**MOTOR CONTROL**

**1) Define the inverse model.**

The inverse model is one of the internal models involved in motor control. Its role is to control the task in a feed-forward loop, by computing the motor commands that will produce as a result the desired trajectory.

**2) Which elements of the primary motor cortex can be associated to the inverse model functions?**

**3) Provide and describe an experimental example, which demonstrates the existence of the direct model.**

The existence of the forward model can be proved with an experimental setup which aims to neglect/bypass the feedback involved in motor commands. For this setup, a subject is required to replicate, on a force-sensitive lever, a force that he has previously felt by the means of an external actuator: in this condition, when the procedure is iterated, a consistent force escalation is recorded. This is due to the lack of the tactile feedback on the subject, which is applying the force on an external body: this proves that proprioceptive signals are attenuated by the forward model.

**REHABILITATION ROBOTICS**

**1) List and explain the advantages and disadvantages of myocontrol in rehabilitation robotics.**

The EMG signal is very easily acquired by surface electrodes placed on the skin, and its high signal-to-noise ratio makes it an optimal candidate as a control variable in a neurorobotics context. Because of such characteristics, it can be used both for triggering purposes and for proportional controlling in a feedforward or feedback loop. The processing of the EMG signal is, also, fundamental in order for it to properly be employed in a robot controller, and in most circumstances cannot rely on standard instrumentation. Plus, the recorded signal heavily relies on electrode placement and is affected by inter-subject variability: a calibration phase is therefore required at any experimental session

**2) Describe an algorithm for myocontrol in a rehabilitation robotic device.**

In a rehabilitation context, the EMG signal recorded from the patient can be used either for triggering assistance (*assistance-as-needed* protocol) or for controlling said assistance in a proportional manner: in the latter case the force provided by the robot is proportional to the power of the signal itself. In this case, the subject has again full control of the triggering and of the trajectories, but additional force can be provided as needed.

**3) What does IIa, B mean in the AHA (American Heart Association) guidelines?**

**NEUROPROSTHESES**

**Consider a motor prosthesis for hand grasping controlled through EEG (i.e. BCI) and one controlled through EMG. The actions to be controlled are: open the hand; close the hand.**

**Suppose to use the neuroprosthesis to restore hand grasping in:**

**1. a SCI patient;**

**2. a post-stroke subject in post-acute phase**

**3. an amputee**

**For each patient (1., 2., 3.) discuss the advantages and disadvantages of the two control strategies (BCI vs EMG-based), explaining the issues that need to be faced to evaluate the appropriateness of the solution.**

* SCI: The neural linking between the CNS and the limb is interrupted, therefore no EMG activity can be recorded. Here, the usage of a BCI implant is the sole option for recovery, but an intensive and long calibration of the prosthesis is necessary, as the EEG signal of the patient must be used to properly train the BCI
* Post-stroke: In this case, the signals generated at brain level correctly reach the muscles, but a portion of these signals is erroneous and uncoordinated. EMG-triggered FES will be, in this case, the optimal solution as it will promote brain plasticity at spinal level when combined with the volitional signals coming downstream from the brain
* Amputee: With a missing limb, both an EEG-based and an EMG-based approach are valid. The EMG must be acquired from a region which is proximal to the amputation site (*e.g.,* electrodes on the forearm for an amputated hand) and correlated to the desired motion of the missing limn. With EEG recording, instead,

**NEUROENGINEERING FOR BIOLOGY**

**1) Consider the following types of *in vitro* neuronal models: dissociated cultured neuronal networks and brain slices. Describe the two models and discuss their advantages and disadvantages.**

“Brain slices” models are obtained by thinly cutting a brain sample and analysing the mature and already developed neuronal networks in the slices themselves, while “dissociated cultured” models are obtained culturing Induced Pluripotent Cells in vitro and observing the evolution of the network that they form over time. Brain slices are an optimal representation of a complete and fully functional brain network but are not patient-specific and may present connectivity artifacts on the sliced plane. On the other hand, dissociated cultures are patient specific as the IPCs are obtained from the subject itself, but as they aren’t grown in the proper physiological context they do not present the morphological/connectivity that characterize a proper cerebellar neural network.

**2) Suppose to acquire extracellular activity from dissociated cultured neurons with MEA. Compare temporal and spatial resolution with respect to patch-clamp. Explain at least two methods that could be used to increase spatial resolution.**

Acquisition with MEA suffers from a low spatial resolution, where probing happens only in the area relatively close to each microelectrode: relevant activity may occur in regions which are not detected by the closest electrodes. On the other hand, neurons can be patch-clamped at any location, but the amount of pipettes for culture is limited. The temporal scale of acquisition can be much longer for MEAs, but is affected by the sampling rate/processing times of the instrumentation; patch clamp can instead be employed for a shorter time, but with increased temporal resolution

**MOTOR CONTROL: THE CEREBELLUM**

**1) Describe the cytological architecture of the cerebellum.**

The cerebellar cortex, which processes motor commands, is a layered structure: deepest is the *granular* layer, where the mossy fibres connect to the granule cells. Here are also located the Deep Cerebellar Nuclei. Above is the *Purkinje* layer, location of the soma of the Purkinje cells and where they are connected by the inhibitory synapses of the climbing fibres. The uppermost layer is the *molecular* one, where the parallel fibres run and connect with the dendrites of the Purkinje cells and the Basket cells.

**2) Define Spike-Time Dependent Plasticity (STDP). Where does STDP take place in the cerebellum?**

Spike-Time Dependent Plasticity is the experimental evidence of the Hebbian learning paradigm: when two neurons involved in a synapses fire without (or with very small) delays, the synapse’s efficiency and strength increase, proportionally to the inter-spike delay (shorter delays induce a higher enhancement). The cerebellar synapses which manifest a STDP behaviour are the ones between the parallel fibres and the dendrites of the Purkinje cells

**3) Describe how plasticity at PF-PC synapses takes place and contributes to cerebellum-driven motor learning.**

The climbing fibres that innervate the Purkinje cells are assumed to carry error signals that either strengthen/depress (LTP/LTD) the parallel fibers’ synapses which instead carry information about the motor command: the synchronization between the error signal and the motor command seems to drive motor learning in the cerebellum

**REHABILITATION ROBOTICS AND ORTHOTICS**

**1) Definition of rehabilitation robotics and orthoses.**

Rehab robotics is a categorization for short-term-usage devices which aim at the functional/anatomical recovery of an impaired limb, which is used by the clinician to promote the rehabilitation of a patient so that he can interact with the environment unassisted. Orthotics, instead, are long-term devices which are used and designed to guide and assist motion of subjects who, due to neurological disorders or permanent disabilities, cannot properly perform motor tasks unassisted, both in terms of coordination and bearing of weights.

