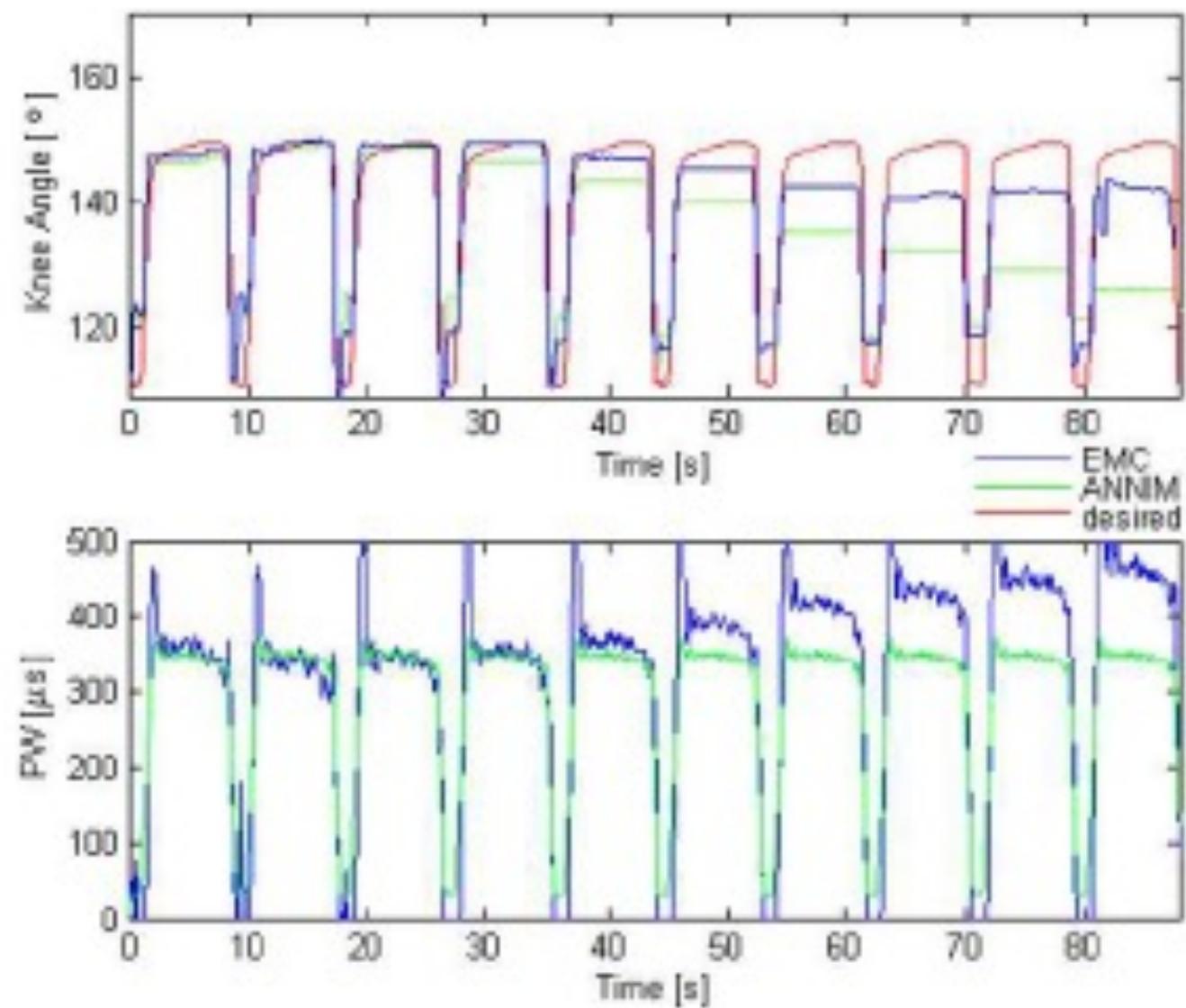
To verify what is the effect of a percentage change of some parameters of the plant (Damping coefficient, Trec and Tfat are the time constant of fatigue, Mass) on the tracking error in the first (without fatigue) and last movement of the knee (with fatigue)



2) SINGLE SESSION Calibration

After an electrode replacement, the current amplitude used by the controller has to be re-calibrated...