**2) Provide an example of a device, which can be used only as orthotics. Describe the population, the mechanical concept and the control strategy. Discuss why it can’t be applied to rehabilitation.**

**3) Provide an example of a device, which can be used only as rehabilitation device. Describe the population, the mechanical concept and the control strategy. Discuss why it can’t be applied as orthotics.**

**NEUROPROSTHESES: FUNCTIONAL ELECTRICAL STIMULATION**

**1) What are the hypothesized principles at the basis of neuroplasticity effect of FES?**

The basis of FES-induced neuroplasticity is the Rashton hypothesis, which states the following: *While the dromic signal from the FES stimulates only the muscular activity, the antidromically-directed stimulus meets, at spinal level, the downwards pulses that are generated from the cerebellum and the motor cortex, which are of volitional nature. The combination of this stimuli at spinal level generates STDP which reinforces the synapses involved in the volitional control.*

**2) What are the reasons to use EMG-controlled FES? What are the technical issues and how these can be solved?**

Controlling the intensity of FES through the EMG signal is a useful approach when aiming at an optimal *assistance-as-needed* protocol: EMG activity can, as a matter of fact, be the triggering variable of the stimulation or the tuning variable in a feedback controller loop, that controls the FES in order to produce a stimulus with intensity proportional to the muscular activity. Moreover, the combination between the neuromuscular command and the FES stimulus may promote neural plasticity.

**3) In the following situations, is EMG controlled FES worthy to be used or not?**

**A. A post stroke patient having no evident residual movement of the district to be trained**

Yes, the signal from the brain is reaching the muscles. Rushton hypothesis will reinforce the healthy synapses

**B. A SCI (Spinal Cord Injury) patient having no evident residual movement of the district to be trained**

No, the brain signal does not reach the muscular level

**C. A post stroke patient showing spasms in the district to be trained**

No, the spasm interferes with the synchronicity at spinal level

**D. A post stroke patient showing poor control in the district to be trained**

Yes, for the same reason as A.

***IN VITRO* NEUROENGINEERING: OPTICAL SOLUTIONS FOR RECORDING *IN VITRO* NEURONAL ACTIVATION**

**1) Explain the principle of working.**

Neuronal cells which are genetically engineered with peculiar photosensitive proteins that activate an electrical stimulus when hit by light. This way, electrical activity in the neurons can be controlled more precisely achieving higher spatiotemporal resolution.

**2) Provide a description of equipment and experimental solution using optical methods to record *in vitro* neuronal activity.**

For optical measurements of the neural activity a Voltage-Sensitive Dye (VSD) is required. The changes in voltage cause a shift in both the emission and absorption spectrum of the chosen VSD. From a fluorescence microscope, a change in the wavelength of the detected light can be reconducted to an electrical signal at a specific point in the microscope field of view.

**3) Discuss advantages and disadvantages with respect to MEA.**

While a MEA samples a batch of neurons close to each probing electrode, VSDs can perform single neuron measurements. Temporal resolution is usually dependent on the framerate of the camera sensor used for the acquisition.

**MOTOR CONTROL**

**1) Describe why motor control is a complex task**

Motor control is a process that involves very noisy signals, which are also non-stationary as they change in both a long-term and short-term time scale. In addition, the limited range of motion of joints and the effect of gravity make motor control a non-linear problem, that becomes highly sensitive to delays between the controller (the brain) and the actuators (the muscles).

**2) List and explain the features of voluntary movement**

1. Invariance from the end effector: The motor is achieved no matter what is the limb involved, but the precision/speed/efficiency are best in the most-trained end-effector

2. Reaction times are inversely proportional with the amount of information that needs to be processed

3. Speed/accuracy trade-off: The faster the speed of the task, the hardest is the processing of the corrective signals, therefore, accuracy is lower

4. Learning and experience increase the task efficiency

**3) Motor learning: what does it mean? What are its features?**

The motor learning paradigm states that the CNS implements strategies that aim at achieving the task in the most efficient way, in terms of accuracy, energy, speed and fatigue. It is therefore an optimization problem that occurs by the co-adaptation of neural control, in terms of electrical activity, and anatomical enhancement, from a kinematical and dynamical point of view. Motor learning is also the result of the coexistence of *innate capacities*, which are hard-wired in the brain and not “plastic” in terms of modification capabilities, and *learned capacities*, that are instead adaptable

**2. REHABILITATION ROBOTICS**

**1) What are the key factors for motor recovery in post-stroke patients and the major limitations of current conventional therapy?**

An effective and goal-directed motor recovery pathway shall cover the following key factors: an early intervention must be followed by a good amount of consistent practice, which gets repeated and adapted over time with activities which are more and more challenging and rewarding. The most important and influential factor is the amount of biofeedback and the proprioceptive signals that the subject experiences. Conventional therapy relies, for most of these aspects, on the activity of the clinician alone, which must follow closely the patient and adapt the exercises in relation to his needs and enhancing the amount of feedback in the right conditions: with a robotic approach, all these aspects are corrected by the robot controller, which is strictly focussed on the patient.

**2) What is neuroplasticity?**

Neuroplasticity is the modification of neuronal synapses in response to external stimuli. The neuronal circuits can recover their function if a correct training/rehabilitative pathway occurs, because in this process the synapses are reinforced, and the functional capability of the neurons is restored

**3) What is intended with the term of Maladaptive plasticity?**

Maladaptive plasticity is the phenomenon of biasing the recovery towards the erroneous tasks: *slacking* is, for example, a type of maladaptive plasticity. It occurs when the training is excessive and not goal-directed

**4) In case of assist-as-needed control strategy, is the EMG triggered solution more valuable than the myocontrolled one in terms of facilitating plasticity? Discuss your answer.**

For *assistance-as-needed* control, both the EMG-triggering and the EMG-feedback strategies are valid. In terms of cost and ease of implementation EMG triggering is superior, but in terms of effectiveness and specificity, a myocontrolled solution is better. A trigger control is, indeed, not adaptive to the subject necessity during the course of the task, but it is only able to detect the support request at the beginning of the action

***IN VITRO* NEUROENGINEERING: OPTICAL SOLUTIONS FOR RECORDING *IN VITRO* NEURONAL ACTIVATION**

**1) Explain the principle of working.**

Neuronal cells which are genetically engineered with peculiar photosensitive proteins that activate an electrical stimulus when hit by light. This way, electrical activity in the neurons can be controlled more precisely achieving higher spatiotemporal resolution.

**2) Provide a description of equipment and experimental solution using optical methods to record *in vitro* neuronal activity.**

For optical measurements of the neural activity a Voltage-Sensitive Dye (VSD) is required. The changes in voltage cause a shift in both the emission and absorption spectrum of the chosen VSD. From a fluorescence microscope, a change in the wavelength of the detected light can be reconducted to an electrical signal at a specific point in the microscope field of view.

**3) Discuss advantages and disadvantages with respect to MEA.**

While a MEA samples a batch of neurons close to each probing electrode, VSDs can perform single neuron measurements. Temporal resolution is usually dependent on the framerate of the camera sensor used for the acquisition.

**CEREBELLUM**

**1) Identify the input and output pathways of the cerebellum within the motor control system, specifying the brain areas sending/receiving projections from the cerebellum.**

The inputs to the cerebellar microcircuits are the Mossy Fibres and the Climbing Fibres, while the output is represented by the Deep Cerebellar Nuclei in the subcortical section. Mossy fibers originate from the spinal cord and the brain stem, from which the cerebellum receives the sensorial information that originates in the periphery, and from the motor cortex which sends information about the motor command, the efferent copy of the forward model; Climbing fibers, instead, originate from the Interior Olive cells, which convey visual sensorial information. The output signal computed in the Deep Cerebellar Nuclei is then sent to the thalamus and the vestibular nuclei.

**2) Describe the main role of the cerebellum in motor control and the cerebellar circuit properties that drive this role.**

The cerebellum is involved in the sensorimotor loop only at a control level: indeed, it does not generate the volitional signal which initiate the motor command, but instead is the *virtual* location of the forward and inverse model which modify and fine-tune the motor command in order to achieve the correct performance. It’s the stratified architecture of the cerebellum that allows for this behaviour. As a matter of facts, plasticity phenomena occur at the molecular layer and involve the synapses between the parallel fibres and the dendrites of the Purkinje cells, which carry information from the deeper layers.

**3) Provide an example of a cerebellum-driven task.**

Equilibrium is a cerebellum-driven task, as the motor commands to the muscles need to be processed and tuned in order to maintain the pose.

**4) If you want to implement a closed-loop neurorobot experiment driven by a bioinspired controller**

**i. – discuss what are the conditions for using compartimental neuronal models.**

A compartimental model offers a fine spatial discretization of the neuron, where multiple functional units are associated to a voltage value. To solve this sort of computationally heavy problem, powerful hardware and software are required, which in most cases come together with long computational time.

**ii. – discuss what are the conditions for using single point neuron models.**

Single neuronal models do not require costly instrumentation or complex algorithms, and they are therefore more practical and affordable, hence they are the models applied on a larger scale. Still, the amount of information produced in output by such models is very limited compared to compartimental ones.

**2. NEUROPROSTHESES (NP)**

**1) What is a myocontrolled NP?**

Myocontrolled neuroprosthesis are devices which deliver an electrical stimulation to a muscular district, and which are controlled in a feedback loop by the EMG signal recorded from the patient itself. A myocontrolled NP may, for example, deliver FES signals to an impaired muscle by the means of the EMG signal that the muscle receives

**2) What are the technological problems to be solved in order to implement a myocontrolled neuroprosthesis?**

EMG is a complex signal to deal with: its acquisition depends heavily on the setup condition (inter-subject variability, electrode placement, skin quality) and, because of this, calibration is required prior to any usage session. Moreover, the amount of noise in the signal itself increases the complexity of the processing step, which require filtering operations that are possible only from advanced instrumentation: most importantly, the FES delivered by the neuroprosthesis must be filtered out of the EMG recorded for the control

**3) Explain possible technological solutions.**

In order to remove the stimulation artifacts, a blanking window can be applied to the signal in order to “cover” the stimulation artifact and maintain an EMG where only the M-wave is visible, this requires an additional low-pass filtering step prior to the windowing. Alternatively, a synchronous averaging of the recorder unfiltered signal could be exploited, under the hypothesis of time-invariance of the FES stimulus. For this approach, to an inter-spike recording is subtracted the time average of the previous batch of recordings: if the time-invariance hypothesis holds, only the M-wave will be present in the resulting signal.

***IN VITRO* NEUROENGINEERING**

**1) What are the possible available solutions for applying stimulation of neurons *in vitro*?**

*In-vitro* stimulations can be achieved with the standard and well-estabilished practice of patch-clamp: through a micropipette that probes the neuron cytosol, the transmembrane voltage can be recorder. Alternatively, Multi Electrode Arrays (MEAs) are a set of equally spaced planar electrodes arranged in a grid-like fashion, which are photolithographed on the culture dish of the neural colony: for this approach, the electrodes sample their nearby area, probing the extracellular voltage generated by the neurons in such proximal region. Last, employing a photosensitive neurotransmitter-cage compound which is provided to the culture in the inactive state, the stimulation can be controlled very precisely by directing a UV-light beam on the stimulation spot

**2) Describe the working principle of two alternatives.**

See the previous answer

**3) Compare the two selected alternatives (advantages and disadvantages).**

Patch-clamping produces signals with a very high temporal resolution, but with a limited spatial resolution. Worse, due to the encumbrance of the patch-clamp setup, only a few neurons can be probed at once. Multi-electrode arrays offer, conversely, a higher number of reachable neurons, still limited by the electrode density: an electrode will most likely probe the extracellular space shared by a group of nearby neurons. For MEAs, the temporal scale in set by the instrumentation.

**MOTOR CONTROL**

**1) Define the function and input/output signals of forward and inverse models in the motor control system**

The inverse model computes the motor commands from the desired input trajectory, which is estimated from the sensorial signals. The forward model, instead, takes as input the efferent copy of the motor command and predicts its effect in terms of the achieved trajectory: together with the sensorial feedback, these two models work cooperatively for the achievement of the desired motor task, where the input of one model flows into the output of the other, and viceversa.

**2) Describe an experiment demonstrating the existence of the internal forward model.**

The existence of the internal model can be demonstrated by eliminating the feedback control from the system: for example when two subjects are required to exert a force on each other, the intensity of which should match the one of the received force, a rapid force escalation is experienced. This is because the consequences of the motor task are not perceived in the direct feedback of the forward model, but only through the sensorial signals of the other subject. In conclusion, this experiment demonstrates that the absence of a feedback forward model, the motion is subjected to a reduced level of control, granted only by the visual sensory feedback and the inverse model.