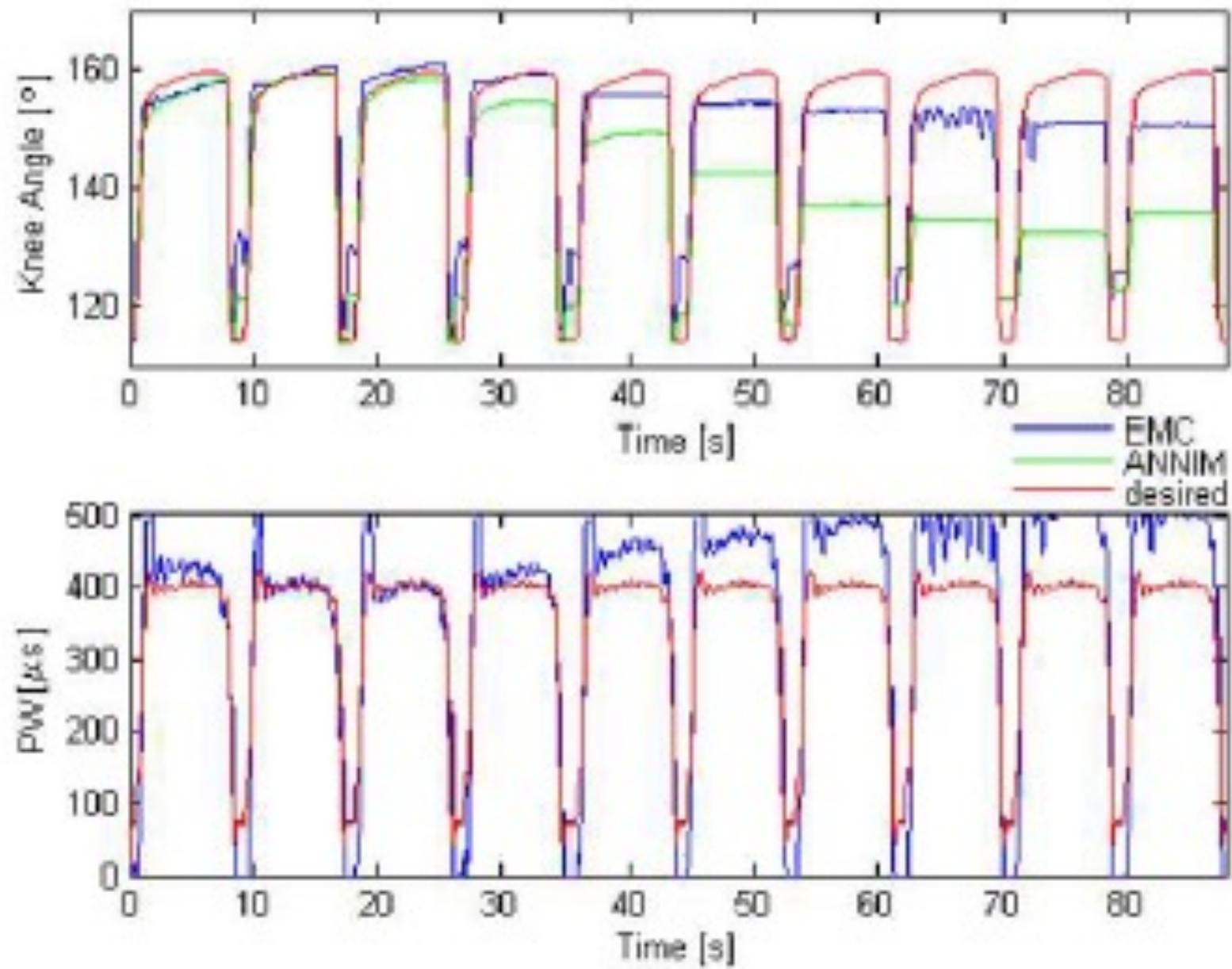
Experiments on one patient





Experiments on one patient

Testing signal



Experiments on one patient Load 0,5Kg