**3) Represent the motor control system in a block diagram, explaining the role of each involved structure. Specifically, identify which of them act as forward and/or inverse controllers.**

**THE CEREBELLUM**

**1) Explain the function of the cerebellum within the motor control system.**

The cerebellum acts as the main controller of the motor command which originates from the motor cortex and, trough the spinal cord, reaches the peripheral muscles. It represents the forward and the inverse model in the sensorimotor loop, which from the desired trajectory computes the errors and sends corrective signals. It is also the main subject of the motor learning process, as the cerebellar synapses are oh Hebbian type.

**2) List and briefly describe the main neural populations in the cerebellar circuit.**

* Granule Cells: Collect the inputs from the mossy fibers, coming from the motor cortex
* Parallel fibers: Connect the Granule cells’ synapses to the Purkinje Cells
* Inferior Olives: Collect the inputs from the visual sensorial signals and direct it towards the Purkinje Cells trough the climbing fibers
* Purkinje Cells: Compute the delays/synchronizations between the input from the parallel fibers and the climbing fibers, outputting towards the DCN
* Deep Cerebellar Nuclei: The output of the cerebellar circuit, directed to the thalamus. They work on the signals coming “up” from the mossy and climbing fibers and “down” from the output of the Purkinje

**3) In designing computational models of the cerebellum, selecting the best model for single neurons is a critical issue. Explain how you would model the neural populations in 2.2 within a spiking neural network model of the cerebellar circuit, highlighting the advantages and limits of your solution.**

When designing a computational model, every neuron can be modelled as a single-point neuron in a Spiking Neural Network, where the number of neurons in each family and the links connecting them must be carefully chosen in relation to the type of experiment that we want to perform. Then, this SNN can be embedded into the microcontroller of a neurorobot so that its physical behaviour can be recorded and associated to the learning process of the SNN itself. The complexity and scale of the SNN influence the required computational power and hardware.

**REHABILITATION ROBOTICS**

**1) List the advantages of using robots in rehabilitation**

**2) Explain the limits of assistive controllers in robotic rehabilitation**

**3) Suggest a solution to overcome the limits described in 3.2 during rehabilitation of the upper limb. Describe the design of the setup, the control strategy and a protocol to test the system.**

**1. NEUROENGINEERING FOR BIOLOGY**

**1.1. Suggest an optical method to record *in vitro* neuronal activity and describe the working**

**principle of this technique.**

**1.2. What are the major technological elements (devices) to run an experiment with the above**

**selected solution**

**1.3. Highlight advantages and disadvantages with respect to other available technologies for**

**recording in vitro neuronal activity.**

**2. Complete the following table**

**Goal of the**

**experiment**

**Experimental technique Possible model to describe**

**collected data**

**Limits/comments**

**Study and model**

**the ionic channels**

**in the axon initial**

**segment**

**Study and model**

**the neural**

**mechanisms**

**underpinning**

**learning**

**behaviour in**

**primates**

**Study and model**

**plasticity between**

**two neural**

**populations**

**Neuroengineering [2] Exam 28th November 2019**

**First Name**

**Last Name**

**Identification Number**

**NEUROENGINEERING [2]**

**Available time: 30 min**

**1. NEUROPROSTHESES (NP)**

**1.1. Define a sensorial NP and a motor NP; present the main components to build each of them,**

**using a block diagram.**

**1.2. Describe the context of application of sensorial NP (target population, goal, end use).**

**1.3. Why do we address the issue of implanted neuroprostheses more for sensorial ones than for**

**motor ones?**

**2. REHABILITATION ROBOTICS**

**2.1. Consider an exoskeleton for the upper limb, adopted to promote motor relearning. Select the**

**context of application (target population and treatment).**

**2.2. Define the best control strategy to be implemented.**

**2.3. Discuss the advantages of the proposed solution with respect to conventional physical therapy.**

**Neuroengineering [2] Exam 22nd January 2020**

**First Name**

**Last Name**

**Identification Number**

**NEUROENGINEERING [2]**

**Step-by-step: available time is 30 min. You have to answer questions 1 and 2 for step-by-step 1,**

**questions 3 and 4 for step-by-step 2.**

**Full exam: available time is 45 min. You have to answer 3 out of the 4 questions.**

**---------------------------------------------------------------------------------------------------------------------------**

**1. CEREBELLUM**

**1.1. List the main neural populations in the cerebellum, describing their role in the circuit.**

**1.2. The E-GLIF neuron model: report basic equations, pointing out which parameters need to be**

**defined and optimized. Suppose to use this model to represent cerebellar neurons: list**

**advantages and disadvantages of the approach.**

**1.3. Present one cerebellum-driven protocol which can be used to test cerebellar properties. Is the**

**model in 1.2 suitable to test the protocol?**

**2. IN VITRO NEUROENGINEERING**

**2.1. Describe the working principle of Multi-Electrode Arrays (MEAs).**

**2.2. List the advantages and disadvantages of MEAs for recording in vitro neuronal activity with**

**respect to the other available technologies (patch clamp and voltage-sensitive dyes).**

**2.3. Describe the main components of a setup for MEA recordings using a block diagram and**

**explaining the function of each block.**

**3. NEUROPROSTHESES (NP):**

**3.1. EMG-controlled NP: what are the main problems you need to face when designing EMGcontrolled**

**NP? Propose a control algorithm to solve them.**

**3.2. What are the reasons for applying EMG-controlled NP?**

**3.3. Describe a situation (patients, diagnosis and conditions) where the use of EMG-controlled NP**

**is not applicable and a situation where it is for sure.**

**4. REHABILITATION ROBOTICS**

**4.1. Consider a robot for assistive walking in a complete SCI patient (Spinal Cord Injury patient**

**with complete lesion at level C7). How the robot can be used? Describe a possible control**

**strategy.**

**4.2. Propose a solution to compute the desired trajectory.**

**4.3. Which are the target application scenarios of the designed robotic platform?**

**Neuroengineering [2] Exam 12th February 2020**

**First Name**

**Last Name**

**Identification Number**

**NEUROENGINEERING [2]**

**Full exam: available time is 45 min.**

**---------------------------------------------------------------------------------------------------------------------------**

**1. MOTOR CONTROL**

**1.1. Define reflexes and voluntary movements; list and explain the laws of voluntary movements.**

**1.2. Represent the main brain areas involved in motor control through a block diagram,**

**highlighting motor and sensory signal flow among them.**

**1.3. Identify and describe the brain area involved in voluntary movement control. What happens if**

**an external perturbation occurs during execution of a voluntary movement?**

**2. BIOMIMETIC CONTROLLERS:**

**2.1. Define biomimetic controllers**

**2.2. Design a biomimetic controller, describing how you define the best control strategy.**

**2.3. Suggest a clinical trial to test the designed solutions (patients, protocol, etc).**

**3. ROBOTICS**

**3.1. Explain the difference between rehabilitation robots and ortheses.**

**3.2. Provide an example of a robot for rehabilitation of the lower limb and one for rehabilitation of**

**the upper limb. What are the main differences in design and control of the device?**

**3.3. Choose one of the robots in 3.2 and provide an example of application: patients, task,**

**rehabilitation plan.**

**First Name**

**Last Name**

**Identification Number**

**NEUROENGINEERING [2] – 27-Jan-2021**

**Available time: 60 min**

**Rehabilitation Robotics**

**1. Design one possible solution for the rehabilitation of a completely plegic upper limb (no**

**volitional movement at all and no residual contraction of any muscle) in a stroke survivor**

**during the post-acute phase. What is the type of control that should be used for the robot?**

**Why facilitating user’s involvement is anyway important also in this condition? How the**

**user involvement can be promoted and how can it be checked?**

**2. Describe the goal of the use of robotics exoskeletons for antigravity support by a disabled**

**person as an assistive technology for activities of daily life. Discuss the main characteristics**

**of the user, accordingly In this context, what are the differences and the pros and cons**

**between active and passive solutions?**

**Neuroprostheses and robotics in rehabilitation**

**3. What are the main limitations of using only standard linear feedback controllers for**

**neuroprostheses?**

**4. Why Artificial Neural Networks (ANNs) can be successfully exploited to control a**

**neuroprostheses, as used as an Inverse model of the neuromuscular system? and what are**

**the assumptions (constraints/conditions) that you need to fulfil to make NN applicable in**

**this case? What the limitations of using ANNs for inverse model neuroprostheses' control?**

**How can you include also fatigue in the NN inverse model?**

**Computational Neuroscience.**

**5. What are the main elements for modelling a large biological inspired brain microcircuit?**

**6. Imagine you want to build a realistic bio-inspired neural network to model the cerebellum.**

**Describe the cerebellum physiological features that make it a suitable benchmark of**

**simulation.**

**7. How would you test your model? Describe one target experiemnt.**

**Neuroengineering [2] Exam 16th February 2021**

**First Name:**

**Last Name:**

**Identification Number:**

**NEUROENGINEERING [2]**

**Available time: 60 min**

**REHABILITATION ROBOTICS**

**1.1 Describe the differences between exoskeletons and end-effector devices. Which are the pros**

**and cons of each category?**

**1.2 Describe the assist-as-needed control strategy.**

**1.3 Describe one possible solution to implement the assist-as-needed control strategy on an**

**exoskeleton device and on an end-effector one (you can choose between upper limb or lower**

**limb devices).**

**DESIGN EXPERIMENTAL STUDIES IN REHABILITATION**

**2.1 What is a meta-analysis? What are the steps to conduct a meta-analysis?**

**2.2 What are the main ingredients of a Randomized Controlled Trial?**

**2.3 What is a crossover design? What are the hypothesis of using a crossover design in a**

**rehabilitation treatment? Do you think it is more appropriate for post-stroke survivors in the**

**subacute phase or in chronic phase?**

**IN VITRO NEUROENGINEERING**

**3.1 What are the characteristics of an experiment where you can use Multi-Electrode Arrays but**

**you cannot use patch clamp.**

**3.2 What are the main advantages and drawbacks of using MEA?**

**3.3 Which solutions can be adopted to reduce the drawbacks of this experimental setup?**

**First Name:**

**Last Name:**

**Identification Number NEUROENGINEERING [2]**

**Available time: 60 min**

**Computational Neuroscience**

**1. Describe the main cerebellar circuit elements.**

**2. The cerebellum plays a central role in learning, what features embed learning capabilities in**

**the cerebellar microcircuit?**

**3. how would you model these learning features in a SNN inspired to the cerebellar**

**microcircuit?**

**In vitro neuroengineering**

**4. What are the main types of in-vitro preparations employed to study brain networks (specify**

**also the goal of such in-vitro preparation)? What are their advantages and disadvantages?**

**5. Which are the technical specifications that must be considered for a technology that aims**

**at conducting a proper analysis on the in vitro network activity.**

**6. Starting from the definition of these technical specifications choose one possible technique**

**you know to acquire signals from neuronal cultures and evaluate it for each specification.**

**Neuroprosthesis**

**7. What are the hypothesized principles at the basis of neuroplasticity effect of FES?**

**8. Describe a possible solution to implement a control strategy for a myocrontrolled**

**neuroprosthesis. Which are the pros and cons of the described solution?**

**9. Describe a situation (patients, diagnosis, and conditions) where the previously described**

**NP is not applicable and a situation where it is for sure.**

**First Name:**

**Last Name:**

**Identification Number**

**NEUROENGINEERING [2]**

**Available time: 60 min**

**Motor Control**

**1. List and explain the elements of the human motor system that make it a complex one.**

**2. List the laws of voluntary movements in humans.**

**3. Define Efference copy, Forward and Inverse models in motor control.**

**In vitro neuroengineering**

**4. What are the possible available solutions for applying stimulation of neurons in vitro?**

**5. Briefly describe the working principle of one solution.**

**6. Compare the selected solution with other possibilities (advantages and disadvantages).**

**Rehabilitation Robotics**

**7. List the advantages and disadvantages of assistance-as-need robotics with respect to**

**conventional therapy in a rehabilitation setting aiming at motor relearning.**

**8. Within the framework of assistance-as-need rehab robotics:**

**a. Describe a robot design features (degrees of freedom, actuated joints, embedded**

**sensors, control strategy)**

**b. Design a clinical trial (study design, target population, goal, experimental setup,**

**outcome measures) to test the efficacy of robotic neurorehabilitation with respect**

**to conventional therapy.**

**9. At the end of your trial, you want to compare the results of the clinical trial described in the**

**previous answer with the studies available in literature conducting a systematic review.**

**Describe the appropriate clinical question to search for studies available in literature**

**through the PICOS format (describe the keywords for each domain).**

**First Name:**

**Last Name:**

**Identification Number**

**NEUROENGINEERING [2]**

**Available time: 60 min**

**Neuroprostheses**

**1. Describe the working principle of Functional Electrical Stimulation (FES) and the main**

**parameters that define the stimulation**

**2. Which are the main differences between natural and artificial muscular contraction?**

**3. Describe a possible solution to detect the human intention in an assistive neuroprosthesis.**

**Rehabilitation Robotics**

**4. Define orthotics (or assistive or for restoration) and rehabilitation robotics**

**5. Describe one possible solution for rehabilitative device:**

**a. define the target users target user (pathology, level of disability, location of**

**intervention)**

**b. the technical design (degree of freedom, actuated joints, embedded sensors),**

**c. the principle for the controller.**

**Motor Control**

**6. Describe the specific role of the cerebellum in the motor control loop, and draw a scheme of**

**the interconnections between the most important areas involved in motor control.**

**7. Describe a cerebellar model explaining how the elements in the cerebellar circuit are**

**represented/simplified.**

**Functional Electrical Stimulation (FES):**

**1.1 describe the principle of working.**

**The functional electrical stimulation (FES) consists of applying a voltage between two electrodes in order to obtain a muscular contraction of the muscles underneath the electrodes. It can be applied both whether or not**

**the subject has partial neuronal activation from higher centres, it is mandatory that the subject still have**

**innervation of the muscle. Two electrodes are used (anode and cathode): the cathode provides a negative**

**current that hyperpolarizes, through the induced ionic currents the area below it; the ions "flow" from the**

**area below the anode that will be depolarized, thus a ionic current flows between the two electrodes. If the**

**depolarization is sufficient to exceed a certain threshold an action potential will be generated causing a**

**muscle contraction with similar dynamic to that generated by a higher command.**

**1.2 describe the possible areas of application for disabled people.**

**The electrical stimulation can be used in different areas, for example in the cochlear stimulation for deaf**

**people, in the deep brain stimulation for people with Parkinson Disease or it can be used to help the recovery**

**of a function in a subject who presents neuromotor impariments (neuro-prosthesis), both as assistive devices**

**or for functional recovery. The neuro-prosthesis can be used for different pathologies, such as Spinal Cord**

**Injury, Stroke, Ataxia and Multiple Sclerosis.**

**1.3 Discuss one application example where the use of artificial neural networks (ANN) could be a good**

**solution for the control of FES. Properly justify and explain your choice.**

**An ANN can be a good solution if the model we are considering is a complex model, if the laws that regulate**

**it are not known and if it is possible to collect a sufficiently redundant training set.**

**An application example is the use of an ANN to provide the feedforward control in a single joint movement,**

**elbow flex-extension. The muscle to be stimulated is the biceps, the subject is sit and the arm is extended**

**along the trunk side. We aim at properly stimulate the biceps so to control the elbow angle time profile. The**

**goal is to train the muscle and to improve fine control. The target population could be MS. The network can**

**be trained to behave like the inverse model (linking the desired movement- angle kinematics time profile- to**

**the correspondent FES sequence of stimuli (controlled for example in PW). This inverse neuromuscular**

**model is complex, nonlinear, strongly personalized and difficult to be inverted, so it is reasonable to explore**

**the use ANN.**

**The collection of the training set could be done by stimulating the subject in the final configuration with a**

**sequence of exploratory FES stimulation profiles and collecting the correspondent achieved angle time**

**profile.**

**The network can be trained on the collected data by using the time profile as input and the sequence of**

**stimulation as output.**

**The collection of training set does not imply difficult operation by the subject and the therapist and can be**

**seen as a preliminary phase of the treatment. Data collection of training set can be amle but anyway, after**

**each therapeutic training the new data collected can be offline used to futher update the ANN so to adapt it to**

**the user’s progression or decrease.**

**1.4 discuss one application example where the use of ANN would not properly cope with the goal.**

**Properly justify and explain your choice.**

**In the case of gait- assisted FES the use of an inverse model ANN-based approach to build the feedforward**

**controller is quite inapplicable because the system has three kinematic degrees of freedom (hip, knee and**

**ankle angle) and multiple muscles to be stimulated (about 8 groups including bilateral muscles). The**

**selection of an exploratory sequence of stimulation a priori to collect the training set could expose the subject**

**to configuration of possible falls or difficult posture. Feedforward controllers based on stereotyped EMG**

**physiological contractions (biomimentic controllers) are much more feasible in such condition.**

**2.1 List the parameters used to modulate the contraction**

**Parameters to control the stimulation:**

**- Amplitude (A) of the current pulse, [mA]**

**- Stimulation frequency (1/period→ 1/T)**

**- Pulse width (PW): width in time of each current pulse [ s]**

**- Monopolar or biphasic pulse Waveform**

**2.2 Discuss the differences between the artificial contraction elicited by FES and the natural muscular**

**contraction**

**1) Muscle fibers are recruited synchronously with the current pulse stimuli – no turnover of fibers. Higher**

**frequency of activation is mandatory to avoid twitches.**

**2) The recruitment of the muscle fibers is spatially fixed and depends on the quantity of charge delivered at**

**the electrodes (it cannot be changed once the parameters of the stimulus are set) – this is exacerbated by the**

**fact that axon threshold are inversely proportional to the diameter of the fiber, inducing a faster activation of**

**Type B fibers, which are larger but are less resistant to fatigue.**

**3) Using external superficial electrodes, the working volume is quite large limiting the capability to control**

**fine smooth movements. Often cross-stimulation to nearby muscles is induced.**

**4) Using intraneural electrodes, the stimuli are more selective but problems of invasiveness and stability of**

**the implant become paramount.**

**Rehabilitation Robotics:**

**1.1 Define rehabilitation robotics (for rehabilitation purpose and not for restorative purpose).**

**Rehabilitation robotics refers to the use of robots to help the physicians in rehabilitation of body parts or**

**functions, which are impaired in patients. The aim is that the functionality is at least partially recovered and**

**the patient can get back moving without being assisted.**

**1.2 Which are the key elements for motor recovery in rehabilitation?**

**The key elements are: frequency and intensity of rehabilitation sessions, functional goal oriented movements,**

**patient active participation.**

**1.3 Which are the main limits of conventional therapy?**

**1) Limited resources for intensive training (one-to-one coupling between therapist and patient) for cost**

**sustainability and organizational reasons in the hospital**

**2) Lack of quantitative evaluation of patient’s improvements, which is necessarily subjective and not precise**

**and limit the capability to tailor the treatment to single patients.**

**3) In addition, some therapies can be difficult to deliver, for example in case of particular movements for**

**overweight people.**

**4) Safety of treatments limits the tasks, which can be trained, so reducing the challenging to the user and the**

**motivation. The training of functional complex tasks is postponed until safety is assured.**

**5) Once patients are discharged from hospital, the continuation of therapy is usually very limited by costs.**

**1.4 How can robot-based rehabilitation tackle the key elements for motor recovery mentioned above?**

**The frequency and intensity of sessions are easy to take on because they depend only on the number of**

**available robots and the therapist supervision can be shared by two/three patients. In addition, after training**

**in the hospital, the patient can use the devices (or simple version of them) at home under remote supervision**

**so to allow continuity of care at home.**

**Robots can assist the patient in goal-oriented tasks, by modulating the difficulty of the tasks and the level of**

**assistance on patient’s current conditions, always assuring proper safety.**

**Patient active participation can be assured in different ways: EMG-based assistance, or “assistance as**

**needed”, with the aim of avoiding the slacking problem. Further training exercises can be immersed in**

**attracting virtual environments or can be designed as games so to sustain subject’s motivation and attention.**

**2.1 discuss the major advantages of the use of robots for the rehabilitation of post-stroke patients.**

**1) Safety in performing also complex tasks since very early after the trauma**

**2) Immersivity and motivation (fancy exercises/games)**

**3) Continuous Monitoring and consequently single user tailoring of therapy.**

**4) Reward: scaling of goal of therapy and assistance by the robot so to assure the completion of the tasks,**

**avoiding frustration and sustaining motivation**

**5) Intensity of repetitive training (for neuroplasticity remapping repetition is crucial)**

**6) Continuity of care: execution of exercises at home under partial/remote supervision after hospital**

**discharge**

**2.1 Robots with impedance controllers: Describe the design of the control solution and the reason for**

**its application.**

**An assistive robot performs a kinematics motion control: as long as the patient's movement remains within**

**the desired trajectory (represented by a proper tunnel around the desired trajectory), there is no correction;**

**when he/she deviates from the ideal tunnel, the robot exerts a force on the patient's limb in order to bring it**

**back to the desired position.**

**The control mechanism is based on a threshold system, which shall cause the robot to intervene if a**

**parameter of interest (distance from the desired path) exceeds a certain threshold (tunnel size).**

**Since the human movements have some variability during the performance of a task, a dead-band (or tunnel)**

**is used: the robot does not correct the motion in case of slight variations from the desired trajectory.**

**The desired position is usually considered as spatial position but also as temporal profile, so that if the**

**patient gets stuck in the tunnel or goes too slow the robot assist the acceleration of the task (back wall**

**assistance).**

**An implementation of this kind of assistance could be the use of adaptive algorithms that tune the control**

**according to the patient's performance so that the subject is constantly forced to make an effort.**

**A control algorithm could be: Pi+1 = f\*Pi + g\*ei where Pi+1 is the parameter at the successive instant, f is the**

**forgetting factor, g is the gain, and ei is the error at the i-th instant.**

**They are used for the motor re-learning of patients suffering from brain damage, but with a residual capacity**

**of nervous control.**

**2.2 discuss the limitations and drawbacks of the use of robots for the rehabilitation of post-stroke**

**patients.**

**1) limited exploration of compensatory strategies (the robot teaches the “target” trajectory and not any**

**possible compensatory alternative), variety of solutions is limited.**

**2) limited translatability of results into daily activities: assistance by the robot simplifies the task execution**

**(for example gravity relief) but at the end of the therapy the goal is to transfer the acquired skills into daily**

**activities performances.**

**3) The subject can learn to let the robot do the movement on his/her behalf: slacking hypothesis.**

**2.3 select one drawback and present the design of a controller for robots which could limit the impact**

**of such drawback.**

**1) Considering the limited translatability: the robotic assisted treatment should be designed so to reduce the**

**assistance as soon as the user is improving till the non-assistance condition, which is the daily living target.**

**The controller should be adaptable and a modulation of assistance (level of antigravity support for example)**

**should scaled of a YY percentage (parameter YY: e.g. -2%) automatically every time the subject succeeds in**

**performing the task in XX trials running (parameter XX: e.g. 5). At the end of each training session, the**

**initial level of assistance and the final one are given back to the therapist/clinician to inform about the**

**progression and to let him/her scale the parameters of the automatic controller XX and YY.**

**2) Considering slacking hypothesis:**

**a. a tunnel-based with backward-wall impedance controller could limit the problem of slacking (describe the**

**principle)**

**b. a proportional myocontroller could help assuring the subject participation throughout the whole task**

**execution. (describe the principle)**

**In-vitro neuronal models:**

**1.1 Report the two main types of in-vitro models used to obtain neuronal networks. Discuss advantages**

**and disadvantages for each of them.**

**1) In vitro cultured neurons: Cultured neurons can be taken directly from embryonic brain tissue and grow in**

**vitro under proper environmental conditions and nutrients delivery. In vitro cultured neurons over time form**

**synapses and grow in network similar to brain tissues.**

**a. Adv:**

**i. the formation of the network can be analysed over time and for long periods (for example studying the**

**pathology pathways or pharmacological kinetics.**

**b. Disadv:**

**i. The network is not natural. Very confined in space and formed by one type of neuron (not mimicking the**

**complex connection between brain areas)**

**2) Brain slices: the slices are taken directly from brain tissue and then put into proper culture medium to**

**preserve the activity of the neurons.**

**a. Adv:**

**i. The network is the very physiological one (or pathological), its formation has not been artificially**

**modified.**

**b. Disadv:**

**i. The slice is extracted from the brain and then its connection to the rest of the brain are cut, this can modify**

**the functioning also of the preserved neurons.**

**ii. The external layers of the slices are the cut dead neurons, they can partly mask the activity of the inside**

**alive neurons (for example in case of MEA recording)**

**iii. Slices can be studied for short term (not possible to use for example for studies on synapses formation or**

**of long term effects of drugs)**

**1.2 Report at least two of the available technologies used to investigate intracellular electrophysiology**

**from in-vitro models.**

**Intracellular electrophysiology can be studied by**

**1) patch clamp electrodes**

**2) Voltage sensitive dyes optical studies**

**(Please note that MEAs record extracellular electrical activities: specific neurons and electrodes coupling**

**models allow to infer information about intracellular electrophysiology from MEA recordings but this should**

**have been clearly clarified in the answer)**

**1.3 Pick one of the two technologies: describe its working principle and discuss its advantages and**

**disadvantages.**

**The first method consists of reading the electrical signals developed by the neuronal units. This technique is**

**useful both for morphological and functional aspects. Unfortunately, the voltage difference given to the cell**

**membrane leads to its degeneration and death. Therefore, this technique is not repeatable and it cannot be**

**made on large scale.**

**For this reason, we moved to the use of MEA (and subsequently to the photoMEA), which are arrays of**

**many electrodes (60 for the old technology, more than 1000 with the latest generation of CMOS). Thanks to**

**a conductive interlude, these allow to study the synapses of neural networks in a bigger scale than with patch**

**clamping. They have another advantage: a high time resolution and high repeatability. On the contrary, they**

**have low selectivity (4-5 neurons per electrode) and no longer morphological meaning as in patch clamping.**

**Cerebellum:**

**1.1 Report its physiological structure (inputs, outputs, cells that make up the tissue and their**

**interconnections)**

**The cerebellum is a structure located at the base of the skull and has many functions. One of the main ones is**

**creating internal models for movement, balance, posture and in general, adaptation and learning in motor**

**control. It contains about half of the total neurons of the brain, with a ratio of INPUT = 40 \* OUTPUT.**

**It is organized in repetitive circuit units, microcomplexes, which can be easily recognized.**

**It includes 3 layers:**

**1) The top layer is the molecular layer, characterized by Stellate cells, Basket cells with inhibitory function**

**and very small dimensions, Parallel fibers, which are made of axonal structures of the underlying Granular**

**cells, over which the dendrites of the Purkinje cells create their synapses.**

**2) The middle layer is characterized by the presence of Purkinje cells somata, with inhibitory function on the**

**output cerebellar neurons, the Deep Cerebellar Nuclei cells. They receive information from climbing fibers**

**and from the parallel fibers (Granuli). Every cell of Purkinje receives only one climbing fiber but the same**

**climbing fibers form synapses with more than one Purkinje cells and receive multiple parallel fibers spatially**

**organized.**

**3) The last layer, i.e. the Granular layer, includes Granular cells that are inhibited by Golgi cells and excited**

**by the Mossy fibers. These are the inputs of the system, carrying sensorial and passage-of-time information,**

**which is processed through a spatio-temporal filtering in this layer.**

**The Mossy fibers also form connections with Deep Cerebellar Nuclei. Instead, the Climbing fibers originate**

**from the Inferior Olivary cells, which are close to the brain stem and carry information on the motor gesture**

**delay and error signals, providing a teaching signal that controls synaptic plasticity.**

**1.2 Explain the reason why the cerebellum represents a relevant test bench for computational neuroscience.**

The cerebellum has significant plasticity properties and constitutes a key element in motor learning; this makes it very interesting for neuroscience. There are two considerations, which makes it a special test bench for computational models in neuroscience:

1) very paradigmatic but, at the same time, simple experiments can be used to test cerebellum properties insimulation or even with real robots: pavlovian association protocols, such as timing association (e.g. EyeBlinking classical Conditioning) or Vestibulo-ocular reflex experiments or reaching experiments under modulation of force fields, that requires continuous tuning of corrective movements.

2) Its structure includes a limited number of cell types (see point above) and their geometrical modular organization as well as their connectivity are rather well known. The level of knowledge of the cerebellum neurophysiology is much higher with respect to other brain areas. In addition, there is a solid literature on the use of computational models to investigate cerebellar learning.

**Computational Neuroscience:**

**1.1 What is Computational Neuroscience;**

Computational neuroscience is the study of neurophysiology or neuropathology, investigating cognitivebrain information processing features, through the use of computational models with the double goal of

- Understanding better the brain functioning

- Advancing computational control solutions mimicking brain performances.

**1.2 Present one example of the cerebellum computational model, identifying the characteristics of the**

**computational model, the similarities with the cerebellum physiology, and the possible testing**

**methods.**

**The cerebellum acts as a feedback/forward controller including an adaptive learning module that allows**

**adjusting the different motor actions.**

**The cerebellum can be schematized with different models. For example, it can be modelled as an inverse**

**model that can be updated thanks to the use of feedback signals (see Figure below). In fact, as known from**

**neurophysiology, the output of the cerebellum (representing motor commands) can be tuned under the**

**supervision of a teaching/error signal encoded by neurons from the Inferior Olive and the corresponding**

**Climbing Fibers. This happens thanks to synaptic plasticity.**

**Embedding the model into a closed-loop circuit reproducing the main cerebellum-driven tasks is**

**fundamental to test the model functioning (therefore, using a simulated or real robotic platform).**

**Example protocols:**

**- Eye-Blinking Classical Conditioning (EBCC): by providing a Conditioned Stimulus, CS (e.g. a sound) and**

**an Unconditioned Stimulus, US (e.g. an air puff, thus a perturbation) with a precise timing, after a learning**

**period, the system learns to provide a conditioned response, eye-blinking, anticipating the US onset.**

**- Vestibulo-Ocular Reflex (VOR): it consists of a movement of the head while looking at a fixed or moving**

**object. Thanks to the adaptive cerebellar module, the system after training will learn that the rotational**

**movement of the head needs a compensatory movement of the eyes in the opposite direction that allows**

**keeping the gaze fixed on the target.**

**- Reaching under external viscous force: while executing a reaching task, if an external force perturbs the**

**movement, the systems learns to produce a compensatory torque to perform successfully the reaching task.**

**Correction depending on the external force is:**

**Gradually the system learns to counterbalance the external force, decreasing the error between the real and**

**ideal trajectory.**

**2.1 Create a block diagram that associates the functioning of the different internal models discussed**

**throughout the course.**

**Motor control is a highly complex physiological mechanism characterized by non-linearity, non-stationarity,**

**noise and multi-dimensionality. This complex process is decomposed by the CNS in different functional**

**modules, each one with different input-output features. An engineering modelling of this mechanism must be**

**based on the distinction into modules as close as possible to the real ones. Two of the best-known internal**

**models are:**

**• The inverse dynamic model: a mechanism that allows generating the torques to be applied to the body**

**segments from a desired trajectory. This is also known as the feedforward controller because it represents the**

**"open-loop control" of the motor control.**

**• The forward model, also called state estimator: it allows to estimate the sensory feedback generated by a**

**certain motor command, in order to subtract the contribution of the patient’s own movements from the**

**sensory feedback.**

**The feedback controller is then the internal model converting the error as fed back to the brain in terms of**

**afferences discrepancies to the error in motor commands. Kalman filter can be added to this network to**

**mimic the capability of our brain to base the action either on current afferences or on a-priori models**

**depending on the current reliability of the afferences.**

**(Also HONDA model can be described to answer this question)**